Spinal Injections for the Diagnosis and Treatment of Chronic Pain

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Pain arising from the spine continues to be a challenging and vexing problem in terms of diagnostic assessment and implementation of therapeutic measures designed to modulate it. There are significant economic, social and health impacts of chronic spinal pain. There are multiple distinct potential and diverse pain generators that may be functioning individually or in tandem to produce a unique pain experience in any given individual. The present discussion will be limited due to space constraints to pain emanating from the cervical and lumbar spinal regions. Additionally, the interventions discussed will include the following: cervical interlaminar and transforaminal injections and medial branch blocks; lumbar interlaminar, caudal and transforaminal injections and medial branch blocks; and sacroiliac joint injections. Admittedly, this is merely a concise overview of an extremely complex topic. The interested reader is referred to the reference section for a somewhat more comprehensive bibliography.

Nature and Scope of the Problem
Chronic pain consists of pain that persists for a minimum of six months following an injury or disease process, extending beyond the typical course of healing of the underlying process, which is associated with chronic pathologic processes that cause continuous or intermittent pain indefinitely, even continuing in the absence of pathology, which may never heal. Prevalence of chronic pain is 2-40% of adults and the lifetime prevalence of spinal pain is 54-80%. The surgical treatment of spinal pain includes more than 285,000 laminectomy/discectomy and close to 300,000 fusion procedures/year in the USA, at an aggregate cost of approximately 15 billion dollars. The utilization of non-surgical remedies including injection therapies are also trending upwards according to CMS data, and represent more than one million lumbar epidural and transforaminal injections/year, costing over sixty-five million dollars. Return to work may be accomplished in many cases by aggressive pain management strategies. This has been demonstrated in a military population exposed to interventional pain management procedures. Recommendations have been published concerning the work-up and treatment of individuals with chronic spinal pain to enhance patient education and improve patient care in terms of shortening the course of the pain experience. The decision on selecting candidates for interventional pain management is typically made following a comprehensive history and physical examination and a demonstration of pathological findings of diagnostic imaging and electrodiagnostic studies. Also, most interventions do not stand alone as pain relieving modalities but actually function as one part of a multifaceted treatment regimen. Evidence from large meta-analyses suggests that spinal pain treatment where radicular pain is present reaches Level I for caudal epidural block; Level II-1 or II-2 for cervical or lumbar facet joint injections for facet joint mediated pain; Level II-1 for cervical interlaminar epidural injections for upper extremity radicular pain; and Level II-1 for lumbar transforaminal (TFESI) epidural injections for radicular pain of the lower extremities using the USPSTF criteria.

Rationale for Lumbar (LESI), Caudal Epidural and Transforaminal Steroid Injections (TFESI) (Figures 1, 2)
Lumbar spinal pain may be localized (LBP), facet-joint mediated, emanate from the intervertebral discs, or it may be radicular, among other etiologies. Lumbar approaches to managing radicular pain typically involve interlaminar injections (Figure 1A-B), caudal injections (Figure 1C-D) or transforaminal injections (Figure 2). The disc has a rich innervation primarily in its outer third of the annulus with elements being contributed by the sinuvertebral nerve, gray rami communicantes, and lumbar ventral rami. Nerves in discs contain calcitonin-gene-related peptide (CGRP), vasoactive intestinal peptide (VIP), Substance P, prostaglandins (Phospholipase A2), histamine, lactate and potassium, each of which is characteristic of nociception. Even so, lavage of the epidural space in volunteers suffering with acute radicular pain did not reveal presence of the aforementioned mediators. However, elevated serum hs-CRP may be an indicator in responsiveness to steroid epidural administration. Steroids remain the most commonly injected chemicals for radicular pain and include Methylprednisolone acetate (MPA), Triamcinolone and Betamethasone. Clearly, steroid epidural injections do not alter herniated disc (HNP) regression. However, steroids may modify enzyme activity and may decrease inflammation by stabilizing leukocyte lysosomal membranes; preventing release of destructive acid hydrolases from leukocytes; inhibiting
macrophage accumulation in inflamed areas; reduce leukocyte adhesion to the capillary endothelium; reducing capillary wall permeability and edema formation; decreasing complement components; antagonizing histamine activity and release of kinins; reducing fibroblast proliferation and collagen disposition; and possibly other mechanisms as well.27

Alternatives to steroids for radicular pain management include epidural administration of TNF-alpha28-30, Indomethacin31, Autologous Conditioned Serum32, as well as intradiscal administration of steroids33, or hypertonic dextrose 50%.34 Spine surgeons do not uniformly refer patients for injection therapy for radicular pain regardless of etiology of the pain.35 More procedures are performed in the Southern USA than in the Northeast. Injection rates are positively correlated with lumbar surgery rates.36

Lumbar, Caudal and Transforaminal Injections (ESI) for Managing Radicular Leg Pain (Figures 1, 2)

*Lumbar epidural injections* may be accomplished using one of three basic approaches-interlaminar, caudal or transforaminal. Steroid injections may be a simple, cost-effective and minimally invasive treatment for sciatic type pain.37 Early meta-analysis data suggested that convincing evidence was lacking for injection therapies in terms of managing low back or radicular pain.38 Some studies suggested ESI were inferior to simple saline injection.39 A newer meta-analysis suggested that evidence for TFESI use in radicular pain was strong; caudal ESI moderate, and LESI limited or inconclusive.40 For degenerative disc disease (DDD) LESI were shown to be beneficial for pain and functional improvement.41 For large HNP, surgical discectomy was shown to be superior to LESI for reducing symptoms.42 Fluoroscopic guidance enhances delivery of steroid to the target of interest.43 LESI seem more effective in the short-term, than for long-term benefit with evidence for short term use being strong for LESI, caudal ESI, and TFESI and moderate for TFESI in long-term pain management.44-49 HNP location and grade of nerve root compression as assessed by pre-procedure MRI may determine clinical outcome following LESI, although spinal canal dimension was found not to be predictive of success or failure of LESI in spinal stenosis.50 In a joint clinical practice guideline from the American College of Physicians and American Pain Society, imaging studies were felt only necessary with severe or progressive neurologic deficits or if patients were deemed candidates for LESI.51 A typically-quoted duration of action of LESI is 3-months.52 LESI done intraoperatively during spinal surgery was shown not to affect outcome in terms of reducing radicular pain although they do appear to shorten the duration of hospital stay when performed in recent laminectomy patients.53 While some would advocate performing a “series” of LESI for radicular pain, the evidence appears scant to support this practice routinely, and in fact, the use of opioids may increase in those who receive 3 or more LESI.54 When 3 LESI are performed, however, it appears that separating the injections by 10 day intervals provides superior pain relief to performing them every 24 hours.55 There appears to be an unresolved conflict in the medical literature concerning the relative efficacy of LESI and other spinal pain treatments, with some authors noting insufficient evidence to support their use in general and others noting substantial benefit from some, but not all therapies.61 Several review articles are available to discuss the relative merits of these treatments.62,63

*Figure 1-A, 1-B; A: L5-S1 Interlaminar Parasagittal Epidural Steroid Injection Showing Unilateral Spread of 3 mL of Contrast and Multiple Nerve Roots Including L3, L4, L5, S1 on the Right. B: Lateral Image of Contrast Spread for Interlaminar Parasagittal Epidural Steroid Injection.*
Caudal Approaches (Figures 1C-1D): The caudal application of local anesthetics for treating sciatic pain dates back to more than 100 years ago\textsuperscript{63}. Steroids in volumes from between 10 mL to 64 mL have been injected through the sacral hiatus, with 10 mL being necessary to attain spread to the L5 segment and 15 mL necessary to reach L4\textsuperscript{64}. The caudal approach is certainly a viable alternative to TFESI when attempting to place medication at a target level in patients who have had previous spinal surgery, which obviates the possibility of interlaminar techniques due to the surgical scar. Studies show a reduction in pain, improved physical functioning, and lowering of opioid usage, persisting up to six months in almost 50% of patients receiving between one and three injections for radicular pain\textsuperscript{65}. When compared to targeted steroid placement onto the affected nerve root using spinal endoscopy, caudal ESI using 11 mL volumes proved superior in terms of analgesia\textsuperscript{66}. Caudal ESI is equally effective for HNP at L4-5 or L5-S1\textsuperscript{67}, and for bilateral radicular pain due to degenerative lumbar spinal stenosis\textsuperscript{68}. Caudal injection with or without steroids (lidocaine 0.5%) appear effective for LBP (70%)\textsuperscript{69}; radicular pain (up to 91% success for average of 35 weeks)\textsuperscript{70}; failed-spine-surgery-syndrome (FBSS) (pain relief in up to 70% and functional status improvement in 55% of patients)\textsuperscript{71}; lumbar spinal stenosis (SS) (60% success rates)\textsuperscript{72}; with the evidence reaching Level I when caudal ESI is done for HNP or radicular pain and discogenic pain alone, and Level I or II-1 when used for FBSS with adhesiolysis\textsuperscript{61}. Even water-for-injection (WFI) proved effective for treating LBP and sciatic pain following caudal administration\textsuperscript{73}. Some have advocated adding hypertonic saline to local anesthetic and steroid for adhesiolysis in SS patients using a caudal technique. Results include pain relief in ¾ of patients for up to one year\textsuperscript{74}. In a retrospective NASS telephone survey of 216 caudal recipients treated for SS, 87.5% improved with a series of injections\textsuperscript{75}. Up to 50 mL of solution injected extends to mid-lumbar segments in a majority of subjects\textsuperscript{76}.

![Caudal Epidural Steroid Injection](image)

Figure 1-C and 1-D: C: Caudal Epidural Steroid Injection With Bilateral S1, S2 and S3 Nerve Root Spread of 5 ML of Contrast Through A Catheter. D: Lateral Image of Contrast Spread for Caudal Epidural Steroid Injection.

Transforaminal Approaches (Figures 2-A, 2-B): Transforaminal techniques have become extremely popular over the past decade or so for treating unilateral radicular pain, while improving standing and walking tolerance in degenerative SS\textsuperscript{77}. Prospective studies showed 84% success rates vs. 48% for trigger-point injections (TPI) in LBP with radiculopathy\textsuperscript{78}. TFESI have shown efficacy for FBSS, SS, and L-S radiculopathy for up to one year or more\textsuperscript{79}. While ventral epidural (88%) and nerve root filling (97%) may occur, intravascular injection may complicate the procedure\textsuperscript{80} which may be missed up to 57% of the time with static fluoroscopy techniques\textsuperscript{81}. TFESI may reduce the requirement for spinal surgical disc decompression\textsuperscript{82}, especially for sciatica symptoms < 6 months in duration\textsuperscript{83}. With injected volumes $\geq$ 0.5 mL, there is no guarantee that TFESI are “selective” to a single specified nerve root level\textsuperscript{84}. Volumes of $\geq$ 2 mL attain ventral epidural spread (i.e., “the target for nociception”) between 75-100% of the time\textsuperscript{85,86}. However, interlaminar techniques have been described which are modifications of standard midline approaches that demonstrate attainment of ventral epidural spread in 100% of cases without the 10% incidence of intravascular injection reported for TFESI\textsuperscript{86,87}. Unilateral epidural spread is attained using interlaminar techniques by
placing the needles parasagittally instead of midline. Interpretation of contrast dispersion may be affected by the experience of the observer, however. In direct comparisons of efficacy of TFESI with interlaminar injections for treating L-S radicular symptoms, some studies have shown superior results from TFESI, while others have shown no difference whatsoever when modifications were undertaken either to the LESI or TFESI component. It is possible that bilateral TFESI may be more effective than single-injection LESI in terms of placing medication into the ventral epidural compartment, provided the LESI is undertaken as a midline, and not parasagittal technique. A recent, but retrospective analysis suggested that both LESI and TFESI were superior in providing pain relief than caudal ESI for SS or HNP, results which are in agreement with previous work but not with meta-analyses of these techniques. Although TFESI may result in surgical sparing in some, selected patients, plasma disc decompression may provide superior pain relief for contained HNP.

**Figure 2-A and 2-B:** A: A-P and B: Lateral Images of Fluoroscopically-Guided Lumbar Transforaminal Steroid Injection. A Left-Sided Approach at the L4-L5 Level was undertaken. Three mL of Iodine-Based Water Soluble Contrast Outlines the Left L4 and L5 Nerve Roots and Extends into the Ventral Epidural Space.

**Complications of Lumbar Epidural Techniques:** Numerous complications from lumbar LESI, TFESI and caudal ESI have been reported and may be procedure-related, medication-related, or patient-related. Glucocorticoids suppress insulin action and should be used cautiously in diabetics, and betamethasone injection LESIs by various routes result in elevation in glucose levels in diabetics lasting approximately 2 days. There is no relationship between cumulative MPA dose and bone mineral density in healthy adults. A single dose of MPA epidurally can cause Cushing’s Syndrome and steroid psychosis has been reported. Rare ocular complications include chorioretinopathy or acute retinal necrosis and transient blindness. Air injected during the LOR technique may cause gas embolism or pneumocephalus if the dura is entered. Central effects include persistent hiccups, bilateral 6th nerve palsy, dysphonia, and facial flushing. Intradiscal injection occurs following both TFESI and LESI but occurs 12 times more commonly in the former case than the latter. Dural puncture and subdural injection occur following both LESI and TFESI, but are more common in the former than the latter. More serious complications include infections including discitis and epidural abscess formation and meningitis, intravascular injections from TFESI, epidural and subdural hematoma formation, cauda equina syndrome, and paralysis and death, primarily from TFESI.

**Cervical Transforaminal (CTFESI) and Interlaminar (CESI) Injection (Figures 3-A, 3-B; 4-A, 4-B):** Treatment of radicular cervical spinal pain may be accomplished using CTFESI or CESI. The strength of evidence using the USPSTF criteria favoring CESI is II-1, with success rates up to 77%. Fluoroscopy improves accuracy of needle placement for interlaminar CESI while ventral epidural spread is noted in between 28%-93% of midline CESI. Depth from skin to the cervical epidural space is > in males and at C6-7 averages 5.1 ± 0.6 cm; in females it is 4.6 ± 0.6 cm with mean width of epidural space of 3 mm (1-4 mm). Some fat (1-2 mm) may be found at C7-T1 but not above that level. At C6-7, 4-6 mL injected will spread up to C-2. The ligamentum flavum may not fuse midline so a lateral fluoroscopic view is important to obtain. Performing CESI using minimal to no
sedation may limit subsequent complication development, particularly since cord penetration may be somewhat
painless155, 158-60. Injection should be undertaken slowly since rapid injection into constricted areas may lead
to neurological complications61 although injection for SS seems to lead to improved outcomes162 and contrast may
spread 3.61 ± 0.84 levels163. It is likely that neurological problems following CEFI occur only after MPA use and
the hanging drop technique164-7. Vascular uptake may occur during CEFI interlaminar injections168-9. While some
suggest that the incidence of complications following CEFI (0.52%-16.8%) is not different than from CTFESI170,
this, as well as the severity of complications after each, is in dispute171. Minor complications include syncope,
headache and facial flushing172-3. Other complications include granuloma formation174; subdural injection175;
pneumocephalus176; epidural and subdural hematoma177-9; epidural abscess180-1; paralysis182; and stroke183. In
summary, it appears that CEFI do help resolve pain and provide short-term benefits in a majority of patients with
HNP184-6.

CTFESI have also been used to treat radicular arm pain. When fluoroscopy is used, intravascular (venous or
arterial) injection occurs 63.4% of the time187, representing a > three-fold higher incidence than previously
reported188. Digital Subtraction Angiography (DSA) may detect twice as many intravascular injections189.
Observational studies suggest that up to 30% of patients receiving CTFESI obtain complete pain relief (CPR) while
30% obtain partial, but lasting relief190. Dural puncture rates are equivalent to interlaminar CEFI191. Some studies
show relatively low rates of minor and transient complications from CTFESI, occurring especially with anterior
needle placement170,192-3, while cadaveric dissection reveals ascending and deep cervical arterial branches entering
the posterior foramen, the classic target site194-6. It appears CTFESI may be more dangerous than previously
reported197 and indeed, there have been cases of temporary198 as well as permanent neurological sequelae199-203 and
death204 during particulate steroid203,205 administration.

Figure 3-A and 3-B: Cervical Transforaminal Injection: A-P View and Lateral Views. A: Right-Sided Approach
at C5-C6 in a Patient With Previous History of Anterior Spinal Discectomy and Fusion Surgery Demonstrates Contrast Spread
Along the Right C-6 Nerve Root. Lighter Shading Represents a Previously Performed Right-Sided C-5 Nerve Root Injection
Cephalad to the Level Represented in these Images. B: Lateral Oblique View of Right

C-6 Nerve Root Spread.

Figure 4-A and 4-B: Cervical Interlaminar Epidural Injection at C6-C7: A-P and Lateral Views. On A-P Imaging
the Needle is Seen Entering the Interlaminar Space in the Midline as Defined by the Dorsal Spinous Processes. On Lateral View, The Spread of 3 mL of Contrast Extends Along the Dorsal Epidural Space for Multiple Levels to C3-C4.
Facet Joint Pain: Role of Cervical Medial Branch Blocks (Figures 5A-5B). The strength of evidence using the USPSTF criteria with 5 levels of evidence (range Level I to III with 3 subcategories in Level II) for accuracy of diagnostic facet joint nerve blocks (MBB) is Level I or II-1 in the diagnosis of lumbar (LMBB) and cervical facet joint pain (CMBB) and is Level II-1 or II-2 for therapeutic cervical and lumbar facet joint nerve blocks61. The rationale for performing these blocks is that pain generators include free and encapsulated nerve endings with nerves containing Substance P and CGRP. The facet joint capsule contains low threshold mechanoreceptors, mechanically sensitive nociceptors and silent nociceptors206. Neck pain following trauma is due to facet joint pain in about 20% of patients207-8. Pain is referred and may be mapped out with the C3-4 and C5-6 levels most commonly affected209,210. False positive rates following single-diagnostic blocks may be 45%211. Early meta-analysis suggested that radiofrequency ablation (RFA) of the medial branches was limited for both cervical and lumbar spinal pain212, but was later found to be moderate (Level III)213. Complications occur with greater frequency if fluoroscopy is not used for CMBB214, as even with fluoro guidance, intravascular injection occurs in up to 4%215. Smaller volume blocks using 0.25 mL of LA may improve precision and accuracy216. Steroids added to local anesthetic do not provide superior pain relief to LA alone217 and intraarticular injections are not indicated in the C-Spine218. RFA of CMB may provide 38 weeks of analgesia using continuous energy techniques219,220, and up to 60 weeks when only successes are considered221-22. When RF of the third occipital nerve (TON) is performed for cervicogenic HA, results may last 10 months, while ataxia, numbness and dysesthesias may develop223; for RF of the DRG of C4, C5, C6, duration of analgesia (DOA) may be 6 weeks224. Pulsed RF techniques may provide analgesia by augmenting C-fos225 and MIB-1 activity226.

![Figure 5-A and 5-B: Cervical Medial Branch Blocks: Lateral and A-P Views Of Three Needles Placed on the Left Side at C3, C4 and C5 Levels, for Block of the C3-C4 and C4-C5 Facet Joint Innervation. Needles sit on the Trapezeoid, Center of the Articular Pillars.](image)

![Figure 6-A and 6-B: A-P and Lateral Views of Lumbar Medial Branch Blocks: A-P and Lateral Views of Four Needles Placed on the Left at L3, L4, L5 and the Sacral Ala.](image)
Lumbar Medial Branch Techniques (Figures 6A-6B): Lumbar facet joint pain (zygapophyseal or “Z” joint) affects up to 15% of patients with axial LBP. Literature supporting the use of diagnostic lumbar facet and MB nerve blocks is controversial. Some meta-analyses purport that there is strong evidence in support of diagnostic Lumbar MBB in terms of accuracy of diagnosing facet joint pain (not MB nerve) are not supported by the preponderance of literature. Some have advocated pre-procedural CT scan (SPECT) as a diagnostic measure to determine suitability for FJB or MBB. With careful patient selection, RF of the lumbar MB may provide effective analgesia lasting many months. Cryolesioning offers alternatives to RFA in selected patients, as well.

Sacroiliac Joint Injections (Figures 7A-7B): As a true synovial joint, the sacroiliac joint (SIJ) is a pain-sensitive structure richly innervated by a combination of unmyelinated free nerve endings and the posterior primary rami of L2-S3. Several muscles have their insertion into the SIJ and include the piriformis; biceps femoris; gluteus maximus and minimus; erector spineae; latissimus dorsi; thoracolumbar fascia; and the iliacus, and any of these may be involved in SIJ related pain. Still, the diagnosis of SIJ pain is difficult to make unequivocally. Intraarticular SIJ injections underestimate the prevalence of SIJ pain due to the influence of extraarticular sources. Furthermore, single-site, single-depth sacral lateral branch injections are not consistent in providing analgesia of the SIJ, while multi-site, multi-depth injections are effective in up to 70%. Double diagnostic SIJ blocks may reduce the false-positive rate of single diagnostic blocks from 20%, but even so, the evidence for short-term and long-term relief from SIJ injections and RF procedures is limited. Recently, SIJ injections have been noted to be effective in cases of spondyloarthropathy. L4-5 dorsal rami and S1-3 lateral branch, water-cooled RF may be provide superior analgesia vs. placebo.

Figure 7-A and 7-B: Sacroiliac Joint Injection: Before and After 3 mL of Contrast Administration, Right-Sided; Oblique Fluoroscopy Angle.

References