Post Thoracotomy Pain Management
Katherine P. Grichnik, MD

Objectives
At the conclusion of this lecture, the participant will be able to:
1. List the most common acute and chronic pain conditions after thoracotomy
2. Analyze the approaches to prevention of acute and chronic pain after thoracotomy
3. Assess the potential for individual genetic markers to improve pain therapy in the future

Selected aspects of each area will be covered, as this topic is too extensive for one lecture

Introduction
The pathway of a pain impulse starts with the primary afferent nerve fibers (C and Aδ) whose axons end in the dorsal horn of the spinal cord. Nociceptive information is passed to the contralateral side of the spinal cord and, after synapsing, ascends in the anterolateral system as spinothalamic tracts. The primary areas of the brain that respond to pain stimuli are the somatosensory corticies, the insular cortex, the anterior cingulate cortex, the prefrontal cortex and several thalamic nuclei. (Boyette-Davis). The insular and anterior cingulate corticies are part of the limbic system, which contribute to the affective or emotional aspect of pain. There is also an elaborate array of pro-nociceptive mediators, which may potentiate the pain, as well as anti-nociceptive chemicals that are released following a tissue insult that leads to pain.

Acute Pain after Thoracotomy
Post thoracotomy pain management can be divided into acute and chronic pain, with the time difference being the perioperative period (up to 30 days) versus 2-6 months after surgery. This acute pain is described as among the most difficult pain conditions to treat and may be caused by the incision, by the intrathoracic manipulations and tissue damage and by the indwelling chest tube. It is usually stated that the best prevention of chronic pain is the use of preemptive analgesia as well as adequate intra- and postoperative analgesia for the thoracotomy patient. There are many approaches to analgesia; a multimodal approach is probably the most effective.

Epidural Analgesia
Thoracic epidural analgesia (TEA) is regarded as the gold standard for pain therapy after thoracic surgery and there are a multitude of studies supporting its efficacy for acute thoracotomy pain. TEA can be delivered in a continuous or via patient controlled epidural analgesia (PCEA) utilizing a variety of opioids and/or local anesthetic combinations. Epidural analgesia is thought to be better than IVPCA (intravenous patient controlled analgesia) alone; for example Behera et al compared PCEA to IVPCA and determined that pain relief was superior, there was less sedation and fewer side effects in the PCEA group. Further, postoperative FVC and PEFR were preserved compared to baseline with PCEA. (Behera). However, epidural catheter placement and use does carry a certain risk; many
anesthesiologists choose to use paravertebral blocks and/or IVPCA for short thoracic procedures that don’t require a chest tube for more than 24-36 hours. Further, chest tube pain is not effectively treated with epidural analgesia and often requires adjunctive modes of analgesia.

**Paravertebral Analgesia**
Some claim that paravertebral analgesia (PVB) is similar to epidural analgesia; for example, based on a small study, Mukherjee stated that PVB were both more effective and lasted longer than epidural analgesia. However, in a systemic review, Norum et al determined that comparative studies indicated that paravertebral block is neither superior nor safer than epidural analgesia for pain after thoracotomy. The authors noted that studies have not compared optimally conducted epidural analgesia to PVB but that PVB may be an alternative for post-thoracotomy pain when TEA is not feasible for various patient-related reasons (Breivik).

**Intrathecal**
Intrathecal analgesia is another mode of analgesia that is available but is rarely used in this population. Mercandante et al compared the effectiveness of continuous intrathecal thoracic analgesia to TEA after abdominal cancer surgery. There were no significant differences in pain, total amount morphine consumed and no technical complications related to the techniques (Mercandante).

**Opiates**
As a stand-alone therapy, opiates are often administered to post-thoracotomy patients, usually in the form of a PCA. This is probably not the most successful form of analgesia when used independently but can be very effective when combined with additional analgesics. However, it must be emphasized that for significant thoracotomy pain, PCA alone is inferior and may be associated with progression to chronic pain. Senturk et al compared the effects of three different analgesia techniques: TEA with and without pre-operative initiation and IV-PCA on postthoracotomy pain. At six months, the patients with pain were clearly the least with pre-TEA (45%) versus IVPCA (78%).

**Nonsteroidal Antiinflammatory Agents (NSAIDs)**
NSAIDs are often considered the mainstay of adjunctive analgesia for thoracotomy pain – especially to treat pain not covered by the spread of epidural solution or paravertebral block. As an example, Senard et al. examined patients who underwent thoracotomy, treated with PCEA and who were randomized to celecoxib or not. They found that postoperative pain scores at rest and with coughing were lower and patient satisfaction was greater in the celecoxib group. However, postoperative functional pulmonary assessments and morbidity were comparable between groups. One of the most commonly used NSAIDs after thoracic surgery is ketorolac but its use must be weighted against the risks of renal dysfunction in hypovolemic patients, the risk of bleeding and should not be used in patients with an aspirin allergy.
**Acetaminophen**

Intravenous acetaminophen is now available in the United States. Extensive studies have not been conducted for its use in thoracic surgery as an adjunctive agent but have proven efficacy in as for many surgical procedures and with many other forms of primary analgesia. Further, some have advocated the combined use of a NSAID and IV acetaminophen to reduce postoperative opioid requirements in general surgery. (Gehling)

**Gabapentin**

Some have advocated the preemptive use of gabapentin to prevent neuropathic chronic thoracic pain. Searle et al assessed (Searle) 100 patients for thoracic surgery utilizing tool to screen for potential or the development of postoperative neuropathic pain. There was a significant association for positive scores in the perioperative period to progress to chronic neuropathic pain at 3 months. Others have not found gabapentin useful to reduce acute shoulder pain in the thoracic patient (Huot).

**Ketamine**

NMDA receptor antagonists such as ketamine are often used as analgesics in surgical settings. Indeed, presurgical administration of ketamine is thought to block the development of central sensitization and hyperalgesia, which are characteristic of chronic pain (Boyette-Davis). Ketamine infusions intraoperatively have been shown to be useful in a multimodal approach to postoperative analgesia.

**Cryoablation**

Some have advocated for the use of cryoablation of the intercostal nerves as a mechanism to reduce the incidence of chronic pain. However, others suspect that cryoablation may actually increase the incidence of chronic pain. Ju et al randomly allocated patients to TEA with bupivacaine and morphine versus intercostal nerve cryoanalgesia. There were no significant differences between the techniques during the first three postoperative days. Both groups showed high incidence of chronic pain (42.1–72.1%), with no significance difference between the groups. However, the cryoablation group reported more allodynia-like pain and had a higher incidence of pain rated as severe that interfered with daily life. They concluded that cryoanalgesia may actually increase the incidence of neuropathic pain. (Ju)

**Transcutaneous Electrical Nerve Stimulation (TENS)**

TENS is a less commonly used therapy for post-thoracotomy pain. Chandra evaluated the effectiveness of TENS as an adjunctive to TEA. TEA with local anestheis and a non-functional TENS apparatus were compared to TEA with a functional TENS unit. They found that adding TENS to epidural analgesia led to a significant reduction in pain with no sequelae; it thus may be a valuable strategy to alleviate postoperative pain following thoracic surgery (Chandra).
Management of Acute Pain

Preemptive multimodal analgesia is now often used. While any one intervention has limited success, combining opiates, local anesthetics, NSAIDS, and/or neuroaxial blockade prior to surgery appears to provide optimal perioperative analgesia and possibly decrease the incidence of chronic pain (Hazelrigg). Some have advocated testing for pain before surgery to predict the level of pain to be anticipated after surgery. Weissman-Fogal et al evaluated patients preoperatively using a “pain temporal summation” survey and found that an individual profile of enhanced pain summation was associated with the greater likelihood of higher postoperative pain scores. (Weissman-Fogal)

Chronic Pain after Thoracotomy

Chronic post-thoracotomy pain is that pain which persists along the thoracotomy incision for at least two months after surgery. Thoracotomy pain syndrome is defined as inflammation in the surgical site stimulates peripheral sensory afferents and is attributed central sensitization or “windup” (Boyette-Davis). Thus, chronic pain may be a maladaptive response to what should be a protective mechanism (acute pain to avoid injury) for an organism. Perioperative physicians may not be aware of the high incidence of chronic pain after thoracotomy. Macguire, et al determined that, in the UK at one year, approximately 50% of patients may have chronic pain after thoracotomy; the incidence decreases to approximately 20% at 7 years. Similarly in a retrospective study, a Dutch group found that the incidence of chronic pain may be as high as 44% of patients at 3 years post surgery. In absolute numbers this may translate to more than 17,000 people with a new diagnosis of chronic pain after thoracotomy each year.

The intercostal, vagus, and phrenic nerves acutely convey pain signals from thoracic surgery. Although all three nerves are at risk, a majority of ongoing chronic pain is usually attributed to direct or indirect intercostal nerve damage. Further, some patients with chronic pain and hyperalgesia have sympathetically maintained pain, whereas in others, the pain is independent of the sympathetic nervous system (Boyette-Davis). Chronic pain is difficult to treat and may be most easily approached by preemptive multimodal analgesia as described above. Chronic treatment is also multimodal and may combine sympathetic nerve blockade (if appropriate), NSAIDs, treatment of neuropathic pain with agents such as gabapentin and mechanical interventions such as TENS units.

What is the Future?: The Genetics of Pain

Is there a role for heritability in chronic pain? Ochroch et al, determined that, in general women have more pain after thoracotomy than men in the first four months after surgery (Ochroch). Others have delved into the notion that certain genetic characteristics can determine the response to a noxious stimulus like thoracic surgery, predict the likelihood of chronic pain and can estimate the response to various analgesic interventions.
A general model for thinking about genetic influences to disease and interventions was proposed by Podgorneau, et al (Figure 1). In explanations, all people have a set of genes that determine one’s responses to perturbations in an environment, leading to health or disease. Then, with the disease response, a patient is again challenged by the ‘controlled trauma’ of an operative procedure; individual response is again dependent on one’s genetic makeup. Currently there are multiple studies to assess 1) the potential to develop (for example) lung cancer, to 2) assess the potential response to medical therapy, and 3) for those needing operative interventions, the potential to develop severe postoperative pain and chronic postoperative thoracic pain syndrome. The results of Shaw et al in this arena will be briefly described.

References

Boyette-Davis and Doughtey Mechanisms of Pain in Thoracic Surgery, in press
Chandra A Indian J Anaesth. 2010 Mar–Apr; 54(2): 116–120
Senturk Anesth Analg 2002;94:11–5