Essential Steps of an Outbreak Investigation

① Confirm the outbreak
② Verify the diagnosis
③ Define and identify cases
   a. Case definition
   b. Case finding and counting
④ Perform descriptive epidemiology
   a. Who is at risk?
   b. Observe
   c. Interview
   d. Case reviews
⑤ Develop hypotheses
⑥ Evaluate hypotheses
⑦ Implement control and prevention measures
⑧ Communicate findings

Learning Objectives

• Define outbreak

• Describe the systematic steps involved in outbreak investigations and generic epidemiologic investigations of infections.

• Explain the importance of outbreak communications
Is it an OUDBREAK? The occurrence of a disease above what is normally expected within a specific place or group of people over a given period of time (CDC definition)

Is it IMPORTANT? i.e. does it require investigation?

The occurrence of a disease above what is normally expected within a specific place or group of people over a given period of time is referred to as an outbreak. Whether an outbreak is important enough to require investigation depends on various factors, including the severity of the disease and the potential for transmission.

Bacteremia in the setting of diversion (1.1)

Confirm outbreak, verify diagnosis, define and identify cases:

- 9 patients in a 50 bed medical-surgical with *Achromobacter xylosoxidans* bacteremia.
- No environmental source identified.

Descriptive epidemiology:

- Bacteremia within 26-62h of admission.
- All 9 on morphine via PCA pump.
- 7/9 in medical-surgical unit.
- Nurse C (1 of 11 nurses starting or changing a PCA pump) associated with all 9 cases (OR, 46; 95% CI, 4.0-525.0; *P* < .001).
- Nurse C, only one who worked from admission to hospital to fever onset.

*Behrens-Muller et al. ICHE 2012;33:180-4*
Bacteremia in the setting of diversion (1.2)

Develop and evaluate hypotheses:
- Unlikely tampering of medication prior to dispensation
- Easy to withdraw morphine after dispensation and before attaching to PCA pump

Implement control and prevention measures:
- PCA pump discontinued
- Nurse C resigned

Behrens-Muller et al. ICHE 2012;33:180-4

HCV Outbreak in the Setting of Diversion (2.1)

Confirm outbreak; define and identify cases:
- Over a 2 year period, 3 incident genetically related HCV infections in transplant patients frequenting an outpatient, integrated, multispecialty clinic without identified breaches in IC or risk behaviors for infection

Descriptive epidemiology:
- Exposure period within 6 weeks of negative HCV RNA and one week before positive HCV RNA
- All 3 had visited the interventional radiology unit
- All 3 had received fentanyl

HCV Outbreak in the Setting of Diversion (2.2)

Develop and evaluate hypotheses:
• 21 employees in IR unit during the study period.
• Only one technician of 21 employees tested was HCV RNA positive.
• Phylogenetic analysis confirmed close genetic relatedness.
• Confessed diversion of fentanyl for many years.

If necessary reconsider, refine hypotheses, perform additional studies:
• Two additional cases identified in case ascertainment.


Hepatitis Clusters/Outbreaks in Healthcare Settings

- Unsafe glucose monitoring practices
- Re-use of lancing device (not lancet itself)
- Diversion
- Contamination of med prep areas/vials
- Syringe re-use
- Indirect syringe re-use
HBV and HCV outbreaks associated with healthcare delivery*, 2001- Sept 2012, US

61 Outbreaks - 28 HCV, 31 HBV, 2 HBV and HCV

- 26 Long-term care
- 20 Outpatient clinics
- 9 Hemodialysis facilities
- 6 Hospitals

*Transmission related to transplant/transfusion are not included

Practices associated with HBV transmission during assisted monitoring of blood glucose

1. Use of fingerstick devices on multiple persons.
2. Failure to clean and disinfect blood glucose testing meters between each use.
3. Failure to change or use gloves, or perform hand hygiene between procedures.

How common are lapses during AMBG?

- Evaluation of practices in sample of ambulatory surgical centers (ASCs)\(^1\)
  - 20.8% of ASCs that performed AMBG used the same fingerstick device for >1 patient
  - 32.1% of ASCs that performed AMBG did not clean and disinfect meters after each use

- Recent outbreaks and/or notification events from lapses during AMBG
  - 2010: Reuse of fingerstick devices at health fair; ~60 individuals at-risk\(^2\)
  - 2012: HBV infections at ALF in VA; reuse of fingerstick devices

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**Sweeping knowledge. Preventing infection.**

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**Indirect syringe reuse and HCV transmission**

Two breaches contributing to transmission of HCV:
- Using same syringe to enter single dose vial.
- Using contents from a single-dose vial on more than one patient.

**MMWR 2008 57(19);513-517**

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1. Schaefer et al. JAMA 2010;303(22):2273-2279
Contamination of products
Multiuse TEE ultrasound gel (1.1)

Confirm outbreak; define and identify cases:
- Increase in the number of positive *Pseudomonas aeruginosa* respiratory cultures in a surgical ICU over 1 month.
- 10 cases of respiratory tract infections identified.

Descriptive epidemiology:
- All patients ventilated and after cardiovascular surgery.
- None of the cultures from surgical sites or blood.
- No clustering by OR, surgeon, OR or nursing staff, ICU room.
- No changes in nursing and respiratory care, equipment management or anesthesia practices.
- Intraoperative TEE used in all patients.

MMWR 2012;61:262-4

Contamination of products
Multiuse TEE ultrasound gel (1.2)

Develop and evaluate hypotheses:
- Intraoperative TEE linked to outbreak.
- Environmental cultures of TEE probes negative.
- Procedures >5 h more frequently associated with infection/colonization.
- Cultures of multiuse US transmission gel (open and sealed) grew *P. aeruginosa*.
- 6 additional cases (all colonizations) were identified.
- In all, 16 cases: 7 infections and 9 colonizations.

Implement control and prevention measures:
- Switch from multiuse to single use transmission gel.

Communication:
- Hospital-wide recall of transmission gel.
- Local and State health departments and FDA notification.

MMWR 2012;61:262-4
Contamination of Devices (1.1)

Confirm outbreak; define and identify cases:

- 4 patients with positive BAL for *P. putida* in a 3 day period, an unusual pathogen at a 935 bed tertiary care hospital in Baltimore.
- A previous *P. aeruginosa* outbreak of respiratory tract infections (RTI) due to a loose bronchoscopy port had led to increased surveillance.

Descriptive epidemiology:

- 4 patients had undergone bronchoscopy with 1 of 2 bronchoscopes with loose biopsy ports.
- None of the patients developed an RTI.
- No important deviation in IC practices in the cleaning and maintenance processes.
- No written protocol nor consistent checks for loose parts.
- Recent switch to third party vendor for repair and maintenance.

Cosgrove S et al. ICHE 2012;33:224-229

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Contamination of Devices (1.2)

**Figure 1.** Stratification of case patients into infection risk groups and case outcomes.

Cosgrove S et al. ICHE 2012;33:224-229
Contamination of devices (1.3)

**Develop and evaluate hypotheses:**
- Loosened biopsy port promoted growth of environmental bacteria.

**Implement control and prevention measures:**
- Immediate removal of bronchoscopes from service.
- Elective bronchoscopy procedures cancelled.
- Recommended maintenance and repair by the manufacturer.

Cosgrove S et al. ICHE 2012;33:224-229

Foodborne (1.1)

**Confirm outbreak; define and identify cases:**
- 2 patients identified with MDR ESBL *K. pneumoniae* at a 500 bed tertiary care hospital in Barcelona, Spain.
- Patients had shared room for 13 days.
- Case defined as any patient admitted to the hospital with cultures positive for MDR ESBL *K. pneumoniae*.
- High prevalence of colonization in surveillance rectal swabs of inpatients.
- Negative environmental cultures in patient care areas.

Calbo E et al. CID 2011;52:743-749
**Figure 1.** Number of New Patients With Faecal Colonization or Infection Due to ESBL-producing *K. pneumoniae* Strain.

Calbo E et al. CID 2011;52:743-749

*Spreading knowledge. Preventing infection.*

**Figure 2.** Prevalence of fecal colonization with an extended-spectrum β-lactamase-producing *Klebsiella pneumoniae* strain among patient in medical wards. Only the ward with the highest proportion of colonized patients is shown.

Calbo E et al. CID 2011;52:743-749

*Spreading knowledge. Preventing infection.*
Foodborne (1.4)

As necessary, reconsider/refine hypotheses, perform additional studies:

- In 9 months, 156 inpatients with colonization/infection were identified.
- 22.4% were infected.
- 2 populations at risk:
  - Urinary catheters
  - Malignancies
- Foodborne source from hospital kitchen suspected because of:
  - High prevalence of colonization/infection in all wards and
  - Negative out-patient and employee rectal surveillance cultures and
  - Rapid and simultaneous spread to all units
  - Early colonization after admission
- 14% of food workers, all on night shift, were fecal carriers.
- 37% of environmental surfaces and 1 food stuff sample contaminated.

Calbo E et al. CID 2011;52:743-749

Foodborne (1.5)

Figure 3. Percentage of urinary colonization in all patients with an indwelling urinary catheter.

Calbo E et al. CID 2011;52:743-749
Use of adherence monitors to control MDR A. baumannii (1.1)

Confirm outbreak; define and identify cases:

- Two significant outbreaks of A. baumannii involving 63 patients admitted to NIH 240-bed research hospital during a 2 year period

Descriptive epidemiology:

- All 63 immunosuppressed patients.
- Most were ICU patients.
- 35% with stem cell transplantation.
- 34 (56%) died after acquisition of A. baumannii:
  - 11 direct cause of death.
  - 11 contributed to death.

Palmore T et al. ICHE 2011;32:1166-1172

Spread knowledge. Preventing infection.

Use of adherence monitors to control MDR A. baumannii (1.2)

Implement control and prevention measures:

- Enhanced contact isolation of all ICU patients.
- Active surveillance cultures on patients not known to be infected/colonized.
- Environmental cultures in proximity of patients, distal to bed and bathroom.
- Environmental cultures of shared equipment.

Because IC staff HH compliance, IC training, and feedback had no effect on transmissions, adherence monitors were placed outside the ICU rooms to monitor staff and visitors.

Palmore T et al. ICHE 2011;32:1166-1172

Spread knowledge. Preventing infection.
Use of adherence monitors to control MDR A. baumannii (1.3)

![Graph showing the number of patients over time for different strains of A. baumannii.]

Source: Epidemic curve of multiresistant Acinetobacter baumanii (MDRAB) acquisition by strain and by month, January 2007 through November 2010. Patients who acquired more than 1 strain of MDRAB were classified with the strain they acquired first or, if both were detected simultaneously, with the strain that predominated on follow-up cultures.

Palmore T et al. ICHE 2011;32:1166-1172

Spreading knowledge. Preventing infection.

Use of adherence monitors to control MDR A. baumannii (1.4)

<table>
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<th>Clinical variable</th>
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Note: CI, confidence interval; ICU, intensive care unit.
* Severe neutropenia is defined as absolute neutrophil count less than 500.
\* The 100% CI could not be computed as a result of invalid standard errors in the multiple conditional logistic regression model using forward selection.

Palmore T et al. ICHE 2011;32:1166-1172

Spreading knowledge. Preventing infection.
Use of adherence monitors to control MDR *A. baumannii* (1.5)

**Lessons learned:**

- Short term IC adherence monitors may be helpful in the control of the outbreak and eradication of HCW patient transmission, particularly in grave epidemic situations.
- Poor adherence was associated with large medical teams making rounds.
- Physicians were most often involved in non-compliance than other staff.
- Total cost for adherence monitors in 2009 was $108,000 for the 10 week outbreak, which may be a limiting factor.

Palmore T et al. ICHE 2011;32:1166-1172

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Environmental Culturing

- **Targeted by good epidemiology**
  - Confirms what you already know/suspect
  - Not a first step
- **Most clinical labs not set up to do this**
  - Best to work with labs that are experienced
Surface Sampling

- Surface contamination has been reported as a source in outbreaks of *Acinetobacter*, VRE, *C. difficile*.
- Surface contamination is not uniform and widely used methods can only sample a very small surface area.
  - Swabsticks allow for sampling of more surface area
- Even with the best methods and a known inoculum the yield in getting bacteria off surface is low.
- Yield is further diminished by residual surface disinfectants.

Compounding Pharmacy Outbreaks

- Compounding critical to maintain availability of specialized medications
- Between 1990 and 2005, FDA learned of 240 illnesses and/or deaths associated with improperly compounded products
- Regulations
  - USP Chapter <797>
  - FDA Good Manufacturing Practices
- Have the potential to be more widespread and potentially more difficult to recognize
Multi-State Fungal Meningitis Outbreak — Jan 2013: Outbreak Timeline

Sep 18 2012
56 y old male diagnosed with Aspergillus meningitis 46 days after an epidural glucocorticoid injection @ Tennessee ambulatory surgical center.

September 26, 27, 28 2012
- Lots 05212012@68, 06292012@26, 08102012@51 recalled.
- Identified 17,675 contaminated vials sent to 76 facilities in 23 states.
- 13,534 patients exposed
- Case finding, disclosure initiated in other states.
- Additional case found in North Carolina.

September 18 2012
56 y old male diagnosed with Aspergillus meningitis 46 days after an epidural glucocorticoid injection @ Tennessee ambulatory surgical center.

September 25 2012
- Local/ state public health and CDC notified.
- 7 other patients with fungal meningitis.
- All the vials of methylprednisolone acetate injections purchased from a single compounding pharmacy, New England Compounding Center, Framingham, MA.

October 2 and 18 2012
- Unopened vials revealed presence of fungi.
- Cultures grew Exserohilum rostratum and other molds.

Multi-State Meningitis Outbreak - Healthcare Facilities

Map of Healthcare Facilities that Received Three Recalled Lots* of Methylprednisolone Acetate (MPA) from New England Compounding Center on September 28, 2012

* Lot #P020120010, 09/27/2012; Lot #P020120020, 09/27/2012; Lot #P020120030, 09/28/2012
** All lots of methylprednisolone acetate that were used/recovered were recalled prior to use.
Fungal Meningitis Outbreak, Case Definitions

Probable Case
A person who received a preservative-free methylprednisolone acetate (MPA) injection, with preservative-free MPA that definitely or likely came from one of the following three lots produced by the New England Compounding Center (NECC) (0521120130468, 062920126726, 081020129051), and subsequently developed any of the following:

- Meningitis of unknown etiology following epidural or paraspinous injection after May 21, 2012;
- Posterior circulation stroke without a cardioembolic source and without documentation of a normal cerebrospinal fluid (CSF) profile, following epidural or paraspinous injection after May 21, 2012; or
- Osteomyelitis, abscesses or other infection (e.g., soft tissue infection) of unknown etiology, in the spinal or paraspinous structures at or near the site of injection following epidural or paraspinous injection after May 21, 2012; or
- Osteomyelitis or worsening inflammatory arthritis of a peripheral joint (e.g., knee, shoulder, or ankle) of unknown etiology diagnosed following joint injection after May 21, 2012.

1 Clinically diagnosed meningitis with one or more of the following symptoms: headache, fever, stiff neck, or photophobia, in addition to a CSF profile showing pleocytosis (>5 white blood cells, adjusting for presence of red blood cells by subtracting 1 white blood cell for every 500 red blood cells present) regardless of glucose or protein levels.

2 Paraspinous injections include, but are not limited to, spinal facet joint injection, sacroiliac joint injection, or spinal or paraspinous nerve root/ganglion block.

3 Patients in this category who do not have any documented CSF results should have a lumbar puncture performed if possible, using a different site than was used for the epidural injection when possible.

Confirmed Case
A probable case with evidence (by culture, histopathology, or molecular assay) of a fungal pathogen associated with the clinical syndrome.

Fungal Meningitis Outbreak, CDC Update, 1-28-13

Persons with Fungal Infections Linked to Steroid Injections, by State

CDC continues to receive reports of persons experiencing extraspinal infections (e.g., epidural abscesses, pleurisy, chest, cranial osteomyelitis, or sepsis) due to use of the implicated steroid injections. These extraspinal infections have occurred without documented spinal involvement.
Fungal Meningitis Outbreak, CDC Update 1-28-13

<table>
<thead>
<tr>
<th>State</th>
<th>Total Case Count</th>
<th>Meningitis Only</th>
<th>Meningitis &amp; Paraspinal/Spinal Infection Only</th>
<th>Stroke w/out Lumbar Puncture Only</th>
<th>Paraspinal/Spinal Infection only</th>
<th>Peripheraial Joint Infection Only</th>
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Spraying knowledge. Preventing infection.

Fungal Outbreak, CDC Update, Jan 28 2013

- Paraspinal/Spinal Infection, 40%
- Meningitis, 24%
- Paraspinal/Spinal Infection & Peripheral Joint Infection, 1.5%
- Peripheral Joint Infection, 31.5%
- Meningitis & Paraspinal/Spinal Infection, 12.8, 18%
- Stroke w/out Lumbar Puncture, 6.1%

Spraying knowledge. Preventing infection.
CDC Recommendations to Clinicians

- Contact patients who have been exposed.
- Infected patients have presented with mild symptoms, only slightly worse than baseline.
- Refer symptomatic patients for an MRI AND diagnostic lumbar puncture.
- Report concerning cases to public health.
- Report suspected cases to their state health department.
- Use appropriate treatment for fungal meningitis, parameningeal infections, and joint infections.

Outbreak Literature Review

- Diversion
- Contamination
- Foodborne
- Adherence monitors
  - Palmere T et al. Use of adherence monitors as part of a team approach to control clonal spread of MDR Acinetobacter baumannii in a research hospital. ICHE 2011: 1166-1172.
- Meningitis Fungal Outbreak