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# Acute Allergic-Type Reactions Among Patients Undergoing Hemodialysis — Multiple States, 2007–2008

CDC is investigating an outbreak of acute allergic-type reactions among patients who have undergone hemodialysis since November 19, 2007. The majority of reactions have occurred among adult hemodialysis patients, with onset within minutes of initiating a hemodialysis session. Although the cause of the outbreak is unknown and remains under investigation, the majority of reactions occurred in patients who received intravenous heparin produced by Baxter Healthcare Corporation (Deerfield, Illinois). Baxter voluntarily recalled nine lots of heparin multidose vials after learning of these adverse events among patients who received heparin during dialysis. This report describes the ongoing investigation.

CDC was first notified on January 7, 2008, by the Missouri Department of Health and Senior Services (MDHSS) of allergic-type reactions among pediatric hemodialysis patients that occurred beginning November 19, 2007, at a pediatric hospital. The reactions had been reported to MDHSS by a health-care provider at the hospital. The symptoms occurred within minutes of dialysis initiation and included facial swelling, tachycardia, hypotension, urticaria, and nausea. A total of eight episodes of acute allergic-type reactions have been identified as occurring among four patients at the pediatric hospital during November 19, 2007–January 15, 2008. These reactions were reviewed by a clinical allergist and were determined to be consistent with anaphylactic or anaphylactoid reaction.

Upon learning of the initial cluster, CDC solicited reports of similar allergic-type reactions among hemodialysis patients nationally through nephrology e-mail lists and public health notifications. In response to these case-finding measures, CDC was contacted on January 9, 2008, by a dialysis supply company that had received reports during the previous 2-week period of approximately 50 similar reactions among adult hemodialysis patients at dialysis facilities in six states. A second supply company reported learning of similar reactions from dialysis facilities as early as December 10, 2007. CDC alerted the Food and Drug Administration (FDA) to these nationwide reports of allergic-type reactions on January 9, 2008, and has been collaborating with FDA on the investigation.

As part of the investigation, CDC has created a working case definition for these reactions. A confirmed case of acute allergic-type reaction has been defined as an episode of anaphylactic or anaphylactoid reaction characterized by angioedema (particularly swelling of lips/mouth, tongue, throat, or eyelids) or urticaria. A probable case has been defined as an episode that includes at least two of the following signs and symptoms: 1) generalized or localized sensations of warmth; 2) numbness or tingling of the extremities; 3) difficulty swallowing; 4) shortness of breath, audible wheezing, or chest tightness; 5) low blood pressure/tachycardia; or 6) nausea or vomiting.

Of the episodes reported as of January 30, CDC has identified 65 confirmed or probable cases among 53 hemodialysis patients that occurred during November 19, 2007–January 21, 2008, at 19 dialysis facilities in 12 states. CDC currently is investigating an additional 36 possible cases. Most reactions resolved after interruption of the dialysis session or treatment with diphenhydramine or steroids at the facility. Other than the eight episodes reported by MDHSS, all cases have occurred among adults.

One common factor among the cases being investigated was receipt of heparin (1,000 units/mL) from 30-mL or 10-mL vials manufactured by Baxter. Intravenous heparin is administered during most hemodialysis sessions to prevent clotting of the access and dialysis circuit. In 61 (94%) of the 65 cases, the affected patient received Baxter heparin during hemodialysis. Dialyzers from four different companies were being used when the reactions occurred. The most commonly used dialyzers, manufactured by Fresenius Medical Care (Waltham, Massachusetts), were being used in 26 (40%) of the episodes. Other exposures have not been ruled out as potential causes of the reactions, and CDC is

conducting additional epidemiologic studies to examine those exposures.

On January 17, 2008, Baxter announced a voluntary recall of nine lots of heparin, based on reports the company had received (*1*). All nine lots were produced at a single plant; eight of the nine lots were produced during September–November 2007. Despite the January 17 recall, an additional reaction occurred on January 21, 2008, after a hemodialysis patient was administered Baxter heparin from one of the recalled lots. CDC has found indications of delays in removing the recalled lots of heparin from distribution, which might result in continued exposures. In addition, these reactions might not be limited to hemodialysis settings. One cardiac-care facility has reported seven allergic-type reactions among cardiac patients who received heparin from lots that were later recalled. CDC and state health departments are investigating these reactions.

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**Editorial Note:** The temporal and geographic distribution of these reactions in a discrete population of patients suggests common exposure to a health-care product with wide distribution in the United States. Previous clusters of acute allergic-type reactions among hemodialysis patients have been attributed to certain types of dialyzer membranes, ethylene oxide (used by the manufacturer as a sterilant), angiotensin-converting enzyme inhibitors, and the reuse of dialyzers (*2,3*). However, based on preliminary findings, these previously recognized causes of allergic-type reactions in dialysis patients are unlikely to explain this outbreak. Heparin is a biologic product rarely associated with anaphylactic reactions (*4*).

CDC is conducting additional case-finding activities and epidemiologic studies to define the scope of the outbreak and is exploring options for laboratory testing to further characterize these reactions. Health-care providers should 1) immediately discontinue use of and segregate the recalled lots of heparin, 2) report medication reactions to MedWatch, the online FDA reporting system for adverse medication events,* and 3) report to their state or local health departments any acute allergic-type reactions that have occurred since November 2007 in patients receiving hemodialysis or intravenous medication infusion. Health departments are asked to report reactions to CDC by telephone (404-639-4514 or 404-639-4273) or e-mail (dblossom@cdc.gov or ppatel@cdc.gov).

## References

1. Baxter Healthcare Corporation. Urgent product recall. Rockville, MD: Food and Drug Administration; 2008. Available at http://www.fda.gov/medwatch/safety/2008/heparin_recall_01-17-2008.pdf.
2. Arduino MJ. CDC investigations of noninfectious outbreaks of adverse events in hemodialysis facilities, 1979–1999. Semin Dial 2000;13:86–91.
3. CDC. Epidemiologic notes and reports of acute allergic reactions associated with reprocessed hemodialyzers—Virginia, 1989. MMWR 1989;38:873–4.
4. Berkun Y, Haviv YS, Schwartz LB, Shalit M. Heparin-induced recurrent anaphylaxis. Clin Exp Allergy 2004;34:1916–8.

* Available at http://www.fda.gov/medwatch.