Notes from the Field

Infections After Receipt of Bacterially Contaminated Umbilical Cord Blood–Derived Stem Cell Products for Other Than Hematopoietic or Immunologic Reconstitution — United States, 2018

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The only Food and Drug Administration (FDA)–approved stem cell products are derived from umbilical cord blood, and their only approved use is hematopoietic and immunologic reconstitution (*1*). On September 17, 2018, the Texas Department of State Health Services received notification of *Enterobacter cloacae* and *Citrobacter freundii* bloodstream infections in three patients who had received injections or infusions of non-FDA–approved umbilical cord blood-derived stem cell products processed by Genetech, Inc., and distributed by Liveyon, LLC, for other than hematopoietic or immunologic reconstitution at an outpatient clinic on September 12. Patient isolates of *E. cloacae* had identical pulsed-field gel electrophoresis patterns, suggesting a common source. On September 22, the Florida Department of Health received notification of *Escherichia coli*, *Enterococcus faecalis,* and *Proteus mirabilis* joint infections in four patients who had received injections of these same products at an orthopedic clinic during February 15–August 30, 2018, also for other than hematopoietic or immunologic reconstitution. Cultures of unopened products from the clinic by a Florida hospital identified contamination with *E. coli* and *E. faecalis*. In response, on September 28, Liveyon issued a voluntary recall and immediately discontinued purchase of the Genetech-processed stem cell products (*2*,*3*). On October 4, CDC issued a nationwide call for reports of culture-confirmed infections in patients who had received the Liveyon product.

As of December 14, CDC has received reports of infections in 12 patients from three states, including the initial Florida and Texas cases: Texas (seven), Florida (four), and Arizona (one). Infection types included bloodstream infections, joint infections, and epidural abscesses, among others. All 12 patients received infusions or injections of Liveyon's product before the recall. Among 11 patients for whom conditions prompting product administration were known, all had nonhematopoietic conditions such as pain or orthopedic conditions. All patients were hospitalized; none died (Table).

CDC tested unopened vials obtained from the Texas and Florida clinics where the initial patients had received the product. The six vials from Texas had the same cord-blood donor and processing date as those that had been administered to the patients with infections. *E. cloacae* was isolated from all six vials; *C. freundii* also was isolated from five. The four vials from Florida were from different donors and processing dates than were the vials from Texas. *E. coli* was isolated from one of two vials from the same cord-blood donor and processing date; *E.coli* and *E. faecalis* were isolated from one of two vials from two unique donors with unique processing dates.

Ongoing investigations include active case finding, additional laboratory testing to compare clinical and product isolates, onsite assessments of health care facility infection control and injection safety practices, and investigation of manufacturing practices (including distribution); initial investigation suggests that bacterial contamination occurred before distribution. Umbilical cord blood cannot be decontaminated after collection because there are currently no validated processes for sterilization, so manufacture of derived products must be highly controlled to prevent distribution of contaminated products (*4*). The Genetech-processed, Liveyon-distributed product is not FDA-approved or lawfully marketed. Though Genetech and Liveyon are registered with FDA, such registration is not a form of FDA approval. FDA registration alone does not demonstrate compliance of firms or their products with the law.

Regardless of when contamination occurred, this investigation highlights the serious potential risks to patients of stem cell therapies administered for unapproved and unproven uses other than hematopoietic or immunologic reconstitution (*5*). Although the safety and efficacy of stem cells for other than hematopoietic or immunologic reconstitution have not been well established (*1*,*4*), many companies, clinics, and clinicians continue to market products from various sources as treatment for orthopedic, neurologic, and rheumatologic conditions without FDA approval. Such clinics and providers operate in outpatient settings, which often have less robust oversight of infection control measures, including injection safety and medication preparation (*6*), potentially amplifying risk to patients. Therefore, FDA has recommended that patients avoid receiving such products outside controlled clinical studies being conducted under an investigational new drug application; these settings help ensure that appropriate manufacturing and safety reporting procedures are followed (*1*). Health care professionals and consumers should report any adverse events related to treatment with the Genetech/Liveyon products or any unapproved stem cell therapies to FDA's MedWatch Safety Information and Adverse Event Reporting Program (https://www.fda.gov/Safety/MedWatch/).

TABLE. Clinical characteristics of patients with culture-confirmed infections after receiving umbilical cord blood-derived stem cell products for other than hematopoietic or immunologic reconstitution — United States, 2018

Patient	Route/Site of administration	Date administered	Setting	Condition prompting product administration*	Specimen collection date, first positive culture	Organism isolated	Infection site	Days of initial hospitalization to treat infection
1	Intra-articular injection, knee and shoulder	Feb 15, 2018	Orthopedic clinic	Degenerative joint disease	Feb 21, 2018	*Escherichia coli, Proteus mirabilis*	Knee	15
2	Intra-articular injection, lumbar spine	Jun 13, 2018	Pain clinic	Pain	Jun 14, 2018	*Escherichia coli*	Bloodstream	4
3	Intra-articular injection, lumbar spine	Jul 27, 2018	Ambulatory surgery center	Pain	Aug 1, 2018	*Escherichia coli, Enterococcus faecalis*	Bloodstream, lumbosacral epidural abscess, discitis, and vertebral osteomyelitis†	58
4	Intra-articular injection, knee and shoulder	Aug 3, 2018	Orthopedic clinic	Unknown	Aug 10, 2018	*Escherichia coli, Enterococcus faecalis*	Knee	30
5	Intra-articular injection, shoulders	Aug 14, 2018	Chiropractic clinic	Osteoarthritis	Aug 29, 2018	*Escherichia coli*	Bloodstream, shoulders	8
6	Intra-articular injection, shoulder	Aug 22, 2018	Orthopedic clinic	Rotator cuff tear with intrasynovial cyst	Sep 9, 2018	*Escherichia coli*	Shoulder	6
7	Intra-articular injection, lumbar spine	Aug 28, 2018	Spine treatment clinic	Lumbar back pain	Sep 1, 2018	*Citrobacter koseri*	Bloodstream	6
8	Intra-articular injection, lumbar spine	Aug 29, 2018	Pain clinic	Pain	Sep 4, 2018	*Escherichia coli, Enterococcus faecalis*	Bloodstream	35
9	Intra-articular injection, knee	Aug 30, 2018	Orthopedic clinic	Osteoarthritis	Sep 7, 2018	*Escherichia coli, Enterococcus faecalis*	Knee	5
10	Intra-articular injection, cervical spine	Sep 12, 2018	Pain clinic	Pain	Sep 15, 2018	*Enterobacter cloacae, Citrobacter freundii*	Bloodstream, cellulitis at injection site§	9
11	Intra-articular injection, cervical and lumbar spine	Sep 12, 2018	Pain clinic	Pain (history of rheumatoid arthritis)	Sep 16, 2018	*Enterobacter cloacae, Citrobacter freundii*	Bloodstream	12
12	Intra-articular injection, lumbar spine and index fingers; intravenous infusion	Sep 12, 2018	Pain clinic	Pain, rheumatoid arthritis, osteoarthritis	Sep 16, 2018	*Enterobacter cloacae*	Bloodstream, lumbar epidural abscess	12

* As reported to CDC by health departments.
† Abscess and vertebrae were not cultured; both organisms were isolated from blood, and *E. faecalis* only was isolated from disc space.
§ No organisms were isolated from skin; both organisms were isolated from blood.

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