

### FOCUS ON: ACUTE PAIN



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### Postoperative pain relief using regional anaesthesia

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KEYWORDS Pain; Postoperative; Anaesthetic technique; Regional; Epidural; Local anaesthesia **Summary** Fear of severe pain after surgery is one of the main concerns of many patients who undergo surgery. There seems to be some justification for this fear. Several recent publications show that the management of postoperative pain is still suboptimal in many institutions. Undertreated postoperative pain may delay discharge and recovery and result in poor rehabilitation and outcomes. Currently, a variety of opioid and non-opioid-based analgesic techniques are used to treat pain. Opioid analgesics, regardless of the route of administration, are associated with a high incidence of adverse effects.

In recent years, there has been a great increase in the use of regional anaesthesia techniques for surgery and postoperative pain management. Catheter techniques are increasingly used in in-patients and ambulatory surgery patients to achieve prolonged pain relief lasting several days. The techniques available for postoperative analgesia include neuraxial (central) blocks, peripheral nerve blocks, wound infiltration techniques, intraperitoneal, intra-articular, and intrabursal techniques. There is overwhelming evidence that epidural technique provides superior analgesic efficacy; however, its effects on reducing morbidity and mortality are controversial. Perineural catheter techniques provide better analgesia and fewer side effects when compared with opioid analgesia and are a good alternative to the more invasive epidural technique, particularly for major orthopaedic extremity surgery. There is good evidence that a simple technique of wound catheter infusion of local anaesthetic provides effective analgesia after a variety of surgical procedures with reduced side effects and high patient satisfaction. With the availability of portable pumps, the technique can be used on ambulatory basis. © 2007 Published by Elsevier Ltd.

Pain relief after surgery continues to be a major medical challenge. In spite of major advances in our understanding of the pathophysiology of acute pain and the development of new analgesic medications and drug delivery techniques, significant numbers of patients continue to suffer from unrelieved postoperative pain. Historically, the

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treatment of postoperative pain has been given low priority by both surgeons and anaesthesiologists. Therefore, patients accepted pain as inevitable in their postoperative experience. Reports of unrelieved pain do not invariably result in corrective measures, and physicians and nurses have not traditionally been held accountable for poor analgesia. Even today, many patients do not receive adequate postoperative pain relief because

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of staff failures to routinely assess pain and pain relief.<sup>1</sup>

Undertreated severe pain has several deleterious effects on neuroendocrine function, respiration, gastrointestinal function, circulation, and autonomic activity. This is particularly relevant for patients undergoing thoracic and major abdominal surgery. Severe postoperative pain is also believed to be a risk factor for the development of chronic pain after surgery.

Unrelieved postoperative pain may delay discharge and recovery and result in an inability to participate in rehabilitation programmes leading to poor outcomes. Recent advances include better understanding of pain mechanisms, physiology, and pharmacology,<sup>2</sup> publications of guidelines<sup>3</sup> establishment of acute pain services, <sup>1,4</sup> initiatives such as "pain as the fifth vital sign", and availability of multiple new drugs and devices. However, these advances have not led to any major improvements and undertreatment of postoperative pain continues to be a considerable problem worldwide.<sup>5,6</sup> A variety of opioid and non-opioid-based analgesic modalities are available. It is well accepted that non-opioid analgesics and techniques be used as the first line of therapy and that opioids should be

Table 1Newer developments in postoperativepain management.

- New drugs (or new use of "old" drugs)
  - Non-opioids (NSAID's (coxibs), ketamine, dextromethorphan, pregabalin, corticosteroids
  - Local anaesthetics (ropivacaine, levobupivacaine)
  - Adjuvants—in techniques such as epidural, perineural, i.v. PCA
- Increasing use of regional analgesia techniques
- Drug delivery systems (transdermal PCA, intranasal, long-acting epidural morphine, sublingual NSAID, perineural/incisional catheter LA at home)
- Concepts (NNT versus PROSPECT, multimodal, preemptive)
- Web-based guidelines (www.postoppain.org, www.esraeurope.org, www.oqp.med.va.gov/ cpg/cpg.htm
- Outcome debate (cost-effectiveness of epidural, evidence-based techniques)
- Organisational issues (APS, role of surgeons, audits)

PCA, patient-controlled analgesia; LA, local anaesthetic; NNT, number-needed-to-treat; PROSPECT, procedure specific pain treatment; APS, acute pain service. reserved for more severe pain. Some of the newer developments are shown in Table 1.

## Why regional analgesia for postoperative analgesia?

Opioid analgesics, the mainstay of postoperative pain management, are associated with substantial adverse effects (especially respiratory depression), regardless of the route of administration and technique. Attempts to limit these adverse effects and improve postoperative analgesia have led to the use of a multimodal approach. The regimen may include several different drugs, such as nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, and local anaesthetics, each acting on different mechanisms along the pain pathway. NSAIDs are used to reduce activation of nociceptors, local anaesthetics block sensory inflow, and opioids work centrally to inhibit pain transmission.

In recent years, there has been a great increase in the use of regional techniques for surgery and postoperative pain management. This increase has been particularly marked in obstetric, orthopaedic, and paediatric surgery. A French survey showed that during a 16-year period between 1980 and 1996, the use of regional techniques had increased 14-fold. In obstetrics, the practice of epidural analgesia increased from 1.5% to 51% of all deliveries in France.<sup>7</sup>

Because they can completely stop pain transmission, regional techniques using local anaesthetics can provide excellent pain control. In addition, they are inexpensive, simple to use, and relatively safe for a wide variety of patients. Local anaesthetics can be applied topically or injected subcutaneously before a procedure to numb a small area, infiltrated pre-operatively into the surgical site, administered as a regional neural blockade to

Table 2Regional techniques for postoperativeanalgesia.

- Central blocks (epidural, spinal, CSE)
- Peripheral n. blocks
  - Proximal and distal nerves
  - Perineural—during surgery (amputation)
  - Intercostal, paravertebral
- Incisional (subcutaneous, subfascial)
- Intraarticular, intrabursal
- Intraperitoneal
- Supraperiosteal

CSE, combined spinal epidural.

cover a large area, given intraspinally for ongoing pain relief, or infused into the operative site via a pump. Table 2 shows the type of regional techniques that can be used for the management of postoperative pain (Table 2).

## Perioperative epidural technique and outcome

The role of perioperative epidural anaesthesia and analgesics in reducing morbidity and mortality is controversial. The high cost of epidural analgesic can be justified only if it shows outcome improvement. A meta-analysis of 141 trials with nearly 10,000 patients showed that perioperative neuraxial anaesthesia reduced overall mortality by about 30%. Furthermore, perioperative anaesthesia and analgesia decreased the risk of deep venous thrombosis, pulmonary embolism, and pneumonia by 39-55%.<sup>8</sup> However, many study design-related guestions have been raised and limited the application of these results to a broader surgical population. At present, the role of perioperative epidural technique on patient outcomes is unclear. It has been speculated that the improvements in perioperative management have increased the safety of the perioperative period to such an extent that the possible analgesia benefits of epidural technique are no longer obvious. Such improvement include use of shorter acting drugs, intensive care units, improved vigilance and monitoring, better preoperative optimisation, minimal invasive surgical techniques, and acute pain services.<sup>9</sup>

## Does postoperative epidural analgesia affect outcome?

Postoperative myocardial infarct is an important predictor of poor outcome after major surgery. Myocardial ischaemia may be present in about 40% of high-risk patients.<sup>10</sup> A thoracic epidural decreases the severity of myocardial ischaemia, blocks sympathetically mediated coronary vasoconstriction and improve coronary flow to the subendocardial areas.<sup>11</sup> However, the effect of postoperative epidural analgesia on the incidence of myocardial ischaemia or infarction in controlled trials has been equivocal.<sup>12,13</sup> A meta-analysis has shown that the use of thoracic, but not lumbar, epidural analgesia significantly decreases the incidence of postoperative myocardial infarction.<sup>14</sup>

Pulmonary complications such as hypoxaemia, pneumonia, atelectasis, and respiratory failure are important causes of postoperative morbidity and mortality, which contribute to, prolonged hospital and ICU stays and account for increased costs. A meta-analysis of perioperative analgesia showed a decrease in the incidence of atelectasis and respiratory complications.<sup>15</sup>

Delays in postoperative gastrointestinal function can contribute to increased postoperative pain. pulmonary complications, and delayed wound healing. Epidural is not a generic term: location of the catheter tip and choice of analgesic drug can independently influence postoperative morbidity. A review of randomised and observational studies showed that when the epidural catheter tip corresponds to the dermatomes of surgical incision all trials (n = 9) noted earlier return of GI function. while only one out of seven trials showed this beneficial effect when the catheter tip did not correspond to surgical dermatomes.<sup>16</sup> A systematic review of randomised controlled trials showed that epidural local anaesthetics in patients undergoing abdominal surgery reduced GI paralysis compared to systemic or epidural opioids, with comparable postoperative analgesia.<sup>17</sup> In a literature review of anaesthetic and analgesic techniques for colon surgery. Liu concluded that randomised controlled trials examining independent effects of epidural analgesia as part of a fast-track clinical pathway have consistently failed to observe a reduction in duration of hospital stay despite superior analgesia, faster recovery from ileus, and faster achievement of discharge criteria after colon surgery.<sup>18</sup>

## Regional techniques to reduce the prevalence of chronic postoperative pain

Chronic pain after surgery is a significant problem. Long-lasting pain has been reported after many surgical procedures including thoracotomy, mastectomy, limb amputation, and hernia repair. The overall incidence varies from 5% to 80% and is related to the type of surgical procedure.<sup>19</sup> Severe postoperative pain in addition to several other factors is a predictor of these chronic conditions, which can have considerable healthcare and economic implications. Many patients report that pain interferes with daily activities after a variety of surgical procedures such as hernia surgery, mastectomy, and thoracotomy.<sup>20</sup> Current evidence shows that intense postoperative pain is a risk factor for chronic pain after surgery. Less-invasive surgical techniques such as laparascopic hernia repair, sentinel-node biopsy for breast cancer, and thoracoscopic chest surgery are associated with less acute and chronic pain. The use of epidural local anaesthesia is associated with less acute and chronic post-thoracotomy pain.<sup>20–22</sup> A recent study showed that pre-incisional paravertebral block provided good acute postoperative analgesia, and reduced pain symptoms at 12 months follow up (43% versus 77% in sham block group). The authors also emphasised that sparing of intercostobrachial nerves in axillary dissection was also important.<sup>23</sup> Furthermore, psychosocial factors are also involved in the progression from acute to chronic pain.

The concepts of "patient-satisfaction" and "quality of life" are complex with many methodological problems. However, comparative studies and systematic reviews have consistently shown superior efficacy of epidural technique above alternative methods to treat postoperative pain, particularly pain during movement.<sup>24,25</sup> These analgesic benefits of epidural analgesia may contribute to higher patient satisfaction and improve quality of life.<sup>25</sup> Overall, on the basis of evidence from seven metaanalyses and three large RCTs, it was concluded that there is a beneficial effect of epidural anaesthesia and analgesia in terms of some measures of cardiac and pulmonary function and there is overwhelming evidence of superior analgesic efficacy.<sup>20</sup>

#### Perineural regional analgesia

The above advantages of epidural analgesia have to be balanced against their risks and costs. The monitoring costs can be reduced considerably if the patients are nursed on surgical wards rather than ICU or postanaesthetic care unit (PACU). A UK survey showed that in over 40% of hospitals, an epidural technique was allowed only in highdependency areas and not on regular surgical wards.<sup>26</sup> Another recent study has shown that the risks of severe neurological complications associated with epidural blocks in elderly patients are far higher than previously presumed.<sup>27</sup> In patients undergoing lower-extremity major orthopaedic surgery, less invasive and less expensive perineural techniques may be as effective as epidural technique.<sup>28,29</sup> A recent meta-analysis showed that continuous peripheral nerve block analgesia, regardless of catheter location, provided superior postoperative analgesia and fewer opioid-related side effects when compared with opioid analgesia.<sup>30</sup> Another meta-analysis confirmed these findings, continuous peripheral analgesic techniques provided superior analgesia, reduced opioid consumption, and reduced opioid-related side effects such as nausea, vomiting, sedation, and pruritus. However, the authors stated that no RCT had addressed effects of these techniques on major morbidity or mortality. The authors also commented that the general applicability of perineural catheter techniques is uncertain because of the required level of technical skill and infrastructure to manage these catheters, especially for outpatients.<sup>20</sup>

#### Incisional catheter techniques

Perineural, incisional, and intra-articular catheter techniques are being used increasingly to manage postoperative pain in hospitalised and day surgery patients. Catheters may be placed within the brachial plexus sheath, perineurally, intra-articularly, into the subacromial space, as well as subcutaneously into the surgical wound. In appropriate patients, simple techniques such as perfusion of local anaesthetic through an incisional catheter may be as effective as the much more invasive epidural technique; this was demonstrated in a recent controlled comparison between the two techniques for pain management after C. section.<sup>31</sup> A meta-analysis of 45 randomised controlled trials (n = 203) of continuous wound catheter technique for postoperative analgesia showed reduced pain scores and/or opioid consumption in the following studies: 5/6 studies of abdominal surgery (upper abdominal, vascular), 13/13 studies of cardiothoracic surgery (thoracotomy, oesophagectomy, sternotomy), 6/7 studies of gynaecologic surgery (C. section, abdominal hysterectomy), and 12/14 studies of orthopaedic surgery (upper and lower extremities and spine surgery). In general, there was a 32% reduction of pain scores at rest and movement, 25% decreased need for opioids, 15% decreased risk of PONV and 30% increase in patient satisfaction. There was also a one day reduction of hospitalisation but the data were from limited number of patients.<sup>32</sup> The role of epidural technique will diminish considerably if further controlled studies confirm the impressive results of incisional catheter techniques. Local anaesthetic drugs can be delivered through such catheters as continuous infusions, on demand self-administered bolus doses by patient-controlled regional analgesia (PCRA) or low-dose background infusions with possibility of on-demand bolus doses. Patients receiving local anaesthetic by infusion or PCRA may achieve more vigorous postoperative physical therapy with improved analgesia than patients receiving only oral opioid analgesics.

## Pain management after ambulatory surgery

One of the most significant changes in surgical practice during the last two decades has been the

growth of ambulatory surgery. In the United States, over 60% of the 79 million surgical procedures performed each year occur in an ambulatory care setting.<sup>33</sup> Also in England ambulatory surgery as a percentage of elective surgery has increased from 34% in 1989–1990 to 65% in 1998–1999.<sup>33</sup> The consensus is that the number of patients undergoing surgery on ambulatory basis will increase particularly in countries with low numbers today.

Adequate postoperative analgesia is a pre-requisite for successful ambulatory surgery. Contrary to the common belief that ambulatory surgery is associated only with mild pain; recent studies have shown that a considerable number of patients have suffered from moderate to severe pain during the first 24–48 h.<sup>34,35</sup> A recent literature review showed that 45% of ambulatory surgery patients experienced pain at home.<sup>36</sup> Postoperative pain is one of the most common reason for delayed discharge, contact with family doctor and the main reason for unanticipated hospital admission. Severe postoperative pain causes extreme discomfort and suffering and is also known to prevent sleep, which contributes to postoperative fatigue. Pain at home also has economic implications due to increased demand on community health services and delayed return to daily activities and employment. Based on results from two surveys McGrath et al. concluded that the problem of pain might be increasing due to increasing complexity of surgery being performed on ambulatory basis. In spite of the implementation of a multimodal analgesia regimen after their first survey, the incidence of moderate to severe pain increased from 26% to 30% and the incidence of severe pain increased two-fold, this is presumably due to recent inclusion of more painful procedures such as laparascopic cholecystectomy and microdiscectomy.<sup>37</sup> The rapid recovery following the use of short-acting anaesthetic agents has led to the concept of fast tracking by bypassing the PACU. However, the success of fast-tracking depends to a considerable extent on effective postoperative pain management routines and the cost saving of outpatient surgery may be negated by unanticipated hospital admission for poorly treated pain.<sup>37</sup> Regional techniques have been shown to facilate fast tracking.

### Regional anaesthesia techniques in ambulatory surgery

In children, the use of regional anaesthesia techniques before the start of surgery (but after the child has been put to sleep) will reduce the requirements of general anaesthetic drugs during surgery, which may result in a more rapid recovery, less nausea and vomiting, earlier alimentation and discharge. Caudal block is easy to perform and provides excellent analgesia for perineal or inguinal surgery. Sympathetic effects on the circulatory system are rare. Blocks may be performed on ilioinguinal, iliohypogastric, dorsal nerve of penis, brachial plexus, femoral nerve, and digital nerves. Ring blocks of wrist or ankle and local infiltration are simple and effective.

#### Peripheral nerve blocks

Peripheral nerve blocks provide excellent analgesia over a limited field and with minimal systemic effects. Peripheral blocks are possible for nearly all kinds of surgery. Even in situations where the block is ineffective for surgery the catheter can often be used for postoperative pain management. The technique is underused both for surgery and postoperative pain treatment. Peripheral nerve blocks have extended the indications for day-case surgical procedures such as major shoulder surgery and knee reconstruction. Comparative studies of interscalene block versus general anaesthesia for daycase shoulder arthroscopic surgery showed that 8% of the patients receiving general anaesthesia alone required unanticipated admission versus none in the patients receiving interscalene block.<sup>38,39</sup> Details about different blocks and techniques can be found in standard books and are beyond the scope of this review.

#### Intra-articular analgesia

Intra-articular drug administration has gained popularity due to its simplicity and efficacy in achieving anaesthesia for diagnostic and operative arthroscopy and for providing postoperative analgesia. The intra-articular technique has been used most frequently for knee and shoulder surgery, particularly for patients undergoing these surgeries on an outpatient basis. The technique has also been used for management of peri- and postoperative analgesia.

Intra-articular local anaesthetics are frequently used in perioperative pain management; however, its analgesic efficacy is controversial. Analgesic effects have been claimed<sup>40</sup> and denied.<sup>41</sup> As some arthroscopic procedures can be successfully performed under intra-articular and incisional local anaesthesia alone, it is surprising that intraarticular local anaesthetics do not consistently provide analgesia. These conflicting reports are due to problems with study designs. There is considerable variation in doses, volumes, and concentrations used in the various studies. A systematic review showed evidence of improved pain relief after intra-articular local anaesthesia in 12 out of 20 studies comprising almost 900 patients. The authors concluded that there was a weak evidence for reduction of postoperative pain and that the technique may be of clinical significance in ambulatory surgery.<sup>42</sup>

#### Intra-articular opioids

The inflammatory response to surgery has been shown to be necessary to express the opioid receptors in the joint. Opioid receptors have been shown in synovial tissues under inflammatory conditions. Blood levels of opioids after intraarticular injection are quite low, suggesting that the effect of morphine is produced peripherally. The analgesic effect of intra-articular morphine and bupivacaine depends on the type of arthroscopic surgery performed. Intra-articular morphine has a better analgesic effect in surgeries with a higher inflammatory response while intra-articular bupivacaine has a better analgesic effect in surgeries such as diagnostic arthroscopies and partial meniscectomies with a lower inflammatory response. Bupivacaine seems more efficient when the synovial layer is intact.43

In a recent systematic review of studies available in the literature, it was concluded that intraarticular morphine produces a definite but mild analgesic effect lasting up to 24 h. This effect may be dose-dependent.<sup>44</sup> This long duration of a single dose of morphine was confirmed by a second systematic review by Kalso et al.<sup>45</sup> These authors separated sensitive and insensitive studies in the reviewed literature. Sensitive studies were those where the experienced pain intensity was  $\geq$  30% of a maximum of 100 on visual analogue scale (VAS) in placebo groups. By including only sensitive studies, the authors could show that 5 mg intra-articular morphine in the knee joint provided up to 27 h analgesia.<sup>45</sup>

# Future prospects—regional techniques at home

Administration of local anaesthetic in the surgical wound is effective and safe but the analgesia lasts only a few hours. We have described a technique using an elastomeric balloon pump, which allows the patient to self-administer local anaesthetic analgesia at home. The technique involves the placement of a multihole, thin (22-gauge) catheters subcutaneously into the surgical wound, subacromially, intra-articularly, or in the axillary brachial plexus sheath (depending on surgical site).<sup>46</sup>

The improvement in, and availability of, catheter techniques and disposable pumps have facilitated the use of local anaesthetic-based analgesic techniques as a means of providing prolonged, effective, and safe postoperative analgesia. A large number of small, portable infusion pumps are currently available, each with benefits and drawbacks. In general, the larger, heavier, more expensive electronic pumps are more reliable than the elastomeric devices. After ambulatory surgery it may be desirable to use one of non-electronic pumps for its simplicity and disposability.<sup>43</sup>

Although this author was the first to report the use of perineural (and incisional and intra-articular) catheter analgesia at home our preference is for incisional and intra-articular catheter techniques because of their simplicity and safety, which are the two most important pre-requisites for such techniques at home. Another reason for restrictive use of ambulatory perineural catheters is that in Sweden (and in most countries outside USA) extensive joint surgery, which is one of the most important indications for perineural catheter techniques, is not an ambulatory procedure at present. The type of procedure that gualifies as ambulatory surgery varies considerably in many countries depending on differences in health care systems and reimbursement policies.

In the ambulatory setting, incisional catheter techniques have been used for the following types of surgery: breast augmentation, maxillofacial surgery, bone harvesting from iliac crest, laparascopic cholecystectomy, inguinal hernia, and hand surgery. For inpatients incisional catheter techniques have been used after hysterectomy, C. section, hip and knee joint replacement, anterior cruciate ligament reconstruction, cardiac surgery, and sternal fracture.<sup>43</sup>

#### Multimodal analgesia

It is generally believed that combing two or more analgesic drugs can provide additive or synergistic effect and reduce the doses of individual analgesics and thereby decrease the adverse effects of each drug especially opioids. Since numerous analgesics and techniques can be a part of such "multimodal analgesia" techniques it is difficult to draw meaningful conclusions from available literature. On the basis of evidence from four meta-analyses and one systematic review it appears that multimodal analgesia (defined as use of NSAIDs, COX-2 inhibitors, or paracetamol in combination with i.v. opioid PCA) results in an opioid-sparing effect, however, this opioid reduction does not consistently result in decreased opioid side effects.<sup>20</sup> The use of NSAIDs may increase some risks such as severe bleeding: number needed to harm (NNH) = 59, renal failure in cardiac patients for COX-2 inhibitors. NNH = 73.<sup>20</sup> Based on current literature, Rathmell et al.<sup>20</sup> concluded that "Despite much rhetoric about combining multiple analgesic techniques to provide multimodal analgesia, only limited evidence suggests that this approach will improve pain control or perioperative outcomes".

### Procedure-specific postoperative pain management

All pain management guidelines advocate generalised "one size fits all" recommendations for use of analgesic drugs and techniques. In clinical practice, it is generally accepted that there is considerable difference in pain intensity and its consequences, for example between thoracotomy versus hysterectomy or hip replacement versus knee replacement. Thus, there is a need for surgical procedure specific guidelines.<sup>47</sup> Two such initiatives are available on public Internet websites.48,49 The US Veterans Health Administration procedure specific guidelines can be accessed at www.ogp.med.va.gov/cpg/cpg.htm;<sup>48</sup> however, the website does not provide the background data or a complete list of references which allow the clinician to make choices based on local conditions, regulatory issues, and economic considerations. The more elaborate procedure specific guidelines are based on the recommendations from an international group of anaesthesiologists and surgeons (PROSPECT Working Group), which can be accessed at www.postoppain.org.<sup>49</sup> The PROSPECT guidelines are based on systematic review of literature for a particular procedure using Cochrane Collaboration and include randomised studies that evaluate the role of analgesic drugs and techniques (including regional anaesthesia techniques) and also the role of anaesthetic and surgical techniques on postoperative pain. Furthermore, gualitative and guantitative (meta-analyses) outcomes are generated. This procedure specific evidence, together with transferable evidence from a similar surgical procedure (where direct procedure specific evidence is not available in the literature) and using the Delphi method forms the basis of PROSPECT recommendations. The recommendations also take into consideration clinical routines and risk-benefit issues, for example the PROSPECT group does not recommend routine use of epidural analgesia for laparascopic cholecystectomy although literature (limited) shows that the technique provides effective analgesia. Readers are presented with the available evidence and can make decisions, which can be adapted to their practice. Currently, PROSPECT recommendations are available for laparoscopic cholecystectomy, inguinal herniorrhaphy, abdominal hysterectomy, total hip arthroplasty, and thoracotomy.<sup>48</sup> Colonic resection, total hip arthroplasty update, thoracotomy, and breast surgery are expected to appear in 2007. It is proposed that about 15-20 of the most common surgical procedures will be included in due course. The recommendations are updated regularly.

The literature that forms the basis of these recommendations including the use of regional techniques can be accessed on the website: www.postoppain.org.

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