second question relates to the fundamental issue of whether such axial spinal procedures in general should be performed *in the first place*. Third, the question is whether the patient fully understands the complexity of the previous two issues and can give meaningful consent for the procedure and the particulate medicine; in particular, whether the patient has *really given* consent for the intervention if they understand that the benefits are likely to be at best modest and transient with the use of particulate steroids, and accompanied by an admittedly small risk of major catastrophic complications.

We will not try to reproduce all the evidence which is available concerning the possible complications of particulate steroids in axial spinal blockade in the literature. This has been more than adequately covered,[1] but we will focus instead on addressing the intersection of the three questions given above.

## The evidence base of particulate steroids causing catastrophic neurological damage in axial spinal procedures

Scientific studies demonstrate that following arterial injection, particulate corticosteroid preparations may form aggregates which may act as emboli to block small terminal arterioles in the brain and spinal cord. Methylprednisolone has the largest particle size, triamcinolone is intermediate and betamethasone has the smallest. Dexamethasone is a solution and does not form particles or aggregates.[2,3]

Arterial injection of particulate methylprednisolone has been shown to cause severe neurological consequences such as unconsciousness and cerebral haemorrhage.[4,5] Particulate corticosteroid preparations have been associated, in published case reports, with neurological damage and vascular complications in humans.[6–8]

As a result of this evidence clinicians instead have turned to using non-particulate (liquid) corticosteroids for axial spinal procedures in an attempt to reduce the chance of such complications but concerns were raised that water soluble corticosteroids were perhaps less clinically efficacious than particulate corticosteroid formulations.[9] Overall, the results following longer term clinical outcomes after treatment comparing particulate and liquid corticosteroid preparations are equivocal. Park et al.[10] demonstrated that triamcinolone (a particulate preparation) reduced the visual analogue score (VAS) better than dexamethasone (a liquid). However, no difference was found between the groups using the McGill Pain Questionnaire or the Oswestry Disability Index. Kim and Brown[11] found dexamethasone phosphate solution comparable to particulate methylprednisolone acetate in the treatment of lumbar radiculopathy, although dexamethasone demonstrated a trend towards less pain relief and a shorter duration of clinical efficacy. Feeley et al.[12] concluded that "particulate steroids are not demonstrably better in relieving pain compared to their non-particulate counterparts" and, in view of the safety concerns of particulate steroids, suggested "it may be prudent to switch to non-particulates, *or at the very least the dangers and alternatives should be flagged with the patient group as part of a shared decision making process*" (our italics).

In a large retrospective observational study (3645 lumbar transforaminal epidural steroid injections (TFESIs) performed on 2634 subjects for radicular pain with or without radiculopathy), there was no evidence that dexamethasone was less effective in pain relief and functional improvement than particulate corticosteroids.[13] A high-quality trial on 78 consecutive subjects found that both triamcinolone and dexamethasone resulted in significant improvements in pain and function at 2 weeks, 3 months and 6 months, but without clear differences between groups, although patients in the dexamethasone group required slightly more injections than the triamcinolone group in order to achieve the same outcomes.[14]

Using the American Society of Anesthesiologists Closed Claims database, epidural corticosteroid injections accounted for 83% of injections and 40% (114/284) of all chronic pain management claims.[15] Significant nerve injury (with seven claims of quadriplegia/paraplegia) was also observed in 28 epidural corticosteroid claims, but it was not specified how many related to use of particulate corticosteroid. Claims related to procedures performed at the level of the cervical spine comprised 22% of all claims related to chronic pain treatment, which suggested a relative increased risk in this area of the spine.[16] Of the 64 cases, there were nine (14%) cervical procedures associated with spinal cord infarction or stroke after intra-arterial injection. In five of these cases, spinal cord infarction followed cervical transforaminal injection of particulate corticosteroid. In three other claims, cervical transforaminal injection of particulate corticosteroid resulted in stroke, presumably by injection into the vertebral artery.

Concerns have also been raised whether corticosteroid formulations used for epidural administration should contain a preservative or not, although no preparations currently in the United Kingdom have a marketing authorisation for epidural administration, so use by this route is currently an 'off-label' indication. There are, however, no documented adverse events from the placement of preservative-containing corticosteroids in the epidural space (although neurological injuries have

been documented when the preservatives have been injected inadvertently by the intrathecal route). There have also been multiple cases of fungal infections caused by epidural and paraspinal injection of a contaminated glucocorticoid product in the United States. Clinicians who elect to use preservative-free corticosteroids must carefully weigh the risks and benefits and address sterility concerns.[17]

There also remains controversy as to any additional benefit from adding a corticosteroid to local anaesthetic for epidural administration. In a recent systematic review, high-quality evidence from multiple high-quality randomised controlled trials identified that the combination of local anaesthetic with corticosteroid was effective in managing chronic spinal pain. Local anaesthetic with corticosteroid and local anaesthetic alone were equally effective in a range of spinal conditions except in disc herniation, where the combination was superior.[18]

Based on the medical evidence, the British Pain Society (BPS) and Faculty of Pain Medicine of the Royal College of Anaesthetists (FPMRCA) produced a Consensus Statement on the Use of Corticosteroids for Neuraxial Procedures in the United Kingdom. They decided that due to the disproportionately large number of case reports of neurological complications related to the cervical region compared to the lumbar region, and also distinguishing between the interlaminar region compared to transforaminal injection, a case could be made for a clinician using different drugs in different regions. This position statement did, however, emphasise patient involvement in the decision-making progress.[19]

The conclusions of the BPS/FPM position statement are given below:

1. Particulate steroids must not be used for transforaminal cervical epidural injections on the basis of the risk of rare but catastrophic complications.
2. While definitive recommendations cannot be given for the choice of soluble or particulate steroid for injections in interlaminar cervical epidurals, clinicians should be aware that serious neurological complications can still occur.
3. While definitive recommendations cannot be given for the choice of soluble or particulate steroid for injections in epidurals undertaken in other areas of the spine (thoracic, lumbar and caudal), clinicians should be aware that serious neurological complications can occur with any route of administration, particularly if there is a history of previous spinal surgery.
4. Steroid preparations for epidural administration may carry a small risk of neurotoxicity with inadvertent intrathecal injection, due to the preservative preparation used. The clinician should carefully consider the formulation used.
5. The doctor must follow current GMC guidance on consent and record the discussion process. The discussion should ideally occur on an occasion prior to the procedure, as well as at the time of the procedure, to allow time for reflection.
6. The consent process should include discussion and documentation regarding indications, efficacy, safety and alternative treatments.
7. The use of corticosteroids in epidural injections is an indication that is outside the marketing authorisation (product licence). This information should also be incorporated into the consent process and documented in the medical records.

The issue arises with the above position statement, of course, that if something is more likely to cause catastrophic neurological injury in the cervical region, why should particulate corticosteroids still be used at all in the lumbar region, even if the ever-present risk might be reduced in the lumbar region? It was accepted, however, that the risk of neurological injury was raised by the presence of altered anatomy (say in the case of prior spinal surgery).

What needs to be considered at this point in the discussion is point 6 in the FPM/BPS guidance, in order to focus on the role of the patient in the decision-making process. In particular, is the clinician entitled to make such a decision on behalf of the patient or should the patient have a greater role in the consenting process, in a scenario where there is likely a raised chance of a rare catastrophic neurological complication with particulate corticosteroid risk, compared to virtually no chance of such a complication with the use of non-particulate steroids?

## Principles of consent

The General Medical Council (GMC) has provided a framework for consent which all medical practitioners are expected to be familiar with and to follow ('Consent: patients and doctors making decisions together').[20] These principles have been strengthened in the draft updating new guidelines which are out for consultation.[21] Briefly, the principles include the following:

(a) listen to patients and respect their views about their health
(b) discuss with patients what their diagnosis, prognosis, treatment and care involve

10. Park CH, Lee SH and Kim BI. Comparison of the effectiveness of lumbar transforaminal epidural injection with particulate and nonparticulate corticosteroids in lumbar radiating pain. *Pain Med* 2010; 11: 1654–1658.
11. Kim D and Brown J. Efficacy and safety of lumbar epidural dexamethasone versus methylprednisolone in the treatment of lumbar radiculopathy: a comparison of soluble versus particulate steroids. *Clin J Pain* 2011; 27(6): 518–522.
12. Feeley IH, Healy EF, Noel J, et al. Particulate and non-particulate steroids in spinal epidurals: a systematic review and meta-analysis. *Eur Spine J* 2017; 26(2): 336–344.
13. El-Yahchouchi C, Geske JR, Carter RE, et al. The non-inferiority of the nonparticulate steroid dexamethasone vs the particulate steroids betamethasone and triamcinolone in lumbar transforaminal epidural steroid injections. *Pain Med* 2013; 14: 1650–1657.
14. Kennedy DJ, Plastaras C, Casey E, et al. Comparative effectiveness of lumbar transforaminal epidural steroid injections with particulate versus nonparticulate corticosteroids for lumbar radicular pain due to intervertebral disc herniation: a prospective, randomized, double-blind trial. *Pain Med* 2014; 15: 548–555.
15. Fitzgibbon DR, Posner KL, Domino KB, et al. Chronic pain management: American Society of Anesthesiologists Closed Claims Project. *Anesthesiology* 2004; 100: 98–105.
16. Rathmell JP, Michna E, Fitzgibbon DR, et al. Injury and liability associated with cervical procedures for chronic pain. *Anesthesiology* 2011; 114(4): 918–926.
17. Smith RM, Schaefer MK, Kainer MA, et al. Fungal infections associated with contaminated methylprednisolone injections. *N Engl J Med* 2013; 369: 1598–1609.
18. Manchikanti L, Nampiaparampil DE, Manchikanti KN, et al. Comparison of the efficacy of saline, local anesthetics, and steroids in epidural and facet joint injections for the management of spinal pain: a systematic review of randomized controlled trials. *Surg Neurol Int* 2015; 6(Suppl. 4): S194–S235.
19. British Pain Society/Faculty of Pain Medicine (RCA) Consensus statement on the use of corticosteroids for neuraxial procedures in the UK, https://www.britishpainsociety.org/static/uploads/resources/files/BPS_FPM_Steroid_Statement_FINAL.pdf
20. General Medical Council. Consent: patients and doctors making decisions together, 2 June 2008, https://www.gmc-uk.org/ethical-guidance/ethical-guidance-for-doctors/consent
21. Review of our consent guidance, https://www.gmc-uk.org/about/get-involved/consultations/review-of-our-consent-guidance
22. Bolam v Friern Hospital Management Committee [1957] 2 All ER 118.
23. Bolitho v City and Hackney Health Authority [1997] 3 WLR 1151.
24. Montgomery v Lanarkshire Health Board [2015] UKSC 11.
25. Sokol DK. Update on the UK law on consent. *BMJ* 2015; 350: h1481
26. Jones v Royal Devon and Exeter NHS Foundation Trust (Lawtel 22 September 2015).
27. *Low back pain and sciatica in over 16s: assessment and management*. NICE guideline [NG59], https://www.nice.org.uk/guidance/ng59
28. Neck pain – cervical radiculopathy. Clinical Knowledge Summaries, National Institute for Health and Care Excellence, https://cks.nice.org.uk/neck-pain-cervical-radiculopathy#!topicSummary
29. Engel A, King W and MacVicar J. The effectiveness and risks of fluoroscopically guided cervical transforaminal injections of steroids: a systematic review with comprehensive analysis of the published data. *Pain Med* 2014; 15(3): 386–402.
30. Munglani R, Eyre G and Sharma M. Consent in pain medicine: law and implications for practise. *Pain News* 2018; 16(2): 60–65.
31. Munglani R, Eyre G and Sharma M. Consent in pain medicine: law and implications for practise. Part 2: what does valid consent look like? *Pain News* 2018; 16(3): 121–126.
32. Sharma M, Knagg R, Munglani R, et al. Consent in pain medicine: law and implications for practise. Part 3: the practicalities of consent in patients with chronic pain? *Pain News* 2018; 16(4): 185–194.

## Appendix 1

List of possible questions that should be addressed during the consenting process for an axial spinal procedure:

1. What is the natural history of this spinal condition? In particular, what are the chances that my condition will improve or deteriorate without this spinal injection and what are likely to be the implications of that for me?
2. What are the risks of (a) minor complications (short-term non-life changing effects) and (b) major complications (life changing effects, including rare catastrophic neurological complications) as a result of the injection?
3. What difference does the addition of corticosteroid make to the efficacy of this injection?
4. Does the use of a non-particulate over particulate corticosteroid make the injection safer, and if so, by how much?
5. Does the use of a non-particulate over particulate corticosteroid make the spinal injections less effective?
6. How do the risks and potential benefits of the injection compare if I have no corticosteroid in it at all?
7. Are cervical injections more dangerous than injections in the thoracic and lumbar region? If so why, and what difference does the use of non-particulate corticosteroids make to that risk?
8. Are there alternatives to this invasive injection such as other oral analgesics or oral corticosteroids, how effective