Pain Physician 2007; 10:185-212 • ISSN 1533-3159

Review

Epidural Steroids in the Management of Chronic Spinal Pain: A Systematic Review

Salahadin Abdi, MD[1], PhD, Sukdeb Datta, MD[2], Andrea M. Trescot, MD[3], David M. Schultz, MD[4], Rajive Adlaka, MD[5], Sairam L. Atluri, MD[6], Howard S. Smith, MD, PhD[7], and Laxmaiah Manchikanti, MD[8]

From: [1]University of Miami, Miller School of Medicine, Miami, FL; [2]Vanderbilt University School of Medicine, Nashville, TN; [3]University of Florida, Gainesville, FL; [4]University of Minnesota Medical School, Minneapolis, MN; [5]Pain Control Associates, Munster, IN; [6]Tristate Pain Management, Loveland, OH; [7]Albany Medical College, Albany, NY; and [8]Pain Management Center of Paducah, KY; and University of Louisville, KY.
Dr. Abdi[1] is Professor and Chief, Division of Pain Medicine, Department of Anesthesiology, Perioperative Medicine and Pain Management, University of Miami, Miller School of Medicine, Miami, FL; Dr. Datta[2] is Assistant Professor, Department of Anesthesiology, Vanderbilt University School of Medicine, and Director, Pain Management Services VA Tennessee Valley Healthcare System, Nashville, TN. Dr. Trescot[3] is Director, Pain Fellowship Program, University of Florida, and The Pain Center, Orange Park, FL. Dr. Schultz[4] is Assistant Professor, Department of Anesthesiology, University of Minnesota Medical School and Medical Director, MAPS Medical Pain Clinics, Minneapolis, MN. Dr. Adlaka[5] is Medical Director, Pain Control Associates, Munster, IN. Dr. Atluri[6], Tristate Pain Management, Loveland, OH. Dr. Smith[7] is Academic Director of Pain Management, Professor of Anesthesiology, Albany Medical College, Albany, NY. Dr. Manchikanti[8] is Medical Director, Pain Management Center of Paducah, KY; and Associate Clinical Professor of Anesthesiology and Perioperative Medicine, University of Louisville, KY.
Address Correspondence: Salahadin Abdi, MD, PhD, Department of Anesthesiology, Perioperative Medicine, and Pain Management, University of Miami, Miller School of Medicine, 1611 NW 12th Ave., SW 303, Miami, FL 33136
E-mail: sabdi@med.miami.edu
Funding: None.
Conflict of Interest: None.

Free full manuscript: www.painphysicianjournal.com

Background: Epidural injection of corticosteroids is one of the most commonly used interventions in managing chronic spinal pain. However, there has been a lack of well-designed randomized, controlled studies to determine the effectiveness of epidural injections. Consequently, debate continues as to the value of epidural steroid injections in managing spinal pain.

Objective: To evaluate the effect of various types of epidural steroid injections (interlaminar, transforaminal, and caudal), in managing various types of chronic spinal pain (axial and radicular) in the neck and low back regions.

Study Design: A systematic review utilizing the criteria established by the Agency for Healthcare Research and Quality (AHRQ) for evaluation of randomized and non-randomized trials, and criteria of Cochrane Musculoskeletal Review Group for randomized trials were used.

Methods: Data sources included relevant English literature performed by a librarian experienced in Evidence Based Medicine (EBM), as well as manual searches of bibliographies of known primary and review articles and abstracts from scientific meetings within the last 2 years. Three reviewers independently assessed the trials for the quality of their methods. Subgroup analyses were performed among trials with different control groups, with different techniques of epidural injections (interlaminar, transforaminal, and caudal), with different injection sites (cervical/thoracic, lumbar/sacral), and with timing of outcome measurement (short- and long-term).

Outcome Measures: The primary outcome measure is pain relief. Other outcome measures were functional improvement, improvement of psychological status, and return to work. Short-term improvement is defined as 6 weeks or less, and long-term relief is defined as 6 weeks or longer.

Results: In managing lumbar radicular pain with interlaminar lumbar epidural steroid injections, the evidence is strong for short-term relief and limited for long-term relief. In managing cervical radiculopathy with cervical interlaminar epidural steroid injections, the evidence is moderate. The evidence for lumbar transforaminal epidural steroid injections in managing lumbar radicular pain is strong for short-term and moderate for long-term relief. The evidence for cervical transforaminal epidural steroid injections in managing cervical nerve root pain is moderate. The evidence is moderate in managing lumbar radicular pain in post lumbar laminectomy syndrome. The evidence for caudal epidural steroid injections is strong for short-term relief and moderate for long-term relief, in managing chronic pain of lumbar radiculopathy and postlumbar laminectomy syndrome.

Conclusion: There is moderate evidence for interlaminar epidurals in the cervical spine and limited evidence in the lumbar spine for long-term relief. The evidence for cervical and lumbar transforaminal epidural steroid injections is moderate for long-term improvement in managing nerve root pain. The evidence for caudal epidural steroid injections is moderate for long-term relief in managing nerve root pain and chronic low back pain.

Key words: Spinal pain, low back pain, cervicalgia, epidural steroids, interlaminar, caudal, transforaminal, radiculopathy, axial pain, postlaminectomy syndrome, failed back surgery syndrome.

Pain Physician 2007; 10:185-212

Epidural injections for managing chronic pain are one of the most commonly performed interventions in the United States (1,2). Utilization statistics in the Medicare population of epidural procedures showed an increase from 802,735 in 1998 to 1,776,153 in 2005, or 121% over a period of 7 years. The projected statistics in the total U.S. population is expected to be 4 times the procedures performed in the Medicare population. Multiple systematic reviews (3-14), a meta-analysis (15), multiple guidelines (16-19), health technology assessments by insurers, and local medical review policies and coverage decisions have been published. However, controversy continues regarding the effectiveness of epidural steroid injections. They have been used to treat radicular pain from herniated discs, spinal stenosis, and chemical discs and axial spinal pain. The evidence is highly variable based on the reviewer and the evidence has been rated from indeterminate to strong in various publications. In addition, 3 types of epidurals, namely interlaminar, transforaminal, and caudal; and administration in 3 separate regions namely lumbar, cervical, and thoracic, with variable results complicate the picture of practice of interventional pain management.

Spinal pain is the most common of all chronic pain disorders. The lifetime prevalence of spinal pain has been reported as 54% to 80% (20-32). Annual prevalence of chronic low back pain ranges from 15% to 45% (22,23,25,30). Studies of the prevalence of low back pain and neck pain (23,25) and impact on general health showed 25% of patients reporting Grade II to Grade IV low back pain (high pain intensity with disability), whereas it was 14% in patients with neck pain. Modern evidence has shown that chronic persistent low back pain and neck pain in children, adults, and elderly are seen in up to 25% to 60% of patients, one year or longer after the initial episode (33-47). In addition, spinal pain is also associated with enormous economic, societal, and health impact (48-65). There are not any interventions which provide definite and long-term improvement in chronic low back pain, neither conservative nor surgical (66-76). Further, postlaminectomy syndrome and other symptoms, such as postsurgery syndrome, representing a cluster of syndromes wherein the expectations of the patient and the spine surgeon are not met, following spine surgery are common phenomena with persistent pain following spine surgery (77-83).

Nevertheless, the benefit and most effective route of administration for epidural steroids remain controversial. Several approaches are available to access the lumbar epidural space; namely, interlaminar, transforaminal, and caudal (3,4,16-19,84,85). There are substantial differences among these 3 approaches. The interlaminar entry can be directed more closely to the assumed site of pathology, requiring less volume than the caudal route. The transforaminal approach is target-specific and requires the smallest volume to reach the primary site of pathology; specifically, the anterior-lateral epidural space as well as the dorsal root ganglion. On the other hand, the caudal entry is relatively easily achieved with minimal risk of inadvertent dural puncture, but requires a relatively high volume (10-20 mL) of injectate to reach the site of pathology.

The underlying mechanism of action of epidurally administered steroid and local anesthetic injections is still not well understood. It is believed that the achieved neural blockade alters or interrupts nociceptive input, reflex mechanisms of the afferent fibers, self-sustaining activity of the neurons, and the pattern of central neuronal activities. Further, it is believed that local anesthetics interrupt the pain-spasm cycle and reverberating nociceptor transmission. On the other hand, corticosteroids reduce inflammation by inhibiting either the synthesis or release of a number of pro-inflammatory mediators and by causing a reversible local anesthetic effect (86-94).

The purpose of this review is to evaluate and update the effects of various types of epidural injections (interlaminar, transforaminal, and caudal) in the management of various types of chronic spinal pain (axial and radicular, cervical and lumbar). Several important studies and complications have been reported since the previous systematic review (3).

Methods

Literature Search

The literature search included using a professional librarian from an academic medical center (Vanderbilt University Medical School, Nashville, TN) utilizing PubMed, EMBASE, and ISI Web of Science (January 1966–October 2006); systematic reviews; narrative reviews; cross-references to the reviews; various published trials; and peer-reviewed abstracts from scientific meetings during the past 2 years, published in the English language. The search strategy including the MeSH terms was performed by the librarian. Results from all 3 databases were combined and duplicates were removed. PubMed strategies included a keyword search of non-

Medline citations to retrieve in-process and supplied by publisher citations. All articles were reviewed by at least 3 authors in the group and results were scored as a mean of the 3 scores rounded up to a whole number. Table 1 in the Systematic Review of Diagnostic Utility of Selective Nerve Root Blocks in this issue of the journal illustrates search strategies utilized.

Selection Criteria

The review focused on randomized and non-randomized evaluations, and reports of complications. The population of interest was patients suffering with chronic spinal pain for at least 3 months. Three techniques of epidural injections (interlaminar, transforaminal, and caudal) with local anesthetic, steroid, or other drugs provided for management of spinal pain were evaluated. All the studies providing appropriate management with outcome evaluations of 3 months or longer and statistical evaluations were reviewed. The primary outcome measure was pain relief at various points in time. The secondary outcome measures were functional or psychological improvement, return to work, and complications.

For evaluating the quality of individual articles, we have used the criteria from the Agency for Healthcare Research and Quality (AHRQ) publication (95). For evaluation of randomized trials, criteria described by Cochrane Review Group for musculoskeletal disorders (96) also have been utilized.

For studies to be included, an algorithmic criterion should have been met and a study should have answered positive questions (at least partially) in all 3 categories (3,4,18,19,97,98). If a study had 10 or more randomized trials meeting inclusion criteria, no observational studies were included. AHRQ criteria, Cochrane Review Group criteria, and algorithmic criteria of inclusion and exclusion are shown in multiple publications (3,4,18,19,95-98) and also in this issue of the journal in the systematic review of percutaneous adhesiolysis.

Analysis of Evidence

Qualitative analysis was conducted, using 5 levels of evidence for effectiveness of epidural steroids as illustrated in Table 1. Pain relief was evaluated on both a short-term (< 6 weeks) and long-term (6 weeks or longer) basis. A study was judged to be positive if the authors concluded that the epidural steroid injection therapy was more effective than the reference treatment in randomized trials or simply concluded that it was effective. All other conclusions were considered negative. If, in the opinion of reviewers, there was conflict with the conclusion, the conclusions were changed with appropriate explanations.

Table 1. *Designation of levels of evidence.*

Level I	Conclusive: Research-based evidence with multiple relevant and high-quality scientific studies or consistent reviews of meta-analyses.
Level II	Strong: Research-based evidence from at least 1 properly designed randomized, controlled trial; or research-based evidence from multiple properly designed studies of smaller size; or multiple low quality trials.
Level III	Moderate: a) Evidence obtained from well-designed pseudorandomized controlled trials (alternate allocation or some other method); b) Evidence obtained from comparative studies with concurrent controls and allocation not randomized (cohort studies, case-controlled studies, or interrupted time series with a control group); c) Evidence obtained from comparative studies with historical control, 2 or more single-arm studies, or interrupted time series without a parallel control group.
Level IV	Limited: Evidence from well-designed, nonexperimental studies from more than 1 center or research group; or conflicting evidence with inconsistent findings in multiple trials.
Level V	Indeterminate: Opinions of respected authorities, based on clinical evidence, descriptive studies, or reports of expert committees.

Adapted from ref 3, 16, 17, 95, 97, 98.

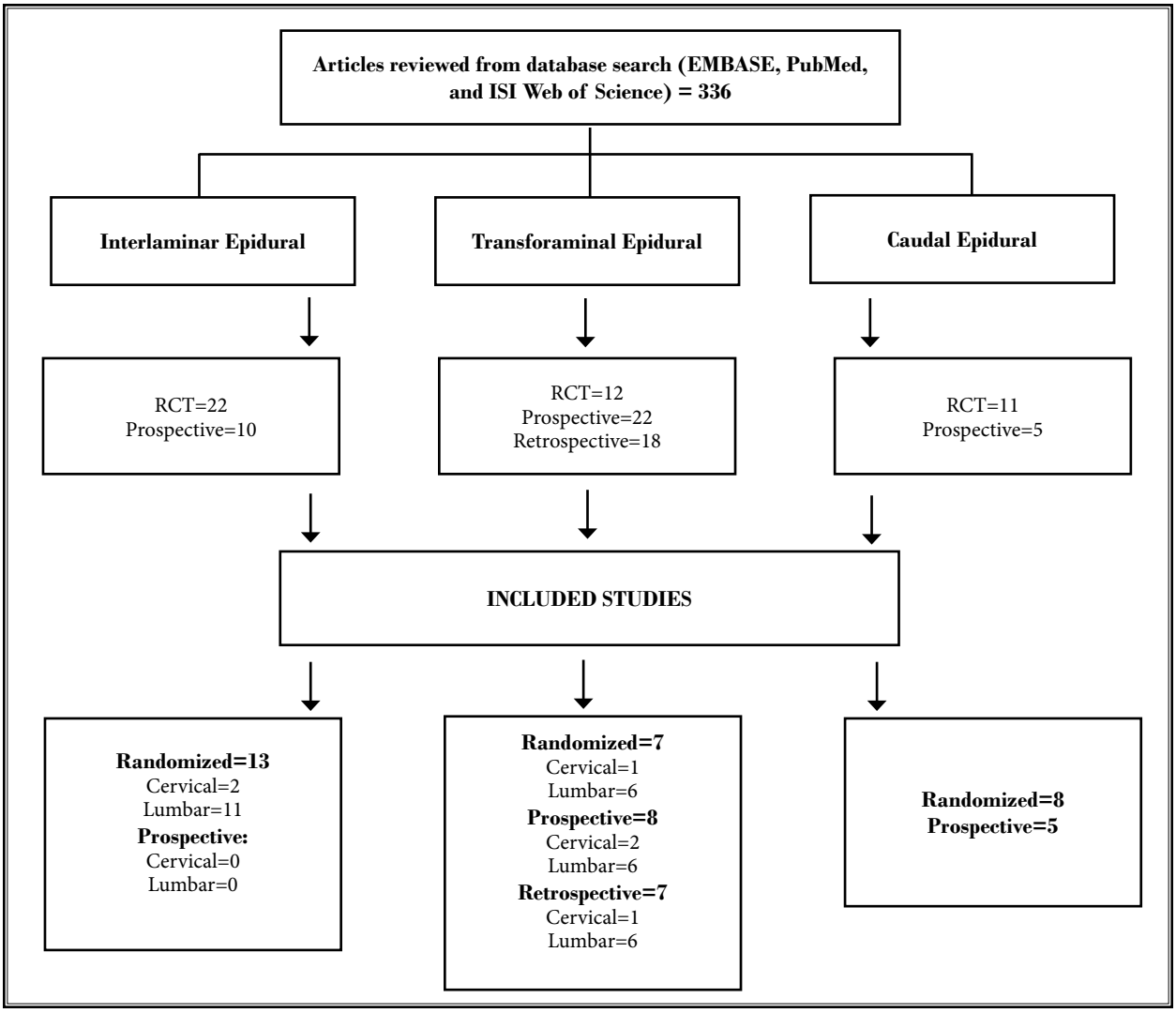

Fig. 1. *Systematic review flow chart.*

Results

The literature search was carried out as described in the methods section. Fig. 1 shows a systematic review flow chart with number of total articles reviewed and included in each category of interlaminar, transforaminal, and caudal epidurals with itemization into randomized, prospective, and retrospective.

Interlaminar Epidural Injections

Our search strategy yielded multiple studies evaluating the effectiveness of interlaminar epidural injections. These included 22 randomized or double-blind trials (99-120), 9 non-randomized prospective trials (121-129), and multiple other observational trials (130-161).

Methodological Criteria

Of the 22 randomized trials, 13 studies met inclusion criteria (99-103,107-109,113,116,117,119,120). One study (104) was excluded as they studied effects of subarachnoid and epidural midazolam. Two studies (110,111) focused on diabetic polyneuropathy and intractable postherpetic neuralgia. One study (114) evaluated only inpatients, whereas 4 evaluations (105,106,115,118) failed to evaluate long-term relief. One study (112) was not included due to lack of data for review. Tables 2 and 3 illustrate various characteristics and results of published randomized trials meeting inclusion criteria. Eleven lumbar trials (99,100-103, 107,108,116,117,119,120) and 2 cervical trials (109,113) were included.

Table 2. *Characteristics of published randomized trials of lumbar interlaminar epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Wilson-McDonald et al (119) Randomized, controlled trial AHRQ score: 10/10 Cochrane score: 7/10	93 pts with MRI evidence of a disc prolapse, spinal stenosis, or a combination. Pts had lumbosacral nerve root pain which had not resolved within 6 wks minimum .	Experimental: epidural injection of bupivacaine 0.5% (40 mg) with methylprednisone 80 mg. Control: intramuscular injection of 0.5% (40 mg) bupivacaine with 80 mg methylprednisone.	Timing: 6 wks, 24 mos. Outcome measures: Oswestry Disability index, pain relief.	In the first 5 wks after epidural injection a useful improvement in nerve root symptoms was seen.	Positive short-term and negative long-term relief
Arden et al (120) Double-blind, randomized placebo controlled: TRIM AHRQ score: 10/10 Cochrane score: 9/10	228 pts with unilateral sciatica .	Experimental: triamcinolone 80 mg and 10 ml of 0.25% bupivacaine Control: interspinous injection with 2 mL of normal saline.	Timing: 3, 6, 12, 26, and 52 weeks. Outcome measures: Oswestry disability index, Likert scale, SF-36, VAS.	Lumbar epidural steroid injection produced a statistically significant improvement in function over placebo in 3 wks. By 6 wks, benefit lost.	Positive short-term and negative long-term relief
Carette et al (100) Randomized, double-blind trial AHRQ score: 10/10 Cochrane score: 10/10	158 pts with sciatica due to a herniated nucleus pulposus. Treatment group: 78 Placebo group: 80.	Experimental: methylprednisolone acetate (80 mg and 8 mL of isotonic saline) Control: isotonic saline 1 mL Frequency: 3 epidural injections 3 wks apart.	Timing: 6 wks, 3 mos, 12 mos Outcome measures: need for surgery Oswestry Disability scores.	Significant improvement was seen in leg pain in the methylprednisolone group after 6 weeks, with no difference after 3 and 12 mos.	Positive short-term and negative long-term relief
McGregor et al (99) Randomized, controlled trial AHRQ score: 6/10 Cochrane score: 5/10	44 pts with low back and leg pain.	Caudal epidural vs lumbar epidural.	Visual analog scale.	No significant improvement.	Negative short-term and long-term relief
Pirbudak et al (117) Randomized non-blinded trial AHRQ score: 7/9 Cochrane score: 6/10	92 pts with sciatica. Experimental with steroids and amitriptyline: 46. Control with benzylprednisolone and bupivacaine steroids: 46.	Experimental: benzylprednisolone (14 mg) + bupivacaine and 10-50 mg oral amitriptyline.	Timing: 2 wks, 6 wks, and 9 mos. Outcome measures: VAS and Oswestry low back pain disability questionnaire.	Lumbar epidural steroid injection reported pain relief up to 6 mos. Additional oral amitriptyline increased pain relief to 9 mos.	Positive short-term and long-term relief
Snoek et al (101) Randomized trial AHRQ score: 7/10 Cochrane score: 6/10	51 pts with lumbar root compression documented by neurological deficit and a concordant abnormality noted on myelography. Experimental: 27 Control: 24.	Experimental: 80 mg of methylprednisolone (2 mL). Control: 2 mL of normal saline Frequency: single injection.	Timing: 3 days and an average of 14 mos. Outcome measures: Pain, sciatic nerve stretch tolerance.	No statistically significant differences were noted in either group.	Negative short-term and long-term relief
Cuckler et al (102) Randomized, double-blind trial AHRQ score: 9/10 Cochrane score: 9/10	73 pts with back pain due to either acute herniated nucleus pulposus or spinal stenosis of > 6 mos. Experimental: 42 Control: 3.1	Experimental: 80 mg (2 mL) of methylprednisolone + 5 mL of procaine 1%. Control group: 2 mL saline + 5 mL of procaine 1%.	Timing: 24 hrs and an average of 20 mos. Outcome measures: subjective improvement, need for surgery.	There was no significant short-term or long-term improvements between both groups.	Negative short-term and long-term relief

Table 2. Continued. *Characteristics of published randomized trials of lumbar interlaminar epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Dilke et al (103) Randomized trial AHRQ score: 7/10 Cochrane score: 7/10	100 pts with low back pain and sciatica of 1 week to more than 2 yrs. Experimental: 51 Control: 48.	Experimental group: 10 mL of saline + 80 mg of methylprednisolone. Control group: 1 mL of saline.	Timing: 2 wks and 3 mos. Outcome measures: pain relief, analgesic use, and resuming work.	Initial Improvement: 60% in the treatment group and 31% in the control group. A greater proportion of actively treated pts improved at 3 mos.	Positive short-term and long-term. relief
Ridley et al (107) Randomized trial AHRQ score: 9/10 Cochrane score: 8/10	35 pts with low back pain and sciatica of mean duration approximately 8 mos. Experimental: 19 Control: 16.	Experimental: 10 mL of saline + 80 mg of methylprednisolone (n=19). Control: saline 2 mL, interspinous ligament (n=16).	Timing: 1 wk, 2 wks, 3 mos, and 6 mos. Outcome measures: pain control improvement in straight leg raising.	90% of the pts in the treated group compared to 19% in the control group showed improvement at 1 wk, 2 wks, and 12 wks. By 24 wks, relief deteriorated to pretreatment levels.	Positive short-term and negative long-term relief
Rogers et al (108) Randomized, single-blind, sequential analysis AHRQ score: 6/10 Cochrane score: 5/10	30 pts with low back pain. Experimental = 15 Control = 15.	Experimental: local anesthetic + steroid. Control: local anesthetic alone.	Timing: 1 month. Outcome measures: pain relief and nerve root tension signs.	Experimental group had significantly better results. Long-term results were similar for both.	Positive short-term relief and negative long-term relief
Kraemer et al (116) Randomized trial AHRQ score: 6/10 Cochrane score: 5/10	Control: 46 Intervention: 40.	Control: paravertebral local injection of local anesthetic, with intramusclar steroid injection. Intervention: lumbar interlaminar steroid injection.	Timing: 3 wks and 3 mos. Outcome measures: pain relief.	Epidural injections were more effective than paravertebral injections.	Positive short-term and negative long-term relief

Since there were multiple randomized trials evaluating lumbar pain (N=1), no prospective or retrospective evaluations were considered for inclusion. The single prospective evaluation of the cervical spine (121) was not included as all the patients who underwent interlaminar epidural steroid injections also underwent transforaminal epidural steroid injections.

Effectiveness

Of the 11 randomized trials (99,100-103,107,108, 116,117,119,120) included in the evaluation of lumbar radiculitis, 7 were positive for short-term relief (100, 103,107,108,116,117,119), whereas only 2 studies were positive for long-term relief (103,117).

In the evaluation of cervical pain and radiculopathy, 2 randomized trials (109,113) were available. Both the randomized trials (109,113) evaluating the effectiveness of interlaminar cervical epidural steroids in managing cervical radiculopathy were positive.

Of the 4 randomized trials, which were positive, Dilke et al (103) studied low back pain and sciatica, and Pirbudak (117) evaluated all patients with sciatica, whereas Castagnera et al (109) and Stav et al (113) studied chronic cervical radicular pain.

Among the studies reporting negative short-term and long-term results, patients with disc herniation, spinal stenosis, and postlumbar laminectomy syndrome with low back and/or sciatica were included.

Description of Study Characteristics

Descriptive characteristics of various studies in-

Table 3. *Characteristics of published randomized trials of cervical interlaminar epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Castagnera et al (109) Randomized trial AHRQ score: 7/10 Cochrane score: 6/10	14 patients: local anesthetic and steroid. 10 patients: local anesthetic, steroid + morphine sulfate.	I. 0.5% lidocaine + triamcinolone acetonide. II. Local anesthetic + steroid + 2.5 mg of morphine sulfate.	Timing: 1 month, 3 mos, and 12 mos. Outcome measures: pain relief.	The success rate was 79% vs. 80% in group I and II. Overall, initial success rate was 96%, 75% at 1 month, 79% at 3 mos, 6 mos, and 12 mos.	Positive short-term and long-term relief
Stav et al (113) Randomized trial AHRQ score: 6/10 Cochrane score: 5/10	Experimental: 25 patients. Control: 17 patients.	Experimental: epidural steroid and lidocaine injections Control: steroid and lidocaine injections into the posterior neck muscles	Timing: 1 week and 1 year. Outcome measures: pain relief, change in range of motion, reduction of daily dose of analgesics, return to work.	One week improvement 36% vs 76%; One year improvement 12% vs 68%.	Positive short-term and long-term relief

cluded in the evidence synthesis is illustrated in Table 2 for lumbar interlaminar epidural injections and Table 3 for cervical interlaminar epidural injections.

Two new interlaminar lumbar epidural steroid injections (119,120) were included in lumbar interlaminar epidural evidence synthesis are described here.

Arden et al (120) evaluated 228 patients with "clinical" unilateral sciatica who were treated with either a lumbar epidural injection (80 mg triamcinolone in 10 mL 0.25% bupivacaine) or an interspinous ligament injection with 2 mL normal saline, performed blindly by "experienced anaesthetists." The patients underwent injections at 0, 3, and 6 weeks, although patients who noted at least 75% improvement in pain did not receive a second or third injection. The epidural injections produced a significant improvement in self-reported function at 3 weeks, but that benefit was lost by 6 weeks.

Wilson-MacDonald et al (119) compared lumbar epidural steroid injections to interspinous ligament steroid injections, to assess whether the epidural location of the steroid was responsible for the subsequent effects. Ninety-three patients with back and leg pain and MRI evidence of a prolapsed disc who had been offered surgery were randomized to receive either a blind lumbar epidural (44 patients) or an injection into the interspinous ligament (48 patients). Each patient was injected with 8 mL 0.5% bupivacaine and 80 mg of methylprednisolone. There was no difference in the rate of subsequent surgery through the period of follow up.

Cost Effectiveness

In the evaluation of cost effectiveness, Manchikanti et al (85) and Price et al (160) concluded that lumbar interlaminar epidural steroid injections were not cost effective.

Level of Evidence

In managing lumbar radicular pain with interlaminar lumbar epidural steroid injections, the level of evidence is strong for short-term relief and limited for long-term relief. In managing cervical radiculopathy with cervical interlaminar epidural steroid injections, the evidence was moderate for short-term improvement and long-term improvement. The evidence is indeterminate in the management of axial neck pain, axial low back pain, and lumbar spinal stenosis.

Transforaminal Epidural Injections

Relevant reports evaluating the effectiveness of transforaminal epidural injections included 12 randomized trials, 20 prospective evaluations, and multiple retrospective reports (121,122,130,161-212).

Methodological Criteria

The evaluation for evidence synthesis led to identification of 12 randomized controlled trials (116,162-

172), and 20 prospective evaluations (121,122,173-190), and multiple retrospective evaluations (130,161,191-206). Of the 12 randomized controlled trials, 7 trials were included in evidence synthesis (162-164,166,167,169,170), whereas of 20 prospective evaluations, 7 were included (121,174,175,187-190). Karppinen et al (166) reported results of 1 study in 2 publications (165,166). Thus, this was considered as one study. Multiple others were excluded for various reasons. A trial by Kolsi et al (168) was not included since the measurements were only of short-term duration. Kraemer et al (116) described lumbar epidural perineural injection, however, using an interlaminar approach, a non-validated technique. A summary of reported studies is listed in Table 4.

Among the 7 randomized trials included in the evidence synthesis meeting inclusion criteria, 6 of them evaluated effectiveness in lumbar disc herniation and radiculopathy (162-164,166,169,170), showing mixed results in 4 of the 6, both in short-term and long-term with 2 negative studies (163,166). The 7th trial (167) studied effectiveness in postsurgery syndrome with negative results.

Among the 7 prospective evaluations included for evaluation, 2 studies evaluated the effectiveness of cervical transforaminal epidurals (121,189), showing positive results. The remaining 5 studies (175,179,187,188,190) evaluated lumbar transforaminal epidural steroid injections. One study (188) compared effectiveness of transforaminal epidural steroid injections in lumbar spine with discectomy. One evaluation reported the effect on spinal stenosis (190). Multiple retrospective evaluations also showed positive results. Only one retrospective evaluation (130) was included in cervical transforaminal evidence synthesis. A summary of lumbar epidural transforaminal injections is described in Table 5, whereas, the summary of cervical transforaminal epidural injections is described in Table 6.

Table 4. *Details of randomized trials studying the effectiveness of lumbar transforaminal epidural steroid injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Riew et al (162,164) Prospective, randomized, controlled, double-blind study AHRQ score: 8/10 Cochrane score: 7/10	55 pts with lumbar disc herniations or spinal stenosis referred for surgical evaluation. 28 pts in experimental group (bupivacaine and betamethasone) and 27 pts in control group (bupivacaine only).	Experimental: transforaminal nerve root or epidural steroid injection with 1 mL of 0.25% bupivacaine and 6 mg of betamethasone Control: 1 mL of 0.25% bupivacaine. As many as 4 injections were given during the follow-up.	Initial outcomes were evaluated at 1 year. Injection was considered as a failure if the patient opted for operative treatment. North American Spine Society questionnaire also used: 20 of 28 patients in steroid group, 9 of 27 patients in control group had no surgery at 1 year. After 5 yrs, with no differences among groups.	17 of the 21 pts still had successful results with no operative intervention.	Positive short-term and long-term relief
Ng et al (163) Randomized, double-blind, controlled trial AHRQ score: 8/10 Cochrane score: 8/10	43 pts were recruited in the bupivacaine and methylprednisolone group and 43 pts in the bupivacaine only group with radicular pain who had unilateral symptoms and also failed conservative management.	One group received bupivacaine and methylprednisolone and the second group received only bupivacaine with a transforaminal injection.	Outcome measures: the Oswestry Disability Index, visual analogue score for back pain and leg pain, claudication in walking distance, and the patient's subjective level of satisfaction of the outcome.	47.5% of pts in the bupivacaine only group had at least 20 mm reduction in leg pain compared to 41.5% of pts in the bupivacaine and steroids group at 3 months.	Negative short-term and long-term relief

Table 4 Continued. *Details of randomized trials studying the effectiveness of lumbar transforaminal epidural steroid injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Karppinen et al (165, 166) Randomized, double-blind trial AHRQ score: 9/10 Cochrane score: 8/10	160 consecutive, eligible pts with sciatica with unilateral symptoms of 1 to 6 mos duration. None of the pts had undergone surgery.	Experimental: local anesthetic and methylprednisolone. Control: normal saline.	Timing: 2 wks, 3 mos, and 6 mos Outcome measures: Pain relief, sick leave, medical costs, and future surgery. Nottingham Health Profile.	Steroid injection produced significant treatment effects and short-term in leg pain, straight leg raising, disability and in Nottingham Health Profile and emotional reactions.	Positive short-term and long-term relief
Vad et al (169) Prospective, randomized trials AHRQ score: 7/10 Cochrane score: 7/10	Pts with leg pain, with documented herniated nucleus pulposus or manifested clinical signs such as radicular pain with lumbar radiculopathy.	Experimental: betamethasone 9 mg, and 2% preservative-free Xylocaine (1.5 mL) per level. Control: trigger point injections.	Timing: 3 wks, 6 wks, 3 mos, 6 mos, and 12 mos. Outcome measures: Roland-Morris score, visual numeric score, finger-to-floor distance, patient satisfaction score.	Group receiving transforaminal epidural steroid injections had 84% success rate compared with 48% for group receiving trigger point injections.	Positive short-term and long-term relief
Devulder (167) Open, non-blind, randomized study AHRQ Score: 6/10 Cochrane Score: 5/10.	60 pts with documented epidural fibrosis in fewer than three nerve roots.	Group A = 1 mL bupivacaine 0.5% with 1500 units hyaluronidase and 1 ml saline per nerve root sleeve. Group B = 1 mL bupivacaine 0.5% with 40 mg methylprednisolone solution per nerve root. Group C = bupivacaine 0.5% combined with 1500 units hyaluronidase and 40 mg methylprednisolone solution. The volume of each injection was 2 ml and each was given twice at an interval of 1 wk.	The pts were evaluated on a verbal pain rating scale 1, 3, and 6 mos after the second injection. The Kruskal-Wallis test was used to detect statistically significant differences among the three groups, and the analysis was refined with the Friedman test.	Overall, although injections induced analgesia at 1 month, these effects were reduced at 3- and 6-month follow-ups. No statistical differences were found between the 3 treatment groups after 1 month.	Negative short-term and long-term relief
Thomas (170) Randomized, controlled trials AHRQ Score: 6/10 Cochrane Score: 5/10	Thirty-one pts (18 females, 13 males) with discal radicular pain of less than 3 mos duration.	Pts were consecutively randomized to receive either radio-guided transforaminal or blindly performed interspinous epidural corticosteroid injections.	Post-treatment outcome was evaluated clinically at 6 and 30 days, and 6 mos. Outcome measures: pain, functional status.	At day 30 and 6 mos, pain relief, daily activities, work, leisure activities, anxiety, and depression, were better in transforaminal group.	Positive short-term and long-term relief

Table 5. *Details and results of nonrandomized trials of lumbar transforaminal epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Lutz et al (179) A prospective case series AHRQ score: 4/8	69 pts with lumbar herniated nucleus pulposus and radiculopathy were recruited.	Transforaminal epidural steroid injections with 1.5 cc of 2% Xylocaine and 9 mg of betamethasone acetate.	Timing: 28 to 144 wks. Outcome measures: At least ±50% reduction in preinjection and postinjection visual numerical pain scores.	A successful outcome was reported by 52 of the 69 pts (75.4%) at an average follow-up of 80 wks (range 28-144 wks).	Positive short-term and long-term relief
Butterman (187) A prospective evaluation AHRQ score: 4/8	232 pts who were referred for treatment of DDD, 171 pts who were possible spinal arthrodesis candidates.	Transforaminal epidural steroid injections or intradiscal steroid injections (ISIs).	Visual analog pain scale, pain drawing, Oswestry Disability. Index, use of pain medication, and opinion of treatment success.	ESI was effective in improving pain and function at short-term follow-up. At 2 years, less than one-third had not had additional invasive treatment.	Positive short-term and negative long-term relief
Butterman (188) A prospective evaluation AHRQ score: 4/8	169 pts with a large herniation of the lumbar nucleus pulposus.	Transforaminal epidural steroid injection or discectomy.	Evaluation was performed with the use of outcomes scales and neurological examination.	42% to 56% of the 50 pts who had epidural steroid injection reported that the treatment had been effective.	Positive short-term and long-term relief
Botwin et al (190) A prospective evaluation AHRQ score: 4/8	34 pts who met our inclusion criteria for the treatment of unilateral radicular pain from degenerative lumbar spinal stenosis.	Injectant: 12 mg of betamethasone acetate and 2 mL of 1% preservative-free lidocaine HCL.	Pts were evaluated by an independent observer at 2 mos, and at 12 mos after the injections. Questionnaires: visual analog scale, Roland 5-point pain scale, standing/walking tolerance, and patient satisfaction scale.	75% of pts had successful long-term outcome, reporting at least a >50% reduction between preinjection and postinjection pain scores, with an average of 1.9 injections per patient. 64% of pts had improved walking tolerance, and 57% had improved standing tolerance at 12 mos.	Positive short-term and long-term relief
Yang et al (175) A prospective evaluation AHRQ score: 4/8	21 patients with lumbar radiculopathy were evaluated. All of them had a CT or MRI visualized disc herniations and were felt to be candidates for discectomy.	Transforaminal epidural steroid injection.	Pain relief and avoidance of surgery.	63% of patients had significant pain relief lasting through the 23-month follow-up, avoiding surgery.	Positive short-term and long-term relief

Description of Study Characteristics

Riew et al (162) performed an evaluation of minimum 5-year follow-up to evaluate nerve root blocks in the treatment of lumbar radicular pain. This was a continuation of a previous randomized, double-blind, controlled study on the effect of nerve root blocks on the need for operative treatment of lumbar radicular pain (164). All of the patients in both studies (162,164) were considered to be operative candidates by the treating surgeon and all had initially requested operative intervention. They had then been randomized to be treated with a selective nerve root block with either bupivacaine or bupivacaine and betamethasone. Both the treating physician and the patient were

Table 6. *Details and results of non-randomized trials of cervical transforaminal epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Bush and Hillier (121) A prospective evaluation AHRQ score: 4/8	68 pts with neck pain and cervical radiculopathy.	Transforaminal cervical epidural steroid injections.	Timing: 1 month to 1 year. Outcome measures: Pain relief.	93% of the pts were reported to have good pain relief lasting for 7 mos.	Positive short-term and long-term relief.
Cyteval et al (189) AHRQ score: 4/8	30 pts with cervical radiculopathy, 16 pts with foraminal degenerative stenosis, 14 pts with disk herniation.	Periradicular foraminal steroid infiltration under CT control.	Timing: 2 wks, 6 mos. Outcome measures: visual analog pain scale (VAS).	Good pain relief was reported in 60% of pts. There was no rebound of pain at the 6-month follow-up.	Positive short-term and long-term relief
Kolstad et al (174) A prospective evaluation AHRQ score: 4/8	21 patients awaiting cervical disc surgery.	Patients were given 2 epidural injections 2 weeks apart.	Outcome assessments: 6 weeks and 4 mos . Outcome measures: VAS, Odom's criterion, and treatment satisfaction.	5 of the 21 patients canceled their surgery due to improvement in pain, and overall, there was a significant decrease in radicular pain at 6 weeks and 4 months.	Positive short-term and long-term relief
Lin et al (130) A retrospective study AHRQ score: 4/8	Patients with herniated cervical discs, otherwise surgical candidates were offered a trial of cervical epidural injections.	Cervical transforaminal with local anesthetic and steroids.	Pain relief and avoidance of surgery.	Of the 70 treated patients, 44 (63%) had significant relief of their symptoms and did not wish to proceed with surgical treatment.	Positive short-term and long-term relief

blinded to the type of medication. Of the 55 randomized patients, 29 avoided an operation in the original study. Twenty-one of those 29 patients were reevaluated with a follow-up questionnaire at a minimum of 5 years after the initial block; 17 of 21 patients still had not had operative intervention. There was no difference between the group treated with bupivacaine alone and the group treated with bupivacaine and betamethasone with regard to the avoidance of surgery for 5 years. At the 5-year follow-up evaluation, all of the patients who had avoided operative treatment had significant decreases in neurological symptoms and back pain compared with baseline values. Authors concluded that the majority of patients with lumbar radicular pain who avoid an operation for at least 1 year after receiving a nerve root injection with bupivacaine along or in combination with betamethasone will continue to avoid operative intervention for a minimum of 5 years.

Ng et al (163) studied periradicular infiltration of nerve roots with local anesthetic and steroid versus local anesthetic alone. They evaluated 86 patients with unilateral leg pain and an MRI showing a lumbar herniated disc or foraminal stenosis at a level compatible with the symptoms. All the patients received a single level injection under fluoroscopy with 2 mL of 0.25% bupivacaine with 40 mg of methylprednisolone in 1 group and the second group receiving only bupivacaine alone. The results showed no significant difference between the groups. In both groups, there was only a modest decrease in VAS at 3 months. Criticism of this study is that only 1 injection was offered.

Karppinen et al (165,166) evaluated transforaminal epidural steroid injections in patients with MRI-confirmed herniated nucleus pulposus. The outcome measures were 50% relief of leg pain and cost effectiveness. Vad et al (169) evaluated transforaminal epidural steroid injections and compared them to

patients undergoing lumbar paraspinal trigger point injections with sodium chloride solution. The outcome measures included improvement in leg pain, Roland-Morris score, and patient satisfaction score.

Thomas et al (170) evaluated the effectiveness of transforaminal epidural and compared it with interspinous corticosteroid injection. Devulder et al (167) used a combination of methylprednisolone, bupivacaine, and hyaluronidase and compared this to a combination of sodium chloride solution, bupivacaine, and hyaluronidase. The outcome measures were reduction in leg pain of at least 50%.

Kolstad et al (174) studied cervical transforaminal epidural steroids on 21 patients awaiting cervical disc surgery. Patients were given 2 epidural injections 2 weeks apart, and followed for 4 months. Three outcome assessments were performed at baseline, 6 weeks, and 4 months. Outcome measures included visual analogue scale pain intensity (0-100 mm) for neck pain, visual analogue scale pain intensity (0-100 mm) for radicular pain, and Odom's Criteria—a grading system to evaluate relief of symptoms and treatment satisfaction (1: Excellent, 2: Good, 3: Fair, 4: Poor). Five of the 21 patients canceled their surgery due to improvement in pain, and overall there was a significant decrease in radicular pain at 6 weeks and 4 months. Neck pain also improved, and patients with spondylosis responded as well as patients with disc herniations.

Among the prospective evaluations, the effect of transforaminal epidural steroids on candidates for discectomy was studied by Yang et al (175). They evaluated 21 lumbar radiculopathy patients, all of whom had CT or MRI visualized disc herniations, all of whom were felt to be candidates for discectomy. Sixty-three percent of the patients had significant pain relief lasting through the 24-month follow-up, avoiding surgery; the transforaminal epidural resulted in significant relief of leg pain and improvement in activities of daily living, but did not improve low back pain.

A retrospective review of cervical transforaminal steroid injections was published by Lin et al (130). They evaluated 70 patients in a retrospective evaluation with cervical disc herniation without myelopathy. The average follow-up was 13 months (6 months to 4 years), and the number of injections ranged from 1 to 4 (mean 1.46). At 1-year follow-up 63% of the patients had improved and avoided surgery.

Cost Effectiveness

Cost effectiveness of transforaminal epidural steroid injections in the management of chronic low back pain showed that cost per 1-year improvement of quality of life was $2,927 per year (85). Further, in patients treated with transforaminal steroids, operations were avoided for contained herniations, costing $12,666 less per responder in the steroid group (166). Cost effectiveness was also demonstrated by avoiding surgical intervention (130,162,164,174).

Level of Evidence

The evidence for lumbar transforaminal epidural steroid injections in managing lumbar nerve root pain is strong for short-term and moderate for long-term improvement. The evidence for cervical transforaminal epidural steroid injections in managing cervical nerve root pain is moderate for short-term and long-term improvement. The evidence is limited in managing lumbar radicular pain in postlumbar laminectomy syndrome. The evidence is indeterminate in managing axial low back pain, axial neck pain, and lumbar disc extrusions.

Caudal Epidural Injections

Relevant reports studying caudal epidural injections included 11 randomized (99,207-216), 5 prospective evaluations (217-221), and multiple retrospective evaluations (3,16-19,84,85,222-224). The results of published reports of the randomized trials are described in Table 7, while Table 8 shows descriptions of prospective evaluations.

Of the 11 randomized trials, 3 trials were excluded (208,212,213). One study (213) was excluded due to non-availability of analyzable information, whereas a second trial (212) was excluded due to lack of long-term data. A recent study (208) was excluded due to poor protocol design and short-term relief and lack of fluoroscopy in the modern era.

Of the 8 randomized trials, 6 trials predominantly evaluated patients with disc herniation or radiculitis (99,207,209-211,214), 2 trials evaluated patients suffering with pain following failed back surgery syndrome (215,216), and one study (214) evaluated a mixed population with 50% postlumbar laminectomy syndrome patients. One study (99) compared blind interlaminar epidurals with caudal epidural steroid injections. One study (208) evaluated the effectiveness of triamcinolone acetonide and methylprednisolone acetate.

Among the 5 nonrandomized evaluations (217-221), disc herniation or radiculitis patients were studied in 2 evaluations (219,220), the role of caudal epidural in chronic low back pain was studied in an additional

2 studies (217,218), and the role of caudal epidural steroids was studied in spinal stenosis in one study (221).

Description of Study Characteristics

Descriptive characteristics of the included randomized trials are shown in Table 7 and non-randomized trials in Table 8.

Dashfield et al (207) compared the effectiveness of caudal steroid epidural with targeted steroid placement during spinal endoscopy for chronic sciatica in a prospective, randomized, double-blind trial. They studied 60 patients referred to their clinic for management of sciatica of greater than 6 months but less than 18 months' duration. The sciatica was defined as pain in the distribution of a lumbar nerve root, accompanied by neurosensory and motor deficits, with or without low back pain. Patients were 18 years of age or older. Patients who had previous spinal surgery, coagulopathy, progressive motor neuron disorders, or peripheral vascular disease were excluded, as were patients who had received an epidural corticosteroid injection within 3 months of being randomized. Patients were allocated randomly into 2 groups. Patients in the caudal group underwent caudal epidural corticosteroid injection with a total of 10 mL of lidocaine 1% with 40 mg of triamcinolone being injected into the epidural space. Patients in the epiduroscopy group underwent epiduroscopy performed by an experienced epiduroscopist with placement of steroid over the nerve root, which included 10 mL of lidocaine 1% with triamcinolone 40 mg. The epiduroscopy group also received infusion of 50 to 150 mg mL of sodium chloride solution. If adhesions were encountered around the painful nerve root, an attempt was made to break adhesions down using saline boluses or by manipulating the endoscope. However, very little scar tissue was encountered in their patient population, as they never had previous surgery.

Table 7. *Characteristics of published randomized trials of caudal epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Dashfield (207) Prospective, randomized, double-blind trial AHRQ score: 9/10 Cochrane score: 8/10	60 pts presenting to the pain management center.	Corticosteroid injection with a total of 10 mL of lidocaine 1% with 40 mg of triamcinolone Epiduroscopy group: delivery of the medication over the painful nerve root with 10 mL of lidocaine 1% with 40 mg of triamcinolone.	Assessments: 6 wks, 3 mos, and 6 mos . Outcome instruments: SF-MPQ and HAD.	Caudal group: significant improvements were found for descriptive pain at 6 mos; VAS at 6 wks, 3 mos, and 6 months; present pain intensity at 3 mos and 6 mos; anxiety at 6 wks, 3 mos, and 6 mos; and depression at 6 mos only.	Positive short-term and long-term relief
McGregor et al (99) Prospective AHRQ score: 6/10 Cochrane score: 5/10	44 pts with low back and leg pain.	Caudal epidural vs lumbar epidural.	Visual Analog Scale.	No significant improvement.	Negative short-term and long-term relief
Breivik et al (209) Randomized, double-blind trial AHRQ score: 8/10 Cochrane score: 7/10	35 pts with incapacitating chronic low back pain and sciatica. Diagnosis based on radiculopathy: arachnoiditis (n=8), no abnormality (n=11), inconclusive findings (n=5). Duration: several mos to several yrs.	Caudal epidural injection: Experimental: 20 mL bupivacaine 0.25% with 80 mg depomethylprednisone (n=16) Placebo: 20 mL bupivacaine 0.25% followed by 100 mL saline (n=19). Frequency: up to three injections at weekly intervals.	Timing: not mentioned. Outcome measures: 1. Pain relief: significant diminution of pain and/or paresis to a degree that enabled return to work. 2. Objective improvement: sensation, Lasègue's test, paresis, spinal reflexes, and sphincter disorders.	56% of the pts reported considerable pain relief in experimental group compared to 26% of the pts in the placebo group.	Positive short-term and long-term relief

Table 7 Continued. *Characteristics of published randomized trials of caudal epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Bush and Hillier (210) Randomized, double-blind trial AHRQ score: 8/10 Cochrane score: 8/10	23 pts with lumbar nerve root compromise randomized into 2 groups.	Experimental: 25 mL: 80 mg triamcinolone acetonide + 0.5% procaine hydrochloride (n=12); Control: 25 mL normal saline (n=11). Frequency: two caudal injections, the first after admission to the trial and a second after 2 wks.	Timing: 4 wks and at 1 year. Outcome measures: 1. Effect on lifestyle; 2. Back and leg pain; 3. Angle of positive SLR.	Significantly better results with pain and straight leg raising in experimental group in short-term. Pain not significantly different but straight leg raise significantly better for long-term relief.	Positive short-term and negative long-term relief
Matthews et al (211) Randomized, double-blind trial AHRQ score: 8/10 Cochrane score: 7/10	57 pts with sciatica with a single root compression Experimental group: male/female: 19/4, median duration of pain: 4 wks . Control group: male/female: 24/10, median duration of pain: 4 wks.	Experimental: 20 mL bupivacaine 0.125% + 2 mL (80 mg) methylprednisolone acetate (n=23). Control: 2 mL lignocaine (over the sacral hiatus or into a tender spot) (n=34) Frequency: fortnightly intervals, up to 3 times as needed.	Timing: 2 wks, 1, 3, 6, and 12 mos. Outcome measures: pain (recovered vs not recovered), range of movement, straight leg raising, neurologic examination.	There was no significant difference between experimental and control group with short-term relief (67% vs 56%). After 3 mos, pts in experimental group reported significantly more pain-free than in control group.	Negative short-term and positive long-term relief
Helsa and Breivik (214) Randomized, double-blind trial with crossover design AHRQ score: 7/10 Cochrane score: 7/10	69 pts with incapacitating chronic low back pain and sciatica. 36 of 69 previously been operated on for herniated disc.	Three caudal epidural injections of either bupivacaine with depomethylprednisolone 80 mg or with bupivacaine followed by normal saline.	Timing: not mentioned. Outcome measures: significant improvement to return to work or to be retrained for another occupation.	34 of the 58 pts (59%) receiving caudal epidural injections of bupivacaine and depomethylprednisolone showed significant improvement. 12 of 49 pts (25%) who received bupivacaine followed by saline were improved.	Positive short-term and long-term relief.
Revel et al (215) Randomized trial AHRQ score: 7/10 Cochrane score: 6/10	60 postlumbar laminectomy pts with chronic low back pain.	Forceful caudal injection: Experimental: 125 mg of prednisolone acetate with 40 mL of normal saline in the treatment group. Control: 125 mg of prednisolone in the control group.	Timing: 6 mos. Outcome measures: pain relief.	The proportion of pts relieved of sciatica was 49% in the forceful injection group compared to 19% in the control group with significant difference.	Positive short-term and negative long-term relief
Meadeb et al (216) Randomized trial Parallel-group study AHRQ score: 6/10 Cochrane score: 6/10	47 postlumbar laminectomy syndrome pts in a multicenter study.	Experimental: forceful injection of 20 mL of normal saline with/without 125 mg of epidural prednisolone acetate. Control: 125 mg of epidural prednisolone. Frequency: each of the 3 treatments were provided once a month for 3 consecutive mos.	Timing: day 1, day 30, and day 120. Outcome measures: Visual Analog Scale.	The VAS scores improved steadily in the forceful injection group, producing a nonsignificant difference on day 120 as compared to the baseline (day 30=120 days).	Negative short-term and long-term relief.

Table 8. *Characteristics of results of prospective studies of caudal epidural injections.*

Study/Methods	Participants	Intervention(s)	Outcome(s)	Result(s)	Conclusion(s) Short-term relief <6 wks Long-term relief > 6 wks
Yates (219) Prospective evaluation AHRQ score: 5/8	20 pts with low back pain and sciatica.	Group I: 60 mg of triamcinolone (3 mL + 47 mL normal saline). Group II: 60 mg of triamcinolone (3 mL + 47 mL lignocaine 0.5%). Group III: 50 mL saline. Group IV: 50 mL lignocaine injections given at weekly intervals in random order.	Timing not mentioned. Subjective and objective criteria of progress. Did not address pain-relief, focused on improvement in straight leg raising which seemed to correlate with pain-relief.	Greatest improvement was noted after the injection-containing steroid. The results suggested that the action of a successful epidural injection is primarily anti-inflammatory and to a lesser extent, hydrodynamic.	Positive short-term and long-term relief
Waldman (220) Prospective evaluation with independent observer review AHRQ score: 5/8	53 pts meeting stringent inclusion criteria with radicular pain distribution anatomically correlating with documented disc herniation and nerve root impingement.	Treatment: 7.5 mL of 1% lidocaine and 80 mg of methylprednisolone with the first block and 40 mg of methyl-prednisolone with subsequent blocks, which were repeated in 48- to 72-hour intervals with the end point being complete pain relief or 4 caudal epidural blocks.	Timing: 6 wks, 3 mos, and 6 mos. Visual Analog Scale and Verbal Analog Scores.	Combined Visual Analog Scale and Verbal Analog Scores for all pts were reduced 63% at 6 wks, 67% at 3 mos, and 71% at 6 mos.	Positive short-term and long-term relief
Manchikanti et al (217) Randomized trial with convenient control group. AHRQ score: 5/10	70 pts after failed conservative management with physical therapy, chiropractic, and medication therapy. All pts were shown to be negative for facet joint pain.	Group I : no treatment Group II: local anesthetic and Sarapin total of 20 mL with 10 mL each. Group III: 10 mL of local anesthetic and 6 mg of betamethasone.	Timing: 2 wks, 1 month, 3 mos, 6 mos, and 1 year. Outcome measures: Average pain, physical health, mental health, and functional status.	Average pain, physical health, mental health, functional status, narcotic intake, and employment improved significantly in Group II and Group III at 2 wks, 1 month, 3 mos, 6 mos, and 1 year.	Positive short-term and long-term relief
Manchikanti et al (218) Prospective evaluation AHRQ score: 5/8	62 pts evaluated. Negative provocative discography: 45 pts. Positive provocative discography: 17 pts.	Caudal epidural injections (1-3) with or without steroids.	Timing: 1 month, 3 mos, and 6 mos. Outcome: average pain, functional status, psychological status, narcotic intake, and employment status.	69% of the pts in the negative discography group and 65% of the pts in the positive discography group were in successful category.	Positive short-term and long-term relief
Ciocon et al (221) Prospective evaluation in elderly pts AHRQ score: 5/8	30 pts with spinal stenosis.	A series of 3 caudal epidural steroid injections, 0.5% xylocaine and 80 mg of Depo-Medrol.	Pain relief, Roland Morris 5-point scale.	Duration of pain relief and improvement ranged from 4-10 months.	Positive short-term and long-term relief.

Patient assessments were carried out before treatment, at 6 weeks, 3 months, and 6 months following treatment. Outcome instruments included SF-MPQ and HAD scores. No significant differences were found between the groups for any of the measures at any time. However, there were significant differences within both groups compared with pretreatment values. For the caudal group, significant improvements were found for descriptive pain at 6 months; VAS at 6 weeks, 3 months, and 6 months; present pain intensity at 3 months and 6 months; anxiety at 6 weeks, 3 months, and 6 months; and depression at 6 months only. Caudal epidural was better than the epiduroscopy group where there were fewer significant changes.

Effectiveness

Of the 8 randomized trials, 5 were positive for short-term pain relief (207,209,210,214,215), and 4 were positive for long-term relief (207,209, 211,214).

Among 8 randomized trials included for analysis, of the 6 trials (99,207,209-211,214) evaluating predominantly radiculopathy, 4 studies were positive (207,209,210,214) and 2 were negative (99,211) for short-term relief, whereas 4 (207,209,211,214) of 6 (99,207,209-211,214) were positive for long-term relief. Of the 2 studies with postlumbar laminectomy syndrome (215,216), only one study (215) was positive for short-term. One study (214) included patients with sciatica, as well as post lumbar laminectomy syndrome. This study showed positive results, both for short-term and long-term.

Among the 5 prospective studies (217-221), 2 studies evaluating radiculopathy or sciatica (219,220) and 2 studies evaluating the effectiveness of caudal epidural steroid injections in chronic low back pain (217,218) were positive, and 1 study evaluating the effectiveness of caudal in lumbar spinal stenosis was positive (221).

Thus, positive long-term relief trials were 71% for radiculopathy or sciatica and 67% for postlumbar laminectomy syndrome. Among the prospective evaluations, 80% were positive for radiculopathy and chronic low back pain.

Cost Effectiveness

The costeffectiveness of fluoroscopically-directed caudal epidural steroids was $3,635 and that of transforaminal steroids was $2,927 per year. In a prospective evaluation, the cost for 1-year improvement for quality-of-life, was $2,550, in patients treated with caudal epidural with local anesthetic and Sarapin or steroids under fluoroscopy (85,217).

Level of Evidence

The evidence of caudal epidural steroid injections with randomized trials and non-randomized reports is strong for short-term relief and moderate for long-term relief in managing chronic pain of lumbar radiculopathy and postlumbar laminectomy syndrome. The evidence is moderate in managing chronic low back pain for short-term and long-term improvement.

Complications

The most common and worrisome complications of caudal, interlaminar, and transforaminal epidural injections are of 2 types: those related to the needle placement and those related to drug administration. Complications include dural puncture, spinal cord trauma, infection, hematoma formation, abscess formation, subdural injection, intracranial air injection, epidural lipomatosis, pneumothorax, nerve damage, headache, death, brain damage, increased intracranial pressure, intravascular injection, vascular injury, cerebral vascular or pulmonary embolus, and effects of steroids (228-291). Spinal cord trauma, and spinal cord or epidural hematoma formation is a catastrophic complication that is rarely seen following interventional procedures in the cervical spine, thoracic spine, or upper lumbar spine.

Botwin et al (225-228) evaluated complications of fluoroscopically-guided epidural steroid injections. Botwin et al (225) reported complications in 207 patients receiving 322 injections of transforaminal lumbar epidural injections. Complications included transient headaches (3.1%), increased back pain (2.4%), increased leg pain (0.6%), facial flushing (1.2%), vasovagal reaction (0.3%), increased blood sugar (0.3%), and hypertension (0.3%). The incidence of minor complications was 9.6% per injection with no major complications.

Botwin et al (226) reported complications of fluoroscopically-guided interlaminar cervical epidural injections. They reported 345 injections in 157 patients. Complications per injection included increased neck pain (6.7%), non-positional headaches (4.6%), insomnia the night of injection (1.7%), vasovagal reactions (1.7%), facial flushing (1.5%), fever the night of the procedure (0.3%), and dural puncture (0.3%). The incidence of all complications per injection was 16.8%.

Botwin et al (227) also reported adverse effects of fluoroscopically guided interlaminar thoracic epidural steroid injections. A total of 21 patients received 39 injections. Adverse effects or complications per injection observed included pain at injection site (7.7%), facial flushing (5.1%), transient non-positional head-

ache (2.6%), insomnia the night of injection (2.6%), and fever the night of the procedure (2.6%). No major complications were reported and adverse effects were reported with a rate of 20.5%.

Botwin et al (228) reported complications of fluoroscopically-guided caudal epidural injections in 139 patients, who received 257 injections. Complications per injection included insomnia the night of injection (4.7%), transient non-positional headaches (3.5%), increased back pain (3.1%), facial flushing (2.3%), vasovagal reactions (0.8%), nausea (0.8%), and increased leg pain (0.4%). The incidence of minor complications was 15.6% per injection.

Furman et al (229) evaluated incidence of intravascular penetration in transforaminal lumbosacral epidural steroid injections in a prospective observational study. Among the 761 transforaminal epidural steroid injections included in the study, the overall rate of intravascular injections was 11.2%, with a higher rate of intravascular injections (21.3%) noted with transforaminal epidural injections at S1 compared with those at the lumbar levels (8.1%).

Furman et al (230) also studied incidence of intravascular penetration in transforaminal cervical epidural steroid injections in 307 patients with 504 treated with transforaminal epidural steroid injections. The overall rate of fluoroscopically-confirmed intravascular contrast injections was 19.4%.

Manchikanti et al (231) reported contrast flow patterns and intravascular needle placement in 100 consecutive patients. Intravenous placement of the needle was noted in 22% of the procedures. With caudal epidurals, Manchikanti et al (231) reported complications with pain during the injection with back pain in 43% of the patients and leg pain in 22% of the patients. They also noted postoperative complications in 34% of the patients with soreness at injection site in 18%, increased pain in 5%, muscle spasms in 4%, swelling in 4%, headache in 3%, minor bleeding in 2%, dizziness in 1%, nausea and vomiting in 1%, fever in 1%, numbness in 1%, and voiding difficulty in 1%. Manchikanti et al (232,233) reported with fluoroscopically-guided caudal epidural injections intravascular placement in 14% of the patients. They (232,233) also reported complications in 7% of the patients with soreness at injection site in 6%, increased pain in 1%, muscle spasms in 1%, headache in 1%, and nausea and vomiting in 1%.

Derby et al (234) surveyed 17 International Spinal Intervention Society (ISIS) instructors who described a total of 5,978 cervical epidurals, interlaminar in 4,389 patients, and transforaminal injections in 1,579 patients. Of the interlaminar injections, there were 23 mild complications (0.5%), while there were 5 cases of minor complications in the transforaminal group (0.32%).

Transforaminal injections have been the cause of some of the most worrisome recent complications. These included cerebellar and cerebral infarct (235,247), spinal cord injury and infarction (236,245,249,256), massive cerebral edema (237), paraplegia (238), visual defects with occlusion following particulate depo-corticosteroids (239), anterior spinal artery syndrome (240), persistent neurological deficits (241), transient quadriplegia (242), cauda equina syndrome (251), subdural hematoma (253), and paraplegia following intracord injection during attempted epidural anesthesia under general anesthesia (255).

Because of the catastrophes associated with cervical transforaminal epidurals, Huntoon (243) dissected 95 nerve roots in 10 embalmed cadavers. He was able to identify 21 foramina where an artery was noted to be proximal to the posterior aspect of the foraminal opening, confirming the potential for injury to a vessel during transforaminal injections.

Although the complications of cervical spinal injections are devastating, they are fortunately rare. Ma et al (244) reviewed the complications of 1,036 fluoroscopically-guided extraforaminal cervical nerve blocks performed on 844 patients over a 4-year period, and found only 14 patients (1.66%) who had even minor complications.

Huston et al (246) reviewed complications of cervical and lumbar selective nerve root injections (SNRs) in 151 consecutive patients who underwent a total of 306 SNRs. There were no major complications noted, and 91% of the patients had no side effects during the injection. The most common side effect noted was increased pain at the injection site after the injection, which was seen in 17.1% of the lumbar patients and 22.7% of the cervical patients.

Paraplegia and quadriplegia have also been reported following interlaminar epidural steroid injections (252).

Infection is occasionally seen with a case of granuloma and intracranial hypertension after 3 cervical epidural steroids (258), thoracic intradural fungal abscess after 3 lumbar epidural steroids (259,270), discitis (267-269,272), and numerous cases of epidural hematoma over the years (262-266).

Other much less common complications include pneumocephalus (273,275,286), transient blindness

(276), retinol necrosis (277), bilateral cirrus chorioretinopathy (278,279), persistent recurrent intractable hiccups (280), dysphonia (281), flushing (282), arterial gas embolus and cortical blindness (283,284), chemical meningitis (287), retinal hemorrhage (288), radiculopathy (289), nerve root damage (290), and cerebral venous thrombosis (291).

Side effects related to the administration of steroids are generally attributed either to the chemistry or to the pharmacology of the steroids. The major theoretical complications of corticosteroid administration include suppression of pituitary-adrenal axis, hypercorticism, Cushing's syndrome, osteoporosis, avascular necrosis of bone, steroid myopathy, epidural lipomatosis, weight gain, fluid retention, and hyperglycemia. The most commonly used steroids in neural blockade in the United States, methylprednisolone acetate, triamcinolone acetonide, betamethasone acetate, and phosphate mixture have all been shown to be safe at epidural therapeutic doses in both clinical and experimental studies (292-301).

Finally, radiation exposure is also a potential problem with damage to eyes, skin, and gonads (302-304).

Discussion

This systematic review evaluated and updated the effectiveness of epidural injections in patients with chronic spinal pain. The evidence was evaluated for 3 types of epidurals separately for cervical and lumbar, and for axial, radicular, and postlaminectomy pain.

The previous systematic review arrived at the following conclusions (3). In managing lumbar radicular pain with interlaminar lumbar epidural steroid injections, the level of evidence was strong for short-term relief and limited for long-term relief. In managing cervical radiculopathy with cervical interlaminar epidural steroid injections, the evidence was moderate for short-term improvement and long-term improvement. However, the evidence was indeterminate in management of axial neck pain, axial low back pain, and lumbar spinal stenosis with lumbar or cervical interlaminar epidural steroid injections.

The evidence for lumbar transforaminal epidural steroid injections in managing lumbar nerve root pain was strong with short-term and long-term improvement. The evidence for cervical transforaminal epidural steroid injections in managing cervical nerve root pain was strong with short-term and long-term improvement. The evidence was moderate in managing lumbar radicular pain in postlumbar laminectomy syndrome, with short-term and long-term improvement. The evidence of lumbar transforaminal epidural steroid injections in managing lumbar spinal stenosis was limited. The evidence was indeterminate in managing axial low back pain, axial neck pain, and lumbar disc extrusions.

The evidence of caudal epidural steroid injections with randomized trials and non-randomized reports was strong for short-term relief and moderate for long-term relief, in managing chronic pain of lumbar radiculopathy and postlumbar laminectomy syndrome. The evidence was moderate in managing chronic low back pain for short-term and long-term improvement. The evidence was limited for lumbar spinal stenosis.

The first systematic review of effectiveness of epidural steroid injections was performed by Kepes and Duncalf in 1985 (5). They concluded that the rationale for epidural and systemic steroids was not proven. However, in 1986 Benzon et al (297), utilizing the same studies, concluded that mechanical causes of low back pain, especially those accompanied by signs of nerve root irritation, may respond to epidural steroid injections. The difference in the conclusion of Kepes and Duncalf (5) and Benzon et al (297) may have been due to the fact that Kepes and Duncalf (5) included studies on systemic steroids whereas Benzon (297) limited their analysis to studies on epidural steroid injections only.

The debate concerning epidural steroid injections is also illustrated by the recommendations of the Australian National Health and Medical Research Council Advisory Committee on epidural steroid injections (84). In this report, Bogduk (10) extensively studied caudal, interlaminar, and transforaminal epidural injections, including all the literature available at the time, and concluded that the balance of the published evidence supports the therapeutic use of caudal epidurals. They also concluded that the results of lumbar interlaminar epidural steroids strongly refute the utility of epidural steroids in acute sciatica. Bogduk et al (84) updated their recommendations in 1999, recommending against epidural steroids by the lumbar route because effective treatment required too high a number for successful treatment, but supporting the potential usefulness of transforaminal steroids for disc prolapse. In 1995, Koes et al (6) reviewed 12 trials of lumbar and caudal epidural steroid injections and reported positive results from only 6 studies. However, review of their analysis showed that there were 5 studies for caudal epidural steroid injections and 7 studies for lumbar epidural steroid injections. Four of the 5 studies involving caudal epidural steroid injections were positive, whereas 5 of 7 studies

were negative for lumbar epidural steroid injections. Koes et al (7) updated their review of epidural steroid injections for low back pain and sciatica, including 3 more studies with a total of 15 trials which met the inclusion criteria. In this study, they concluded that of the 15 trials, 8 reported positive results of epidural steroid injections. Both reviews mostly reflected the quality of studies, rather than any meaningful conclusion.

Nelemans et al's (8) Cochrane review of injection therapy for subacute and chronic benign low back pain included 21 randomized trials. Of these, 9 were of epidural steroids. They failed to separate caudal from interlaminar epidural injections, but still concluded that convincing evidence is lacking regarding the effects of injection therapy on low back pain. Rozenberg et al (9), in a systematic review, identified 13 trials of epidural steroid therapy. They concluded that 5 trials demonstrated greater pain relief within the first month in the steroid group as compared to the control group. Eight trials found no measurable benefits. They noticed many obstacles for meaningful comparison of cross studies, which included differences in the patient populations, steroid used, volume injected, and number of injections. These authors were unable to determine whether epidural steroids are effective in common low back pain and sciatica based on their review. Rozenburg et al (9) concluded that 3 of the top 5 rated studies did not demonstrate significant benefit of the steroid over the non-steroid group. Hopayiank and Mugford (305) expressed frustration over the conflicting conclusions from two systematic reviews of epidural steroid injections for sciatica and asked which evidence should general practitioners heed. Multiple previous reviews have criticized the studies evaluating the effectiveness of epidural injections. Criticisms ranged from methodology, small size of the study populations, and other limitations, including long-term follow-up and outcome parameters.

Overall the evidence for lumbar interlaminar epidural steroid injections is limited for long-term relief. However, for cervical interlaminar epidural steroid injections, the evidence is moderate. Evidence is indeterminate in management of the axial neck pain, axial low back pain, and lumbar spinal stenosis with lumbar or cervical interlaminar epidural steroid injections.

In this study, the evidence for lumbar transforaminal epidural steroid injections in managing lumbar and cervical nerve root pain is moderate; however, the evidence is limited in managing lumbar radicular pain in postlumbar laminectomy syndrome. The evidence is indeterminate in managing axial low back pain, neck pain, and lumbar disc extrusions.

The evidence of caudal epidural steroid injections is moderate in managing lumbar radiculopathy and postlumbar laminectomy syndrome. In contrast to interlaminar and transforaminal epidural injections the evidence is moderate in managing chronic low back pain. Airaksinen et al (11) in European Guidelines for the Management of Chronic Nonspecific Low Back Pain, published in 2006, which only included the literature up to 2002, concluded that epidural corticosteroid injections would only be considered for radicular pain if it contained disc prolapse as the cause of the pain and if the corticosteroid is injected close to the target or the nerve root. In addition, they also stated that the injection should be fluoroscopically-guided and should aim at the ventral part of the epidural space, near the spinal nerve root or the spinal nerve root through a transforaminal approach. They also concluded that there is conflicting evidence that conventional epidural steroids with a blind approach without fluoroscopic guidance are effective in radicular pain.

The present review is similar to 2 previous systematic reviews and also the guidelines published (16-19). However, it is vastly different from a multitude of other systematic reviews. It is close to European Guidelines for the Management of Chronic Nonspecific Low Back Pain, which advises that fluoroscopically-guided epidurals have better prognosis than the blind epidurals. The present systematic review, similar to the ones performed by Abdi et al (3) and Boswell et al (4), has several additional features.

Finally, all types of epidural steroid injections can be associated with complications and adverse events as described earlier. Therefore attention to detail and caution should be taken when performing any of the 3 techniques discussed in order to improve safety and minimize complications.

This systematic review included multiple new articles not described in the previous reviews.

Arden's study (120) compared 10 mL of epidural bupivacaine and steroid to 2 mL normal saline in the interspinous ligament. The use of local anesthetic in one and not the other makes true patient blinding unlikely. Wilson-MacDonald (119) injected the same local and steroid into each patient, either epidurally or in the ligament, but the large volume injected (8 mL) would be expected to be very painful and disruptive in the relative closed space of the interspinous ligament, again calling the patient blinding into ques-

tion. Therefore no significant new information can be gathered from these 2 studies. They also published 2 different manuscripts from 1 study.

In the 2 new cervical transforaminal studies, Kolstad et al (174) and Line et al (130) both showed that cervical epidural transforaminal injections can lead to pain relief significant enough to prevent patients from having to undergo surgery. Yang et al (175) also concluded that lumbar transforaminal injections reduce the need for lumbar surgical decompression.

One could argue that scientific evidence supporting the efficacy of transforaminal epidural steroid injection indirectly supports the efficacy of epidural administration by any route of administration. This argument makes sense in view of the anatomy of the epidural space and the pathophysiology of radiculopathy. To elaborate, the epidural space is a continuous anatomic compartment extending from the base of the skull to the sacrum that can be entered at various levels and by various routes to achieve the same end. The space itself consists of adipose tissue interspersed with random bands of fibrous tissue and venous vessels. The ventral epidural space is closest to the posterior disc margin and the traversing nerve root, which is the presumed site of pathology in lumbar radiculopathy. Although the most direct method to deposit medication into this region is by using a transforaminal approach to needle insertion, it is conceivable that medication may reach this target equally well using a caudal, interlaminar, or catheter route of administration.

Regarding pathophysiology, investigations into the biochemistry of disc degeneration and herniation indicate that intraspinal inflammation is a major cause of radicular pain (253,255-257,272,283,284). The neurotoxic, inflammatory mediator phospholipase A2 (PLA2) is contained within the disc nucleus and is released after annular injury. PLA2 in turn triggers the arachidonic acid cascade, leading to localized inflammation mediated by prostaglandins and leukotrienes. Inflammatory neuropeptides such as calcitonin gene-related peptide (CGrP) and substance P are contained within the dorsal root ganglion and perpetuate inflammation as they are released from irritated nerve roots. Corticosteroids have powerful anti-inflammatory effects, which include inhibition of prostaglandin synthesis, blockade of PLA2 activity, and stabilization of inflammatory cell membranes. Injecting corticosteroids into the epidural space should result in higher concentrations of the active medication at the site of inflammation when compared to oral or parenteral routes of steroid administration. The spinal injection route of administration is the only method of drug delivery that does not rely on blood flow to deliver the medication to its site of action and blood flow may be impaired in the region of compressive disc herniation. Even with normal spinal circulation, blood flow delivers steroid preferentially to high blood flow organs with presumably low concentrations arriving at the site of spinal pathology.

References

1. Manchikanti L. Medicare in interventional pain management: a critical analysis. *Pain Physician* 2006; 9:171-198.
2. Specialty utilization data files from CMS available at: http://www.cms.hhs.gov/physicians/pfs.
3. Abdi S, Lucas LF, Datta S. Role of epidural steroids in the management of chronic spinal pain: a systematic review of effectiveness and complications. *Pain Physician* 2005; 8:127-143.
4. Boswell M, Hansen H, Trescot A, Hirsch J. Epidural steroids in the management of chronic spinal pain and radiculopathy. *Pain Physician* 2003; 6:319-334.
5. Kepes ER, Duncalf D. Treatment of backache with spinal injections of local anesthetics, spinal and systemic steroids. *Pain* 1985; 22:33-47.
6. Koes BW, Scholten RJ, Mens JM, Bouter LM. Efficacy of epidural steroid injections for low back pain and sciatica: a systematic review of randomized clinical trials. *Pain* 1995; 63:279-288.
7. Koes BW, Scholten RJ, Mens JMA, Bouter LM. Epidural steroid injections for low back pain and sciatica: an updated systematic review of randomized clinical trials. *Pain Digest* 1999; 9:241-247.
8. Nelemans PJ, deBie RA, deVet HC, Sturmans F. Injection therapy for subacute and chronic benign low back pain. *Spine* 2001; 26:501-515.
9. Rozenberg S, Dubourg G, Khalifa P, Paolozzi L, Maheu E, Ravaud P. Efficacy of epidural steroids in low back pain and sciatica: a critical appraisal by a French task force of randomized trials. *Revue du Rhumatisme* 1999; 66:79-85.
10. Bogduk N. Epidural steroids for low back pain and sciatica. *Pain Digest* 1999; 9:226-227.
11. Airaksinen O, Brox JI, Cedraschi C, Hildebrandt J, Klaber-Moffett J, Kovacs F, Mannion AF, Reis S, Staal JB, Ursin H and Zanoli G. Chapter 4: European guidelines for the management of chronic nonspecific low back pain. *Eur Spine J* 2006; 15:S192-S300.
12. Cannon DT, April CN. Lumbosacral epidural steroid injections. *Arch Phys Med Rehabil* 2000; 83:S87-S98.
13. McQuay HJ, Moore RA, Eccleston C, Morley S, Williams AC. Systematic review of outpatient services for chronic pain control. *Health Technol Assess* 1997; 1:1-135.
14. Tonkovich-Quaranta LA, Winkler SR. Use of epidural corticosteroids in low back pain. *Ann Pharmacother* 2000; 34:1165-1172.
15. Watts RW, Silagy CA. A meta-analysis on the efficacy of epidural corticosteroids in the treatment of sciatica. *Anaesth Intensive Care* 1995; 23:564-569.
16. Boswell MV, Shah RV, Everett CR, Sehgal N, Mckenzie-Brown AM, Abdi S, Bowman RC, Deer TR, Datta S, Colson JD, Spillane WF, Smith HS, Lucas-Levin

LF, Burton AW, Chopra P, Staats PS, Wasserman RA, Manchikanti L. Interventional techniques in the management of chronic spinal pain: evidence-based practice guidelines. *Pain Physician* 2005; 8:1-47.

17. Manchikanti L, Staats PS, Singh V, Schultz DM, Vilims BD, Jasper JF, Kloth DS, Trescot AM, Hansen HC, Falasca TD, Racz GB, Deer T, Burton AW, Helm S, Lou L, Bakhit CE, Dunbar EE, Atluri SL, Calodney AK, Hassenbusch S, Feler CA. Evidence-based practice guidelines for interventional techniques in the management of chronic spinal pain. *Pain Physician* 2003; 6:3-80.
18. Manchikanti L, Singh V, Kloth DS, Slipman CW, Jasper JF, Trescot AM, Varley KG, Atluri SL, Giron C, Curran MJ, Rivera JJ, Baha A, Bakhit CE, Reuter M. Interventional techniques in the management of chronic pain: part 2.0. *Pain Physician* 2001; 4:24-96.
19. Manchikanti L, Singh V, Bakhit CE, Fellows B. Interventional techniques in the management of chronic pain: part 1.0. *Pain Physician* 2000; 3:7-42.
20. Verhaak PF, Kerssens JJ, Dekker J, Sorbi MJ, Bensing JM. Prevalence of chronic benign pain disorder among adults: a review of the literature. *Pain* 1998; 77:231-239.
21. Elliott AM, Smith BH, Hannaford PC, Smith WC, Chambers WA. The course of chronic pain in the community: results of a 4-year follow-up study. *Pain* 2002; 99:299-307.
22. Lawrence RC, Helmick CG, Arnett FC. Estimates of the prevalence of arthritis and selected musculoskeletal disorders in the United States. *Arthritis Rheum* 1998; 41:778-799.
23. Cassidy JD, Carroll LJ, Cotê P. The Saskatchewan Health and Back Pain Survey: the prevalence of low back pain and related disability in Saskatchewan adults. *Spine* 1998; 23:1860-1867.
24. Guo HR, Tanaka S, Halperin WE, Cameron LL. Back pain prevalence in US industry and estimates of lost workdays. *Am J Public Health* 1999; 89:1029-1035.
25. Côté P, Cassidy JD, Carroll L. The Saskatchewan Health and Back Pain Survey. The prevalence of neck pain and related disability in Saskatchewan adults. *Spine* 1998; 23:1689-1698.
26. Linton SJ, Hellsing AL, Hallden K. A population based study of spinal pain among 35–45-year old individuals. *Spine* 1998, 23:1457-1463.
27. Miemelainen R, Videman T, Battie MC. Prevalence and characteristics of upper or mid-back pain in Finnish men. *Spine* 2006; 31:1846-1849.
28. Walker BF, Muller R, Grant WD. Low back pain in Australian adults: prevalence and associated disability. *J Manip Physiol Ther* 2004; 27:238-244.
29. Bot SD, van der Waal JM, Terwee CB, van der Windt DA, Schellevis FG, Bouter LM, Dekker J. Incidence and prevalence of complaints of the neck and upper extremity in general practice. *Ann Rheum Dis* 2005; 64:118-123.
30. Bressler HB, Keyes WJ, Rochon PA, Badley E. The prevalence of low back pain in the elderly. A systemic review of the literature. *Spine* 1999; 24:1813-1819.
31. Cecchi F, Debolini P, Lova RM, Macchi C, Bandinelli S, Bartali B, Lauretani F, Benvenuti E, Hicks G, Ferrucci L. Epidemiology of back pain in a representative cohort of Italian persons 65 years of age and older: the InCHIANTI study. *Spine* 2006; 31:1149-1155.
32. Mortimer M, Pernold G, Wiktorin C. Low back pain in a general population. Natural course and influence of physical exercise--a 5-year follow-up of the Musculoskeletal Intervention Center-Norrtalje Study. *Spine* 2006; 31:3045-3051.
33. Cassidy JD, Cote P, Carroll LJ, Kristman V. Incidence and course of low back pain episodes in the general population. *Spine* 2005; 30:2817-2823.
34. Hestbaek L, Leboeuf-Yde C, Manniche C. Low back pain: what is the long-term course? A review of studies of general patient populations. *Eur Spine J* 2003; 12:149-165.
35. Croft PR, Lewis M, Papageorgiou AC, Thomas E, Jayson MI, Macfarlane GJ, Silman AJ. Risk factors for neck pain: a longitudinal study in the general population. *Pain* 2001; 93:317-325.
36. Côté P, Cassidy JD, Carroll LJ, Kristman V. The annual incidence and course of neck pain in the general population: a population-based cohort study. *Pain* 2004; 112:267-273.
37. Enthoven P, Skargren E, Oberg B. Clinical course in patients seeking primary care for back or neck pain: a prospective 5-year follow-up of outcome and health care consumption with subgroup analysis. *Spine* 2004; 29:2458-2465.
38. Elder LA, Burdorf A. Prevalence, incidence, and recurrence of low back pain in scaffolders during a 3-year follow-up study. *Spine* 2004; 29:E101-E106.
39. Croft PR, Papageorgiou AC, Thomas E, Macfarlane GJ, Silman AJ. Short-term physical risk factors for new episodes of low back pain. Prospective evidence from the South Manchester Back Pain Study. *Spine* 1999; 24:1556-1561.
40. Miedema HS, Chorus AM, Wevers CW, van der Linden S. Chronicity of back problems during working life. *Spine* 1998; 23:2021-2028.
41. Thomas E, Silman AJ, Croft PR, Papageorgiou AC, Jayson MI, Macfarlane GJ. Predicting who develops chronic low back pain in primary care: a prospective study. *Brit Med J* 1999; 318:1662-1667.
42. Jackson JL, Passamonti M. The outcomes among patients presenting in primary care with a physical symptom at 5 years. *J Gen Intern Med* 2005; 20:1032-1037.
43. Jones GT, Johnson RE, Wiles NJ, Chaddock C, Potter RG, Roberts C, Symmons DP, Macfarlane GJ. Predicting persistent disabling low back pain in general practice: a prospective cohort study. *Br J Gen Pract* 2006; 56:334-341.
44. Kaaria S, Luukkonen R, Riihimaki H, Kirjonen J, Leino-Arjas P. Persistence of low back pain reporting among a cohort of employees in a metal corporation: A study with 5-, 10-, and 28-year follow-ups. *Pain* 2006; 120:131-137.
45. Leboeuf-Yde C, Gronstvedt A, Borge JA, Lothe J, Magnesen E, Nilsson O, Rosok G, Stig LC, Larsen K. The Nordic back pain subpopulation program: a 1-year prospective multicenter study of outcomes of persistent low-back pain in chiropractic patients. *J Manipulative Physiol Ther* 2005; 28:90-96.
46. Kadam UT, Thomas E, Croft PR. Is chronic widespread pain a predictor of all-cause morbidity? A 3 year prospective population based study in family practice. *J Rheumatol* 2005; 32:1341-1348.
47. Kovacs FM, Fernández C, Cordero A, Muriel A, Gonzalez-Lujan L, Gil del Real MT. Spanish Back Pain Research Network. Non-specific low back pain in primary care in the Spanish National Health Service: a prospective study on clinical outcomes and determinants of management. *BMC Health Serv Res* 2006; 6:57.
48. Saastamoinen P, Leino-Arjas P, Laaksonen M, Lahelma E. Socio-economic differences in the prevalence of acute, chronic and disabling chronic pain among ageing employees. *Pain* 2005; 114:364-371.
49. Bunketorp L, Stener-Victorin E, Carlsson J. Neck pain and disability following motor vehicle accidents: a cohort

study. *Eur Spine J* 2005; 14:84-89.

50. Frank AO, De Souza LH, Frank CA. Neck pain and disability: a cross-sectional survey of the demographic and clinical characteristics of neck pain seen in a rheumatology clinic. *Int J Clin Pract* 2005; 59:173-182.
51. Hartvigsen J, Frederiksen H, Christensen K. Physical and mental function and incident low back pain in seniors: a population-based two-year prospective study of 1387 Danish Twins aged 70 to 100 years. *Spine* 2006; 31:1628-1632.
52. Jacob T. Low back pain incident episodes: a community-based study. *Spine J* 2006; 6:306-310.
53. Weiner DK, Kim YS, Bonino P, Wang T. Low back pain in older adults: are we utilizing healthcare resources wisely? *Pain Med* 2006; 7:143-150.
54. Ekman M, Jönhagen S, Hunsche E, Jonsson L. Burden of illness of chronic low back pain in Sweden: a cross-sectional, retrospective study in primary care setting. *Spine* 2005; 30:1777-1785.
55. Ritzwoller DP, Crounse L, Shetterly S, Rublee D. The association of comorbidities, utilization and costs for patients identified with low back pain. *BMC Musculoskelet Disord* 2006; 7:72.
56. Vogt MT, Kwoh CK, Cope DK, Osial TA, Culyba M, Starz TW. Analgesic usage for low back pain: impact on health care costs and service use. *Spine* 2005; 30:1075-1081.
57. Ricci JA, Stewart WF, Chee E, Leotta C, Foley K, Hochberg MC. Back pain exacerbations and lost productive time costs in United States workers. *Spine* 2006; 31:3052-3060.
58. White AG, Birnbaum HG, Mareva MN, Daher M, Vallow S, Schein J, Katz N. Direct costs of opioid abuse in an insured population in the United States. *J Manag Care Pharm* 2005; 11:469-479.
59. Luo X, Pietrobon R, Sun SX, Liu GG, Hey L. Estimates and patterns of direct health care expenditures among individuals with back pain in the United States. *Spine* 2004; 29:79-86.
60. Leigh JP, Markowitz SB, Fahs M, Shin C, Landrigan PJ. Occupational injury and illness in the United States. Estimates of costs, morbidity, and mortality. *Arch Intern Med* 1997; 157:1557-1568.
61. Freedman VA, Martin LG, Schoeni RF. Recent trends in disability and functioning among older adults in the united states. *JAMA* 2002; 288:3137-3146.
62. Hurwitz EL, Morgenstern H, Yu F. Cross-sectional and longitudinal associations of low-back pain and related disability with psychological distress among patients enrolled in the UCLA Low-Back Pain Study. *J Clin Epidemiol* 2003; 56:463-471.
63. Maetzel A, Li L. The economic burden of low back pain: a review of studies published between 1996 and 2001. *Best Pract Res Clin Rheumatol* 2002; 16:23-30.
64. Bell G, Kidd D, North R. Cost-effectiveness analysis of spinal cord stimulation in treatment of failed back surgery syndrome. *J Pain Symp Manage* 1997; 13:286-295.
65. de Lissovoy G, Brown RE, Halpern M, Hassenbusch SJ, Ross E. Cost-effectiveness of long-term intrathecal morphine therapy for pain associated with failed back surgery syndrome. *Clin Ther* 1997; 19:96-112.
66. Macario A, Pergolizzi JV. Systematic literature review of spinal decompression via motorized traction for chronic discogenic low back pain. *Spine* 2006; 6:171-178.
67. Murtagh J, Foerster V. Radiofrequency neurotomy for lumbar pain [Issues in emerging health technologies, issue 83]. Ottawa: Canadian Agency for Drugs and Technologies in Health; 2006.
68. Khadilkar A, Milne S, Brosseau L, Robinson V, Saginur M, Shea B, Tugwell P, Wells G. Transcutaneous electrical nerve stimulation (TENS) for chronic low-back pain. *Cochrane Database Syst Rev* 2005; 3:CD003008.
69. French SD, Cameron M, Walker BF, Reggars JW, Esterman AJ. A Cochrane review of superficial heat or cold for low back pain. *Spine* 2006; 31:998-1006.
70. Clarke JA, van Tulder MW, Blomberg SE, de Vet HC, van der Heijden GJ, Bronfort G. Traction for low-back pain with or without sciatica. *Cochrane Database Syst Rev* 2005; 4:CD003010.
71. Kay TM, Gross A, Goldsmith C, Santaguida PL, Hoving J, Bronfort G, Cervical Overview Group. Exercises for mechanical neck disorders. *Cochrane Database Syst Rev* 2005; 3:CD004250.
72. Chow RT, Barnsley L. Systematic review of the literature of low-level laser therapy (LLLT) in the management of neck pain. *Laser Surg Med* 2005; 37:46-52.
73. Singh K, Ledet E, Carl A. Intradiscal therapy: a review of current treatment modalities. *Spine* 2005; 30:S20-S26.
74. Taylor RS, Taylor RJ, Fritzell P. Balloon kyphoplasty and vertebroplasty for vertebral compression fractures: a comparative systematic review of efficacy and safety. *Spine* 2006; 31:2747-2755.
75. Gibson JN, Waddell G. Surgery for degenerative lumbar spondylosis: updated Cochrane Review. *Spine* 2005; 30:2312-2320.
76. Weinstein JN, Tosteson TD, Lurie JD, Tosteson AN, Hanscom B, Skinner JS, Abdu WA, Hilibrand AS, Boden SD, Deyo RA. Surgical vs nonoperative treatment for lumbar disk herniation: the Spine Patient Outcomes Research Trial (SPORT): a randomized trial. *JAMA* 2006; 296:2441-2450.
77. Schofferman J, Reynolds J, Herzog R, Covington E, Dreyfuss P, O'Neill C. Failed back surgery: etiology and diagnostic evaluation. *Spine J* 2003; 3:400-403.
78. Slipman CW, Shin CH, Patel RK, Isaac Z, Huston CW, Lipetz JS, Lenrow DA, Braverman DL, Vresilovic EJ Jr. Etiologies of failed back surgery syndrome. *Pain Med* 2002; 3:200-214.
79. Waguespack A, Schofferman J, Slosar P, Reynolds J. Etiology of long-term failures of lumbar spine surgery. *Pain Med* 2002; 3:18-22.
80. Boden S, Bohlman H. *The Failed Spine*. Lippincott, Williams & Wilkins, Philadelphia, PA, 2003.
81. Sampath P, Bendebba M, Davis JD, Ducker T. Outcome in patients with cervical radiculopathy. Prospective, multicenter study with independent clinical review. *Spine* 1999; 24:591-597.
82. Law JD, Lehman RAW, Kirsch WM. Reoperation after lumbar intervertebral disc surgery. *J Neurosurg* 1978; 48:259-263.
83. Waddell G, Kummel EG, Lotto WN, Graham JD, Hall H, McCulloch JA. Failed lumbar disc surgery and repeat surgery following industrial injury. *J Bone Joint Surg (Am)* 1979; 61:201-207.
84. Bogduk N, Christophidis N, Cherry D. Epidural use of steroids in the management of back pain. Report of working party on epidural use of steroids in the management of back pain. National Health and Medical Research Council. Canberra, Commonwealth of Australia, 1994, pp 1-76.
85. Manchikanti L, Pakanati RR, Pampati V. Comparison of three routes of epidural steroid injections in low back pain. *Pain Digest* 1999; 9:277-285.
86. Byrod G, Otani K, Brisby H, Rydevik B, Olmarker K. Methylprednisolone reduces the early vascular permeability increase in spinal nerve roots induced by epidural nucleus pulposus application. *J Orthop Res* 2000; 18:983-987.
87. Flower RJ, Blackwell GJ. Anti-inflammatory steroid induced biosynthesis of a

phospholipase A2 inhibitor which prevents prostaglandin generation. *Nature* 1979; 278:456-459.

88. Lundin A, Magnuson A, Axelsson K, Nilsson O, Samuelsson L. Corticosteroids preoperatively diminishes damage to the C-fibers in microscopic lumbar disc surgery. *Spine* 2005; 30:2362-2367.
89. Nicol GD, Klingberg DK, Vasko MR. Prostaglandin E2 enhances calcium conductance and stimulates release of substance P in avian sensory neurons. *J Neurosci* 1992; 12:1917-1927.
90. Hua SY, Chen YZ. Membrane receptor-mediated electrophysiological effects of glucocorticoid on mammalian neurons. *Endocrinology* 1989; 124:687-691.
91. Hayashi N, Weinstein JN, Meller ST, Lee HM, Spratt KF, Gebhart GF. The effect of epidural injection of betamethasone or bupivacaine in a rat model of lumbar radiculopathy. *Spine* 1998; 23:877-885.
92. Lee HM, Weinstein JN, Meller ST, Hayashi N, Spratt KF, Gebhart GF. The role of steroids and their effects on phospholipase A2: an animal model of radiculopathy. *Spine* 1998; 23:1191-1196.
93. Minamide A, Tamaki T, Hashizume H, Yoshida M, Kawakami M, Hayashi N. Effects of steroids and lipopolysaccharide on spontaneous resorption of herniated intervertebral discs: an experience study in the rabbit. *Spine* 1998; 23:870-876.
94. Kingery WS, Castellote JM, Maze M. Methylprednisolone prevents the development of autotomy and neuropathic edema in rats, but has no effect on nociceptive thresholds. *Pain* 1999; 80:555-566.
95. West S, King V, Carey T, Lohr K, McKoy N, Sutton S, Lux L. Systems to rate the strength of scientific evidence. Evidence Report/Technology Assessment No. 47 University of North Carolina: Agency for Healthcare Research and Quality. AHRQ Publication No. 02-E016; April 2002.
96. van Tulder M, Assendelft W, Koes B, Bouter LM. Method guidelines for systematic reviews in the Cochrane Collaboration Back Review Group for Spinal Disorders. *Spine* 1997; 22:2323-2330.
97. Manchikanti L, Abdi S, Lucas LF. Evidence synthesis and development of guidelines in interventional pain management. *Pain Physician* 2005; 8:73-86.
98. Shekelle PG, Andersson G, Bombardier C, Cherkin D, Deyo R, Keller R, Lee C, Liang M, Lipscomb B, Spratt K. A brief introduction to the critical reading of the clinical literature. *Spine* 1994; 19(suppl):2028S-2031S.
99. McGregor AH, Anjarwalla NK, Stambach T. Does the method of injection alter the outcome of epidural injections? *J Spinal Disord* 2001; 14:507-510.
100. Carette S, Leclaire R, Marcoux S, Morin F, Blaise GA, St-Pierre A, Truchon R, Parent F, Levesque J, Bergeron V, Montminy P, Blanchette C. Epidural corticosteroid injections for sciatica due to herniated nucleus pulposus. *N Engl J Med* 1997; 336:1634-1640.
101. Snoek W, Weber H, Jorgensen B. Double-blind evaluation of extradural methylprednisolone for herniated lumbar disc. *Acta Orthop Scand* 1977; 48:635-641.
102. Cuckler JM, Bernini PA, Wiesel SW, Booth RE Jr, Rothman RH, Pickens GT. The use of epidural steroid in the treatment of radicular pain. *J Bone Joint Surg* 1985; 67:63-66.
103. Dilke TF, Burry HC, Grahame R. Extradural corticosteroid injection in the management of lumbar nerve root compression. *Br Med J* 1973; 2:635-637.
104. Serrao JM, Marks RL, Morley SJ, Goodchild CS. Intrathecal midazolam for the treatment of chronic mechanical low back pain: a controlled comparison with epidural steroid in a pilot study. *Pain* 1992; 48:5-12.
105. Klenerman L, Greenwood R, Davenport HT, White DC, Peskett S. Lumbar epidural injections in the treatment of sciatica. *Br J Rheumatol* 1984; 23:35-38.
106. Rocco AG, Frank E, Kaul AF, Lipson SJ, Gallo JP. Epidural steroids, epidural morphine and epidural steroids combined with morphine in the treatment of post-laminectomy syndrome. *Pain* 1989; 36:297-303.
107. Ridley MG, Kingsley GH, Gibson T, Grahame R. Outpatient lumbar epidural corticosteroid injection in the management of sciatica. *Br J Rheumatol* 1988; 27:295-299.
108. Rogers P, Nash T, Schiller D and Norman J. Epidural steroids for sciatica. *Pain Clinic* 1992; 5:67-72.
109. Castagnera L, Maurette P, Pointillart V, Vital JM, Erny P, Senegas J. Long-term results of cervical epidural steroid injection with and without morphine in chronic cervical radicular pain. *Pain* 1994; 58:239-243.
110. Hernandez R, Lopez F. Assessment of pain intensity in patients with diabetic polyneuropathy treated with peridural 2% lidocaine methylprednisolone acetate vs peridural 2% lidocaine. *Anestesia en Mexico* 1999; 11:65-69.
111. Kikuchi A, Kotani N, Sato T, Takamura K, Sakai I, Matsuki A. Comparative therapeutic evaluation of intrathecal versus epidural methylprednisolone for long-term analgesia in patients with intractable postherpetic neuralgia. *Reg Anesth Pain Med* 1999; 24:287-293.
112. Helliwell M, Robertson JC, Ellia RM. Outpatient treatment of low back pain and sciatica by a single extradural corticosteroid injection. *Br J Clin Pract* 1985; 39:228-231.
113. Stav A, Ovadia L, Sternberg A, Kaadan M, Weksler N. Cervical epidural steroid injection for cervicobrachialgia. *Acta Anaesthesiol Scand* 1993; 37:562-566.
114. Buchner M, Zeifang F, Brocai DR, Schiltenwolf M. Epidural corticosteroid injection in the conservative management of sciatica. *Clin Orth Rel Res* 2000; 375:149-156.
115. Valat JP, Giraudeau B, Rozenberg S, Goupille P, Bourgeois P, Micheau-Beaugendre V, Soubrier M, Richard S, Thomas E. Epidural corticosteroid injections for sciatica: a randomised, double blind, controlled clinical trial. *Ann Rheum Dis* 2003; 62:639-43.
116. Kraemer J, Ludwig J, Bickert U, Owczarek V, Traupe M. Lumbar epidural perineural injection: a new technique. *Eur Spine J* 1997; 6:357-361.
117. Pirbudak L, Karakurum G Oner U, Gulec A, Karadasli H. Epidural corticosteroid injection and amitriptyline for the treatment of chronic low back pain associated with radiculopathy. *Pain Clinic* 2003; 15:247-253.
118. Bronfort G, Evans RL, Maiers M, Anderson AV. Spinal manipulation, epidural injections, and self-care for sciatica: a pilot study for a randomized clinical trial. *J Manipulative Physiol Ther* 2004; 278:503-508.
119. Wilson-MacDonald J, Burt G, Griffin D, Glynn C. Epidural steroid injection for nerve root compression: a randomized, controlled trial. *J Bone Joint Surg Br* 2005; 87-B:352-355.
120. Arden NK, Price C, Reading I, Stubbing J, Hazelgrove J, Dunne C, Michel M, Rogers P, Cooper C, WEST Study Group. A multicentre randomized controlled trial of epidural corticosteroid injections for sciatica: the WEST study. *Rheumatology (Oxford)* 2005; 44:1399-1406.
121. Bush K, Hillier S. Outcome of cervical radiculopathy treated with periradicular/epidural corticosteroid injections: a prospective study with independent clinical review. *Eur Spine J* 1996;

5:319-325.
122. Rull BM, Miralles M, Aure S. Therapeutic epidural infiltrations in the lumbar nerve roots. *Revista de Ortopedia y Traumatologia* 1996; 40:209-217.
123. Caglar S, Erdine S, Aldemir T. The results of the epidural steroid injections in patients with radiculopathies due to lumbar disc herniations. *Fizik Tedavi Rehabilitasyon Dergisi* 1995; 19:186-190.
124. Rivest C, Katz JN, Ferrante FM, Jamison RN. Effects of epidural steroid injection on pain due to lumbar spinal stenosis or herniated discs: a prospective study. *Arthritis Care Res* 1998; 11:291-297.
125. Koning HM, Koning AJ; Bruinen TCM; Koster HG; Heybroek E. The period of pain relief following a successful epidural steroid injection for low back pain. *Pain Clinic* 2002; 13:331-338.
126. Andersen KH, Mosdal C. Epidural application of corticosteroids in low back pain and sciatica. *Acta Neurochir* 1987; 87:52-53.
127. Warfield CA, Crews DA. Epidural steroid injection as a predictor of surgical outcome. *Surg Gyn Obstet* 1987; 164:457-458.
128. Fukusaki M, Kobayashi I, Hara T, Sumikawa K. Symptoms of spinal stenosis do not improve after epidural steroid injection. *Clin J Pain* 1998; 14:148-151.
129. Stav A, Ovadia L, Landau M, Weksler N, Berman M. Epidural steroid injection in the treatment of lumbar and cervical pain syndromes: a preliminary retrospective comparison. *Pain Clinic* 1991; 4:95-112.
130. Lin EL, Lieu V, Halevi L, Shamie AN, Wang JC. Cervical epidural steroid injections for symptomatic disc herniations. *J Spinal Disord Tech* 2006; 19:183-186.
131. Mangar D, Thomas PB. Epidural steroid injections in the treatment of cervical and lumbar pain syndromes. *Reg Anesth* 1991; 16:246.
132. Shulman M. Treatment of neck pain with cervical epidural steroid injection. *Reg Anesth* 1986; 11:92-94.
133. Catchlove RFH, Braha R. The use of cervical epidural nerve blocks in the management of chronic head and neck pain. *Can Anaesth Soc J* 1984; 31:188-191.
134. Berman AT, Garbarino JL Jr, Fisher SM, Bosacco SJ. The effects of epidural injection of local anesthetics and corticosteroids in patients with lumbosciatic pain. *Clin Orthop* 1984; 188:144-151.
135. Purkis IE. Cervical epidural steroids. *Pain Clinic* 1986; 1:3-7.
136. Rowlingson JC, Kirschenbaum LP. Epidural analgesic techniques in the management of cervical pain. *Anesth Analg* 1986; 65:938-942.
137. Warfield CA, Biber MP, Crews DA, Dwarakanath,GK. Epidural steroid injection as a treatment for cervical radiculitis. *Clin J Pain* 1988; 4:201-204.
138. Cicala RS, Thoni K, Angel JJ. Long-term results of cervical epidural steroid injections. *Clin J Pain* 1989; 5:143-145.
139. Pawl RP, Anderson W, Shulman M. Effect of epidural steroids in the cervical and lumbar region on surgical intervention for discogenic spondylosis. *Clin J Pain* 1985; 1:181-185.
140. Ferrante FM, Wilson SP, Iacobo C, Orav EJ, Rocco AG, Lipson S. Clinical classification as a predictor of therapeutic outcome after cervical epidural steroid injection. *Spine* 1993; 18:730-736.
141. Klein GR, Vaccaro AR, Cwik J, Seitchik S, Viscusi ER, Albert TJ. Efficacy of cervical epidural steroids in the treatment of cervical spine disorders. *Am J Anesthesiol* 2000; 9:547-552.
142. Ozyalcin S, Yucel A, Erdine S. Epidural steroid injection in the treatment of cervical pain syndromes: a retrospective follow up study. *Angri Dergisi* 1996; 8:9-14.
143. Hickey RF. Outpatient epidural steroid injections for low back pain and lumbosacral radiculopathy. *NZ Med J* 1987; 100:54-59.
144. Heyse-Moore GH. A rational approach to the use of epidural medication in the treatment of sciatic pain. *Acta Orthop Scand* 1978; 49:366-370.
145. Harley C. Extradural corticosteroid infiltration: a follow-up study of 50 cases. *Ann Phy Med* 1966; 9:22-28.
146. Sharma S, Stedman R. Epidural steroids: a retrospective analysis of the efficacy of high and low dose therapy. *Anesthesiology* 1998; 3A:A1135.
147. Rosen CD, Kahanovitz N, Bernstein R, Viola K. A retrospective analysis of the efficacy of epidural steroid injections. *Clin Orthop* 1988; 228:270-272.
148. Arnhoff FN, Triplett HB, Pokorney B. Follow-up status of patients treated with nerve blocks for low back pain. *Anesthesiology* 1977; 46:170-178.
149. Jamison RN, VadeBoncouer T, Ferrante FM. Low back pain patients unresponsive to an epidural steroid injection: identifying predictive factors. *Clin J Pain* 1991; 7:311-317.
150. Hopwood MB, Abram SE. Factors associated with failure of lumbar epidural steroids. *Reg Anesth* 1993; 18:238-243.
151. Reale C, Turkiewicz AM, Reale CA, Stabile S, Borgonuovo P, Apponi F. Epidural steroids as a pharmacological approach. *Clin Exp Rheumatol* 2000; 18: S65-S66.
152. Bowman SJ, Wedderburn L, Whaley A, Grahame R, Newman S. Outcome assessment after epidural corticosteroid injection for low back pain and sciatica. *Spine* 1993; 18:1345-1350.
153. Jurmand SH. Cortiotherapie peridurale des lombalgies et des sciatiques d'origine discale. *Concours Medicale* 1972; 94:5061-5070.
154. Ito R. The treatment of low back pain and sciatica with epidural corticosteroids injection and its pathophysiologic basis. *J Jpn Orthop Assoc* 1971; 45:769-777.
155. Brown FW. Management of discogenic pain using epidural and intrathecal steroids. *Clin Orthop* 1977; 129:72-78.
156. Warr AC, Wilkinson JA, Burn JM, Langdon L. Chronic lumbosciatica syndrome treated by epidural injection and manipulation. *Practitioner* 1977; 209:53-59.
157. Papagelopoulos PJ, Petrou HG, Triantafyllidis PG, Vlamis JA, Psomas-Pasalis M, Korres DS, Stamos KG. Treatment of lumbosacral radicular pain with epidural steroid injections. *Orthopedics* 2001; 24:145-149.
158. Silva J, Costa AO, Simoes MT, Neto RR. Management of radicular pain from lumbar herniated disc using betamethasone epidural injection. *Revista Brasileira de Ortopedia* 1999; 34:165-168.
159. Wang JC, Lin E, Brodke DS, Youssef JA. Epidural injections for the treatment of symptomatic lumbar herniated discs. *J Spinal Disord Tech* 2002; 15:269-272.
160. Price C, Arden N, Coglan L, Rogers P. Cost-effectiveness and safety of epidural steroids in the management of sciatica. *Health Technol Assess* 2005; 9:1-58, iii.
161. Schaufele MK, Hatch L, Jones W. Interlaminar versus transforaminal epidural injections for the treatment of symptomatic lumbar intervertebral disc herniations. *Pain Physician* 2006; 9:361-366.
162. Riew KD, Park JB, Cho YS, Gilula L, Patel A, Lenke LG, Bridwell KH. Nerve root blocks in the treatment of lumbar radicular pain: a minimum five-year follow-up. *J Bone Joint Surg Am* 2006; 88:1722-1725.
163. Ng L, Chaudhary N, Sell P. The efficacy of corticosteroids in periradicular infiltration for chronic radicular pain: a ran-

domized, double-blind, controlled trial. *Spine* 2005; 30:857-862.

164. Riew KD, Yin Y, Gilula L, Bridwell KH, Lenke LG, Lauryssen C, Goette K. The effect of nerve-root injections on the need for operative treatment of lumbar radicular pain. *J Bone Joint Surg AM* 2000; 82: 1589-1593.
165. Karppinen J, Malmivaara A, Kurunlahti M, Kyllonen E, Pienimaki T, Nieminen P, Ohinmaa A, Tervonen O, Vanharanta H. Periradicular infiltration for sciatica. *Spine* 2001; 26:1059-1067.
166. Karppinen J, Ohinmaa A, Malmivaara A, Kurunlahti M, Kyllonen E, Pienimaki T, Nieminen P, Tervonen O, Vanharanta H. Cost effectiveness of periradicular infiltration for sciatica. *Spine* 2001; 26:2587-2595.
167. Devulder J, Deene P, De Laat M, Van Bastelaere M, Brusselmans G, Rolly G. Nerve root sleeve injections in patients with failed back surgery syndrome: a comparison of three solutions. *Clin J Pain* 1999; 15:132-135.
168. Kolsi I, Delecrin J, Berthelot JM, Thomas L, Prost A, Maugars Y. Efficacy of nerve root versus interspinous injections of glucocorticoids in the treatment of disc-related sciatica: a pilot, prospective, randomized, double-blind study. *Joint Bone Spine* 2000; 67:113-118.
169. Vad VB, Bhat AL, Lutz GE, Cammisa F. Transforaminal epidural steroid injections in lumbosacral radiculopathy: a prospective randomized study. *Spine* 2002; 27:11-16.
170. Thomas E, Cyteval C, Abiad L, Picot MC, Taourel P, Blotman F. Efficacy of transforaminal versus interspinous corticosteroid injection in discal radiculalgia: a prospective, randomised, double-blind study. *Clin Rheumatol* 2003; 22:299-304.
171. Anderberg L, Annertz M, Persson L, Brandt L, Saveland H. Transforaminal steroid injections for the treatment of cervical radiculopathy: a prospective and randomised study. *Eur Spine J* 2006; Epub ahead of print.
172. Autio RA, Karppinen J, Niinimaki J, Ojala R, Kurunlahti M, Haapea M, Vanharanta H, Tervonen O. Determinants of spontaneous resorption of intervertebral disc herniations. *Spine* 2006; 31:1247-1252.
173. Tong HC, Williams JC, Haig AJ, Geisser ME, Chiodo A. Predicting outcomes of transforaminal epidural injections for sciatica. *Spine J* 2003; 3:430-434.
174. Kolstad F, Leivseth G and Nygaard O. Transforaminal steroid injections in the treatment of cervical radiculopathy. A prospective outcome study. *Acta Neurochir (Wien)* 2005; 147:1065-1070.
175. Yang SC, Fu TS, Lai PL, Niu CC, Chen LH, Chen WJ. Transforaminal epidural steroid injection for discectomy candidates: an outcome study with a minimum of two-year follow-up. *Chang Gung Med J* 2006; 29:93-99.
176. Ng LC, Sell P. Outcomes of a prospective cohort study on peri-radicular infiltration for radicular pain in patients with lumbar disc herniation and spinal stenosis. *Eur Spine J* 2004; 13:325-329.
177. Karaeminogullari O, Sahin O, Boyvat F, Akgun RC, Gurun U, Demirors H, Tuncay IC, Tandogan RN. Transforaminal epidural steroid injection under computed tomography guidance in relieving lumbosacral radicular pain. *Acta Orthop Traumatol Turc* 2005; 39:416-420.
178. Michel JL, Lemaire S, Bourbon H, Reynier C, Lhoste A, Soubrier S, Dubost JJ, Ristori JM. Fluoroscopy guided L5-S1 transforaminal injection as a treatment for s1 radiculopathy. *J Radiol* 2004; 85:1937-1941.
179. Lutz GE, Vad VB, Wisneski RJ. Fluoroscopic transforaminal lumbar epidural steroids: an outcome study. *Arch Phys Med Rehabil* 1998; 79:1362-1366.
180. Dreyfuss P, Baker R, Bogduk N. Comparative effectiveness of cervical transforaminal injections with particulate and nonparticulate corticosteroid preparations for cervical radicular pain. *Pain Med* 2006; 7:237-242.
181. Berger O, Dousset V, Delmer O, Pointillart V, Vital JM, Caille JM. Evaluation of the efficacy of foraminal infusions of corticosteroids guided by computed tomography in the treatment of radicular pain by foraminal injection. *J Radiol* 1999; 80:917-925.
182. Melzer A, Seibel RM. Magnetic resonance (MR)-guided percutaneous pain therapy of degenerative spinal diseases. *Semin Interv Radiol* 1999; 16:143-150.
183. Sequeiros RB, Ojala RO, Klemola R, Vaara TJ, Jyrkinen L, Tervonen OA. MRI-guided periradicular nerve root infiltration therapy in low-field (0.23-T) MRI system using optical instrument tracking. *Eur Radiol* 2002; 12:1331-1337.
184. Zennaro H, Dousset V, Viaud B, Allard M, Dehais J, Senegas J, Caille JM. Periganglionic foraminal steroid injections performed under CT control. *Am J Neuroradiol* 1998; 19:349-352.
185. Groenemeyer DH, Gevargez A, Schindler O, Schirp S, Braun M. CT-guided periradicular injections of corticosteroids in the management of lumbar radiculopathy associated with disk herniation. *J Radiol* 2002; 1-12.
186. Buttermann GR. Lumbar disc herniation regression after successful epidural steroid injection. *J Spinal Disord Tech* 2002; 15:469-476.
187. Buttermann GR. The effect of spinal steroid injections for degenerative disc disease. *Spine J* 2004; 4:495-505.
188. Buttermann GR. Treatment of lumbar disc herniation: epidural steroid injection compared with discectomy. A prospective, randomized study. *J Bone Joint Surg Am* 2004; 86-A:670-679.
189. Cyteval C, Thomas E, Decoux E, Sarrabere MP, Cottin A, Blotman F, Taourel P. Cervical radiculopathy: open study on percutaneous periradicular foraminal steroid infiltration performed under CT control in 30 patients. *AJNR Am J Neuroradiol* 2004; 25:441-445.
190. Botwin KP, Gruber RD, Bouchlas CG, Torres-Ramos FM, Sanelli JT, Freeman ED, Slaten WK, Rao S. Fluoroscopically guided lumbar transformational epidural steroid injections in degenerative lumbar stenosis: an outcome study. *Am J Phys Med Rehabil* 2002; 81:898-905.
191. Lee JW, Kim SH, Lee IS, Choi JA, Choi JY, Hong SH, Kang HS. Therapeutic effect and outcome predictors of sciatica treated using transforaminal epidural steroid injection. *AJR Am J Roentgenol* 2006; 187:1427-1431.
192. Slipman CW, Lipetz JS, DePalma MJ, Jackson HB. Therapeutic selective nerve root block in the nonsurgical treatment of traumatically induced cervical spondylotic radicular pain. *Am J Phys Med Rehabil* 2004; 83:446-454.
193. Slipman C, Lipetz J, Jackson H, Plastaras C, Vresilovic E. Outcomes of therapeutic selective nerve root blocks for whiplash induced cervical radicular pain. *Pain Physician* 2001; 4:167-174.
194. Lutze M, Stendel R, Vesper J, Brock M. Periradicular therapy in lumbar radicular syndromes: methodology and results. *Acta Neurochir* 1997; 139:719-724.
195. Uhlenbrock D, Arlinghaus J. Results of CT-guided periradicular pain therapy. *Rofo* 1997; 166:528-534.
196. Le Chevallier PL, Videgrain M, Roulleau P, Delvert JC, Valat JP, Castaing J. Injection of the sacrolumbar roots: a complementary method of staging sciatica. 18 cases. *Rev Rhum Mal Osteoartic* 1978; 45:473-477.
197. Devulder J. Transforaminal nerve root

sleeve injection with corticosteroids, hyaluronidase, and local anesthetic in the failed back surgery syndrome. *J Spinal Disord* 1998; 11:151-154.

198. Weiner BK, Fraser RD. Foraminal injection for lateral lumbar disc herniation. *J Bone Joint Surg* 1997; 79-B:804-807.
199. Narozny M, Zanetti M, Boos N. Therapeutic efficacy of selective nerve root blocks in the treatment of lumbar radicular leg pain. *Swiss Med Wkly* 2001; 131:75-80.
200. Friedman R, Li V, Mehrotra D, Mosuro Y, Atkinson G. Foraminal injection of a painful sacral nerve root using an epidural catheter: case report. *Reg Anesth Pain Med* 2002; 27:214-216.
201. Rosenberg SK, Grabinsky A, Kooser C, Boswell M. Effectiveness of transforaminal epidural steroid injections in low back pain: a one year experience. *Pain Physician* 2002; 5:266-270.
202. Schmid G, Vetter S, Gottmann D, Strecker EP. CT-guided epidural/perineural injections in painful disorders of the lumbar spine: short- and extended-term results. *Cardiovasc Intervent Radiol* 1999; 22:493-498.
203. Groenmeyer DH, Seibel R, Schindler O, Schattauer K, Lange S, Schmidt A. Microinvasive CT guided periradicular therapy for treatment of chronical functional disorders of the spine. *Weiner Medizinische Wochenschrift* 1995; 145:129-139.
204. Slipman CW, Lipetz JS, Jackson HB, Rogers DP, Vresilovic EJ. Therapeutic selective nerve root block in the nonsurgical treatment of atraumatic cervical spondylotic radicular pain: a retrospective analysis with independent clinical review. *Arch Phys Med Rehabil* 2000; 81:741-746.
205. Lee KS, Lin CL, Hwang SL, Howng SL, Wang CK. Transforaminal periradicular infiltration guided by CT for unilateral sciatica: an outcome study. *Clin Imaging* 2005; 29:211-214.
206. Sasso RC, Macadaeg K, Nordmann D, Smith M. Selective nerve root injections can predict surgical outcome for lumbar and cervical radiculopathy: comparison to magnetic resonance imaging. *J Spinal Disord Tech* 2005; 18:471-478.
207. Dashfield AK, Taylor MB, Cleaver JS, Farrow D. Comparison of caudal epidural with targeted steroid placement during spinal endoscopy for chronic sciatica: a prospective, randomized, double-blind trial. *Br J Anaesth* 2005; 94:514-519.
208. Anwar A, Zaidah I, Rozita R. Prospective randomized single blind study of epidural steroid injection comparing triamcinolone acetonide with methylprednisolone acetate. *APLAR J Rheumatology* 2005; 8:1-53.
209. Breivik H, Hesla PE, Molnar I, Lind B. Treatment of chronic low back pain and sciatica. Comparison of caudal epidural injections of bupivacaine and methylprednisolone with bupivacaine followed by saline. In: Bonica JJ, AlbeFesard D (eds). *Advances in pain research and therapy. Vol. 1.* Raven Press, New York, 1976, pp 927-932.
210. Bush K, Hillier S. A controlled study of caudal epidural injections of triamcinolone plus procaine for the management of intractable sciatica. *Spine* 1991; 16:572-575.
211. Mathews JA, Mills SB, Jenkins VM, Grimes SM, Morkel MJ, Mathews W, Scott CM, Sittampalam Y. Back pain and sciatica: controlled trials of manipulation, traction, sclerosant and epidural injections. *Brit J Rheumatol* 1987; 26:416-423.
212. Beliveau P. A comparison between epidural anesthesia with and without corticosteroids in the treatment of sciatica. *Rheum Phys Med* 1971; 11:40-43.
213. Blankenbaker DG, De Smet AA, Stanczak JD, Fine JP. Lumbar radiculopathy: treatment with selective lumbar nerve blocks: comparison of effectiveness of triamcinolone and betamethasone injectable suspensions. *Radiology* 2005; 237:738-741.
214. Helsa PE, Breivik H. Epidural analgesia and epidural steroid injection for treatment of chronic low back pain and sciatica. *Tidsskr Nor Laegeforen* 1979; 99:936-939.
215. Revel M, Auleley GR, Alaoui S, Nguyen M, Duruoz T, Eck-Michaud S, Roux C, Amor B. Forceful epidural injections for the treatment of lumbosciatic pain with post-operative lumbar spinal fibrosis. *Rev Rhum Engl Ed* 1996; 63:270-277.
216. Meadeb J, Rozenberg S, Duquesnoy B, Kuntz JL, Le Loet X, Sebert JL, Le Goff P, Fallut M, Marty M, Blevin S, Guggenbuhl P, Chales G, Duvauferrier R. Forceful sacrococcygeal injections in the treatment of postdiscectomy sciatica. A controlled study versus glucocorticoid injections. *Joint Bone Spine* 2001; 68:43-49.
217. Manchikanti L, Pampati V, Rivera JJ, Beyer CD, Damron KS, Barnhill RC. Caudal epidural injections with sarapin steroids in chronic low back pain. *Pain Physician* 2001; 4:322-335.
218. Manchikanti L., Singh V, Rivera JJ, Pampati V, Beyer CD, Damron KS, Barnhill RC. Effectiveness of caudal epidural injections in discogram positive and negative chronic low back pain. *Pain Physician* 2002; 5:18-29.
219. Yates DW. A comparison of the types of epidural injection commonly used in the treatment of low back pain and sciatica. *Rheum Rehab* 1978; 17:181-186.
220. Waldman SD. The caudal epidural administration of steroids in combination with local anesthetics in the palliation of pain secondary to radiographically documented lumbar herniated disc: a prospective outcome study with 6-months follow-up. *Pain Clinic* 1998; 11:43-49.
221. Ciocon JO, Galindo-Ciocon D, Amaranath L, Galindo D. Caudal epidural blocks for elderly patients with lumbar canal stenosis. *J Am Geriatr Soc* 1994; 42:593-596.
222. Barré L, Lutz GE, Southern D, and Cooper G. Fluoroscopically Guided Caudal Epidural Steroid Injections for Lumbar Spinal Stenosis: a restrospective evaluation of long term efficacy. *Pain Physician* 2004; 7:187-193.
223. Hauswirth R, Michot F. Caudal epidural injection in the treatment of low back pain. *Ischweizerische Medizinische Wochenschrift* 1982; 112:222-225.
224. Goebert HW Jr, Jallo SJ, Gardner WJ, Wasmuth CE. Painful radiculopathy treated with epidural injections of procaine and hydrocortisone acetate: results in 113 patients. *Anesth Analg* 1961; 140:130-134.
225. Botwin KP, Gruber RD, Bouchlas CG, Torres-Ramos FM, Freeman TL, Slaten WK. Complications of fluoroscopically guided transforaminal lumbar epidural injections. *Arch Phys Med Rehabil* 2000; 81:1045-1050.
226. Botwin KP, Castellanos R, Rao S, Hanna AF, Torres-Ramos FM, Gruber RD, Bouchlas CG, Fuoco GS. Complications of fluoroscopically guided interlaminar cervical epidural injections. *Arch Phys Med Rehabil* 2003; 84:627-633.
227. Botwin KP, Baskin M, and Rao S. Adverse effects of fluoroscopically guided interlaminar thoracic epidural steroid injections. *Am J Phys Med Rehabil* 2006; 85:14-23.
228. Botwin KP, Gruber RD, Bouchlas CG, Torres-Ramos FM, Hanna A, Rittenberg J, Thomas SA. Complications of fluoroscopically guided caudal epidural injections. *Arch Phys Med Rehabil* 2001; 80:416-424.
229. Furman MB, O'Brien EM, Zgleszewski TM. Incidence of intravascular penetration in transforaminal lumbosacral epi-

dural steroid injections. *Spine* 2000; 25:2628-2632.

230. Furman MB, Giovanniello MT, O'Brien EM. Incidence of intravascular penetration in transforaminal cervical epidural steroid injections. *Spine* 2003; 28:21-25.
231. Manchikanti L, Cash KA, Pampati V, Damron KS, McManus CD. Evaluation of lumbar transforaminal epidural injections with needle placement and contrast flow patterns: a prospective, descriptive report. *Pain Physician* 2004; 7:217-224.
232. Manchikanti L, Bakhit CE, Pampati V. The role of epidurography in caudal neuroplasty. *Pain Digest* 1998; 8:277-281.234.
233. Manchikanti L, Cash KA, Pampati V, McManus CD, Damron KS. Evaluation of fluoroscopically guided caudal epidural injections. *Pain Physician* 2004; 7:81-92.
234. Derby R, Lee SH, Kim BJ, Chen Y, and Seo KS. Complications following cervical epidural steroid injections by expert interventionalists in 2003. *Pain Physician* 2004; 7:445-449.
235. Beckman WA, Mendez RJ, Paine GF, Mazzilli MA. Cerebellar herniation after cervical transforaminal epidural injection. *Reg Anesth Pain Med* 2006; 31:282-285.
236. Ludwig MA and Burns SP. Spinal cord infarction following cervical transforaminal epidural injection: a case report. *Spine* 2005; 30:E266-E268.
237. Rozin L, Rozin R, Koehler SA, Shakir A, Ladham S, Barmada M, Dominick J, Wecht CH. Death during transforaminal epidural steroid nerve root block (C7) due to perforation of the left vertebral artery. *Am J Forensic Med Pathol* 2003; 24:351-355.
238. Houten JK, Errico TJ. Paraplegia after lumbosacral nerve root block: report of three cases. *Spine J* 2002; 2:70-75.
239. Cousins MJ. An additional dimension to the efficacy of epidural steroids. *Anesthesiology* 2000; 93:565.
240. Brouwers PJ, Kottink EJ, Simon MA, Prevo RL. A cervical anterior spinal artery syndrome after diagnostic blockade of the right C6-nerve root. *Pain* 2001; 91:397-399.
241. Nash TP. Comment on A cervical anterior spinal artery syndrome after diagnostic blockade of the right C6-nerve root. *Pain* 2002; 91:217-218.
242. Karasek M and Bogduk N. Temporary neurologic deficit after cervical transforaminal injection of local anesthetic. *Pain Med* 2004; 5:202-205.
243. Huntoon MA. Anatomy of the cervical intervertebral foramina: vulnerable arteries and ischemic neurologic injuries after transforaminal epidural injections. *Pain* 2005; 117:104-111.
244. Ma DJ, Gilula LA, Riew KD. Complications of fluoroscopically guided extraforaminal cervical nerve blocks: an analysis of 1036 injections. *J Bone Joint Surg Am* 2005; 87:1025-1030.
245. Glaser SE and Falco F. Paraplegia following a thoracolumbar transforaminal epidural steroid injection. *Pain Physician* 2005; 8:309-314.
246. Huston CW, Slipman CW, Garvin C. Complications and side effects of cervical and lumbosacral selective nerve root injections. *Arch Phys Med Rehabil* 2005; 86:277-283.
247. Tiso RL, Cutler T, Catania JA, Whalen K. Adverse central nervous system sequelae after selective transforaminal block: the role of corticosteroids. *Spine J* 2004; 4:468-474.
248. Quintero N, Laffont I, Bouhmidi L, Rech C, Schneider AE, Garvardin T, Dizien O. Transforaminal epidural steroid injection and paraplegia: case report and bibliographic review. *Ann Readapt Med Phys* 2006; 49:242-247.
249. Bose B. Quadriparesis following cervical epidural steroid injections: case report and review of the literature. *Spine J* 2005; 5:558-563.
250. Huntoon MA, Martin DP. Paralysis after transforaminal epidural injection and previous spinal surgery. *Reg Anesth Pain Med* 2004; 29:494-495.
251. Bilir A, Gulec S. Cauda equina syndrome after epidural steroid injection: a case report. *J Manipulative Physiol Ther* 2006; 29:492-494.
252. Tripathi M, Nath SS, Gupta RK. Paraplegia after intracord injection during attempted epidural steroid injection in an awake-patient. *Anesth Analg* 2005; 100:1209-1211.
253. Reitman CA, Watters W. Subdural hematoma after cervical epidural steroid injection. *Spine* 2002; 27:E174-E176.
254. Ziai WC, Ardelt AA, Llinas RH. Brainstem stroke following uncomplicated cervical epidural steroid injection. *Arch Neurol* 2006; 63:1643-1646.
255. Bromage RP, Benumof JL. Paraplegia following intracord injection during attempted epidural anesthesia under general anesthesia. *Reg Anesth Pain Med* 1998; 23:104-107.
256. Hodges SD, Castleberg RL, Miller T, Ward R, Thornburg C. Cervical epidural steroid injection with intrinsic spinal cord damage: two case reports. *Spine* 1998; 23:2137-2142.
257. Williams KN, Jackowski A, Evans PJ. Epidural hematoma requiring surgical decompression following repeated cervical epidural steroid injections for chronic pain. *Pain* 1990; 42:197-199.
258. Dietrich CL, Smith CE. Epidural granuloma and intracranial hypotension resulting from cervical epidural steroid injection. *Anesthesiology* 2004; 100:445-447.
259. Saigal G, Donovan PMJ, Kozic D. Thoracic intradural Aspergillus abscess formation following epidural steroid injection. *Am J Neuroradiol* 2004; 25:642-644.
260. Waldman SD. Cervical epidural abscess after cervical epidural nerve block with steroids (Letter). *Anesth Anal* 1991; 72:717.
261. Mamourian AC, Dickman CA, Drayer BP, Sonntag VK. Spinal epidural abscess: three cases following spinal epidural injection demonstrated with magnetic resonance imaging. *Anesthesiology* 1993; 78:204-207.
262. Knight JW, Cordingley JJ, Palazzo MG. Epidural abscess following epidural steroid and local anesthetic injection. *Anaesthesia* 1997; 52:576-578.
263. Kaul S, Meena AK, Sundaram C, Reddy JM, Naik RT, Murthy JM. Spinal extradural abscess following local steroid injection. *Neurol India* 2000; 48:181-183.
264. Sabel M, Felsberg J, Neuen-Jacob E, Lichota A, Schnitzler A, Herdmann J. Enlargement of a chronic aseptic lumbar epidural abscess by intraspinal injections—a rare cause of progressive paraparesis. *Zentralbl Neurochir* 2000; 61:111-114.
265. Huang RC, Shapiro GS, Lim M, Sandhu HS, Lutz GE, Herzog RJ. Cervical epidural abscess after epidural steroid injection. *Spine* 2004; 29:E7-E9.
266. Parlier-Cuau C, Carlier RY, David P, Silva M, Doyon D. Subdural abscess. Rare complication of epidural infiltration: apropos of a case and review of the literature. *J Radiol* 1993; 74:205-209.
267. Hooten WM, Mizerak A, Carns PE. Discitis after lumbar epidural corticosteroid injection: a case report and analysis of the case report literature. *Pain Med* 2006; 7:46-51.
268. Finn KP and Case JL. Disk entry: a complication of transforaminal epidural injection--a case report. *Arch Phys Med Rehabil* 2005; 86:1489-1491.
269. Huang J, Kwa A. Lumbar discogram resulting from lumbar interlaminar epi-

dural injection. *J Clin Anesth* 2004; 16:296-298.

270. Kabbara AK, Rosenberg SK, and Untal C. Methecillin-resistant staphyloccus aureus epidural abscess after transforaminal epidural steroid injection. *Pain Physician* 2004; 7:269-272.
271. Hooten WM, Kinney MO, Huntoon MA. Epidural abscess and meningitis after epidural corticosteroid injection. *Mayo Clin Proc* 2004; 79:682-686.
272. Yue WM, Tan SB. Distant skip level discitis and vertebral osteomyelitis after caudal epidural injection: s case report of a rare complication of epidural injections. *Spine* 2003; 28:E209-E211.
273. Simopoulos T, Peeters-Asdourian C. Pneumocephalus after cervical epidural steroid injection. *Anesth & Anal* 2001; 92:1576-1577.
274. Nishimura H, Uemura Y, Fukuda S, Kamada Y, Moriwaki T. Two cases of pyogenic cervical discitis presenting tetraparesis. *No Shinkei Geka* 2000; 28:631-637.
275. Hawley JS, J. P. Ney, and M. M. Swanberg. Subarachnoid pneumocephalus from epidural steroid injection. *Headache* 2005; 45:247-248.
276. Young WF. Transient blindness after lumbar epidural steroid injection: a case report and literature review. *Spine* 2002; 27:E476-E477.
277. Browning DJ. Acute retinal necrosis following epidural steroid injections. *Am J Ophthalmol 2003;* 136:192-194.
278. Iida T, Spaide RF, Negrao SG, Carvalho CA, and Yannuzzi LA. Central serous chorioretinopathy after epidural corticosteroid injection. *Am J Ophthalmol* 2001; 132:423-425.
279. Pizzimenti JJ, Daniel KP. Central serous chorioretinopathy after epidural steroids. *Pharmacotherapy* 2005; 25:1141-1146.
280. McAllister RK, McDavid AJ, Meyer TA, Bittenbinder TM. Recurrent persistent hiccups after epidural steroid injection and analgesia with bupivacaine. *Anesth Analg* 2005; 100:1834-1836.
281. Slipman CW, Chow DW, Lenrow DA, Blaugrund JE, and Chou LH. Dysphonia associated with epidural steroid injection: a case report. *Arch Phys Med Rehabil* 2002; 83:1309-1310.
282. Everett CR, Baskin MN, Novoseletsky D, Speach D, and Patel R. Flushing as a side effect following lumbar transforaminal epidural steroid injection. *Pain Physician* 2004; 7:427-429.
283. MacLean CA, Bachman DT. Documented arterial gas embolism after spinal epidural injection. *Ann Emerg Med* 2001; 38:592-595.
284. McMillan MR, Crumpton C. Cortical blindness and neurologic injury complicating cervical transforaminal injection for cervical radiculopathy. *Anesthesiology* 2003; 99:509-511.
285. Mateo E, Lopez-Alarcon MD, Moliner S, Calabuig E, Vivo M, De Andres J, Grau F. Epidural and subarachnoid pneumocephalus after epidural technique. *Eur J Anesthesiol* 1999; 16:413-417.
286. Katz JA, Lukin R, Bridenbaugh PO, Gunzenhauser L. Subdural intracranial air: an unusual cause of headache after epidural steroid injection. *Anesthesiology* 1991; 74:615-618.
287. Gutknecht DR. Chemical meningitis following epidural injections of corticosteroids (Letter). *Am J Med* 1987; 82:570.
288. Kusher FH, Olson JC. Retinal hemorrhage as a consequence of epidural steroid injection. *Arch Opthalmol* 1995; 113:309-313.
289. Elias M. A rare cause of radiculopathy following transforaminal epidural steroid injection. *Pain Clinic* 1998; 11:159-160.
290. Stohr M, Mayer K. Nerve-root damage from local injections. *Dtsch Med Wochenschr* 1976; 101:1218-1220.
291. Milhaud D, Heroum C, Charif M, Saulnier P, Pages M, Blard JM. Dural puncture and corticotherapy as risks factors for cerebral venous sinus thrombosis. *Eur J Neruol* 2000; 7:123-124.
292. Nelson DA, Landau WM. Intraspinal steroids: history, efficacy, accidentality, and controversy with review of United States Food and Drug Administration reports. *J Neurol Neurosurg Psychiatry* 2001; 70:433-443.
293. Manchikanti L. Role of neuraxial steroids in interventional pain management. *Pain Physician* 2002; 5:182-199.
294. Delaney TJ, Rowlingson JC, Carron H, Butler A. Epidural steroid effects on nerves and meninges. *Anesth Analg* 1980; 58:610-614.
295. MacKinnon Se, Hudson AR, Gentilli R. Peripheral nerve injection injury with steroid agents. *Plast Reconstr Surg* 1982; 69:482-489.
296. Chino N, Awad EA, Kottke FJ. Pathology of propylene glycol administered by perineural and intramuscular injection in rats. *Arch Phys Med Rehab* 1974; 55:33-38.
297. Benzon HT, Gissen AJ, Strichartz GR, Avram MJ, Covino BG. The effect of polyethylene glycol on mammalian nerve impulses. *Anesth Analg* 1987; 66:553-559.
298. Abram SE, Marsala M, Yaksh TL. Analgesic and neurotoxic effects of intrathecal corticosteroids in rats. *Anesthesiology* 1994; 81:1198-1205.
299. Latham JM, Fraser RD, Moore RJ, Blumbergs PC, Bogduk N. The pathologic effects of intrathecal betamethasone. *Spine* 1997; 22:1558-1562.
300. Robustelli della Cuna FS, Mella M, Magistrali G, Ricci M, Losurdo A, Goglio AM. Stability and compatibility of methylprednisolone acetate and ropivacaine hydrochloride in polypropylene syringes for epidural administration. *Am J Health Syst Pharm* 2001; 58:1753-1756.
301. Manchikanti L, Pampati V, Beyer CD, Damron KS, Cash KA, Moss TL. The effect of neuraxial steroids on weight and bone mass density: a prospective evaluation. *Pain Physician* 2000; 3:357-366.
302. Manchikanti L, Cash KA, Moss TL, Pampati V. Effectiveness of protective measures in reducing risk of radiation exposure in interventional pain management: a prospective evaluation. *Pain Physician* 2003; 6:301-305.
303. Manchikanti L, Cash KA, Moss TL, Rivera JJ, Pampati V. Risk of whole body radiation exposure and protective measures in fluoroscopically guided interventional techniques: a prospective evaluation. *BMC Anesthesiol* 2003; 3:2.
304. Manchikanti L, Cash KA, Moss TL, Pampati V. Radiation exposure to the physician in interventional pain management. *Pain Physician* 2002; 5:385-393.
305. Hopayiank K, Mugford M. Conflicting conclusions from two systematic reviews of epidural steroid injections for sciatica: which evidence should general practitioners heed? *Br J Gen Pract* 1999; 49:57-60.