

Letter to the Editor

RE: The risks of epidural and transforaminal steroid injections in the spine: Commentary and a comprehensive review of the literature

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Dear Editor,

We read with interest the comprehensive literature review and commentary by Dr. Epstein of the risks of epidural and transforaminal steroid injections in the spine.^[5] While this manuscript appears to be comprehensive, we are concerned with the lack of evidence in the opinions offered. We disagree with Dr. Epstein's understanding of the literature and makes unusual claims discrediting all interventional techniques even though the title says "epidural and transforaminal steroid injections in the spine." Further, the author appears to not recognize that transforaminal injections and caudal epidural injections are in facet epidural injections.^[8,9]

Dr. Epstein has selected all the negative studies and provided seemingly erroneous interpretations of other literature leading to what we believe are best termed inappropriate conclusions. It would appear that her focus may have been on the contaminated epidural steroid injections resulting in meningitis. However, she postulated a multitude of other issues based on incidence of infection from contaminated steroids, projecting that epidural injections are typically short-acting and ineffective over the long-term, exposing patients to major risks and complications, with delay in surgery. Even the very unusually high and unimaginable complications she is describing in these manuscripts of adhesive arachnoiditis of 6-16%, intravascular injections, etc., along with other life-threatening complications are not based on the literature she has reviewed. Even with the extraordinary statements re: Complications in interventional pain procedures, they may well be

less when compared with the risks of intraspinal fusion devices in which Dr. Epstein described maximal complication rates of 38%, reoperation rates of 85%, poor outcomes in 77%, along with high costs of the device.^[7] Additionally, per Dr. Epstein many operations that are recommended are not necessary or are too complex.^[6]

The author, in the description of complications and outcomes of interlaminar and transforaminal epidural injections, seems to use the manuscript of facet joint nerve blocks by Manchikanti *et al.*^[20] alleging 11.4% intravascular injury and 76.3% bleeding. This would be a gross misinterpretation of that study. There was no intravascular injury described in this manuscript by Manchikanti *et al.*,^[20] which rather described intravascular entry, unrelated to epidural injections.

An assessment of outcomes should describe at least all randomized trials. Instead Dr. Epstein appears to have picked only a few studies with negative results. Based on inadequate utilization of literature, she describes that patients are subject to major life-threatening risks, while delaying potential requisite surgery. Per above, prior reports by Dr. Epstein of surgical complications are enormous.^[7]

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Overall this manuscript would be appropriate for describing the infectious complications based on contaminated steroid injection. Multiple manuscripts in literature^[8,10-16,18,19,21-26] have shown equal effectiveness of epidural injections on a long-term basis, along with facet joint nerve blocks, even though that was not the subject of this review, and have shown significant improvement with outcomes of at least 50% pain relief with functional status improvement of 50% over a period of 2 years. A recent systematic review also confirmed these findings.^[3]

Multiple complications related to transforaminal epidural injections are justifiable;^[8,9] however, these complications are related to mainly cervical epidural injections and based on the radicular entry and injection of particulate steroids. The author seems to make multiple statements not substantiated by literature. This trend extended to the clinical effectiveness, complications, and also costs and provides misinterpretations. She quotes Manchikanti *et al.*^[20] as providing a multitude of data, which was not related to this manuscript or to other manuscripts.^[17] The author has also made multiple statements regarding financial incentives not described in any of the manuscripts.

The author also describes two major types of epidural spinal injections, translaminar and transforaminal; however, there is also a caudal epidural injection. In assessment of the efficacy of epidural injections, one would review all the literature; however, this review is lacking focus on selective literature and using the literature related to the complications in the efficacy. She also described one study by Manchikanti;^[14] which was a positive study, and made no comments. Parr *et al.*^[27] is cited in reference to short-term pain relief for disc herniation and radiculitis and evidence was lacking for both short- and long-term treatment from an earlier systematic review published in 2009 rather than using the manuscript published by Benyamin *et al.*^[1] In fact, recent guidelines^[8] and multiple systematic reviews^[1,2,4,9,28] have provided similar evidence for interlaminar epidural injections, caudal epidural injections, and lumbar transforaminal epidural injections performed in interventional pain management settings under fluoroscopy with proper selection of patients. However, there is no evidence for transforaminal cervical epidural injections.

Overall, this manuscript is confusing. It is our opinion that it provides multiple elements of misinformation rather than evidence-based opinions.

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TO THE EDITOR

Query

We read with interest the comprehensive literature review and commentary by Dr. Epstein of the risks of epidural and transforaminal steroid injections in the spine.^[5] While this manuscript appears to be a comprehensive, we are concerned with the lack of evidence in the opinions offered.

Response from Dr. Epstein

The individual writing the letter to the editor comments that this manuscript just appears “to be comprehensive,” I would respond that it includes 43 references, and covers over 62 manuscript (prior to pdf) pages [Table 1]. Furthermore, the data predominantly include a summary of different authors’ findings, rather than just Dr. Epstein’s subjective conclusions. Therefore, there is no “lack of evidence” as the so called “opinions” offered are actually the data from multiple articles written by the various authors.

Query

We disagree with Dr. Epstein’s understanding of the literature and makes unusual claims discrediting all interventional techniques even though the title says “epidural and transforaminal steroid injections in the spine.” Further, the author appears to not recognize that transforaminal injections and caudal epidural injections are in facet epidural injections.^[8,9]

Response from Dr. Epstein:

I would ask the author of this query, where are the “unusual claims discrediting all interventional techniques? In each section, the data cited comes from the various studies written by multiple authors [Table 1].

One example of this comes from the following section entitled: *Increase of 160% of Steroid Injections Over 10 Years Driven by Aging/Desperate Patients and Monetary Considerations*

Here, Dr. Manchikanti, Chairman of the American Society of Interventional Pain Physicians observed: “We

are doing too many of these (spinal injections), and many of those don’t meet the proper criteria”.^[25] He further observed, “about 20 percent of doctors who perform the procedures were not adequately trained.” When reviewing Medicare records, he found that the frequency of these injections increased by 160% from 2000 to 2010. He attributed this to the needs of older patients in desperate need of pain relief, and by financial incentives. “Medicare and private insurers pay \$100 to several hundred dollars for an injection, and there are pain clinics that do almost nothing but injections.”^[25] Here, an expert in the field is clearly stating that there has been a marked increase in the incidence of these injections performed, and that many are done that “don’t meet the proper criteria”. Those are the words of Dr. Manchikanti; they are they are not Dr. Epstein’s words. Furthermore Dr. Manchikanti himself brings up the financial incentive. Perhaps a closer analysis/review of the article would change the mind of the author of this QUERY.

Query

Dr. Epstein has selected all the negative studies and provided seemingly erroneous interpretations of other literature leading to what we believe are best termed inappropriate conclusions.

Response from Dr. Epstein

Again, if you look at the article, there are many studies that presented both the pros and cons for performing these injections [Table 1].

Presentation of Multiple Articles Supporting the Use of Epidural and Transforaminal Injection

For example, under the section *Indications for Epidural and Transforaminal Injections*, Dr. Epstein presented Landa *et al.* findings, citing two major types of epidural spinal injections employed in the cervical and lumbar regions; translaminar (TLESI) and transforaminal (TFESI) approaches.^[19] The translaminar procedure is utilized to address more diffuse symptoms, while the transforaminal approach is employed to directly treat a single nerve root. Note that Dr. Epstein did not edit out Landa *et al.* positive conclusions. In fact she quoted Landa *et al.* who found that these injections

demonstrated “efficacy for up to 6 months of pain relief, though long-term benefits are less reliable.”^[19] Dr. Epstein also did not exclude Dr. Landa’s acknowledgement that “these injections can also result in severe complications.” Landa *et al.*’s words were included to present Landa’s balanced views, and his statements/conclusions were not Dr. Epstein’s “erroneous interpretations.”

Query

It would appear that her focus may have been on the contaminated epidural steroid injections resulting in meningitis.

Response from Dr. Epstein

Indeed, one of the purposes of this commentary was to review the data surrounding the “epidemic” of contaminated epidural steroid injections performed in 2012 [Table 1]. In the manuscript, under *News of Infections Attributed to Epidural/Transforaminal Steroid Injections*, the Morbidity Mortality Weekly Report of the Centers for Disease Control and Prevention published on October 19, 2012 the following statement: Multistate outbreak of fungal infection associated with injection of methylprednisolone acetate solution from a single compounding pharmacy (United States, 2012).^[12] The Tennessee Department of Health was alerted that a patient tested positive for *Aspergillus fumigatus* meningitis 46 days after an epidural steroid injection (preservative-free methylprednisolone acetate solution (MPA) that had been “compounded at New England Compounding Center (NECC) in Framingham, Massachusetts.” By October 10, 2012, the CDC, multiple health departments, and the Food and Drug Administration (FDA) found 137 cases and 12 deaths in 10 states. By October 29, 2012, the Center for Disease Control had identified 25 deaths due to epidural steroid-related meningitis (many due to *Aspergillus*), with 337 patients sickened in 18 states, and an additional 14,000 patients likely exposed to contaminated steroids.^[3]

These data, as documented by the references, had already been published in major national newspapers and other medical journals prior to being presented in this commentary. The purpose of presenting this information to spine surgeons and others who read *Surgical Neurology International Spine Supplement* (a free downloadable internet journal) was to highlight what can happen if contaminated steroid material is injected in the spine, thus focusing attention on whether these “invasive” procedures are necessary, and whether the inherent risks warrant the benefits. Furthermore, attention was focused on the lack of uniform regulations for many of these compounding pharmacies, a shortfall which contributed to the epidemic of epidural steroid (ESI)-related infections. Under the title: *The Failure to Adequately Regulate Specialty Pharmacies* the failure to adequately regulate specialty pharmacies is the present focus of

discussion, as “greenish black foreign matter” and “white filamentous tissue” have been found in contaminated vials of steroids.^[3] The New York Times also reported in October of 2012 “greenish-yellow residue on sterilization equipment, surfaces coated with levels of mold, and bacteria that exceeded the company’s own environmental limits” in one of the specialty pharmacies.^[29]

Additionally, Dr. Epstein cited OTHER authors who emphasized OTHER complications attributed to epidural steroid injections (ESIs) beyond contamination/infection. Under the section *News of Meningitis Attributed to Epidural/Transforaminal Steroid Injections Plus Other Risks of Nerve Damage, Paralysis, and Strokes*, Pollack noted that the recent outbreak of fungal meningitis resulted from epidural/transforaminal spinal injections, but also highlighted that these “same injections have also long been linked to other rare but devastating complications, including nerve damage, paralysis and strokes.”^[3,29] He specifically detailed that epidural injections utilizing steroids, “while approved for uses like relieving inflammation in joints, have not been approved by the FDA for epidural injections, next to the spinal cord.”^[29] Also referring to those who died of meningitis, Dr. William Landau, professor of neurology at Washington University in St. Louis, Missouri, noted: “Not only were these people killed, but there was no ethical reason to give this treatment.”^[29] So in short, Dr. Epstein cited other authors’ concerns regarding not only fungal meningitis associated with ESI, but also regarding ESI’s other complications.

Query

However, she postulated a multitude of other issues based on incidence of infection from contaminated steroids, projecting that epidural injections are typically short-acting and ineffective over the long-term, exposing patients to major risks and complications, with delay in surgery.

Response from Dr. Epstein

Actually, in order to provide balance to this review article, Dr. Epstein included reviews/sections from at least 15 studies favoring epidural steroid injections. This “review article”, therefore, was hardly “one sided” [Table 1].

Pros for Epidural Steroid Injections: References to 15 Articles With Summary of 3 of the 15

Under the section *Benefits for the Efficacy of Epidural Injections, Utility of Epidural Steroid Injections in Averting Surgery in Patients Originally Deemed Surgical Candidates*, Riew *et al.* designed a prospective, randomized, controlled, double-blind study to determine how effective selective nerve root injections utilizing steroids vs. bupivacaine alone could be in avoiding surgery for patients with demonstrated “surgical” disc herniations.^[30] All 55 patients had radiculopathy that

Table 1: Sections and summaries

News of Infections Attributed to Epidural/Transforaminal Steroid Injections The Failure to Adequately Regulate Specialty Pharmacies New England Compounding Center	The Center for Disease Control (October 29, 2012) reported 25 deaths due to meningitis, 337 patients sickened in 18 states, and an additional 14,000 patients probably exposed to contaminated steroids. ^[12] Greater Food and Drug Administration regulation of compounding centers is warranted to avert such exposures/outbreaks in the future
News of Meningitis Attributed to Epidural/Transforaminal Steroid Injections Plus Other Risks of Nerve Damage, Paralysis, and Strokes Frequency of Epidural/Transforaminal Fluoroscopic Spinal Injections Interlaminar Lumbar Epidural Injections Increase of 160% of Steroid Injections Over 10 Years Driven by Aging/Desperate Patients and Monetary Considerations	Epidural/transforaminal spinal injections may not only result in fungal meningitis, but are also associated with other devastating complications, that include nerve damage/paralysis, and strokes Rosas <i>et al.</i> note estimated frequency of low back pain/sciatica is prevalent, accounting for 13% (the second most common) reason for (medical) office visits in the US. ^[34] Dr. Manchikanti, Chairman of the American Society of Interventional Pain Physicians, observed that there has been a 160% increase in epidural injections from 2000 to 2010, and that too many are being performed without meeting proper criteria. Furthermore, 20% of physicians performing these procedures are not adequately trained. He raised the issue of “financial incentives” being responsible for this marked increase in procedures
Indications for Epidural and Transforaminal Injections	Landa <i>et al.</i> defined two major types of cervical and lumbar spinal injections; the translaminar (TLESI) and transforaminal (TFESI) approaches. ^[19] The former best addresses diffuse symptoms, while the latter; typically focus on single nerve root pathology
Benefits for the Efficacy of Epidural Injections Utility of Epidural Steroid Injections in Averting Surgery in Patients Originally Deemed Surgical Candidates	In a prospective, randomized, controlled, double-blind study involving 55 patients with lumbar radiculopathy, more patients receiving selective nerve root injections of bupivacaine with betamethasone vs. bupivacaine alone opted over the long-term (13-28 months) for nonoperative management (“success”). ^[30]
Minimal Complications of 10,000 Fluoroscopic-Guided Epidural Injections	Manchikanti <i>et al.</i> determined that in 10,000 fluoroscopic-guided epidural injections, the risk of intravascular complications was highest for adhesiolysis (11.6%) and lumbar transforaminal procedures (7.9%), while the frequency of dural punctures was 0.5% (highest for adhesiolysis 1.8% followed by thoracic procedures). ^[26]
Efficacy of Lumbosacral Transforaminal Steroid Injections 30% or Greater Reduction in Radicular Pain with Transforaminal Epidural Injections Utilizing Three Different Doses of Dexamethasone	Ahadian <i>et al.</i> documented the comparable safety and efficacy of transforaminal epidural injections utilizing 4 mg (33 patients), 8 mg (33 patients), and 12 mg (32 patients) of Dexamethasone at 4, 8, and 12 weeks postinjection. ^[2] By the 12 th postinjection week, VAS scores declined to 26.6%, the ODI showed minimal residual findings, and there were no adverse events
Evidence Based Literature Documents Efficacy of Lumbosacral Transforaminal Steroid Injections Performed Under Fluoroscopy or CT Guidance Efficacy of Multiple Types of Spinal Injections, Including Transforaminal Epidural Steroids In Resolving Radicular Pain	Benny <i>et al.</i> documented that lumbosacral transforaminal injections (8 of 10 randomized control studies and 9 prospective trials) performed under CT or fluoroscopic guidance injections showed positive short- and long-term outcomes. ^[6] Roberts <i>et al.</i> identified nine randomized studies which utilized fluoroscopy to perform transforaminal epidural steroid injections for the treatment of radiculopathy. ^[32] They noted that TFESI were not only better than placebo, but also superior to interlaminar and caudal injections. The one exception was subacute/chronic radiculopathy, where a single TFESI was as effective as a single transforaminal injection of bupivacaine or saline
Better Outcomes with Transforaminal Epidural Steroid Injections vs. Interlaminar Injections for Lumbar Disc Disease Greater Effectiveness of Bilateral Transforaminal Epidural Steroid Injections for Treating Patients with Spinal Stenosis	Schaufele <i>et al.</i> retrospectively analyzed the efficacy of TFESI vs. TLESI, and found that those undergoing TFESI experienced better resolution of pain, required fewer subsequent injections, and fewer subsequent operations. ^[37] Bilateral TFESI produced more effective control of symptoms in patients with spinal stenosis (SS) vs. TLESI. ^[20] This was likely attributed to higher concentrations of steroids achieved in the ventral epidural space vs. dorsal compartment which is typically occupied by not only scar and fibrosis, but marked ossification/hypertrophy of the yellow ligament that blocks steroid dissemination
Comparable Efficacy of Different Spinal Injections Comparable Efficacy of Epidural Steroid Injections vs. Intramuscular Injections of Steroids with a Local Anesthetic	In the Wilson-MacDonald <i>et al.</i> study, 93 patients who were considered potential surgical candidates, exhibited comparable 2-year outcomes (Oxford Pain Chart and ODI) utilizing epidural steroid injections or intramuscular injections of steroids combined with a local anesthetic. ^[42] They found no substantial difference over the longer term, and the incidence of subsequent surgery was similar for both groups

(Contd...)

Table 1: Continued

Relative Efficacy of Caudal Epidural Injections with Local Anesthetic With or Without Steroids	In a 2-year randomized, double-blind, controlled trial of fluoroscopic caudal epidural injections (with or without steroids), Manchikanti <i>et al.</i> concluded that both types of injection were an effective treatment for a select group of patients who have chronic function-limiting low back and lower extremity pain secondary to central spinal stenosis. ^[24]
Blind (without Fluoroscopy) Interlaminar Spinal Epidural Steroid Injections Provide Short-term Relief for Disc Herniations and Radiculitis But Not Spinal Stenosis	Epidural steroid spinal injections performed blindly (without fluoroscopy), are one of the most common procedures performed in the US for chronic low back pain. Although Parr <i>et al.</i> demonstrated short-term pain relief for disc herniations and radiculitis, the evidence is lacking for both short and long-term treatment of spinal stenosis. ^[28]
Risks of Epidural/Transforaminal Epidural Spinal Injections Limited Efficacy of Injections	Deyo observed that in multiple clinical trials utilizing epidural spinal injections performed at the University of Washington, that "seven clinical trials showed the injections were helpful, another seven found them no better or even worse than a placebo, and three (had) unclear results." ^[3]
Epidural Steroid Injections Provide No Additional Improvement	Valat <i>et al.</i> compared the efficacy of epidural steroid injections vs. isotonic saline, finding that "the efficacy of isotonic saline administered epidurally for sciatica cannot be excluded, but epidural steroid injections provide no additional improvement." ^[39]
Epidural Steroids Offer No Significant Functional Benefits or Reduction in the Need for Surgery	Carette <i>et al.</i> , in a double-blind, randomized trial, determined that for 158 patients with herniated discs evaluated utilizing the ODI at 3, 6, 12 weeks. and 1 year following injections, that even if epidural methylprednisolone resulted in some short-term benefits, it offers no significant functional benefit, nor does it reduce the need for surgery. ^[10]
Epidural Steroids Offer No Sustained Benefits or Reduce the Need for Surgery	Arden <i>et al.</i> evaluated the efficacy of three ESI vs. interligamentous saline injections (3 weeks apart) in patients with unilateral sciatica for 1-18 months. ^[5] They found that ESI offered transient benefit in symptoms at 3 weeks in patients with sciatica, but no sustained benefits in terms of pain, function or need for surgery
Rare Major But Common Minor Complications of Fluoroscopic Facet Joint Nerve Blocks.	Manchikanti <i>et al.</i> reported on 43,000 intermittent fluoroscopically guided facet joint nerve blocks injections performed during 7500 visits, and observed the following complications: intravascular injection (11.4%), local bleeding (76.3%), oozing (19.6%), local hematoma with profuse bleeding (1.2%) with less than 1% experiencing other complications (e.g., dural puncture, spinal cord irritation, infection). ^[25]
Safety of Cervical Epidural Steroid Injections Comparable Long-term Efficacy of Cervical Epidural Steroid Injections Performed with/without Morphine	Castagnera <i>et al.</i> noted that long-term results (48 postinjection months) did not differ between two patient groups with nonsurgical cervical disease, receiving one dose of epidural steroids without (S) and with Morphine Sulfate (S+M). Success rates were 78.5% (S), and 80% (S+M), while specific pain relief was also comparable (86.8% (S) and 86.9% (S+M)). ^[11]
Minimal Complications of Cervical Epidural Steroid Spinal Injections Performed Under Fluoroscopy	In the Botwin <i>et al.</i> series involving 157 patients undergoing 354 cervical epidural steroid injections at the C6-C7 or C7-T1 levels, although 16.8% of patients exhibited complications, none required hospital stays or developed persistent morbidity. ^[9]
Few Complications of Cervical Epidural Steroid Injections	Abbasi <i>et al.</i> concluded that a review of the literature revealed 0-16.8% incidence of complications associated with cervical epidural spinal injections, but acknowledged that the design of most studies was suboptimal (e.g., future prospective, randomized studies were warranted). ^[1]
Efficacy and Safety (64%) of Cervical Epidural Steroids for Radiculopathy	Rowlingson and Kirschenbaum series, performing 45 cervical epidural steroid injections in 25 patients with cervical radiculopathy, resulted in 64% incidence of good or excellent responses. ^[35]
Few Complications Attributed to 1036 Extraforaminal Cervical Nerve blocks	Performing 1036 extraforaminal cervical nerve blocks in 844 patients resulted in no major but 14 (1.66%) minor complications that more frequently occurred with deep rather than superficial injections. ^[23]
Rare Cervical Complications Following 790 Steroid Epidural Nerve Blocks	Waldman evaluated 215 patients undergoing 790 cervical epidural nerve blocks, finding 2 dural punctures, 3 vasovagal events, and 1 delayed superficial infection. ^[40]
Risks of Cervical Epidural Steroid Injections No Long-standing Benefit of Epidural Steroids/Local Anesthetic vs. Sterile Saline/Local Anesthetic	In the Anderberg <i>et al.</i> prospective randomized study of 40 patients undergoing either cervical ESI/local anesthetic vs. sterile saline/local anesthetic, at 5 postinjection weeks, patients receiving steroid injections had less pain, but not over the longer-term. ^[4]
Permanent Neurological Complications (e.g., Quadriplegia) Associated with Cervical Epidural or Transforaminal Steroid Injections	Scanlon <i>et al.</i> cited 8 instances of inadvertent intravascular injections leading to brain and spinal cord injury and identified an additional four cases of major particulate corticosteroid embolic injury to the cerebellum and brainstem in the literature. ^[36] In their own survey of members of the American Pain Society, the 21.4% response rate (287 of 1340) revealed 78 complications including 16 vertebral brain infarcts, 12 cervical spinal cord infarcts, and 2 combined brain/spinal cord infarcts, with 13 fatal outcomes

(Contd...)

Table 1: Continued

Clinical Example of Irreversible Paraplegia Secondary to Adhesive Arachnoiditis	In Rodriguez Luna <i>et al.</i> reported that adhesive arachnoiditis occurs in between 6% and 16% of patients having primary or revision lumbar surgery. ^[33]
Clinical Example of Postoperative Spinal Adhesive Arachnoiditis Resulting in Hydrocephalus and Equina Syndrome	Koerts <i>et al.</i> reported that 86% of cases of spinal adhesive arachnoiditis occur in the lumbar region, and are due to: Contamination of the subarchnoid space with blood (e.g., CSF leak/dural tear), infection, myelography (especially oil-based), epidural steroid injections, spinal surgery (disc/stenosis), and trauma. ^[18]
Increased Risks of Adhesive Arachnoiditis and Subdural Hematoma with Epidural Blood Patch for Postdural Puncture Headaches in two Patients	Riley and Spiegel documented subdural hematoma and subdural hematoma with adhesive arachnoiditis with chronic sacral radiculopathy as the result of utilizing large volume epidural blood patches in two respective patients with postdural puncture headaches. ^[31]
Direct Contraindications for Epidural Steroid Injections	Direct contraindications to performing epidural steroid injections include prior surgery and infection
Costs of Epidural Injections: Facility and Physician Fees	Many insurance companies motivate physicians (with higher reimbursements) to perform epidural injections in their office (typically without fluoroscopy, which is often not reimbursed yet costs \$100.00) to avoid facility fees. Fees quoted for nerve blocks ranged from \$83 in an ASC vs. \$183 in an office, while those for epidural injections performed in an ASC averaged \$107 vs. \$247 in an office; facility fees varied typically from \$300 to \$650. ^[27]
Conclusion	<p>Epidural Injections Are the Most Common Nerve Blocks</p> <p>Increased Frequency of Epidural/Transforaminal Injections</p> <p>Epidural/Transforaminal Injections are Ineffective</p> <p>Comparable Efficacy of Epidural Steroids vs. Epidural Saline Injections</p> <p>Comparable Outcomes and No Reduction in Need for Surgery</p> <p>Risks of Epidural/Transforaminal Injections</p> <p>Risks of Meningitis</p> <p>Facet Joint Injections: Ineffective and Associated with Multiple Complications</p> <p>Complication Rate 0-16.8% for Cervical Epidural/Transforaminal Injections</p> <p>Specific Risks of Inadvertent Intravascular Injections Leading to Brain/Cord Injury</p> <p>Risk of Quadriplegia with Intramedullary Cervical Injection</p> <p>Risk of Adhesive Arachnoiditis</p> <p>Animal Series</p> <p>Clinical Series</p> <p>Insurers Promoting Unsafe Practices</p>

CSF: Cerebrospinal fluid, CSF: Cerebrospinal Fluid, TLESI: Translaminar lumbar epidural steroid injections, TFLEI: Transforaminal lumbar epidural steroid injections, ESI: Epidural steroid injections, ASC: Ambulatory surgical center, SEA: Spinal epidural abscess

correlated with radiographically documented surgical disease (e.g. herniated discs). Patients were randomly selected for selective nerve-root injection with bupivacaine vs. bupivacaine with betamethasone, and could choose to receive up to 4 injections. Over the follow-up duration of 13-28 months, 9 of 27 patients receiving bupivacaine alone, but a higher 20 of 28 receiving bupivacaine with the steroid, decided against surgery (defined as a "success"): this difference was significant ($P < 0.004$). The authors projected that in the future, more patients with radiculopathy (1-2 level discs) should first undergo selective nerve-root injections with corticosteroids before opting for surgery.

A second study concerned the *Minimal Complications of 10,000 Fluoroscopic-Guided Epidural Injections*. It was authored by Manchikanti *et al.* and was a prospective, nonrandomized study involving 10,000 patients who over 20 months received: 39% caudal epidurals, 23% cervical interlaminar epidurals, 14% lumbar interlaminar epidurals, 13% lumbar transforaminal epidurals, 8% percutaneous adhesiolysis, and 3% thoracic interlaminar

epidural procedures."^[26] All procedures were performed in an Ambulatory Surgical Center (ASC) by three physicians. Intravascular complications were greater for adhesiolysis (11.6%) and lumbar transforaminal (7.9%) injections vs. 0.5% for lumbar, 3.1% for caudal, 4% for thoracic, and 4.1% for cervical epidurals. Dural punctures, observed in 0.5% of patients occurred in the following: 1% cervical, 1.3% thoracic, 0.8% lumbar, and 1.8% adhesiolysis. The authors concluded that major complications were rare, but minor side effects were common.

A third study by Ahadian *et al.* noted the *Efficacy of Lumbosacral Transforaminal Steroid Injections: 30% or Greater Reduction in Radicular Pain with Transforaminal Epidural Injections Utilizing three Different Doses of Dexamethasone*. Ahadian *et al.*'s prospective, randomized, double-blind trial, the relative efficacy of transforaminal epidural injections utilizing 4 mg (33 patients), 8 mg (33 patients), and 12 mg (32 patients) of Dexamethasone were studied at four time intervals: 1, 4, 8, and 12 weeks postinjection.^[2]

A 30% or greater reduction in radicular pain utilizing the Visual Analog Scale (VAS) was considered a “success”. Other outcome measures included the: Oswestry Low Back Disability Index (ODI), Subject Global Impression of Change, Subject Global Satisfaction Scale, and adverse events (AE). Over the 4, 8, and 12 postprocedure weeks, the average reduction in radicular pain based on the VAS was 41.7%, 33.5%, and 26.6%, respectively. The ODI revealed minimal residual findings by the 12th week after injection, and no AE were encountered. They concluded that results were comparable for all three-dosage groups, and that Dexamethasone was both safe and effective for transforaminal injections.

There were many other sections/articles as cited below that reviewed additional “pros” for different types of spinal injections. These included:

Evidence-Based Literature Documents Efficacy of Lumbosacral Transforaminal Steroid Injections Performed Under Fluoroscopy or CT Guidance by Benny and Azari.^[6]

Efficacy of Multiple Types of Spinal Injections, Including Transforaminal Epidural Steroids In Resolving Radicular Pain by Roberts *et al.*^[32]

Better Outcomes with Transforaminal Epidural Steroid Injections vs. Interlaminar Injections for Lumbar Disc Disease by Schaufele *et al.*^[37]

Greater Effectiveness of Bilateral Transforaminal Epidural Steroid Injections for Treating Patients with Spinal Stenosis by Lee *et al.*^[20]

Comparable Efficacy of Different Spinal Injections; Comparable Efficacy of Epidural Steroid Injections vs. Intramuscular Injections of Steroids with a Local Anesthetic by Wilson-MacDonald *et al.*^[42]

Relative Efficacy of Caudal Epidural Injections with Local Anesthetic With or Without Steroids by Manchikanti *et al.*^[24]

Blind (without Fluoroscopy) Interlaminar Spinal Epidural Steroid Injections Provide Short-term Relief for Disc Herniations and Radiculitis But Not Spinal Stenosis by Parr *et al.*^[28] Safety of Cervical Epidural Steroid Injections

Comparable Long-term Efficacy of Cervical Epidural Steroid Injections Performed with/without Morphine by Castagnera *et al.*^[11]

Minimal Complications of Cervical Epidural Steroid Spinal Injections Performed Under Fluoroscopy by Botwin *et al.*^[9]

Few Complications of Cervical Epidural Steroid Injections by Abbasi *et al.*^[1]

Efficacy and Safety (64%) of Cervical Epidural Steroids for Radiculopathy by Rowlingson and Kirschenbaum^[35]

Few Complications Attributed to 1036 Extraforaminal Cervical Nerve Blocks by Ma *et al.*^[23]

And there are other sections as well. Therefore the accusation that Dr. Epstein only “projected that epidural injections are typically short-acting and ineffective over the long-term, exposing patients to major risks and complications, with delay in surgery” was simply not true as the 16 articles cited above will attest to.

Under the section *Risks of Epidural/Transforaminal Epidural Spinal Injections*, Limited Efficacy of Injections, Dr. Epstein also presented the “cons” from other studies/articles. One article noted that ESI were “typically short-acting and ineffective over the long-term, exposing patients to major risks and complications, with delay in surgery.”^[3] Dr. Epstein directly cited Dr. Deyo’s comment that despite the increase in steroid spinal injections, “people with back pain are reporting more functional and work limitations, rather than less.”^[3] Dr. Deyo further cited a University of Washington study in which “seven clinical trials showed the injections were helpful, another seven found them no better or even worse than a placebo, and three (had) unclear results.”^[3] Dr. Deyo also observed other risks of these injections that included: Infection, injections into the spinal fluid, intravascular injections, nerve damage, hemorrhages, and arachnoiditis. Again, these were not my quotes, but rather quotes from others that did not reflect a purely one-sided view.

In another section, *Epidural Steroid Injections Provide No Additional Improvement*, Valat *et al.*’s article compared the efficacy of epidural corticosteroid injections (2 mL prednisolone acetate (50 mg)) vs. 2 mL isotonic saline (both administered ×3) for patients with sciatica for between 15 and 180 postinjection days.^[39] In 42 patients in the control group (CG), and 43 in the steroid-treated cohort, finding “the efficacy of isotonic saline administered epidurally for sciatica cannot be excluded, but epidural steroid injections provide no additional improvement.”^[39] In another section, *Epidural Steroids Offer No Significant Functional Benefits or Reduction in the Need for Surgery*, Carrette *et al.*, in a double-blind, randomized trial, determined that for 158 patients with herniated discs evaluated utilizing the ODI at 3, 6, 12 weeks, and 1 year following injections, that even if epidural methylprednisolone resulted in some short-term benefits, it “offers no significant functional benefit, nor does it reduce the need for surgery.”^[10] In the section *Epidural Steroids Offer No Sustained Benefits or Reduce the Need for Surgery*, Arden *et al.* evaluated the efficacy of three ESI vs. interligamentous saline injections (3 weeks apart) in patients with unilateral sciatica for 1-18 months.^[5] They found that ESI offered transient benefit in symptoms at 3 weeks in patients with sciatica, but no sustained benefits in terms of pain, function, or need for surgery. In the section *Risks of*

Cervical Epidural Steroid Injections, No Long-standing Benefit of Epidural Steroids/Local Anesthetic vs. Sterile. Anderberg *et al.* found in their prospective randomized study of 40 patients undergoing either cervical ESI/local anesthetic vs. sterile saline/local anesthetic, that at 5 postinjection weeks, patients receiving steroid injections had less pain, but not over the long-term.^[4] In the section *Permanent Neurological Complications (e.g. Quadriplegia) Associated with Cervical Epidural or Transforaminal Steroid Injections.* Scanlon *et al.* cited eight instances of inadvertent intravascular injections leading to brain and spinal cord injury and identified an additional four cases of major particulate corticosteroid embolic injury to the cerebellum and brainstem in the literature.^[36] In their own survey of members of the American Pain Society, the 21.4% response rate (287 of 1340) revealed 78 complications including: 16 vertebrobasilar brain infarcts, 12 cervical spinal cord infarcts, and 2 combined brain/spinal cord infarcts, with 13 fatal outcomes. In yet another section entitled *Risks of Inadvertent Intravascular Injections During Under Attempted Cervical Steroid Injections, Inadvertent “Vascular Injections” Result in Quadriplegia During Attempted Epidural Cervical Steroid Injections.* Bose *et al.* presented a patient who developed quadriplegia and a respiratory arrest following an attempted cervical epidural steroid injection at the C6-C7 level, concluding that it was likely a “vascular event” that left the patient with a major permanent neurological deficit.^[8] And like the “pros” section, many other “cons” were also presented.

Therefore, the “pros” and “cons” of ESI were presented from multiple articles as detailed above, indicating that this review article was indeed, not simply one-sided; that accusation is clearly spurious [Table 1].

Query

Even the very unusually high and unimaginable complications she is describing in these manuscripts of adhesive arachnoiditis of 6-16%, intravascular injections, etc., along with other life-threatening complications are not based on the literature she has reviewed. Even with the extraordinary statements re: Complications in interventional pain procedures, they may well be less when compared with the risks of intraspinal fusion devices in which Dr. Epstein described maximal complication rates of 38%, reoperation rates of 85%, poor outcomes in 77%, along with high costs of the device.^[7] Additionally, per Dr. Epstein many operations that are recommended are not necessary or are too complex.^[6]

Response from Dr. Epstein

The complication rates that I cited in this review article were those drawn directly from the literature. Indeed, I have written over 300 original and/or review articles/

chapters on multiple subjects that similarly provide careful assessment of the appropriate literature. I am glad, however, to see that the QUERY, author has read some of these articles. Nevertheless, I fail to see their relevance in the context of this discussion.

Query

The author, in the description of complications and outcomes of interlaminar and transforaminal epidural injections, seems to use the manuscript of facet joint nerve blocks by Manchikanti *et al.*^[20] alleging 11.4% intravascular injury and 76.3% bleeding. This would be a gross misinterpretation of that study. There was no intravascular injury described in this manuscript by Manchikanti *et al.*,^[20] which rather described intravascular entry, unrelated to epidural injections.

Response from Dr. Epstein

I have already responded in prior sections regarding the complications of these injections, which do, however, include intravascular injuries resulting in quadriplegia [Table 1]. The sections relevant to this include the following; Under the section *Permanent Neurological Complications (e.g. Quadriplegia) Associated with Cervical Epidural or Transforaminal Steroid Injections,* Scanlon *et al.* cited eight instances of inadvertent intravascular injections leading to brain and spinal cord injury and identified an additional four cases of major particulate corticosteroid embolic injury to the cerebellum and brainstem in the literature.^[36] In their own survey of members of the American Pain Society, the 21.4% response rate (287 of 1340) revealed 78 complications including: 16 vertebrobasilar brain infarcts, 12 cervical spinal cord infarcts, and 2 combined brain/spinal cord infarcts, with 13 fatal outcomes. The next section dealt with *Risks of Inadvertent Intravascular Injections During Attempted Cervical Steroid Injections, Inadvertent “Vascular Injections” Result in Quadriplegia During Attempted Epidural Cervical Steroid.* Injections in which Bose *et al.* noted that 64-76% of patients undergoing cervical epidural steroid injections for pain/radiculopathy subjectively improved, and major adverse events (AE) attributed to these injections were rarely reported in the literature.^[8] They felt that few clinicians report AE (due the risk of medicolegal suits and other factors), but also that few journals accept such case reports, much less those with negative outcomes. Bose *et al.*'s patient developed quadriplegia and respiratory arrest following an epidural steroid injection at the C6-C7 level and remained unchanged at 6 postinjection months. The injection was performed by “a fellowship-trained pain management specialist in an outpatient surgicenter using C-arm fluoroscopic guidance.”^[8] Despite the patient's quadriplegia, Magnetic resonance (MR) studies performed 6 h after the injection and 6 months later failed to show

any significant radiographic findings. The authors attributed the deficit/quadruplegia to an intravascular injection (“vascular event”). In another section, *Transforaminal Cervical Injection Resulted in Vascular Infarction to Cord*, following a left C6 transforaminal epidural steroid injection, Ludwig’s 53-year-old patient developed left arm and bilateral lower extremity weakness, and MR confirmed intramedullary cord signal changes within 24 h from the odontoid to the C4-C5 levels consistent with diffuse vascular infarction.^[22] In the section *Inadvertent “Intravascular Injections” of Cervical Local Anesthesia Result in Transient Quadriplegia*, Karasek and Bogduk noted the adverse consequences of performing a C6-7 transforaminal injection utilizing local anesthesia that resulted in an inadvertent injection into a cervical radicular artery.^[17] Their patient’s immediate quadriplegia resolved within 20 min; however, had this been a steroid injection, particulate matter may have acted as an embolus and caused a permanent injury. In another section: *Cardiac Arrest Due to Cervical Epidural Steroid Injection* Stabuer and Nazair’s 67-year-old female patient following a C6-C7 epidural cervical steroid injection sustained pneumocephalus and a cardiopulmonary arrest.^[38] The latter was likely attributed to blockade of the sympathetics resulting in bradycardia/arrest.

There are multiple other sections that continue to review complications from other studies. *In yet another section, Multiple Complications of Epidural or Transforaminal Injections*

Multiple Complications of Epidural/Transforaminal Injections Are Often Underreported

Landa *et al.* noted that serious complications of epidural/transforaminal spinal injections are often underreported.^[7,14,15,19,41,43] Risks of epidural/transforaminal injections include: infection, epidural hematoma (0-1.9%), intravascular injections, nerve damage, cerebrospinal fluid (CSF) fistulas/headaches, air embolism, urinary retention, allergic reactions, seizures, blindness, and others.^[7,14,15,19,41,43]

Of interest, the multiple sections of this review article were overwhelmingly devoted to assessment of different articles, and were not simply my opinion pieces. I did offer, however, one short section *Author’s Personal Communication with Pediatric Neurosurgeons* regarding personal communication with pediatric neurosurgeons regarding a 16-year-old female who following a cervical epidural injection performed by an outside physician became quadriplegic. The MR immediately demonstrated a fluid signal within the cord itself, consistent with a direct intramedullary cord injection. Despite treatment with hyperbaric oxygen, she did not fully recover (personal communication).

Query

An assessment of outcomes should describe at least all randomized trials. Instead Dr. Epstein appears to have picked only a few studies with negative results. Based on inadequate utilization of literature, she describes that patients are subject to major life-threatening risks, while delaying potential requisite surgery. Per above, prior reports by Dr. Epstein of surgical complications are enormous.^[7]

Response from Dr. Epstein

I have already demonstrated that I did not just “pick only a few studies with negative results” [Table 1]. If the QUERY individual believes this, then he/she has not read the article carefully. Furthermore, I already presented the multitude of articles reflecting both the pros as and cons of ESI. Finally, the QUERY individual’s last comment is not even relevant to the discussion.

Query

Overall this manuscript would be appropriate for describing the infectious complications based on contaminated steroid injection.

Response from Dr. Epstein

Thank you for this comment.

Query

Multiple manuscripts in literature^[8,10-16,18,19,21-26] have shown equal effectiveness of epidural injections on a long-term basis, along with facet joint nerve blocks, even though that was not the subject of this review, and have shown significant improvement with outcomes of at least 50% pain relief with functional status improvement of 50% over a period of 2 years. A recent systematic review also confirmed these findings.^[3]

Response from Dr. Epstein

As indicated in the review article, there are many articles that demonstrate the lack of long-term effectiveness [Table 1].

Query

Multiple complications related to transforaminal epidural injections are justifiable;^[8,9] however, these complications are related to mainly cervical epidural injections and based on the radicular entry and injection of particulate steroids. The author seems to make multiple statements not substantiated by literature.

Response from Dr. Epstein

The multiple sections and articles citing intravascular injections resulting in major neurological deficits have already previously been quoted [Table 1]. These sections accurately report/summarize the data from the different references, and are not just the musings/opinions of the author. I invite you to read the primary sources, which

will substantiate the summaries I have provided in this review article.

Query

This trend extended to the clinical effectiveness, complications, and also costs and provides misinterpretations. She quotes Manchikanti *et al.*^[20] as providing a multitude of data, which was not related to this manuscript, nor other manuscripts.^[17] The author has also made multiple statements regarding financial incentives not described in any of the manuscripts.

Response from Dr. Epstein

I have already responded to similar comments made earlier. However, for your reference look again under *Increase of 160% of Steroid Injections Over 10 Years Driven by Aging/Desperate Patients and Monetary Considerations*. You will find that Dr. Manchikanti, Chairman of the American Society of Interventional Pain Physicians observed: “We are doing too many of these (spinal injections), and many of those don’t meet the proper criteria”.^[25] He further observed, “about 20 percent of doctors who perform the procedures were not adequately trained.” When reviewing Medicare records, he found that the frequency of these injections increased by 160% from 2000 to 2010. He attributed this to the needs of older patients in desperate need of pain relief, and by financial incentives. “Medicare and private insurers pay \$100 to several hundred dollars for an injection, and there are pain clinics that do almost nothing but injections.”^[25] It was clearly his statements above rather than my own as the quotes indicate. His concern regarding adequate training, adequate indications, and financial considerations are rather clear. This clearly, therefore, documents the inaccuracy of the Query’s last sentence.

Query

The author also describes two major types of epidural spinal injections, translaminal and transforaminal; however, there is also a caudal epidural injection. In assessment of the efficacy of epidural injections, one would review all the literature; however, this review is lacking focus on selective literature and using the literature-related complications in the efficacy. She also described one study by Manchikanti;^[14] that was a positive study, and made no comments. Parr *et al.*^[27] is cited in reference to short-term pain relief for disc herniation and radiculitis and evidence was lacking for both short- and long-term treatment from an earlier systematic review published in 2009 rather than using the manuscript published by Benyamin *et al.*^[1] In fact, recent guidelines^[8] and multiple systematic reviews^[1,2,4,9,28] have provided similar evidence for interlaminar epidural injections, caudal epidural injections, and lumbar transforaminal epidural injections performed in interventional pain management settings under fluoroscopy with proper selection of patients. However, there is no evidence for transforaminal cervical epidural injections.

Response from Dr. Epstein

I would recommend that the Query read the review article more carefully to find answers to these comments/questions/accusations [Table 1].

Query

Overall, this manuscript is confusing. It is our opinion that it provides multiple elements of misinformation rather than evidence-based opinions.

Response from Dr. Epstein

First of all, I would question the source of this conclusion. Second, the information provided comes from a multitude of studies gleaned from the literature, and included data regarding the pros and cons of these injections [Table 1]. I would strongly recommend that the Query author undertake a more concerted review of this article to fully glean its benefits.

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