Magnetic Resonance Imaging Screening to Identify Spinal and Paraspinal Infections Associated With Injections of Contaminated Methylprednisolone Acetate

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FUNGAL CONTAMINATION OF METHylprednisolone prepared by a compounding pharmacy resulted in an unprecedented multistate outbreak of meningitis in the fall of 2012.[1-4] Michigan has had the highest state-specific attack rate for fungal infection associated with the contaminated spinal or paraspinal injections.[5,6] Initially, these injections were complicated by meningitis. Within 6 weeks of the outbreak, meningitis became less frequent and localized spinal and paraspinal infections became the principal manifestations of contaminated steroid injections. In contrast to the relatively brief period in which meningitis cases appeared, a steady stream of spinal and paraspinal infections continue to present long after the injections were last administered.

For editorial comment see p 2493.

Author Video Interview available at www.jama.com.

Importance Injection of contaminated methylprednisolone has resulted in an unprecedented nationwide outbreak of *Exserohilum rostratum* fungal infections, manifested initially as meningitis and/or basilar stroke. Insidious onset of spinal or paraspinal infection at the injection site has been increasingly reported and is occurring months after receipt of injection with the contaminated drug. The clinical findings are often subtle and similar to those that led the patient to undergo the methylprednisolone injection.

Objective To determine if patients who had not presented for medical care but who had received contaminated methylprednisolone developed spinal or paraspinal infection at the injection site using contrast-enhanced magnetic resonance imaging (MRI) screening.

Design, Setting, and Participants There were 172 patients who had received an injection of contaminated methylprednisolone from a highly contaminated lot (No. 06292012@26) at a pain facility but had not presented for medical care related to adverse effects after the injection. Screening MRI was performed between November 9, 2012, and April 30, 2013.

Main Outcomes and Measures Number of persons identified with previously undiagnosed spinal or paraspinal infection.

Results Of the 172 patients screened, MRI was abnormal in 36 (21%), showing epidural or paraspinal abscess or phlegmon, arachnoiditis, spinal osteomyelitis or diskitis, or moderate to severe epidural, paraspinal, or intradural enhancement. Of the 115 patients asked about new or worsening back or neck pain, lower extremity weakness, or radiculopathy symptoms, 35 (30%) had at least 1 symptom. Thirty-five of the 36 patients with abnormal MRIs met the Centers for Disease Control and Prevention (CDC) case definition for probable (17 patients) or confirmed (18 patients) fungal spinal or paraspinal infection. All 35 patients were treated with antifungal agents (voriconazole, with or without liposomal amphotericin B), and 24 required surgical debridement. At the time of surgery, 17 of 24 patients (71%), including 5 patients who denied having symptoms, had laboratory evidence of fungal infection.

Conclusions and Relevance Among patients who underwent screening MRI to look for infection at the site of injection of contaminated methylprednisolone, 21% had an abnormal MRI, and all but one met CDC criteria for probable or confirmed fungal spinal or paraspinal infection. Screening MRI led to identification of patients who had minimal or no symptoms of spinal or paraspinal infection and allowed early initiation of medical and surgical treatment.

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Box 1. Centers for Disease Control and Prevention Definitions[5]

Probable fungal meningitis: A patient who received epidural or paraspinal injection with contaminated methylprednisolone with signs or symptoms of meningitis including white blood cell count of 5/μL or higher in cerebrospinal fluid after accounting for the presence of any red blood cells without any other explanation. Fungal meningitis was also diagnosed when there was a posterior circulation stroke without a cardioembolic source.

Probable spinal or paraspinal infection: Magnetic resonance imaging evidence of osteomyelitis, abscess, or other infection (eg, soft tissue infection) of otherwise unknown origin in the spinal or paraspinal structures, at or near the site of epidural or paraspinal injection with contaminated methylprednisolone.

Confirmed case: If findings for probable fungal meningitis or spinal or paraspinal infection were present and there was microbiological, molecular, or histopathological evidence of a fungal pathogen, the case was reclassified as a confirmed case.

Because patients received these injections to treat back pain or neuropathic symptoms, the presentation of a slowly developing spinal or paraspinal infection has been obscured. Early identification of these infections with subsequent early intervention should benefit these patients. Consequently, a magnetic resonance imaging (MRI) screening protocol was initiated to identify patients who might have spinal or paraspinal infection related to injection of contaminated methylprednisolone.

METHODS

Screening Protocol and Study Definitions Used for Classification of Patients

A series of patients were studied who received contaminated methylprednisolone injections at a pain treatment facility but had not presented for medical care related to the contaminated injection. These patients did not have meningitis or symptoms of spinal or paraspinal infection suggestive of the need for evaluation. Patients were evaluated at St Joseph Mercy Hospital (SJMH), a 537-bed, non–university-affiliated, community teaching hospital belonging to a 6-hospital network that is part of Trinity Health. The institutional review board at SJMH reviewed and approved the study protocol with a waiver of informed consent.

A fungal outbreak registry was established to include all patients receiving an injection from lot No. 06292012@26 of preservative-free methylprednisolone prepared at New England Compounding Center. The dates and site of injection were recorded in the registry. A fungal outbreak clinic was established to coordinate care for exposed patients. Because of concern for patients with spinal or paraspinal infections with little to no change in their baseline chronic back pain, an MRI screening protocol was launched on November 9, 2012, and the follow-up reported herein was continued until April 30, 2013. All patients underwent gadolinium-contrast MRI evaluation with fat suppression to evaluate the postcontrast images.

Patients were asked about worsening back or neck pain, radiculopathy, or lower-extremity weakness at the time the MRI was scheduled. These patients were classified as symptomatic or asymptomatic. Patients who could not be reached were classified as unknown. Results of imaging and patient symptom classification were entered into the fungal outbreak registry. Some of the patients had standing orders for screening MRIs. These patients were notified about the results and asked whether they had symptoms at the time the MRI was scheduled. The Centers for Disease Control and Prevention (CDC) case definitions for meningitis and spinal or paraspinal infection were used (Box 1).[5] The medical records for all hospitalized patients having an abnormal MRI were reviewed to assess for the type of antifungal treatment given, length of hospital stay, spinal surgery intervention, and results of culture, histopathology, immunohistochemistry, and fungal polymerase chain reaction studies.

Interpretation of MRI

Neuroradiologists read the MRI studies and classified them as abnormal, equivocal, or normal. If the MRI interpretation was uncertain, its classification was established by conferring with a team of neuroradiologists and physicians specializing in infectious diseases at a weekly multidisciplinary conference. Abnormal radiological findings included abscess, phlegmon, spinal osteomyelitis or diskitis, arachnoiditis, epidural or paraspinal enhancement, and intradural enhancement. Severity of enhancement was noted for epidural, paraspinal, and intradural lesions. Radiological findings classified as equivocal included mild epidural, paraspinal, or intradural enhancement. All abnormal or equivocal images were reviewed a second time by another neuroradiologist (there were 3 fellowship-trained neuroradiologists available to review MRIs). A common nomenclature was used for classification purposes (Box 2).

Data Analysis

We used SAS version 9.2 (SAS Institute Inc) to analyze demographic, MRI, and other clinical information. Demographic and clinical variables were summarized using mean, median, or percentage, as appropriate. Data abstracted from the medical record and the independent neuroradiology readings were entered into an Excel spreadsheet (Microsoft) by trained data abstractors. Duplicate databases were created and then compared using a SAS procedure (PROC COMPARE) to identify data entry errors between the 2 data sets. No discrepancies were found.

RESULTS

Patients

Between August 9, 2012, and November 8, 2012, there were 218 patients identified who had received spinal or

paraspinal injections with the contaminated methylprednisolone lot No. 06292102@26 who had not presented for medical care related to the injection (FIGURE 1). Each patient received at least 1 injection between August 9, 2012, and October 2, 2012, which was the day when the contaminated steroid was removed from the pain facility.

The mean (SD) age of the patients was 63.2 (14.0) years (range, 17-93 years); women accounted for 136 patients (62% of cohort). The monthly number of admissions for meningitis, spinal or paraspinal infections, and joint infections appear in FIGURE 2.

Of the 218 patients eligible for screening MRI, 47 had already been scheduled for an MRI by their physicians when contacted by the study team. The remaining 171 were contacted by nurses from the fungal outbreak clinic.

By April 30, 2013, 172 of the 218 patients (79%) had at least 1 MRI performed. Twelve patients (6%) received care outside of the SJMH system. Eight patients (4%) had contraindications to MRI, which included spinal stimulators and cardiac devices. A total of 26 patients (12%) were scheduled for an MRI after April 30, 2013, or did not respond to the study team's request to schedule an MRI.

Results of Screening MRI

Of the 172 patients who had an initial screening MRI performed, 34 (20%) were noted to have an abnormal MRI, 30 (17%) an equivocal result, and 108 (63%) a normal MRI. Twenty-five of the 30 patients with equivocal findings on the first MRI underwent repeat imaging; 2 of these subsequent studies were abnormal, 13 remained equivocal, and 10 were read as normal. Of the findings on the 36 abnormal MRI studies (34 initial MRIs with 2 abnormal studies on repeat examination), phlegmon was found in 30, there was an abscess in 13, spinal osteomyelitis or diskitis in 7, and arachnoiditis in 6 (FIGURE 3 and FIGURE 4). Enhancement was classified as severe in 6 and as moderate in 30 (TABLE 1). Twenty-eight patients had multiple simultaneous MRI abnormalities. The median time from last spinal or paraspinal injection to an abnormal MRI was 87 days (range, 44-192 days). None of the MRI studies interpreted as normal had pathological evidence of enhancement at the injection site. Pathological enhancement is defined as enhancement not related to normal vascular enhancement; instead it implies disease.

Risk Factors

Medical history information was available for 34 of the 35 patients with infections. Of these, none had chronic renal insufficiency, immunosuppression (defined as having human immunodeficiency virus/AIDS, receiving chronic immunosuppressive therapy, or being a transplant recipient), connective tissue disease, chronic liver disease, or a history of cerebrovascular accident or stroke. Three patients had a history of malignancy (solid or hematopoietic), 8 had diabetes, 5 had coronary artery disease, 22 had hypertension, and 13 had hyperlipidemia.

Box 2. A Common Nomenclature

Abscess: defined as a peripherally enhancing fluid collection

Phlegmon: showed abnormal enhancement, but lacked central fluid signal

Spinal osteomyelitis or diskitis: identified when there was evidence of bone marrow edema, enhancement, and/or abnormal signal in the disk

Arachnoiditis: characterized by nodular or linear enhancement of the nerve roots of the cauda equina

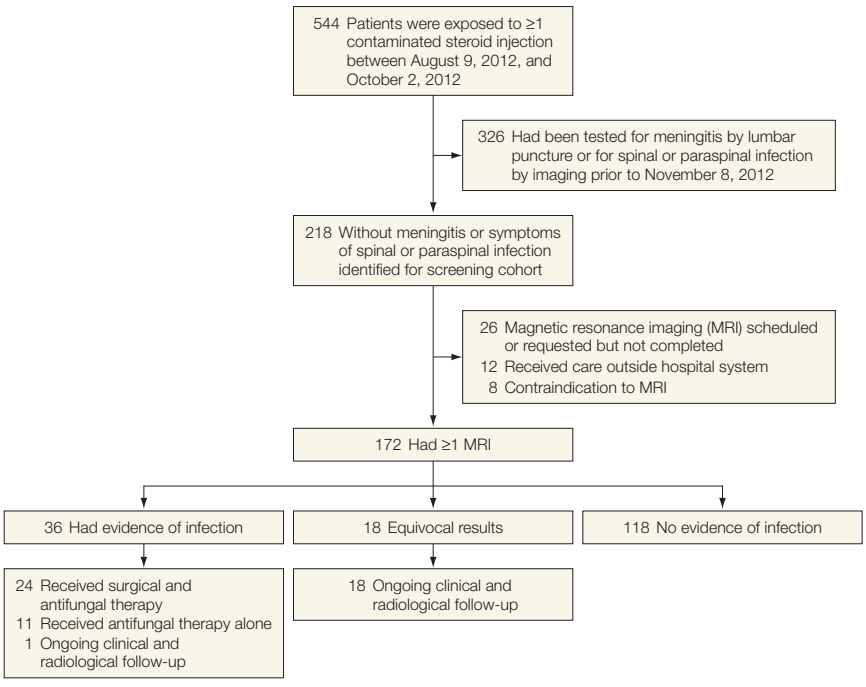
Intradural: defined as within or beneath the dura

Epidural: defined as above the dura

Paraspinal space: included the paravertebral muscles, facet joints, and structural ligaments

Enhancement: characterized as abnormal signal intensity related to the T1 relaxivity effect of a contrast agent

Figure 1. Process of Identifying Spinal and Paraspinal Infections After Patients Were Exposed to Contaminated Methylprednisolone in 2012



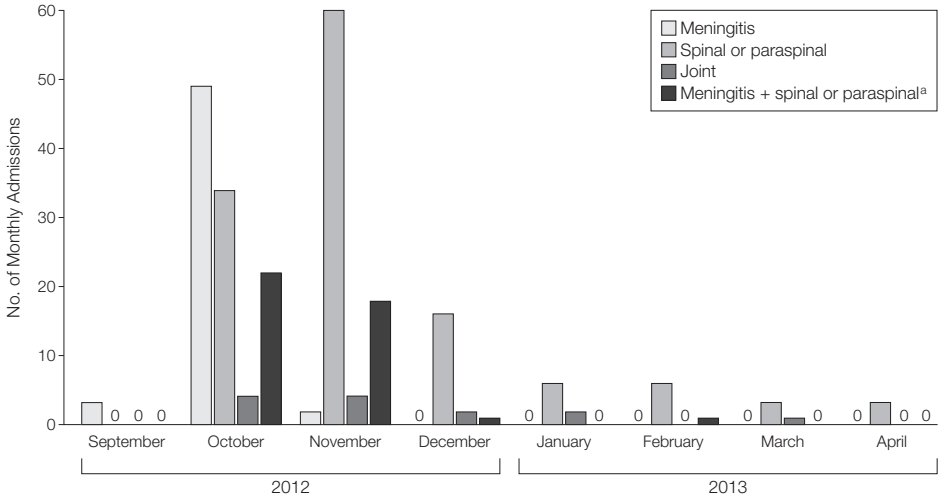
Symptoms

Data were obtained from 115 patients regarding the presence of new or worsening back or neck pain, radiculopathy, or lower-extremity weakness. Thirty-five of the 115 patients (30%) had at least 1 of these symptoms. Thirteen patients had no change in back or neck pain, no lower-extremity weakness, and no evidence of radiculopathy, but had an abnormal MRI. Of these, 7 patients underwent surgery and 5 were documented to have fungal infection.

Treatment and Outcomes

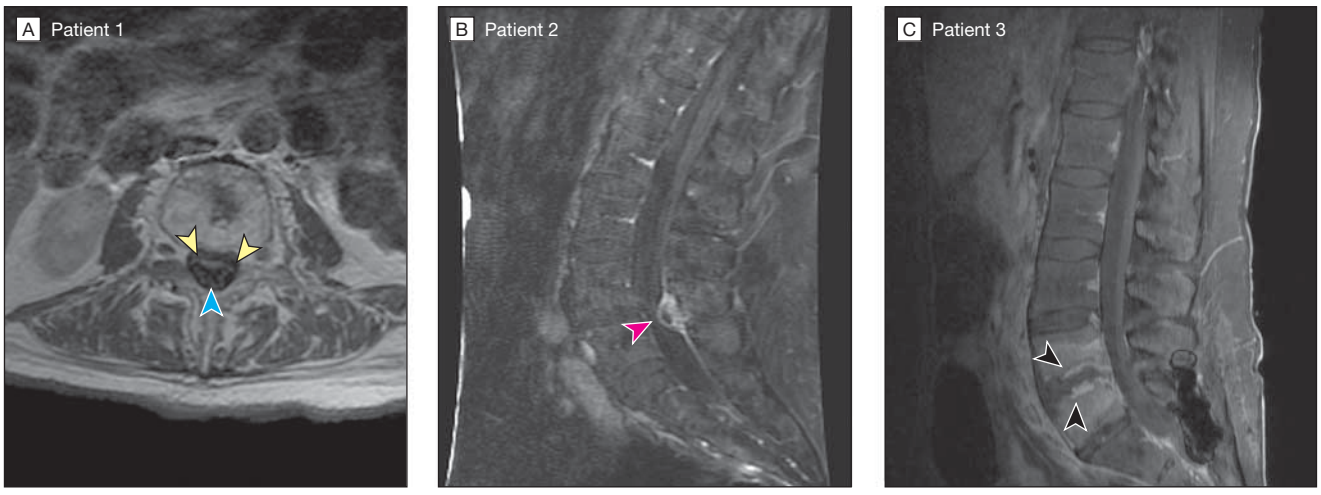
All 36 patients who had a screening MRI classified as abnormal were hospitalized, 32 at SJMH and 4 at other local hospitals. Thirty-five patients met the CDC case definition[5] for probable spinal or paraspinal infection (**TABLE 2** and Box 1). Of the 35 patients, 3 were between the ages of 20 to 40 years; 10 between the ages of 41 to 60 years; 16 between the ages of 61 to 80 years; and 6 between the ages of 81 to 100 years.

Figure 2. Monthly Admissions for Meningitis, Spinal or Paraspinal Infections, and Joint Infections Related to Contaminated Methylprednisolone Injections



[a]Reflects date of abnormal magnetic resonance imaging result. Of the 54 cases of fungal meningitis, 42 developed spinal or paraspinal infection.

Figure 3. Images From Magnetic Resonance Imaging of 3 Patients Exposed to Spinal and Paraspinal Injections With Contaminated Methylprednisolone



A, Axial T1 postcontrast image shows avid enhancement of nerve roots (yellow arrowheads) as well as clumped intradural enhancement (blue arrowhead) consistent with arachnoiditis. Tissue obtained during operation showed fungal hyphae, and polymerase chain reaction was positive for *Exserohilum* species. B, Sagittal T1 fat-saturated, postcontrast images of the lumbar spine shows a rim-enhancing fluid collection in the dorsal epidural space (pink arrowhead) in a patient who was asymptomatic. Tissue obtained at surgery showed fungal hyphae. C, Linear end-plate enhancement (black arrowheads) consistent with diskitis or osteomyelitis in another patient in whom tissue obtained at surgery showed fungal hyphae; cultures yielded *Exserohilum* species.

All of these patients received antifungal therapy; 25 were given voriconazole and liposomal amphotericin B and 10 received voriconazole alone. One patient who did not meet the criteria for probable fungal infection was admitted to another hospital and was followed up with serial imaging of her lumbar spine but had not been treated with antifungal therapy.

Twenty-four of the 35 patients (69%) meeting the CDC case definition for probable spinal or paraspinal infection required operative intervention. Of these 24 patients, 22 had MRI findings of epidural or paraspinal abscess or phlegmon. The remaining 2 had only paraspinal enhancement. Seventeen patients (71%) have had confirmed evidence of fungal infection by positive histopathology, cultures, polymerase chain reaction (PCR), or immunohistochemistry. Cultures grew *Exserohilum* species in 5 patients, and PCR testing was positive for *Exserohilum* in 5 of 12 tests that were performed. Two patients who underwent surgery for paraspinal enhancement alone had positive PCR testing on tissues for *Exserohilum*. Of 7 asymptomatic patients who underwent surgery, 5 had fungal infection confirmed, and another asymptomatic patient had evidence of septate hyphae on ultrasound-guided aspiration of a paraspinal abscess.

The median length of stay for the 32 patients who received care at SJMH was 15 days (range, 3-38 days). Thirty-one patients were discharged from SJMH while continuing to take oral voriconazole therapy, and 1 elderly patient who died had extensive confirmed epidural and intradural infection with *Exserohilum*.

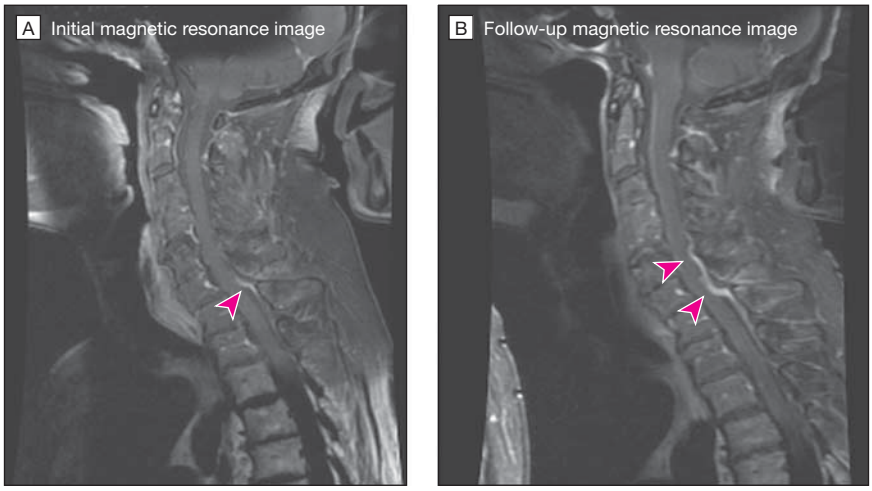
DISCUSSION

A proactive health system intervention was instituted by MRI screening of at-risk patients in response to an unprecedented outbreak of fungal infection. This resulted in earlier identification of patients with probable and confirmed infection. Thirteen of 36 screened patients (36%) found to have an abnormal MRI did not have changes in baseline pain or neuropathic symptoms at the spinal or paraspinal injection site. As of April 30, 2013, all of these patients were treated with antifungal drugs for spinal or paraspinal infection. Of these patients, 7 required surgical intervention; 5 of the 7 had laboratory confirmation of fungal infection.

Even though some patients reported worsening clinical symptoms, they had not presented for care before being contacted through our screening program. These patients were unable to distinguish whether the pain was from their chronic condition that prompted the methylprednisolone injection or from some new problem. Of 35 patients who reported worsening symptoms following spinal or paraspinal steroid injections, 22 were identified as having a fungal infection as a result of our screening program. Seventeen required surgical intervention. Twelve of these patients had a laboratory-confirmed fungal infection.

During the initial weeks of the outbreak, 260 patients presented to SJMH's emergency department for lumbar puncture in response to the CDC's recommendations for the evaluation of patients exposed to contaminated

Figure 4. Initial and Follow-up Magnetic Resonance Images of 1 Patient



A, Sagittal T1 fat-saturated, postcontrast image of the cervical spine shows thin linear dorsal epidural enhancement at the C5-C6 level (arrowhead). B, Follow-up imaging performed 19 days later shows thickening of the area of enhancement (arrowheads). The patient had become increasingly symptomatic with neck pain at the cervical injection site prior to the second magnetic resonance imaging. Subsequent biopsy showed evidence of fungal hyphae and cultures grew *Exserohilum* species.

Table 1. Radiological Findings in Patients With Abnormal Magnetic Resonance Imaging (MRI) Screening Results

	No. of Findings in 36 Patients With Abnormal MRI			
	Location			
	Epidural	Paraspinal	Intradural	Total[a]
Phlegmon	12	18	0	30
Abscess	4	9	0	13
Spinal osteomyelitis[b]	NA	NA	NA	7
Arachnoiditis	NA	NA	6	6
Enhancement				
Moderate	11	18	1	30
Severe	1	5	0	6

Abbreviation: NA, not applicable.
[a] Some patients had more than 1 finding on MRI.
[b] Includes diskitis.

Table 2. Clinical Findings in 35 Cases of Probable and Confirmed Fungal Spinal or Paraspinal Infections

Sex	CDC Case Status[a]	Symptoms[b]	Time From Last Injection to Abnormal MRI, d	MRI Findings	Initial Treatment	Operative Intervention	Outcome[c]
Female	Confirmed	Yes	63	Epidural infection[d] Paraspinal infection[e] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Confirmed	Yes	44	Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Probable	Yes	60	Paraspinal infection[e] Enhancement[f]	Voriconazole	No	Improved
Female	Confirmed	Yes	82	Epidural infection[d] Paraspinal infection[e] Arachnoiditis Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Probable	No	122	Epidural infection[d] Paraspinal infection[e] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Probable	No	78	Epidural infection[d] Paraspinal infection[e]	Voriconazole + liposomal amphotericin B	Yes	Improved
Male	Confirmed	Yes	81	Paraspinal infection[e] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Male	Probable	Yes	104	Arachnoiditis	Voriconazole + liposomal amphotericin B	No	Improved
Male	Probable	No	87	Arachnoiditis	Voriconazole + liposomal amphotericin B	No	Improved
Female	Probable	Yes	105	Epidural infection[d] Paraspinal infection[e] Spinal osteomyelitis[g] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Confirmed	Yes	56	Epidural infection[d] Paraspinal infection[e] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Probable	No	118	Epidural infection[d] Paraspinal infection[e] Spinal osteomyelitis[g]	Voriconazole	No	Improved
Female	Confirmed	Yes	69	Paraspinal infection[e] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Confirmed	No	85	Paraspinal infection[e] Enhancement[f]	Voriconazole	Yes	Improved
Female	Probable	Yes	106	Paraspinal infection[e] Enhancement[f]	Voriconazole	Yes	Improved
Male	Confirmed	No	115	Epidural infection[d] Paraspinal infection[e] Spinal osteomyelitis[g] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Probable	Yes	96	Equivocal[h]	Voriconazole	No	Improved
Female	Probable	No	121	Spinal osteomyelitis[g] Enhancement[f]	Voriconazole	No	Improved
Female	Confirmed	Yes	91	Paraspinal infection[e] Spinal osteomyelitis[g]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Confirmed	No	74	Paraspinal infection[e]	Voriconazole	No	Improved
Male	Confirmed	No	59	Epidural infection[d] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Probable	Yes	108	Arachnoiditis	Voriconazole + liposomal amphotericin B	No	Improved
Male	Confirmed	No	80	Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Confirmed	No	88	Epidural infection[d] Paraspinal infection[e] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Confirmed	Yes	68	Epidural infection[d] Arachnoiditis Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Death
Female	Probable	Yes	86	Paraspinal infection[e] Enhancement[f]	Voriconazole	No	Improved
Male	Probable	Yes	94	Epidural infection[d] Paraspinal infection[e] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Probable	Yes	61	Epidural infection[d] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Male	Probable	No	57	Arachnoiditis	Voriconazole + liposomal amphotericin B	No	Improved

(continued)

Table 2. Clinical Findings in 35 Cases of Probable and Confirmed Fungal Spinal or Paraspinal Infections (continued)

Sex	CDC Case Status[a]	Symptoms[b]	Time From Last Injection to Abnormal MRI, d	MRI Findings	Initial Treatment	Operative Intervention	Outcome[c]
Female	Confirmed	Yes	61	Paraspinal infection[e] Enhancement[f]	Voriconazole	Yes	Improved
Female	Confirmed	Yes	126	Epidural infection[d] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Confirmed	Yes	156	Paraspinal infection[e] Enhancement[f] Spinal osteomyelitis[g]	Voriconazole	Yes	Improved
Female	Probable	No	172	Spinal osteomyelits[g]	Voriconazole + liposomal amphotericin B	No	Improved
Female	Confirmed	Yes	154	Epidural infection[d] Paraspinal infection[e] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved
Female	Probable	Yes	192	Epidural infection[d] Enhancement[f]	Voriconazole + liposomal amphotericin B	Yes	Improved

Abbreviation: CDC, Centers for Disease Control and Prevention.
[a] Probable spinal or paraspinal infection defined as MRI evidence of osteomyelitis, abscess, or other infection (eg, soft tissue infection) of unknown origin in the spinal or paraspinal structures at or near the site of epidural or paraspinal injection with contaminated methylprednisolone. Confirmed spinal or paraspinal infection defined as having had any of the above findings plus microbiological, molecular, or histopathological evidence of a fungal pathogen.
[b] Worsening back or neck pain, radiculopathy symptoms, or lower-extremity weakness.
[c] Improved outcome indicates that the patient was discharged from the hospital while continuing to take voriconazole.
[d] Any abscess and/or phlegmon above the dura.
[e] Any abscess and/or phlegmon in the paravertebral muscles, facet joints, or structural ligaments.
[f] Moderate or severe epidural or paraspinal enhancement.
[g] Includes diskitis.
[h] Mild paraspinal enhancement.

steroids during spinal injections. Of these patients, 206 did not meet the CDC case definition for meningitis.[5] Many of the 54 patients who were found to have meningitis subsequently developed concomitant spinal or paraspinal infections; 42 developed concomitant infection (last recorded concomitant infection developed in mid-February 2013). This observation prompted our decision to proactively screen all patients exposed to contaminated spinal or paraspinal steroid injections for the development of these localized infections using screening MRI.

One limitation of this screening program was a high rate of equivocal MRI studies. The reasons these occurred include variable sensitivity thresholds of different neuroradiologists and the screening modality (MRI) itself. In this context, sensitivity refers to the ability of MRI to identify the disease. Sensitivity thresholds can vary by scanner and sequences. Fat suppression–contrast sequence has higher sensitivity to establish a diagnosis than does a conventional examination. Cases in which an accurate site of injection was not provided accounted for several equivocal diagnoses; we found that focusing on the specific injection site was helpful. Fat-suppressed postcontrast sequences were particularly sensitive and helped differentiate infection from other causes of enhancement. An epidural venous plexus can show enhancement and can be asymmetrical, which can lead a neuroradiologist to question whether infection is present. Moreover, inflammatory and degenerative arthropathy, particularly of the facet joints, can show strong enhancement and mimic infection. Diagnostic accuracy improved as the study team gained experience with the MRI findings of this infection and as the presence of fungal infection was confirmed by tissue examination of patients who underwent operations.

Development of a fungal outbreak registry, which included all exposed patients and their respective dates and sites of injections, and a specific fungal outbreak clinic provided strong foundations for the design and implementation of a screening program. In addition, multidisciplinary conferences including neuroradiology, infectious diseases, anesthesiology, and neurosurgery were critical to interpreting MRI studies and standardizing our medical and surgical approach.

There are several limitations to our study. First, the numbers of patients screened and found to have probable or confirmed fungal infection is relatively small. Second, our presumption that early treatment initiated when MRI abnormalities are found will improve outcomes has not been established. In addition, these results may not be generalizable to all patients exposed to contaminated methylprednisolone, especially those who received injections from the presumably less heavily contaminated lots of this drug.

Health Alert Network guidance from the CDC calls for clinicians to remain vigilant when following up patients who have received spinal or paraspinal injections of contaminated methylprednisolone.[7] The CDC recommends that anyone who received these injections and who has new or worsening symptoms at or near the injection site, undergo a contrast-enhanced MRI. In addition, the CDC recommends that clinicians should consider obtaining an MRI with contrast of the injection site in patients with persistent but baseline symptoms.

Our findings support obtaining contrast-enhanced MRI of the injec-

tion site in patients with persistent back pain even when their pain disorder has not worsened. Such patients have been found to have abscesses, phlegmons, and spinal osteomyelitis or diskitis with MRI. A proactive outreach to patients receiving injections from a highly contaminated lot, especially lot No. 06292012@26, is needed. Magnetic resonance imaging may detect infection earlier in some patients, leading to more efficacious medical and surgical treatment and improved outcomes.

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Study concept and design: Malani, Vandenberg, Singal, Kasotakis, Kaakaji.
Acquisition of data: Malani, Vandenberg, Singal, Kasotakis, Moudgal, Jagarlamudi, Neelakanta, Kaakaji.
Analysis and interpretation of data: Malani, Vandenberg, Singal, Kasotakis, Koch, Halasyamani, Kaakaji, Kauffman.
Drafting of the manuscript: Malani, Vandenberg, Singal, Kasotakis, Koch, Kaakaji, Kauffman.
Critical revision of the manuscript for important intellectual content: Malani, Vandenberg, Singal, Kasotakis, Koch, Moudgal, Jagarlamudi, Neelakanta, Otto, Halasyamani, Kauffman.
Statistical analysis: Malani, Singal.
Administrative, technical, or material support: Malani, Kasotakis, Koch, Moudgal, Jagarlamudi, Neelakanta, Halasyamani, Kaakaji.
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Online-Only Material: The Author Video Interview is available at www.jama.com.

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Many persons have a wrong idea of what constitutes true happiness. It is not attained through self-gratification but through fidelity to a worthy purpose.

—Helen Keller (1880-1968)