

### Introduction

Mulligan and Rowlingson ( [11](#) ) in 2001, remarked: "Although possessing a long history of use, the therapeutic use of epidural steroid injections still needs substantiation."

### How they are performed:

Cervical, thoracic, and lumbar epidural injections can be approached through translaminar (interlaminar) and transforaminal injections.

The translaminar approach is in the midline or paramedian and requires the needle to penetrate skin, subcutaneous tissue, paraspinal muscles (paramedian approach) or interspinous ligament (midline approach), and ligamentum flavum.

The needle is advanced in an oblique approach until its tip touches the posterior lateral portion of the vertebral body, located superior to the intervertebral foramen just under the pedicle.

Transforaminal approach is performed by placing the needle in the neuroforamen (hole) ventral (anterior) to the nerve root.

In addition, there is a third possible approach for lumbar injections: caudal. This involves

inserting the needle through the sacral hiatus into the epidural space at the sacral canal.

Bevacqua, Haas and Brand ( [\[iii\]](#) ) investigated the depth of the posterior epidural space (ES). They found:

“The posterior ES has been found to be somewhat larger and more variable than previously described.

The findings provide clinical confirmation of recent radiologic and cadaveric studies, which portray a posterior ES of variable size and complex shape.

These findings have implications for cannulation and use of epidural therapy as well as for the combined catheter epidural and single-dose spinal technique.”

This emphasises the considerable variation between individuals, which makes accurate placement of drugs more difficult.

In patients who have had previous spinal surgery, there may be scarring in the epidural space, which further confounds accuracy of needle siting.

Mechanism of action: Lee et al. ( [\[iii\]](#) ) looked at the effects of steroids on prostaglandin phospholipase A2 in an animal model.

It is thought that some disc-related pain is due to inflammatory mediators such as this phospholipase.

They found that the level of phospholipase A2 activity was at its maximum at 1 week after

surgery in Groups I (saline injection, loose ligature of nerve root surgery) and IV (betamethasone 3 days after surgery).

It showed a steady reduction in the steroid group, whereas it remained relatively high and dropped rapidly after 3 weeks in the saline-treated group, and returned to the level of a normal nerve root at 6 weeks after surgery.

They suggested that the irritated nerve root was caused in part by a high level of phospholipase A2 activity initiated by inflammation, and that the mechanism of action of epidural steroid injection is inhibition of phospholipase A2 activity.

The other steroid groups (II and III) were given betamethasone 0.1 ml a day before surgery (II), or a day after (III). There was no significant difference in recovery time among steroid injection groups.

Epidural steroid injections are administered in an attempt to reduce inflammation of affected nerve roots.

Slucky et al. ( [iv](#) ), in their dog study, were unable to demonstrate any material effect of the steroid on the dura on the collagen matrix, although they did see a significant decrease in the number of intracytoplasmic mitochondria (cell energy generators) of dural fibroblasts in steroid-injected animals, suggesting a metabolic inhibitory effect.

Abram stated ( [v](#) ):

“Radiculopathy following disc herniation appears to be produced by either mechanical or chemical nerve root inflammation. Epidurally injected corticosteroids most likely exert a beneficial effect through anti-inflammatory rather than direct analgesic mechanisms.”

### Types of approach

Carrino et al. ( [\[vi\]](#) ) looked at spinal steroid injections in the US from 1993-1999. They found that

"Despite an overall increase in spinal injection procedure volume and reimbursement... nonradiologists performed most of these procedures. Epidural steroid and facet joint injections had the highest volume and reimbursement ... and were performed almost exclusively by nonradiologists (predominantly anesthesiologists)."

Cluff et al, at Massachusetts General Hospital, Boston, ( [\[vii\]](#) ) looked at practice of epidural steroid injection across the United States.

They noted:

"it is not clear whether there is consensus on their technical aspects. The current literature suggests that variations in technical aspects may affect ESI outcomes."

They found that private practices use significantly more fluoroscopy than academic centres, especially with cervical injections (73% of private practices compared with only 39% of academic institutions polled use fluoroscopic guidance).

After laminectomy 61% of private practices, but only 15% of academic centres, use the transforaminal approach. They concluded that there remains no consensus as to treatment and practice still varies widely.

Price et al. ( [\[viii\]](#) ) compared caudal and lumbar approaches. 93% of lumbar and 64% of caudal epidural injections were correctly placed. 97% of lumbar and 85% of caudal epidural injections, which were clinically judged as being correctly placed were confirmed radiographically.

In those where clinical judgement was uncertain (&quot;maybe&quot;), 91% of lumbar injections, but only 45% of caudal injections were found to actually correctly placed.

The authors suggested,

&quot;In the non-obese patient, lumbar epidural injections can be accurately placed without x ray screening, but caudal epidural injections, to be placed accurately, require x ray screening no matter what the weight of the patient.&quot;

Chen and Foye in an online article on epidural steroids updated in March 2002 ( [\[ix\]](#) ) noted that epidural injections using a caudal approach were first performed in 1901 when cocaine was injected to treat lumbago and sciatica.

In the 1920s-40s high volumes of normal saline and local anesthetics were used. Epidural corticosteroid injection as part of the conservative (non-surgical) management of lumbar radicular pain was first recorded in 1952.

The most commonly used steroid compounds include betamethasone sodium phosphate and betamethasone acetate (Celestone Soluspan), methylprednisolone acetate (Depo-Medrol), and triamcinolone hexacetonide (Aristospan).

Each millilitre of Celestone Soluspan contains 3 mg of highly soluble betamethasone sodium and 3 mg of the relatively insoluble acetate salt.

Thus, Celestone Soluspan provides both rapid onset and extended anti-inflammatory activity.

Depo-Medrol and Aristospan, in contrast, being relatively insoluble, provide a sustained anti-inflammatory effect.

As Chen and Foye pointed out, as injected methylprednisolone remains in situ for approximately 2 weeks, there should be a 2 week delay after the injection before assessment of the patient's response and administration of a repeat injection.

This interval could be shorter if an alternative, short-acting steroid had been used.

Debi et al. ( [\[x\]](#) ), in Israel, reported on a technique of applying 80 mg methylprednisolone acetate (Depomedrol) or the same amount (2 mL) of saline, soaked in 2.5 x 2.5 cm of collagen absorbable haemostat (Instat) that was left on the decompressed nerve root after lumbar laminectomy.

At 1 year post-op, no difference in outcome was reported. However, one should note that here again is a potential for arachnoiditis, with increased exposure time and a foreign body which could trigger an inflammatory reaction and hence, arachnoiditis.

### Fluoroscopy

Fluoroscopy is rather like the X-ray equivalent of a camcorder compared with a camera; instead of a static picture, there is a dynamic film from a continuous X-ray beam, transmitted to a monitor screen so that the doctor can observe the progress of the procedure.

It is used in various procedures, including cardiac catheterisation, barium studies etc.

Some authors advocate the use of fluoroscopy to ensure correct placement of epidural steroid injections. However, others point out that it is only with use of contrast agent that one can be sure not to have hit a blood vessel.

"As mentioned previously, reports suggest that injection without fluoroscopic guidance (i.e., blind injection) result in 30-40% of needle misplacement, including needle tip placement outside the epidural space (e.g., intravascular injection) and not at presumed level of pathological process.

Therefore, although it is not a standard, it is recommended that ESIs be performed under fluoroscopic guidance and with radiographic contrast documenting appropriate placement in order to improve safety, accuracy, and potential efficacy of ESIs." ([xi](#))

Fredman et al published a paper in February of 1999( [xii](#) ) in which they concluded that in cases of "failed back surgery syndrome" (for which ESIs are often used) "surface anatomy is unreliable and may result in inaccurate steroid placement.

Finally, despite accurate placement, the depot-steroid solution will spread to reach the level of pathology in only 26% of cases."

Renfrew et al, published their study in 1999( [xiii](#) ), and concluded that "fluoroscopy is essential for correct placement of epidural steroid injection."

The use of fluoroscopy has been adopted by the International Spinal Injection Society (ISIS). Firstly, in August 2000, Botwin et al ( [xiv](#) ) reported an incidence of 9.6% 'minor' complications per fluoroscopically guided transforaminal lumbar epidural injection.

Amongst these were: 8 cases of increased back pain (2.4% of the total participants), 2 increased leg pain (0.6%).

The authors did not report any major complications, but the follow up of only 1-3 weeks after each injection (a series being given over 4 months) would have failed to include such long term effects as arachnoiditis.

Furman et al ( [\[xv\]](#) ) published in *Spine* in October 2000 a study in which the authors contended that "there is a high incidence of intravascular injections in transforaminal ESIs that is significantly increased at S1."

They conclude that

"Fluoroscopically guided procedures without contrast confirmation are instilling medications intravascularly and therefore not into the desired epidural location."

As they point out, this requires that contrast injections should be performed in order to ensure correct placement of the steroid preparation.

More recently, Furman et al. ( [\[xvi\]](#) ) looked at the incidence of intravascular injection in cervical transforaminal injections.

They found out of 504 transforaminal epidural steroid injections, the overall rate of fluoroscopically confirmed intravascular contrast injections was 19.4%.

This was higher than for lumbosacral injections, confirming the need for fluoroscopic guidance.

The authors also recommended use of contrast agent to exclude positioning intravascularly.

Stitz and Sommer ( [\[xvii\]](#) ) looked at the accuracy of blind versus fluoroscopically guided caudal epidural injections in 54 patients.

Successful injection placement on the first attempt occurred in 74.1% of the patients, as confirmed by fluoroscopy.



The authors remarked that whilst

“Caudal epidural injection is performed ideally with fluoroscopic guidance as the gold standard for accurate drug placement,”

should fluoroscopy be impossible (contraindicated or not available),

“the presence of readily palpable anatomic landmarks at the sacral hiatus and the absence of palpable subcutaneous airflow over the sacrum significantly increase the operator's confidence in the likelihood of an accurate injection”.

This was based on their observations that using these criteria, injections were confirmed on fluoroscopy as being 87.5% and 82.9% accurate respectively.

However, that leaves over 10% inaccuracy, even allowing professional expertise at reading these signs.

Vad et al. ( [xviii](#) ) compared fluoroscopically guided transforaminal epidural steroid injections with saline trigger point injections in treating lumbosacral radiculopathy.

Their prospective study required pain reduction greater than 50% at least 1 year after treatment to class as successful outcome.

The group receiving transforaminal epidural steroid injections had a success rate of 84%, as compared with 48% for the group receiving trigger-point injections.

This indicates the possible success for epidural steroid injections provided fluoroscopic guidance is used. However, as we have seen, practice varies widely.

### EFFICACY:

Bernstein ( [\[xix\]](#) ) looked at injection therapies in chronic pain and concluded:

"There was limited evidence of effectiveness (level 3) of intraoperative steroid at discectomy, epidural steroid injection for sciatica with low back pain, caudal steroid injection for low back pain...There was limited evidence (level 3) that there is no additional benefit of adding steroid to local anesthetic in caudal epidural injections."

McQuay ( [\[xx\]](#) ) cites an NNT (number needed to treat one patient successfully) of 7.3 for greater than 75% pain relief in the short term(1-60 days) and 13 for more than 50% pain relief in the long term (12 weeks to 1 year). In comparison to adjuvant analgesics such as antidepressants and anticonvulsants, which have NNTs of between 2 and 3 for intractable neuropathic pain, ESIs are patently much less effective.

The recent Cochrane Review on Injection therapy for subacute and chronic benign low back pain concluded: "Convincing evidence is lacking on the effects of injection therapies for low back pain."( [\[xxi\]](#) )

In New Zealand in 2002, a statement on the use of ESIs, prepared for distribution to members of the NZ Society of Anaesthetists stated:

"We suggest epidural steroids should be offered only in acute cases of disc herniation or nerve root ("radicular") irritation with either symptomatic criteria and/or with minor neurological signs.....

Equivocal cases or those with major neurological signs should be fully investigated, with MRI if necessary, prior to referral.....

It is our opinion, supported by the literature, that in carefully selected cases epidural steroid injection can produce rapid and sustained pain relief.&quot;

In December 2001, a Finnish group published a paper in the prestigious journal Spine ( [\[xxii\]](#) ), in which the authors suggested that with use of a methylprednisolone-bupivacaine combination,

&quot;In the case of contained herniations, the steroid injection produced significant treatment effects and short-term efficacy...

For symptomatic lesions at L3-L4-L5... By 1 year, steroid seemed to have prevented operations for contained herniations&quot;

However, they noted that

&quot;For extrusions, steroid seemed to increase the operation rate.&quot;

They therefore concluded that steroids were &quot;counterproductive&quot; for extrusions.

This carries important implications in the cases where peridural injections are performed without the benefit of MRI diagnosis.

The diagnosis is critical: other sources of back and leg pain, including sacroiliac arthropathy, facet joint or myofascial pain are not likely to be relieved by this treatment. Patients who have had previous spinal surgery are unlikely to benefit, or those with long duration of symptoms, or spinal stenosis.

Fukusaki et al. ( [\[xxiii\]](#) ) evaluated the therapeutic effect of epidural steroids in lumbar

degenerative spinal canal stenosis.

They found that epidural block with saline (group 1) 8 ml of 1% mepivacaine (Group 2) or 8 ml of 1% mepivacaine and 40 mg of methylprednisolone Group 3. Results showed that there was no significant difference in the effectiveness of treatment between group 2 and group 3 throughout the time course.

In group 2, 55.5% showed a good or excellent result after 1 week, 16.7% after 1 month, and 5.6% after 3 months whereas in group 3, 63.2% after 1 week, 15.8% after 1 month, and 5.3% after 3 months.

They concluded that epidural steroid injection was not beneficial in combating pseudoclaudication (stenosis symptom of leg pain on walking).

Rozenberg et al ( [xxiv](#) ) reviewed 13 trials from 1996-1997. 5 trials showed some benefit, 8 found no measurable benefits.

Rosen et al ( [xxv](#) ) concluded in 1988, "overall results were poor", with only approximately 50% of patients receive temporary relief, whilst long-term relief occurs in less than 25% of patients.

Anderson and Mosdal ( [xxvi](#) ) found that epidural steroid injection was "useless" in patients with long-lasting complaints and previous disc operations.

This finding was also seen in the study by Cuckler et al ( [xxvii](#) ), which failed to demonstrate ESI efficacy, with the authors also raising the issue of published reports of "serious complications".

More recently, in 1997, Carette et al ( [xxviii](#) ) studied patients with prolapsed nucleus pulposus and found that epidural steroid

"offers no significant functional benefit, nor does it reduce the need for surgery," although there may be short-term improvement in pain and sensory deficit.

Ringsdal et al ( [xxix](#) ) proposed that

"future correctly designed studies are necessary to clarify whether the injection should be a supplement to the established treatment of low back pain and sciatica,"

as they found that previous studies showed conflicting results.

The NHMRC report ( [xxx](#) ) suggests that ESI are of greater use in sciatica when there is a substantial inflammatory component (especially if acute) but are less useful if there is a predominantly compressive radiculopathy.

The AHCPR Clinical Practice Guideline ( [xxxi](#) ) clearly states that

"Epidural injections are invasive and pose rare but serious potential risks. There was no evidence that epidural steroids are effective in treating acute radiculopathy."

Lafuma et al ( [xxxii](#) ) conducted a randomised multicentre study to evaluate the benefits and costs of routine epidural steroid injections , using the primary criterion of whether other treatments were required following 1 to 3 injections: they concluded "adding an epidural injection as a first-line treatment .....for the treatment of lumbosciatic syndrome requiring in-hospital management results in additional costs and no gain in efficacy."

Again, this viewpoint was echoed by Schneeberger et al in 1998( [xxxiii](#) ), who commented thus

"To the present time no conclusive data have been published to prove that these procedures reduced the need for surgery in the case of herniated nucleus pulposus or spinal stenosis.

Their efficacy on the intensity of pain is also controversial. Some improvement on pain and functional scores may be observed for a few weeks but this positive effect disappears 2 or 3 months post-injection."

The NZHTA Report in 2001 concluded:

"Because of the lack of definitive evidence (either way), or the lack of well designed trials, a solid foundation for the effectiveness of steroids is lacking."

### Adverse reactions

These were clearly outlined by Kaplan and Derby ( [xxxiv](#) ):

"Risks associated with needle placement or with the injection of diagnostic/therapeutic substances, including the local anesthetic and steroid suspension, include, infection, bleeding, nerve injury, transient numbness or weakness, paralysis, contrast reaction (allergy), adrenal suppression, and fluid retention with systemic manifestations which may include peripheral swelling.

Pneumothorax may occur if undergoing a thoracic procedure. Total spinal blockade is possible with cervical procedures.

There is also a potential for minor subcutaneous infection, vasovagal episode, as well as failure to obtain a definitive diagnosis or positive therapeutic injection with persistence of chronic pain."

Since the withdrawal of oil-based myelography, Depo-Medrone (Depo-Medrol) is one of the principal causes of adhesive arachnoiditis in the Western world.

Dr. Burton maintains that almost all diffuse cases of clinically significant adhesive arachnoiditis are caused by Depo-Medrone.

However, the scale of the problem has yet to be recognised within the medical profession:

The State of Colorado Invasive Treatment Procedures 1998 ( [\[xxxv\]](#) ) states that "permanent paresis (weakness), anaphylaxis (acute allergic reaction of a life-threatening degree) and arachnoiditis have rarely been reported with the use of epidural steroids."

McLain et al. ( [\[xxxvi\]](#) ) noted that although epidural steroids are "commonly applied", this type of therapy "is not inherently benign".

They reported a case of acute paraplegia resulting after an epidural injection carried out under fluoroscopic control, which was complicated by dural puncture.

Radiographic studies showed a focal space-occupying lesion which spontaneously resolved within 2-3 hours.

The patient recovered motor, sensory and bladder function over 48 hours.

There were 3 possible explanations:

1. Inadvertent atypical anaesthetic block,

2. Loculation of the injectate caused a transient compressive lesion,

3. Intrathecal injection may have produced an arachnoid cyst.

Although in itself beneficial, the drug is in a solution that contains preservatives such as polyethylene glycol (also used in antifreeze).

Nelson ( [xxxviii](#) ) states:

“Methylprednisolone acetate contains approximately 30 mg of polyethylene glycol per milliliter”

Other preparations such as Kenalog use benzyl alcohol.

It should be noted that alcohol is a recognised cause of toxic neuropathy, so adverse reactions are unsurprising.

The manufacturers, Upjohn, stated in 1981 that

“we would advise against the epidural/extradural routes of administration because of possible adverse reactions”.

However, this specific recommendation was withdrawn from the data sheet in 1997.

Upjohn included the following information in their 1988 data sheet:



"Adverse effects reported with some non-recommended routes of administration... Intrathecal/epidural: **arachnoiditis**, meningitis, paraparesis/paraplegia, sensory disturbances, bowel and bladder dysfunction, headaches, seizures."

Currently, literature on Depo-Medrone states that it is contraindicated for intrathecal administration and that it contains benzyl alcohol, which is potentially toxic when administered locally to neural tissue.

However, Bristol Myers Squibb, manufacturers of Kenalog, another steroid drug used in epidural injections, issues a data sheet stating

"not recommended for administration via the epidural route".

Both drugs remain unlicensed for use around the spine, the use being left to the individual doctor's discretion and clinical judgement.

Their use in the UK is extensive and epidural steroid injection (ESI) is practised by a variety of clinicians including GPs and specially trained physiotherapists.

In 1993, David Blunkett raised the issue of Depo-Medrone in Parliament, but the Government's response was

"The Department has issued no specific advice to doctors on this issue."

Later, in February of 1994, David Blunkett issued a news release calling for the halt of

"all unrecommended use of this drug (depo-medrone)".

The Clinical Affairs Committee of the British Society of Rheumatology issued a statement to its members (1994) on epidural injection of Depo-medrone, which advises that because of the risks attached; if a doctor wishes to use it INDIVIDUAL INFORMED CONSENT would have to be obtained, &quot;IN VIEW OF THE POTENTIAL SERIOUS COMPLICATIONS.&quot;

They also recommended avoiding use of Depo-Medrol, suggesting other preparations.

Unfortunately this is not being adhered to. Department of Health statistics for 1995 suggest that approximately 30,000 epidural injections were performed that year in the UK.

The numbers in the United States are likely to be considerably higher.

The most commonly used preparation in the UK is Depo-Medrone.

In 1995, a letter in the British Medical Journal with the title, &quot;A shot in the back&quot; ( [xx xviii](#) ), responded to a World in Action programme that investigated claims that the drug manufacturer had pressurised doctors into giving the drug by an unauthorised route.

The author concluded:

&quot;I had a clear impression that this was a specialised procedure to be used by experts and only by experts, entirely on their own responsibility.

The drug company, in my view, had been wise not to press for an extension of the approval to include the epidural route.

They have no control over the point of an anaesthetist's needle.&quot;

Nelson ( [\[xxxix\]](#) ) cites a 2.5% risk of inadvertent injection directly into the subarachnoid space.

The Mackinnon studies on rats ( [\[xl\]](#) ) showed that a variety of injectable steroids may damage peripheral nerves if injected directly into the nerve.

Furthermore, the NHMRC report from 1994 suggested that the risk of dural puncture is, on average, "at least 5%". The authors also warn,

"Particular care must be taken if attempting an epidural injection in patients previously treated by spinal surgery. Complete obliteration of the epidural space occurs following decompressive laminectomy and in such cases an attempted epidural injection carries a very high risk of dural tap."

Nelson maintains that

"the epidural space is not wholly separate from the subdural and/or subarachnoid space" and that the spaces are "not only contiguous, but continuous".

He therefore concludes that epidural delivery of drugs may not guarantee that the substance will remain isolated in the epidural space.

Byrod and Olmarker ( [\[xli\]](#) ) found evidence that the potential barrier properties of the dura/arachnoid "seem less than effective" for preventing substances in the epidural space from reaching the endoneural space of nerve roots.

Wood ( [\[xlii\]](#) ) studied the effects of injections of methylprednisolone acetate into rat sciatic nerves. Nerves treated with either the steroid or its vehicle showed damage, including collagen (scar) formation and demyelination.

Note that Crowhurst (in the context of epidural anaesthesia) maintains:

"A drug placed in the epidural space will be re-distributed into various other compartments...fat, connective tissues, blood, epineurium sheaths, nerve roots and the spinal CSF. Only a fraction of the drug reaches the thecal nerve roots, its intended target. ....Unfortunately, the remainder of the dose is not without its unwanted effects..." ( [\[xliii\]](#) )

Recently, Nelson and Landau ( [\[xliv\]](#) ) again raised in the medical arena, the issue of the safety of ESIs, although their recent letter in the New England Journal of Medicine dealt with the use of intrathecal methylprednisolone to treat postherpetic neuralgia, as studied by Kotani et al. ( [\[xlv\]](#) )

Nelson and Landau noted that chemical meningitis accounts for half the serious sequelae of a single intrathecal injection of methylprednisolone. (40-80mg).

Amongst the other adverse events, they cited cauda equina syndrome and chronic arachnoiditis, although they did concede that the latter was more often associated with multiple injections.

They very pertinently mention the neurotoxic preservatives in the steroid preparation.

This is taken up by the Editor of the Journal, Dr. Watson ( [\[xlvi\]](#) ) who, in his Editorial reply clearly states that the manufacturers, Pharmacia-Upjohn do not recommend their products either for intrathecal or epidural administration.

Whilst they concede that it is possible to manufacture a preservative-free preparation, they feel a delay before marketing is a substantial barrier i.e. it is not commercially advantageous to develop such a preparation.

A German practitioner, Dr. Henner Niebergall, of Freiberg, has questioned the use of a combination of methylprednisolone and lidocaine ( [\[xlvii\]](#) ).

He pointed out that:

"lidocaine is neurotoxic not only when injected into the nerves but also when injected intrathecally at concentrations greater than 2 percent."

Note that in most cases, epidural steroid injections involve a combination of local anaesthetic for immediate effect and steroid preparation for sustained anti-inflammatory action.

In reply, Kotani et al, the authors of the original study, remarked that they were fully aware that "intrathecal methylprednisolone can be neurotoxic" ( [\[xlviii\]](#) ).

They excluded patients with neurologic disease from the study, based on the observations that complications had been seen in multiple sclerosis patients.

They admitted that their consent form clearly stated in detail about

"the possibility of serious adverse effects, including life-long paralysis, exacerbation of pain, recurrence of herpes zoster, and even death."

More recently still, Marinangeli et al. in July 2002, published a paper ( [\[xlix\]](#) ) on the clinical use of epidural and spinal steroids.

The authors noted:

"Complications associated with intrathecal steroids are more frequent and severe than epidural injections and include: adhesive arachnoiditis, aseptic meningitis, cauda equina syndrome. Steroidal toxicity seems to be related to the polyethylenic glycol vehicle."

Nelson and Landau published a detailed account of the history of the use of intraspinal steroid preparations ( [\[ii\]](#) ) in 2001.

Whilst they stated that serious permanent complications including arachnoiditis are "a rare but certain risk", they went on to stress that

"We must conclude that the adverse drug reactions of intraspinal steroid therapy submitted to the FDA (and especially individual case reports in the literature) comprise only the ?tip of the iceberg."

Other reports of complications:

Recently, Parsons and Hawboldt reported on herpes zoster as a complication ( [\[iii\]](#) )

In 1997, Siegfried reported a case of CRPS (RSD) development after cervical epidural steroid injection.

This condition has similarities with arachnoiditis (see below). ( [\[lii\]](#) )

Jarrier et al. reported a case of Cauda Equina Syndrome. ( [\[liii\]](#) )

Staphylococcal meningitis and cauda equina syndrome were reported in a Canadian patient after a series of epidural steroid injections. ( [\[liv\]](#) )

Intrinsic cord damage as a result of 'pithing' the cervical cord with the needle has also been reported. ( [\[iv\]](#) )

Chronic arachnoiditis after use of paramethasone, a steroid available outside the USA, was reported in 1997. ( [\[vii\]](#) )

Enlargement of a chronic aseptic epidural abscess by epidural injections was reported by Sabel et al. ( [\[viii\]](#) ) who suggested:

"The frequent use of invasive procedures at the spinal cord such as epidural injections has led to an increased incidence of iatrogenic abscesses."

Temporary complications include retinal haemorrhage ( [\[viii\]](#) ) Young ( [\[ix\]](#) ) reported in 2002 on a case of transient blindness after lumbar epidural steroid injection.

The author noted that there had been 9 previous cases of retinal haemorrhages such as in this case.

Whilst the patient recovered most of his sight, he did not regain full sight. The author concluded:

"Transient blindness is a rare complication of lumbar epidural injection."

Gibran et al. ( [\[ix\]](#) ) reported a case of unilateral vitreous haemorrhage secondary to a caudal epidural injection, which they suggested was a variant of a condition known as Terson's syndrome.

Stoll and Sanchez ( [\[xi\]](#) ) reported a case of epidural haematoma after spinal puncture for

delivery of steroid, presenting 8 days after the procedure.

This has more usually been reported in association with impaired haemostasis (not seen in this case) and epidural anaesthesia.

Of note is the delay between procedure and clinical presentation, and the potential for later arachnoiditis due to the inflammatory properties of blood within the haematoma. ....

Other case reports of epidural haematoma include: ( [\[lxii\]](#) ; [\[lxiii\]](#) )

Reitman and Watters ( [\[lxiv\]](#) ) reported a fatality after a cervical epidural steroid injection. The patient developed an anterior subdural haematoma, which was surgically decompressed (and a patch applied), but she subsequently developed meningitis and succumbed to repeated cardiac arrests.

Conus medullaris syndrome was reported by Cohen in 1979, after multiple intrathecal steroid injections. ( [\[lxv\]](#) )

A further important point was raised by Lowell et al ( [\[lxvi\]](#) ) when they reported on 3 cases of epidural abscess after intrathecal methylprednisolone administered after discectomy.

They concluded that the use of perioperative epidural steroid injections may predispose to infection and that a prospective study is needed to examine the use of this procedure:

"Therapy was discontinued after an increased postoperative deep infection rate was noted."

There have been a number of case reports of epidural abscess. ( [\[lxvii\]](#) ; [\[lxviii\]](#) ; [\[lix\]](#) , [\[lxx\]](#) , [\[lxxi\]](#) )



O'Brien and Rawluk described an unusual case involving Mycobacterium organism. Histology of the excised inflammatory lesion showed chronic granulomatous inflammation. ( [\[lxxii\]](#) )

Kaul et al. ( [\[lxxiii\]](#) ) reported an extradural abscess in a 26 year old presenting as an external swelling.

Horlocker et al. ( [\[lxxiv\]](#) ) looked at patients taking non-steroidal inflammatory drugs (NSAIDs) who underwent ESIs, to evaluate any increased risk of haemorrhagic complications such as spinal haematoma.

In their series, only 28% of cases involved fluoroscopic guidance; paraesthesia was elicited in 3% and dural puncture occurred in 0.8%.

The mean volume of injectant was 8 +/- 3 mL. 61% included local anaesthetic agent (52% lidocaine, 9% bupivacaine).

The steroid used in 98% was triamcinolone.

Blood was noticed during needle or catheter placement in 5.2% of the patients (including frank blood in 12 patients), but NSAID therapy did not appear to affect the incidence of traumatic (bloody) tap.

The authors noted, however, that there was an increased frequency of minor haemorrhagic complications with increasing age, large gauge needles, needle placement at multiple interspaces, multiple needle passes, larger injectant volume and accidental dural puncture. 42 out of 1035 patients experienced new neurological symptoms or worsening of previous complaints; 18 had bilateral symptoms.

This was more common in women than men. It is unclear as to the extent of follow-up in these

cases.

The authors noted in their discussion that new antiplatelet drugs such as ticlopidine and clopidogrel have been associated with cases of spinal haematoma including one patient undergoing a series of epidural steroid injections.

Vandermeulen et al. ( [\[lxxv\]](#) ) attributed 3 of 61 cases of spinal haematoma after spinal or epidural injections, to antiplatelet medication.

However, other studies have claimed that spinal injection given to patients taking aspirin or other NSAIDs is relatively safe.

Indeed, the American Society of Regional Anesthesia Consensus Conference on Neuraxial Anesthesia and Anticoagulation concluded:

“antiplatelet drugs, by themselves, appear to represent no added significant risk for the development of spinal hematoma in patients having epidural or spinal anesthesia.”

In commenting on the 42 patients with transient worsening of neurological function, Horlocker and her colleagues initially attributed this to the local anaesthetic in the injectant, but decided that the duration of symptoms over a number of days and the fact that patients not receiving LA, militated against this.

They speculated on a pressure (ischaemic) effect of the injection or an inflammatory response. Either scenario could be a precursor to arachnoiditis.

Chemical meningitis

Gutknecht ( [\[lxxvi\]](#) ) described chemical meningitis after epidural steroid injections.

Karmochkine et al. ( [\[lxxvii\]](#) ) described a case simulating infectious meningitis after intradural

steroid injection.

Dougherty and Fraser ( [\[lxxviii\]](#) ) also reported 2 cases of severe meningitis following intraspinal steroid administration.

The authors concluded:

"It is suggested that the value of intraspinal steroids in the treatment of disc-related sciatica is unproven and if they are used, one must be alert to the complications."

THE TIRANTI CASE On February 3, 2000, a 38year old woman in New Jersey, USA was awarded \$12 million as compensation for arachnoiditis which developed as a result of Depo-medrol injected into the subarachnoid space in 1986.

The size of the award was in compensation for her past and future disability as well as her pain and suffering.

Conclusion:

In summary, in 1985 Kepes and Duncalf ( [\[lxxix\]](#) ) wrote:

"Low back pain and sciatica have been treated with peridural local anesthetics for over 80 years and with epidural and subarachnoid steroid injections for a quarter of a century.

Good results from this treatment which vary from 20 to 95% decrease on long-term follow up.

Statistical significance is absent if compared with other forms of therapy.

It is the authors' opinion that the rationale for the use of spinal local analgesics or steroids or intramuscular steroids has not been scientifically proven.

Complications with the use of subarachnoid steroids are sufficiently serious that this form of therapy should be condemned.

In this age of accountability it is imperative that therapies with questionable benefits should be critically evaluated.&quot;

Nearly 15 years later, Dr. Burton, one of the leading experts on arachnoiditis, wrote in 1999, ( [\[ xxx\]](#) )

&quot;A universally popular treatment is the percutaneous deposition of steroids into the epidural space of the spinal canal in order to decrease inflammation and assist with the natural healing processes.

Unfortunately, because of physician failure to know about, or to understand, the potentially dangerous potential of certain steroid substances known to be able of creating disabling adhesive arachnoiditis this disease process still remains rampant throughout the world.&quot;

Quantifying the overall risk of developing symptomatic adhesive arachnoiditis solely as a result of epidural steroid administration is fraught with difficulties because most cases involve a variety of other invasive procedures and also there is unlikely to be direct MRI evidence to permit a comparison of pre- and post- epidural scans.

However, in broad terms, bearing in mind Nelson's suggestion of 90% incidence of radiological arachnoiditis following *intrathecal methylprednisolone*, and the NHMRC estimate of 5% dural

puncture, one can estimate an approximate rate of radiological arachnoiditis of 5% after epidural steroids.

Add in results from Johnson et al.( [\[lxxxi\]](#) ) who found that 20% of those with radiological arachnoiditis subsequently developed symptoms, and one can suggest an overall estimate of 1% for the risk of symptomatic adhesive arachnoiditis following epidural steroid injection.

This is far higher than the figure suggested by most published medical literature, which may be accounted for by the confounding presence of other precipitating factors, and also the overall low rate of detection of the condition.

"The complications of ill-advised epidural steroid injection represent one of the most serious and under appreciated public health problems in the world today. Because many have not learned from the past adhesive arachnoiditis continues to be caused in unsuspecting patients by physicians who don't do the "right thing" because they don't know what it is."( [\[lxxxii\]](#) )

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