Outbreak Summary Report
385146 – A: NECC Fungal Outbreak

Maine Center for Disease Control and Prevention
An Office of the Department of Health and Human Services
Paul R. LePage, Governor Mary C. Mayhew, Commissioner

Executive Summary

Federal Centers for Disease Control and Prevention (CDC), in collaboration with state and local health departments and the Food and Drug Administration (FDA) investigated a multistate outbreak of fungal meningitis and other infections among patients who received contaminated steroid injections. This form of meningitis is not contagious. The investigation also includes fungal infections associated with the injection site, both spinal and peripheral joints, such as a knee, shoulder or ankle.

Maine facilities did not receive any of the implicated contaminated lots, but did perform patient notifications for any patient who received an injectable, ophthalmic or surgical solution from the implicated facility. Some Maine residents received contaminated product in another state.

Timeline of Multistate Outbreak of Fungal Infections, Maine 2012-13

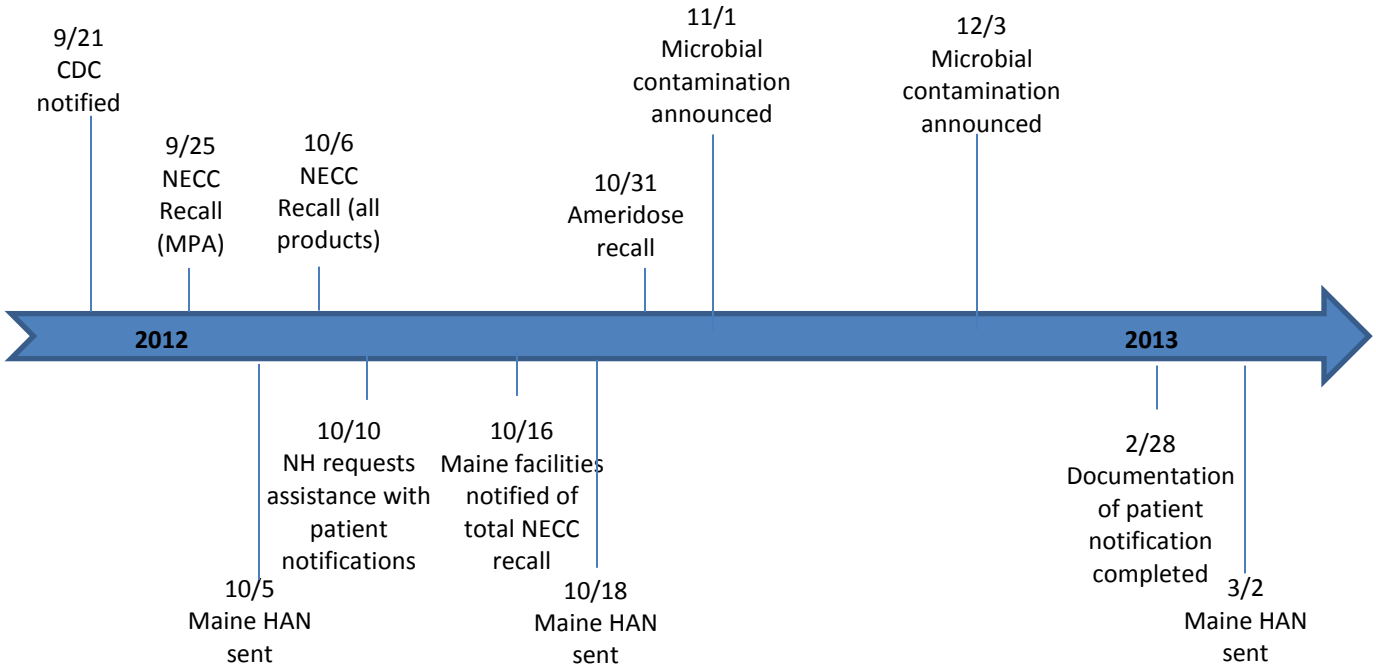


Table of Contents

Background 2
Current Status 2
Maine Response 3
MPA Recall 3
Total NECC Recall 3
Ameridose Recall 6
Outreach 6
Maine Notifications (Health Alerts) 6
Discussion 6
Appendix 1: Types of Products Received from NECC 8
Appendix 2: NECC Exposure Response Script 10
Appendix 3: NECC Exposure Report Form 11

Background

On September 21, 2012, the Tennessee Department of Health notified federal CDC of a patient with onset of meningitis approximately 19 days following epidural steroid injection at a Tennessee ambulatory surgery center. Initial cultures of cerebrospinal fluid (CSF) and blood were negative; subsequently, *Aspergillus fumigatus* was isolated from CSF by fungal culture. On September 28, investigators identified a case outside of Tennessee, possibly indicating contamination of a widely distributed medication.

On September 25, 2012, the New England Compounding Center (NECC) located in Framingham, Massachusetts voluntarily recalled the following lots of methylprednisolone acetate (MPA) (PF) 80mg/ml:

Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #05212012@68, BUD 11/17/2012

Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #06292012@26, BUD 12/26/2012

Methylprednisolone Acetate (PF) 80 mg/ml Injection, Lot #08102012@51, BUD 2/6/2013

Twenty-three states received these recalled lots including Connecticut, New Hampshire, New York, Pennsylvania, and Rhode Island in the Northeast.

On October 3, 2012, the compounding center ceased all production and initiated recall of all MPA and other drug products prepared for intrathecal administration. On October 4, 2012, the FDA advised healthcare providers to not use any NECC products. On October 6, NECC announced a recall of all its products.

As a result of the ongoing investigation of NECC, a patient with possible meningitis potentially associated with epidural injection of an additional NECC product, triamcinolone acetonide, was identified. A transplant patient with *Aspergillus fumigatus* infection who was administered NECC cardioplegic solution during surgery was also reported. On October 15, 2012, FDA questioned the sterility of any injectable drugs, including ophthalmic drugs that are injectable or used in conjunction with eye surgery, and cardioplegic solutions produced by NECC. Out of an abundance of caution, FDA recommended alerting all patients who may have received those products.

On October 31, 2012, a second compounding company, Ameridose, announced a voluntary recall of all unexpired products in circulation.

On November 1 and December 3, 2012 FDA announced the identification of microbial contamination in unopened vials of betamethasone, cardioplegia, and triamcinolone solutions distributed and recalled from NECC. This included bacteria known as *Bacillus*, and fungal species including *Aspergillus tubingensis, Aspergillus fumigatus*, *Cladosporium* species, and *Penicillium* species.

Current Status (as of April 8, 2013):

Case classification, including confirmed and probable cases, is according to the current CDC case definition. Cases are counted in the state where they received the medication, not in the state of residence.

- # of states with cases: 20
- # of cases: 733
    - # of cases in Maine residents (counted as New Hampshire cases): 2

- # of deaths: 53

Cases are still being identified, primarily associated with the 3 contaminated lots of MPA.

Source: http://www.cdc.gov/hai/outbreaks/meningitis.html

Maine Response

MPA Recall

No Maine facilities received the three recalled lots of MPA. However, multiple Maine residents received injections at a Pain Clinic in New Hampshire. The New Hampshire Department of Health and Human Services, Division of Public Health Services identified 76 Maine residents who received product in New Hampshire, 16 of which were epidural injections.

On October 10, 2012, the New Hampshire Department of Public Health requested assistance in notifying three Maine residents they had been unable to reach. Maine Center for Disease Control (Maine CDC) followed the following protocol:

- Attempted to reach the patient by phone. If unable to contact;
- Made a home visit. If patient was not at home, left a letter at the residence requesting a call back. If patient did not call back within three days;
- Sent a letter to the patient's home (assuming forwarding service if the patient no longer resided at that residence) requesting a call back.

Using this method, Maine CDC was able to contact two of the three patients. The letter sent to the third patient was returned 'Unable to Forward.' On November 21, 2012, New Hampshire notified Maine that the third patient had presented for care and was evaluated – completing all Maine notifications

Maine CDC continued to respond to consult requests from Maine residents, and assist New Hampshire in reaching patients for follow up or obtaining case information. For all patients that were symptomatic, Maine CDC completed the New Hampshire case report form, and forwarded all completed forms to New Hampshire for follow up.

Of the 76 identified Maine residents, two are considered cases and are included in New Hampshire's 14 cases. Both cases met the probable case definition for meningitis.

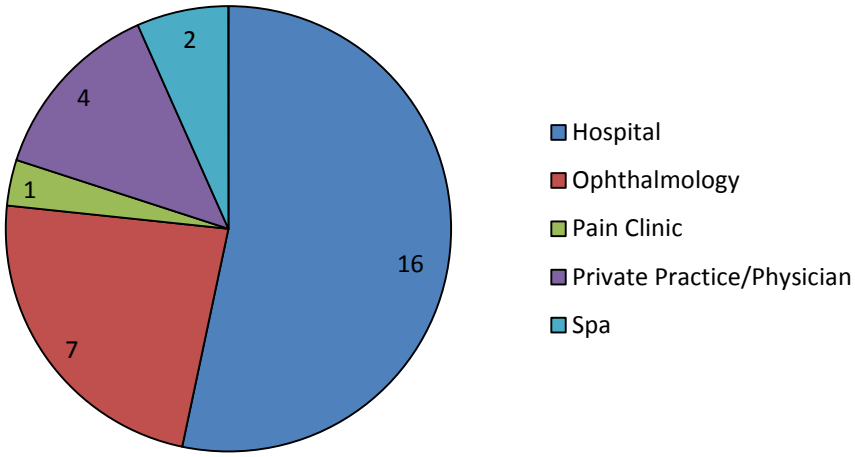
Maine CDC also followed up on one case of meningitis in a Minnesota resident who was hospitalized in Maine. This patient received an MPA injection in Minnesota, but it was determined to be from a lot other than the recalled lots. Maine CDC completed Minnesota's case report form, and forwarded the completed form to Minnesota for follow up.

Total NECC Recall

Maine CDC received an invoice list of all Maine facilities that had ordered product from NECC from May 2012 to October 2012. Maine CDC identified 30 facilities that received NECC product within this time frame. These 30 facilities were in ten counties including: Androscoggin, Aroostook, Cumberland, Hancock, Kennebec, Lincoln, Penobscot, Piscataquis, Waldo, and York.

Of the 30 facilities identified, just over half were hospitals. Other types of facilities included ophthalmology, pain clinics, private practices, and spas (Figure 1).

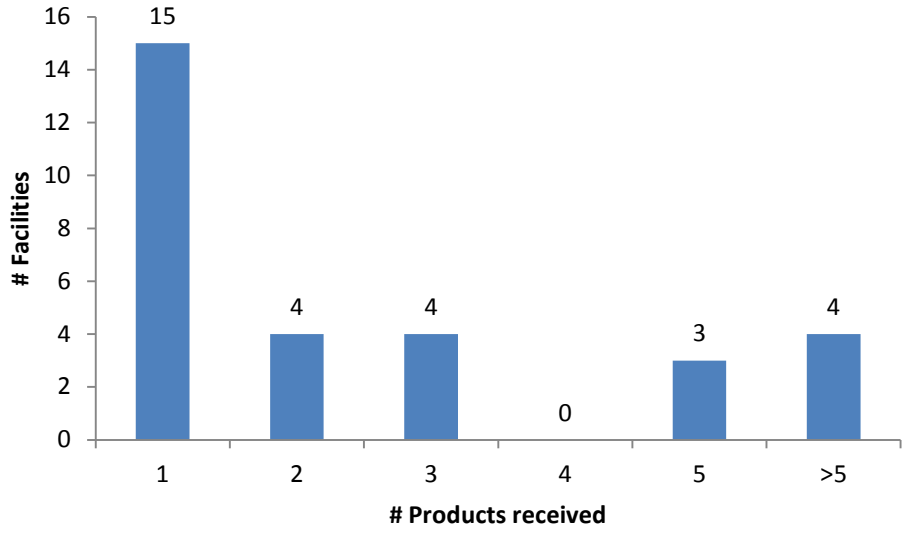
Figure 1: Type of Facilities that received NECC product, Maine May – October 2012



There were 253 invoices from Maine facilities from May 2012 through October 2012, encompassing 66 product formulations (Appendix 1).

The number of product type received per facility ranged from 1 to 17 with a mean number of 3.9 products. Fifteen facilities only received one product (Figure 2).

Figure 2: Number of Products Received per Facility, Maine May – October 2012

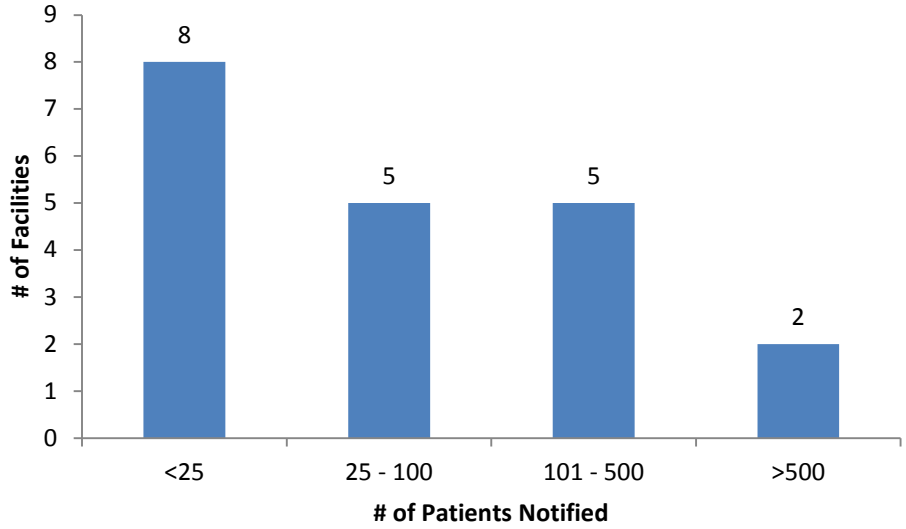


On October 16, 2012, Maine CDC began calling each facility to make sure they were aware of the notification recommendations, provide information, and answer any questions. A standardized script was created for all phone calls (Appendix 2). The recommended point of contact for hospitals was the Chief of Pharmacy, and for other settings either a licensed clinician or practice manager. An information packet was sent to all sites either by email or fax, which included an exposure report form that was requested to be returned to Maine CDC after all notifications were completed (Appendix 3). Maine CDC reached the appropriate personnel at all sites by October 18, 2012.

Maine CDC kept all partners aware of federal updates through an e-mail list serve. Maine CDC sent reminder notifications for the NECC report forms in November, December and January, and had all reports returned by February 2013.

Of the 30 sites that received any NECC product, 21 completed patient notification. The other nine sites determined that notification was not necessary (the product was not injectable, ophthalmic, or used during surgery). For the 21 sites that did notify patients, the minimum number of patients notified was 1 and the maximum number was 1,400 (Figure 3). At least 3,766 patients were notified of their potential exposure (some facilities did not have an exact number of notifications completed).

Figure 3: Number of Patients Notified by Facility, Maine 2012*



* One facility did not provide a number

The majority of facilities used multiple methods to complete patient notification. The two most common methods included letter and phone (Table 1).

Table 1: Methods Used for Patient Notification, Maine 2012*

How Notifications Were Completed	# of Facilities
Call Center	1
In Person (office visits)	3
Letter	17
Phone	12
Website	2

* Facilities may have used more than 1 method for notification

In addition to notifying patients of their potential exposure, Maine CDC notified all hospital laboratories in the state to be aware of the potential risk, and to provide the standard testing recommendations. This notification was sent through MicroNet, an informal statewide network of microbiologists. Maine CDC also requested reports of positive fungal cultures on invasive specimens from hospitals throughout the state. Maine CDC followed up on five reports of suspect fungal meningitis or septic arthritis, none of

which met the case definition to be included in the outbreak. No Maine cases were identified in relation to the NECC products received in the state.

Ameridose Recall
Federal CDC and the FDA did not recommend follow up for patient who received Ameridose products, therefore Maine CDC did not recommend any patient notifications.

Outreach
As part of Maine CDC's response to the multistate fungal infections outbreak, we notified our partners of the situation and requested that they notify us of any unusual activity or reports. Maine CDC communicated with the following entities:

- Poison Control
- Laboratories (MicroNet)
- Maine Medical Examiner's office

Maine Notifications (Health Alerts)
Maine CDC sent three health alerts to healthcare providers regarding the fungal infections outbreak.

- October 5, 2012: Meningitis and Stroke Associated with Potentially Contaminated Product
- October 18, 2012: Update on Fungal Infections Outbreak and FDA Recall
- March 12, 2013: Fungal Infections Update

Discussion

This was a very complex outbreak, involving large numbers of partners from multiple state and federal agencies. The response changed very rapidly, and required daily conference calls with federal partners to remain aware of the situation. It was an unusual outbreak in that cases were counted in the state where they were treated, and not in their state of residence. There were many facets to this outbreak that warrant future work to improve response in future situations including:

- Difficulty in contacting facilities. Maine CDC has good relationships with the Infection Practioners at hospitals, but little to no experience in working with pharmacies. Many of the facilities were not hospitals, and do not routinely interact with Maine CDC which created many questions.
- Difficulty in identifying patients who had received product. Some facilities track each dose of medication by individual through a barcoded medication dispensing and tracking system, but many outpatient facilities were unable to determine exactly who received what. They were able to identify patient who had received the medication, but they were unable to ascertain whether that product was an NECC product or not, making patient notification extremely difficult and time consuming.
- Difficult messaging. Maine did not receive any of the contaminated product, so messaging around the outbreak was difficult. Maine also had no cases (because the 2 cases counted in New Hampshire) which made the urgency difficult to ascertain. Messaging around the NECC recall and notification was also difficult, as federal partners made it clear that the notifications were being done "out of an abundance of caution." It was difficult to determine or define the risk for facilities, and in turn for their patients who were exposed.
- Communication. This was a multistate outbreak with major federal implications. Maine had multiple residents being notified by other states, but we were not always aware of the exposure. Maine also did not have an easy secure way to exchange large amounts of data between states in an electronic form. New Hampshire provided access to their Health Alert System so that we could share data for this event.

- Volume of work. Maine did not have any cases to follow up on, but this outbreak response still required a large volume of work in order to stay aware of the situation, and assist our partners with their questions and patient notifications.

Although the outbreak continues for states that received the contaminated lots of MPA, Maine completed all the requested activities for this outbreak. Overall, the response to the outbreak took many months, and required a great deal of follow up. Many lessons were learned that could be applied to future large national outbreaks.

Appendix 1: Types of Products Received from NECC, Maine May – October 2012

Product	Number	Percent
ATROPINE 1mg/mL/1	4	1.58
AVASTIN (RP)	23	9.09
B1000	2	0.79
BETA-PHONO 0.05% GEL	8	3.16
BRD GEL, 1ML	3	1.19
CAFFEINE BENZ 250MG/ML,2ML	3	1.19
CEFTAZ	5	1.98
DEX S.P 4/2(PF)	3	1.19
DIPH 50/1ML Vial	1	0.4
EDTA 1%, PF, 10ML	3	1.19
ETHA20%,10ML	2	0.79
ETHA20%,5ML	2	0.79
FUROS 10/10 VIAL	1	0.4
FUROS 10/4 VIAL	2	0.79
GLYC (ORAL)	1	0.4
GLYC-INJ 5ML	2	0.79
GLYC-OP	2	0.79
H10	4	1.58
HB10/2.5	3	1.19
HB50/19.4	1	0.4
HBC20/5/100	2	0.79
HY150/1	2	0.79
HY150/1 PF	9	3.56
HY150/10 PF	2	0.79
HY150/5	2	0.79
HYDROXYPROG/1	7	2.77
INTERFERON (PF) 1MU/ML	2	0.79
KETOR 30MG/ML,1ML SYR	2	0.79
LET 3ML	1	0.4
LET GEL 3ML SYRINGE	25	9.88
M50	3	1.19
MB2.6/2000	1	0.4
MB25/9.6	1	0.4
MB50/10	2	0.79
MB50/14.7	1	0.4
MB50/6.1	1	0.4
MB50/6.9	3	1.19

MB50/9.23	1	0.4
MB7/20	1	0.4
MBC30/1024/509.5	2	0.79
MC10/30	1	0.4
MC50/38.4	1	0.4
METHACHOLINE (M) KIT/5	1	0.4
METHACHOLINE KIT/5	16	6.32
METOC 5MG/ML, 2ML SYR	8	3.16
MISOP 800MCG SUPP	2	0.79
MITOMYCIN 0.2, 1ML	5	1.98
MITOMYCIN 0.4, 1ML	3	1.19
MITOMYCIN 0.5, 1ML	5	1.98
NALBUPH(PF)10MG/ML,1ML	4	1.58
PE/CY/BU/FL 2.5	20	7.91
PE/LIDO 2.5-1	4	1.58
PHENYL 1.5%/1 PF	3	1.19
PHOSCHOLINE 50MG-50	3	1.19
POTAS PHOSPH 3MMOL/ML,10ML	1	0.4
POTASS CHLOR 2 MEQ-10 ML	1	0.4
POTASSIUM/CHLORIDE	1	0.4
PROCH5/2 PF	6	2.37
SBB300/20/3.5	3	1.19
SOD BICARB/50 PF SYR	3	1.19
STS 1/30	1	0.4
SUL.BLUE(PF)	4	1.58
THIAM100MG/ML, 1ML	3	1.19
TRIAC 20-6-4-30	1	0.4
TRIAM AC 40/1 PF	3	1.19
VANCO10	5	1.98

Appendix 2: NECC Exposure Response Script

Facility Name:

Point of Contact:
manager

Phone number:

Maine CDC team member:

Recommended Points of Contact
Hospital: Chief of Pharmacy
Other settings: Licensed clinician or Practice

Date:

NECC Exposure Response script

Good afternoon! My name is _____ and I am calling from Maine CDC regarding the recent fungal meningitis and septic arthritis outbreak. As you have probably heard the New England Compounding Center (NECC) and FDA have expanded the recall to all NECC products. We have identified your facility as receiving NECC product since May of this year. Have you seen the FDA statement regarding this expanded recall?

☐ Yes ☐ No

If NO:
Okay, I will summarize it for you. Based on new information, out of an abundance of caution, FDA advises facilities who received product for NECC to follow-up with patients for whom your facility administered:

- an injectable product,
  - including an ophthalmic drug that is injectable or used in conjunction with eye surgery,
- or a cardioplegic solution (only used in open heart surgery).

Your facility should inform patients who received the NECC products noted above of the symptoms of possible infection and instruct them to contact you or another healthcare provider immediately if they experience any symptoms of infection.

If YES:
Great. Then you are aware that FDA is recommending that you follow up with patients for whom your facility administered an:

- injectable product,
  - including an ophthalmic drug that is injectable or used in conjunction with eye surgery,
- or a cardioplegic solution (only used in open heart surgery).

Have you begun this process?

☐ Yes (if yes – who is coordinating the effort?_____)
☐ No

CONCLUSION :
At Maine CDC, we are working to monitor the progress of this effort, and we are requesting that you report back to us:

- the amount of product received,
- the amount distributed,
- the number of patients you notified, and
- the method you used to notify them.

We would like to send you a copy of the FDA statement, draft text that can be used in a letter or e-mail to your patients, and the reporting form that will need to be returned to Maine CDC. Who should this information go to? -
_____

What is the best way to get this information to the correct person?

☐ E-mail _____
☐ Fax _____

We will send this information to you within 24 hours. Do you have any additional questions?

If you think of any additional questions you can call us at 1-800-821-5821, or e-mail us at disease.reporting@maine.gov. Thank you for your time.

Appendix 3: NECC Recall Exposure Form

Maine Center for Disease Control and Prevention
An Office of the Department of Health and Human Services
Paul R. LePage, Governor Mary C. Mayhew, Commissioner

Department of Health and Human Services
Maine Center for Disease Control and Prevention
286 Water Street
11 State House Station
Augusta, Maine 04333-0011
Tel.: (207) 287-8016; Fax: (207) 287-9058
TTY Users: Dial 711 (Maine Relay)

NECC exposure report form

Name of facility:

Person reporting:

Contact phone:

Contact e-mail:

Name of Product	Amount received	Amount used	# patients contacted
1.			
2.			
3.			
4.			
5.			
6.			
7.			
8.			
9.			
10.			
11.			
12.			

Patients were contacted by:

☐ Phone ☐ E-mail ☐ Letter ☐ Other means:

Date contacts complete:

Please attach a copy of the letter, or script that was used to notify patients. This form should be returned by e-mail to disease.reporting@maine.gov or by fax to 207-287-6865.