Letters

RESEARCH LETTER

Response to Mold Contamination of Intravenous Magnesium Sulfate Produced by a Compounding Pharmacy

An increasing number of contaminated medications produced by compounding pharmacies have placed patients at risk, created unnecessary burdens on health care facilities, and illustrate the need for better oversight of the industry.[1-3] We describe a hospital's response to fungal contamination of intravenous magnesium sulfate ($MgSO_4$) produced by a compounding pharmacy.

Methods | On March 13, 2013, a nurse discovered "floaters" in a bag of $MgSO_4$. The hospital pharmacy immediately recalled all units of $MgSO_4$ produced by the compounding pharmacy and found floaters in a second lot of $MgSO_4$ recalled from a different hospital ward. The following day, pharmacy personnel recalled all 12 000 units of 44 types of products received from the compounding pharmacy from all patient care areas at the hospital and at 2 other system-related hospitals. Appropriate state agencies, the US Food and Drug Administration (FDA), and the Centers for Disease Control and Prevention (CDC) were notified. Products from the compounding pharmacy were sequestered and examined by hospital pharmacy employees and FDA personnel for visible evidence of contamination, and samples were obtained for investigation by the FDA and CDC. The hospital microbiology laboratory performed DNA sequencing of material from the contaminated $MgSO_4$.

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Because multiple lots of $MgSO_4$ produced by the compounding pharmacy, including lots without visible contamination, were in use at the hospital concurrently, and lot numbers are not embedded in medication barcodes recorded in patient medical records, we could not identify only those patients who received $MgSO_4$ from contaminated lots. Therefore, a list of all patients who received $MgSO_4$ during the exposure period was generated. Hospital personnel notified potentially exposed patients by telephone and certified letter and informed their physicians by telephone. Prophylactic voriconazole was administered to patients with allogeneic stem cell transplants who were potentially exposed.

From mid-March through mid-June 2013, medical records of potentially exposed patients who were readmitted were reviewed for evidence of fungal infection, and microbiology laboratories at the 3 system hospitals reported growth of any mold from sterile body sites twice weekly to the infection control program.

Results | DNA sequencing performed by the hospital microbiology laboratory directly on particulate material from contaminated bags and sequencing of fungal growth recovered from 2 lots of contaminated $MgSO_4$ was consistent with *Hamigera* spp, subsequently identified by the CDC as *Hamigera insecticola*. Sequencing of fungal growth from 1 of the 2 lots also yielded an *Aspergillus*-like organism, identified by the CDC as *Neosartorya hiratsukae*. Investigations by the CDC and a reference laboratory used by the compounding pharmacy found that 4 lots of $MgSO_4$ and a lot of dexamethasone sodium phosphate were contaminated with fungi, including *Penicillium chrysogenum* and *Penicillium rubens* (**Table 1**).

A total of 1309 patients and 460 physicians were notified regarding possible exposures to contaminated $MgSO_4$. As of mid-June 2013, responses to hotline calls, laboratory-based surveillance, and review of 545 readmissions of potentially exposed patients revealed no fungal infections attributable to the contaminating fungi. The hospital's response involved an estimated 14 915 hours of personnel time, and estimated costs to the hospital system were $874 989 (**Table 2**). An FDA investigation revealed that the source of contamination was the compounding pharmacy, where all contaminated products prepared for our hospital were compounded on a separate (unique) laminar flow work bench, and uncovered unsanitary conditions and numerous violations of good manufacturing practice requirements for drugs.[4]

Table 1. Contaminated Lots of Magnesium Sulfate From a Compounding Pharmacy and Fungal Contaminates Identified

Lot No.	Product	Date		Contaminant	No. of Units in Lot	No. of Units Infused
		Produced	Received			
1	$MgSO_4$	February 13, 2013	February 18, 2013	*Hamigera insecticola*, *Neosartorya hiratsukae*	50	23
2	$MgSO_4$	February 20, 2013	February 22, 2013	*H insecticola*, *Penicillium chrysogenum*	600	562
3	$MgSO_4$	February 27, 2013	March 1, 2013	*Penicillium rubens*	20	None
4	$MgSO_4$	January 31, 2013	February 1, 2013	*P chrysogenum*	400	374
	Dexamethasone sodium phosphate	February 27, 2013	March 1, 2013	*P rubens*	20	None

Abbreviation: $MgSO_4$, magnesium sulfate.

Table 2. Hospital System Costs Associated With Fungal Contamination of Magnesium Sulfate

Activity	Expenses, US$	Hours
Patient and physician notification	80 038	1286
Drug costs	386 777	
Patient disease surveillance	26 434	220
Administrative time (legal, regulatory, finance, and administrative)	204 873	1288
Pharmacy in-house admixture services	485 845	10 825
Pharmacy recall (sequester, inventory, and formulary)	59 202	1296
System hospital B total (drug cost and resources)	109 165	
System hospital C total (drug cost only)	3655	
Subtotal	1 355 989	
CP-A fee savings (no products purchased × 6 mo)	(481 000)	
Total	**874 989**	**14 915**

Abbreviation: CP-A, compounding pharmacy.

Discussion | Fungal contamination of $MgSO_4$ required extensive pharmacy, laboratory, infection control, and hospital administrative support; substantial hospital resources for patient and physician notification; ongoing surveillance; and prophylactic treatment of high-risk patients. Inclusion of lot numbers in medication barcodes would have greatly simplified notification and surveillance efforts by identifying only those patients who were exposed to contaminated lots. Our experience adds to the increasing body of evidence that improved oversight of compounding pharmacies by the FDA is needed.[5,6]

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Sexual Activity in Midlife Women: Importance of Sex Matters

Sexual function is associated with health-related quality of life (HRQoL).[1,2] Understanding the factors that affect aging women's sexual activity has implications for maintenance of HRQoL in this population.

In this study, we used a longitudinal cohort to examine the factors that predict maintenance of sexual activity among midlife women. We hypothesized that higher sexual function and higher importance of sex at baseline would predict maintenance of sexual activity.

Methods | Do Stage Transitions Result in Detectable Effects (STRIDE) is a longitudinal cohort study of women ages 40 to 65 years enrolled in 2005 from a general internal medicine practice. All English-speaking women who completed written informed consent were enrolled. This study was approved by the University of Pittsburgh's institutional review board. Women completed annual questionnaires regarding demographic variables, menopausal status and symptoms, and medical comorbidities. In year 4 of the study, women completed the Female Sexual Function Index (FSFI).[3] Lower scores indicate worse sexual function. Importance of sex was assessed by a single question. Menopausal status was assigned based on self-reported bleeding history. Body mass index and medication use were abstracted from the electronic health record.

The primary outcome was sexual activity at year 8, assessed by the question: "During the past 6 months, have you engaged in *any* sexual activities with a partner?" Women who did not answer the questions on sexual function or who answered "No sexual activity in the prior 4 weeks" on any FSFI question were excluded.

Descriptive statistics were used to compare sexually active and inactive women at baseline. We used univariable logistic regression models to examine characteristics associated with sexual activity maintenance at study year 8. Variables that may change over time were examined longitudinally using random effects mixed models. Variables that attained clinical or marginal statistical significance ($P < .20$) were entered into a multivariable model.