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FactFinders

FactFinders for patient safety: Understanding potential procedure-related complications: RFN/multifidus atrophy, intradiscal biologics, and facet cyst rupture

Minh Nguyen [a,1,*], Mathew Saffarian [b,1], Clark C. Smith [c,1], Eric K. Holder [d], Haewon Lee [e], Benjamin J. Marshall [f], Ryan Mattie [g], Jaymin Patel [h], Byron Schneider [i,j], Zachary L. McCormick [k], on behalf of the Spine Intervention Society's Patient Safety Committee

[a] University of Texas Southwestern, Department of Physical Medicine and Rehabilitation, Dallas, TX, USA
[b] Michigan State University, Department of Physical Medicine and Rehabilitation, East Lansing, MI, USA
[c] Columbia University Medical Center, Rehabilitation and Regenerative Medicine, New York, NY, USA
[d] Yale University School of Medicine, Department of Orthopedics and Rehabilitation, New Haven, CT, USA
[e] University of California, San Diego, Department of Orthopedic Surgery, San Diego, CA, USA
[f] Department of Physical Medicine and Rehabilitation, University of Colorado, School of Medicine, Denver, CO, USA
[g] Providence Cedars-Sinai Tarzana Medical Center, Department of Interventional Pain & Spine, Los Angeles, CA, USA
[h] Emory University, Department of Orthopaedics, Atlanta, GA, USA
[i] Vanderbilt University Medical Center, Dept of Physical Medicine & Rehabilitation, Nashville, TN, USA
[j] Vanderbilt University Medical Center, Center for Musculoskeletal Research, Nashville, TN, USA
[k] University of Utah, Division of Physical Medicine and Rehabilitation, Salt Lake City, UT, USA

A B S T R A C T

This series of FactFinders presents a brief summary of the evidence and outlines recommendations to improve our understanding and management of several potential procedure-related complications.

The evidence in support of the following facts is presented: (1) *Multifidus Atrophy After Lumbar Medial Branch Radiofrequency Neurotomy (LMBRFN)* – There is no conclusive published literature indicating that LMBRFN leads to increased multifidus atrophy relative to natural history. High-quality prospective studies with a natural history comparison group evaluating immediate pre-procedure as well as post-procedure longitudinal cross-sectional imaging are needed to accurately assess for any possible influence of LMBRFN on multifidus atrophy as well as the clinical relevance. (2) *Intradiscal Biologics* – Although the available evidence on intradiscal biologic interventions is limited, it nonetheless shows a non-zero risk of complications. Until larger sample sizes are reported, the actual magnitude of the risk cannot be ascertained. In the meantime, physicians who perform intradiscal injections of biologics should conscientiously consider the risk-benefit of these procedures. (3) *Lumbar Facet Synovial Cyst Rupture* – There have been few reports of complications secondary to lumbar facet synovial cyst rupture. Risks of may include increased pain, infection, and nerve root compression.

Does Lumbar Medial Branch Radiofrequency Neurotomy Cause Multifidus Atrophy?

Minh Nguyen, MD, MPH; Eric K. Holder, MD; Benjamin J. Marshall, DO; Clark C. Smith, MD, MPH; Jaymin Patel, MD; and Zachary L. McCormick, MD on behalf of the Spine Intervention Society's Patient Safety Committee

Myth: Lumbar medial branch radiofrequency neurotomy (LMBRFN) causes increased segmental spinal muscle atrophy due to multifidus denervation.

Fact: Presently, there is no conclusive published literature indicating that LMBRFN leads to increased multifidus atrophy relative to natural history. High-quality prospective studies with a natural history comparison group evaluating immediate pre-procedure as well as post-procedure longitudinal cross-sectional imaging are needed to accurately assess for any possible influence of LMBRFN on multifidus atrophy as well as the clinical relevance.

Lumbar medial branch radiofrequency neurotomy (LMBRFN) is a procedure commonly used to treat pain arising from the lumbar medial branch nerves that innervate the lumbar zygapophysial (facet) joint(s)

* Corresponding Author.
E-mail address: Minh.nguyen3@utsouthwestern.edu (M. Nguyen).
[1] denotes co-first authors.

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[1–3]. Each lumbar facet joint is dually innervated from the lumbar medial branch at the same level and one level above the facet joint [4]. However, lumbar medial branches also innervate other nearby structures, including the interspinous ligament, supraspinous ligament, and paraspinal multifidus muscles [5]. The multifidus muscle is the largest and most medial muscle of the deep lumbar paraspinal muscles [6]. The multifidi are arranged in a segmental manner, arising from the spinous processes medially and attaching more laterally at the mammillary processes of more caudal vertebral segments, the aponeurosis of the erector spinae muscles, the posterior superior iliac spine, or the sacrum and dorsal sacral ligaments. As such, the multifidi generally span and influence stability at multiple lumbar vertebral levels [6,7]. There is some evidence that each lumbar multifidus muscle is innervated by lumbar medial branches from multiple vertebral segments [8]. One study of an L5 nerve root lesion demonstrated electromyographic spontaneous activity three levels cranial (L2) to the injury [9]. The lumbar multifidus muscle functions as the principal posterior spine stabilizer, and impairment of the multifidi has been associated with increased low back pain [10]. It has been proposed that denervation of the lumbar medial branch(es) through LMBRFN may lead to multifidus atrophy.

A 2009 prospective study examining multifidus atrophy after unilateral LMBRFN followed five patients for 17–26 months [11]. These patients underwent electromyography (EMG) sampling of the paraspinal muscles before and after LMBRFN. In this small study, at 6 weeks post-LMBRFN, all patients were found to have EMG-documented denervation of the lumbar paraspinal muscles. At 21 months post-procedure, all patients had MRIs of the lumbar spine that were reviewed by three radiologists who were blinded to the side of the LMBRFN procedure. Lumbar multifidus atrophy was documented in all cases; however, post-procedural MRIs were not compared to pre-procedural imaging. Therefore, it is unknown whether the observed atrophy was directly attributable to the LMBRFN. Furthermore, cross-sectional or volume-based measurements to quantify atrophy on the treated versus untreated side were not performed. Interestingly, the radiologists could not agree as to which side or level(s) had been treated. In fact, accurate consensus amongst the radiologists regarding the side and level of LMBRFN was achieved in only one patient. Ultimately, all patients were relieved of their chronic low back pain and did not request any additional therapy or service. No functional testing of the multifidus was evaluated.

A 2015 retrospective cohort study involving 27 patients examined the cross-sectional-area (CSA) of multifidus atrophy after a LMBRFN procedure [12]. These patients underwent pre- and post-procedural MRI studies. MR images were taken a mean 12.7 months before the procedures and 7.5 months after the procedures. Untreated multifidi at the contralateral segmental levels were used as controls for comparison. Mean multifidus CSA pre-treatment was 6.2 cm^2 and mean multifidus CSA post-treatment was 5.7 cm^2 compared to 5.9 cm^2 in the control multifidi. The observed decrease in multifidus CSA at the treated versus control side showed a trend but did not reach statistical significance ($p = .06$). No data regarding patient's pain or function after the procedure were provided. A possible confounding factor must be mentioned as baseline MRIs for pre-to post-treatment comparison occurred at various intervals (12.7 months on average) before LMBRFN, rather than immediately prior to treatment. Given that these patients had unilateral low back pain, asymmetric multifidus atrophy may have occurred to a greater extent on the painful side (that subsequently underwent treatment) compared to the non-painful side in the months prior to LMBRFN due to pain-inhibition and associated disuse. Prior research has demonstrated that patients with unilateral low back pain show greater multifidus atrophy on the painful side [13,14].

A 2023 single-site retrospective study analyzed the relative paraspinal autochthonous intramuscular adipose volume before and after RFN in 20 patients [15]. The authors report that the RFN procedure was performed in accordance with the technique described by the Spine Interventional Society (SIS) guidelines (20°oblique, 20–30° decline). Patients had received an MRI at a median of 0.8 ± 0.30 [0.2–1.1] years pre-RFN and an MRI at a median of 1.4 [0.9–2.6] years post-RFN. The volume of interest included mono- (Mm. rotatores), multi- (Mm. multifidi), and pluri-segmental (M. erector spinae) muscles at the disc level of interest. Adipose volume was calculated by comparing the same spinal level pre- and post-RFN. Additionally, unilateral procedures were compared to the non-treated sided for comparison of fat and muscle volume change. Furthermore, the investigators calculated the intramuscular adipose volume within the multifidus and rotatores muscles separately, as these muscles are solely innervated by the medial branch (unlike other adjacent paraspinal muscles). The authors found that the relative paraspinal adipose volume did not differ before and after RFN ((42 ± 16.3 [9–81]) versus (43 ± 22.8 [4–90]), percent; $P = .726$). When comparing the superficial paraspinal muscle (innervated by the lateral branch) versus the deep layer of the paraspinal muscles (innervated by the medial branch), before ($P = .723$) and after RFN ($P = .805$), no significant statistical difference was observed. Unilateral procedures did not show a significant difference in segmental intramuscular adipose volume when compared to the non-treated side before ($P = .481$) and after ($P = .578$) RFN. There was no statistically significant difference in patients who met the responder definition for pain direction following RFN ($P = .147$) and those who did not meet this definition ($P = .461$). In this study, it should be noted that the authors used intraarticular facet infiltration as a diagnostic test to select patients and did not provide the number of facet levels that underwent LMBRFN. No functional testing of the multifidus was evaluated.

Summary and conclusions

There has been minimal published research that addresses whether LMBRFN leads to multifidus atrophy relative to natural history.

- A small prospective study found that blinded radiologists could not reliably determine the laterality and level(s) of treatment with LMBRFN [11].
- A small retrospective study reported no significant difference in multifidus atrophy CSA post-unilateral LMBRFN compared to control levels [12].
- No study has evaluated the significance of repeat RFN on multifidus atrophy, or motor function and medial branch recovery.
- There is a dearth of evidence addressing clinical effectiveness for denervating more than three joints. The preponderance of current evidence has specifically investigated targeting of the lower lumbosacral levels (*i.e.,* L4-S1) where there is traditionally believed to be a natural increase in muscular atrophy with age.
- It should be stated that given the nature of the LMBRFN procedure, some degree of multifidus denervation and atrophy is plausible. However, the degree of multifidus denervation and recovery as well as clinical relevance requires future high-quality study.

Complications from Intradiscal Biologic Interventions

Mathew Saffarian, DO; Ryan Mattie, MD; Haewon Lee, MD; Byron Schneider, MD; Zachary L. McCormick, MD; and Jaymin Patel, MD on behalf of the Spine Intervention Society's Patient Safety Committee

Fact: Although the available evidence on intradiscal biologic interventions is limited, it nonetheless shows a non-zero risk of complications. Until larger sample sizes are reported, the actual magnitude of the risk cannot be ascertained. In the meantime, physicians who perform intradiscal injections of biologics should conscientiously consider the risk-benefit of these procedures.

The lumbosacral intervertebral discs (IVDs) are believed to be a common source of chronic low back pain (LBP). The IVD is the largest avascular structure in the body. Intradiscal biologic interventions are being increasingly used for patients suffering from chronic severe LBP [16]. There are various types of biologic injectates, including platelet rich plasma (PRP), bone marrow aspirate concentrate (BMAC), allogenic

stromal cells, mesenchymal precursor cells, adipose-derived stem cells, as well as cultured and expanded stem cells. The risks of performing intradiscal biologic injections must be understood by any physician performing them, particularly since the efficacy of intradiscal biologic injections remains uncertain [16]. Accordingly, the risk-benefit ratio of potentially proceeding with such procedures must consider this uncertainty regarding potential benefit.

Published case reports of adverse events

The first published case of an infection following an IVD biologic injection was described in 2012 [17]. A 61-year-old male underwent "bone marrow aspirate, unseparated harvested adipose tissue autograft, and plasma from peripheral blood draw injection into his L3-L4 and L5-S1 IVDs." Authors did not comment on the use of prophylactic antibiotics, either orally or injected within the disc, nor did they comment on the use of single- or double-needle technique. About 1 month later, the patient began experiencing fevers, increasing low back pain, and signs of acute cauda equina syndrome. A subsequent MRI revealed discitis, osteomyelitis, and an epidural abscess. The patient underwent emergency decompression, and cultures identified methicillin-resistant *Staphyloccocus epidermidis*. Treatment consisted of IV and PO antibiotics and spinal fusion surgery. The patient eventually regained bladder function and motor control. The authors did not state whether there were any permanent partial neurological deficits.

A case of spondylodiscitis following a PRP injection into the L5-S1 IVD using a double-needle extrapedicular technique has also been reported [18]. No prophylactic antibiotics were administered. Symptoms began several weeks later with increased LBP, night sweats, and decreased mobility. The authors did not comment on specific neurological deficits. A biopsy showed *Cutibacterium acnes*. IV Ceftriaxone was given for 6 weeks, and at 1-year post-injection, the patient had no signs of infection and required no surgical intervention. The authors did not state whether there were any permanent partial neurological deficits.

A 32-year-old male underwent a biologic treatment to the L4-L5 IVD [19]. The exact details of the procedure were not provided as the injection was not performed by the study authors; however, he was thought to have been injected with a combination of PRP and BMAC. The authors did not specify if prophylactic antibiotics were administered, nor did they comment on the use of single- or double-needle technique. Two weeks later, he presented to the emergency department (ED) with lower extremity radicular pain, weakness, saddle anesthesia, and progressive low back pain. Laboratory results were within normal limits. An MRI of the lumbar spine did not demonstrate any signs of discitis or osteomyelitis. Two separate image-guided aspirations demonstrated no bacterial growth. A repeat biopsy was performed, and again, no signs of osteomyelitis or malignancy were noted. About 1 month later, the patient returned to the ED with worsening symptoms. The MRI showed evidence of discitis and osteomyelitis at L4-5 and L5-S1. A biopsy was performed, and *Cutibacterium acnes* was found. IV daptomycin was given for 12 weeks, and at 1-year follow-up he had stable LBP without radiculopathy.

Another publication reported three additional cases of adverse events [20]. The first case included a 55-year-old male who underwent BMAC injections to the L4-L5 and L5-S1 IVDs along with the left L4-L5 and L5-S1 facet joints via double-needle technique. Prophylactic IV cefazolin and 500 mcg of intradiscal gentamicin were administered. The patient experienced post-procedure pain that increased until day 19 post-injection, at which point, he sought treatment. He was found to have an elevated C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) but a normal white blood cell (WBC) count. An MRI with and without contrast demonstrated L5-S1 spondylodiscitis and enhancement of the L4-5 facet joints with extension into the right L4-L5 paravertebral space and right psoas muscle. He was treated with IV cloxacillin for 6 weeks followed by oral rifampicin and moxifloxacin for an additional 6 weeks. At 3-month follow-up, no further signs of infection were observed, and a subsequent MRI showed resolution of the spondylodiscitis. The authors did not state whether there were any permanent neurological deficits.

An additional case involved a 35-year-old male who presented for treatment of spondylodiscitis following BMAC injection to the L3-L4 and L4-L5 IVDs. Prior to the BMAC injection procedure he had prophylactically received 1 g of IV cefazolin. The authors did not comment on the use of single- or double-needle technique. Seven days after the injection, he was hospitalized for worsening, intractable pain along with fever and constipation. He was found to have an elevated CRP and ESR, but normal WBC. Blood cultures were negative. An MRI revealed L3-L4 discitis and an epidural abscess. He underwent a CT-guided aspiration of the cerebrospinal fluid, and culture results showed no bacterial growth. He was treated with IV cefepime and vancomycin for 6 weeks. Intractable pain persisted, and he subsequently was treated with high-dose dexamethasone. There was significant improvement within 24 h; however, he continued to report pain for 5 months following the procedure. At the time of the publication, there was no confirmation of the infectious organism. The authors did not state whether there were any permanent neurological deficits.

A final case involved a 34-year-old male who underwent leukocyte-poor two-level PRP injection to the L4-L5 and L5-S1 IVDs on two separate occasions. It is unknown whether he received prophylactic antibiotics prior to the PRP treatments. The authors did not comment on the use of single- or double-needle technique. Due to continued pain, he underwent BMAC injections at the same IVDs. Prior to the BMC injections, he was treated with prophylactic IV cefazolin. At 2 weeks, he had persistent, severe pain and underwent an MRI that showed mildly increased T2 signal in the L4-L5 high intensity zone and an increased disc protrusion at L5-S1. It is not clear from the articles whether these were new imaging findings compared to pre-injection lumbar MRI. He subsequently developed a fever, and a CT-guided biopsy was performed showing *Cutibacterium acnes* within the L5-S1 IVD. CRP and ESR were elevated, while his WBC count remained normal. A repeat MRI was performed at 4 weeks, which showed increased endplate changes and central vertebral body remodeling at L5 and the sacrum. He was treated with IV ceftriaxone for 42 days followed by oral amoxicillin for another 42 days. At three months, his blood work normalized, his pain improved to baseline, and he had no ongoing neurological or infectious symptoms.

Published research studies reporting adverse events

A recently published study reported data on the efficacy and safety of allogenic stromal antigen-3 mesenchymal precursor cells combined with hyaluronic acid into a single lumbar IVD in 100 patients [21]. Each patient received both a diagnostic injection and either a therapeutic or a control injection. Prophylactic IV antibiotics were given, but specifics were not described. Single needle disc access technique was used. Adverse events were documented as treatment-emergent adverse events (TEAE). Worsening LBP was found to be the most common post-procedural complaint. Three subjects discontinued the study due to worsening LBP; the investigators did not believe this was related to the procedure. One patient experienced severe LBP thought to be related to the study agent and did not continue with the study. One patient experienced "implant site infection," which was not further defined. The patient continued with the study. The adverse outcomes and their causes were not clearly reported. However, it appears that there were four cases of severe LBP leading to participant withdrawal from the study and another case of possible infection that did not lead to withdrawal from further participation.

Another recent study explored the effectiveness of intradiscal PRP for discogenic low back pain without Modic changes [22]. A single needle technique was used to access the disc in 49 patients who received intradiscal PRP without prophylactic antibiotics. One patient suffered from spondylodiscitis and recovered with antibiotic treatment and surgical debridement. It was not reported whether there were any residual neurologic deficits.

Published research studies without adverse events

In all of the published cohort studies, a total of 378 patients underwent biologic lumbosacral IVD injections [20]. Injectates included bone marrow mesenchymal stem cells, adipose-derived stem cells, PRP, cultured and expanded stem cells, and activated platelet-derived growth factors. No infections or major complications were reported in any of the 378 participants. The majority of the studies reported follow-up of 6–12 months [23–35]. Several studies reported follow-up as far out as 4–9 years [36–41]. Five studies treated subjects (n = 69) with prophylactic IV antibiotics prior to injection [27,30,32,33,35]. One study (n = 22) utilized intradiscal injection of gentamicin along with PRP [28].

Discussion

Studies investigating biologic treatments for the lumbosacral IVDs have had small sample sizes, and in aggregate, total fewer than 500 patients. There are six case reports and one published research study documenting infectious adverse events. There are no large cohort studies that have documented safety or allow for a high degree of confidence in the precise incidence of complications. Further research including larger patient populations is needed to better define the scope of complications as well as to define more accurate incidence rates.

Two types of complications have been reported in case studies – increased pain and spinal infection. The etiology of the infections is unclear. The multi-step process of preparing biologic injectates – from tissue collection, processing, and transfer prior to the injection – provides a greater number of opportunities for an infection to occur when compared to other procedures that access the intervertebral disc. There is therefore likely an increase in the risk of infection inherent in biologic injections when compared to other intradiscal procedures based on this logic, but currently insufficient evidence to support this theory.

The role of prophylactic intradiscal antibiotics in intradiscal biologic injections has been debated given the possible deleterious effects of antibiotics on cell proliferation [41]. Infections have occurred in patients who received prophylactic antibiotics as well as in those who did not. A previous FactFinder has been published outlining the use of antibiotics for non-biologic disc injections [42]. With regard to infectious complications, additional research is needed to better delineate the role of prophylactic antibiotics, both IV and intradiscal, single-versus double--needle disc access technique, as well as to identify both modifiable and non-modifiable risk factors for spinal infection. Such information will help inform the shared decision-making process between physicians and patients regarding the risk-benefit ratio unique to each individual who is considering an IVD biologic injection.

Complications of Lumbar Facet Synovial Cyst Rupture

Clark C. Smith, MD, MPH; Haewon Lee, MD; and Zachary L. McCormick, MD on behalf of the Spine Intervention Society's Patient Safety Committee

Myth: Lumbar facet synovial cyst rupture carries a high risk for complications such as acute cauda equina syndrome and epidural hematoma.

Fact: There have been few reports of complications secondary to this procedure. Risks of lumbar facet cyst rupture may include increased pain, infection, and nerve root compression.

Background

Lumbar facet synovial cysts (LFSC) arise from the facet joint capsule and are thought to be part of a degenerative process or increased segmental mobility that impose additional stress on the facet joints. These cysts are benign and, in many cases, cause no symptoms. Depending on size, location, and contents, these cysts can cause nerve root compression, radicular pain, or claudication [43,44]. These should be distinguished from Tarlov cysts or discal cysts.

Using CT or fluoroscopic guidance, LFSC rupture is a commonly used treatment option. After needle guidance into the facet joint, and using contrast medium to confirm intra-articular access, saline, local anesthetic (LA) alone, or a mixture of LA and steroid can be used to rupture the LFSC via pressurization. One retrospective study included 100 patients who underwent LFSC rupture, defined by the authors as a contrast pattern consistent with spill into the epidural space [43]. The study included 81 patients with successful rupture. Fifty-five percent of those patients ultimately required decompression surgery to remove the cyst. Final categorical success rates were not published. There was no mention of complications of the LFSC rupture procedure. Subsequent studies have delineated MRI characteristics of LFSCs that correlate with a greater likelihood of a positive treatment outcome following facet cyst rupture. LFSCs that demonstrate a hyperintense or intermediate signal on T2-weighted imaging are associated with higher rates of successful rupture, possibly because such cysts contain a greater proportion of fluid versus viscous or calcified material [44].

Risk of complications

Data suggest that, while rare, significant complications of LFSC rupture can occur. Two studies did not specifically address or include reports of any complications associated with LFSC rupture [43,45]. One study reported complications including worsening pain, epidural hematoma, and infection [46], while other studies have described cases of increased pain that resolved with medication or time alone [47,48]. Cases of worsened pain have required surgical decompression [43,44,49] to relieve the pain. Two cases of symptomatic epidural hematoma requiring surgical decompression have been reported following spontaneous LFSC rupture [50]. In neither case was the epidural hematoma attributed to an intervention. The effect of anticoagulant/antiplatelet medication on developing an epidural hematoma is unknown. There is at least one case of cellulitis after LFSC rupture that resolved with oral antibiotic treatment [46]. An epidural or spinal abscess has never been reported in association with cyst rupture. Other complications include LFSC rupture into an unintended space. Cambron et al. reported two cases of rupture of LFSC contents into the subarachnoid space, without any sequalae [44].

Sometimes a LFSC that does not appear to contain blood on imaging may, in fact, be hemorrhagic. In theory, if a hemorrhagic cyst were ruptured percutaneously, this may cause blood to enter the epidural space. Due to the low volume of LFSC, it is unlikely this would result in a symptomatic, let alone clinically significant epidural hematoma.

Alternative procedures

The alternative to percutaneous LFSC rupture is decompressive surgery, which carries significant risks. A large systematic review of 82 published studies, including a total of 966 patients, demonstrated that many patients who underwent surgery for the treatment of LFSC continued to suffer from pain (22%), and 2% experienced recurrence of a cyst. The overall surgical complication rate was 4.8%. Complications included deep venous thrombosis, cerebrospinal fluid leak, dural tear, and death [51].

Other interventional procedures have been described to treat lumbar LFSC. One small retrospective study examined intra-articular facet joint injection in combination with a lumbar transforaminal steroid injection and reported no complications [52]. Another study investigated the long-term effectiveness of direct CT-guided aspiration and fenestration of symptomatic lumbar facet synovial cysts [53]. This study did not explicitly address or report on any complications.

Conclusions and recommendations

- Large studies investigating the safety and effectiveness of LFSC rupture have not been conducted. Patients undergoing LFSC rupture should be advised on effectiveness and risks of the procedure, based on the published evidence, acknowledging its shortcomings.
- As with all interventional spine procedures, universal infection control precautions should be employed.
- There is insufficient data to conclude whether or not concurrent treatment with antiplatelet or anticoagulant medication increases the likelihood of a spinal epidural hematoma.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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