How to detect and investigate outbreaks in the healthcare setting

Maria Luisa Moro
LESSONS FROM AN EPIDEMIC, AGAIN

IT seemed like a simple plan. After the rubber top of a vial was swiped with an alcohol-soaked pledget and pierced with a needle, a dose of medication was aspirated, and any residual content was pooled for later use. What could go wrong? But this procedure carries as much as a 2 percent risk of introducing bacteria into the container,\(^1\) and that can trigger a dangerous cascade. If the hands of the operator are contaminated, if there is a nearby reservoir of potential pathogens (e.g., contaminated soap or hand lotion), if the medication is preservative-free, if the contaminant can grow in the medication, and if the medication is introduced into the bloodstream of a susceptible patient, the consequences can be disastrous. Although exceedingly unlikely, this sequence of events occurred in a dialysis center in Colorado where the staff pooled preservative-free epoetin alfa for later use. This practice led to a cluster of patients with *Serratia liquefaciens* bacteremia and pyrogenic reactions from extrinsic contamination of the pooled medication, as reported by Grohskopf et al. in this issue of the *Journal*.\(^2\)

ROBERT A. WEINSTEIN, M.D.
Cook County Hospital
Chicago, IL 60612

NEJM 2001
How frequent outbreaks are?

<table>
<thead>
<tr>
<th>Author</th>
<th>Years</th>
<th>Setting</th>
<th>Incidence/10,000 admissions</th>
<th>% of all HAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haley</td>
<td>1970-1980</td>
<td>7 community hospitals, USA</td>
<td>0.8/10,000</td>
<td>2%</td>
</tr>
<tr>
<td>Wenzel</td>
<td>1978-1982</td>
<td>- University Virginia - Other hospitals USA</td>
<td>1/10,000</td>
<td>- 3.7% - 3%</td>
</tr>
<tr>
<td>Ostrosky-Zeichner</td>
<td>1985-1998</td>
<td>Tertiary care referral center, Mexico</td>
<td>3/10,000</td>
<td>1.5%</td>
</tr>
</tbody>
</table>
And when clusters are also taken into account?

Outbreak: a significant increase of the infection rate

1.5% - 4% of all HAIs

Cluster: two or more related cases (place, time or other factors)

6% of all HAIs

\[
\text{10\% = } \frac{5}{1000} \text{ admissions (if infection rate 5\%)}
\]
Microorganisms causing outbreaks

- Gram negative
  - Enterobacteriaceae
  - Pseudomonas
- S. aureus
- GI infections
- MRSA
- MDR
- MDR-TB
- VRE
- MRSA, VISA, MDR-GN
The majority (849; 83.1%) of the outbreaks were from hospitals, with more than half of them (474) occurring in intensive care units. One hundred twenty-two outbreak investigations were from outpatient care and 51 from nursing homes.
HOW OUTBREAKS CAN CONTRIBUTE TO PREVENTION OF NOSOCOMIAL INFECTION: ANALYSIS OF 1,022 OUTBREAKS

Petra Gastmeier, MD; Sabine Stamm-Balderjahn, MD; Sonja Hansen, MD; Frauke Nitzschke-Tiemann, MD; Irina Zuschneid, MD; Katrin Groneberg, MD; Henning Rüden, MD

- 37% of the outbreaks no identified sources.
- 263 patient
- 122 medical equipment or devices
- 119 the environment
- 112 the staff
- 37 contaminated drugs
- 34 contaminated food
- 33 contaminated care equipment

Infect Control Hosp Epidemiol 2005;26:357-361
Investigation?

Epi/lab?

Control?
Relative priority of investigative and control efforts during an outbreak, based on level of knowledge of the source, mode of transmission, and causative agent

<table>
<thead>
<tr>
<th>Source/Mode of Transmission</th>
<th>Known</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Known</td>
<td>Investigation +++ Control +++</td>
<td>Investigation +++ Control +</td>
</tr>
<tr>
<td>Unknown</td>
<td>Investigation +++ Control +++</td>
<td>Investigation +++ Control +</td>
</tr>
</tbody>
</table>

+++ = highest priority  
+ = lower priority

Goodman RA, Am J Epidemiol 1990
PATIENT-TO-PATIENT TRANSMISSION OF NOSOCOMIAL MALARIA IN ITALY

Maria Luisa Moro, MD; Roberto Romi, PhD; Carlo Severini, PhD; Gian Paolo Casadio, MD; Giovanni Sarta, MD; Guido Tampieri, MD; Antonio Scardovi, MD; Cinzia Pozzetti, RN, CIC; the Malaria Outbreak Group

✓ malaria diagnosed in 1 patient that was admitted for bronchopulmonary disease to the ICU 20 days before the onset of the malaria symptoms (no other exposure)
✓ 3 days of stay in the ICU concomitantly to another patient with malaria
✓ molecular genotyping showed that the two strains were identical
✓ common procedures: CVC, NPT, stick for glicemia
✓ Infection control: no multidose vials, “safe” fingerstick device
✓ The likely source of infection was identified during a training course 6 months later: a nurse reported that, when collecting blood, she placed patients’ fingers directly on the blood glucose meter, a practice she had learned from a poster advertising the device.
Outbreak identification & investigation

Start: Recognize the outbreak timely
Step 1: Verify the diagnosis & establish the existence of an outbreak
Step 2: Report the outbreak & search for information
Step 3: Study the event & first control measures
   - Define and identify cases (case definition, identify and count cases)
   - Perform descriptive epidemiology
   - Develop hypotheses
   - Evaluate hypotheses
   - As necessary, reconsider/refine hypotheses and execute additional studies
   - additional epidemiologic studies
   - other types of studies – laboratory, environmental
Step 4: Implement control and prevention measures and communicate findings
Detection of outbreaks of healthcare infections

- Alert from an effective surveillance system
- Alert from
  - the physician
  - the nurse
  - the hospital microbiologist
  - the hospital epidemiologist
Detection of outbreaks of healthcare infections

- Alert from an effective surveillance system
  - alert organisms surveillance
  - lab softwares (automatic screening of laboratory data)
Computer-Assisted Surveillance for Detecting Clonal Outbreaks of Nosocomial Infection

Donna M. Hacek,1* Ralph L. Cordell,2 Gary A. Noskin,3,4 and Lance R. Peterson1,4

Evanston Northwestern Healthcare, Evanston,1 and Northwestern Memorial Hospital,2 Northwestern University’s Feinberg School of Medicine,4 Chicago, Illinois, and Health Outcomes Branch, Division of Healthcare Quality Promotion, Centers for Disease Control and Prevention, Atlanta, Georgia2

Received 28 August 2003/Returned for modification 22 October 2003/Accepted 4 November 2003

Whole-house surveillance for healthcare-associated infection is no longer the recommended practice because of the large personnel time investment required. We developed a computer-based tracking system using microbiologic data as an aid in detecting potential outbreaks of healthcare-associated infections on a hospital-wide basis. Monthly total isolates of 25 clinically significant hospital pathogens were tallied from 1991 to 1998 to form a database for future comparison. Two different algorithm tools (based on increases of organism numbers over baseline) were applied to determine alert thresholds for suspected outbreaks using this infor-
Detection of outbreaks of healthcare infections

Microrganismo: 1928 - Staphylococcus aureus
Periodo Selezionato: January 1, 2003 - December 31, 2004
Periodicità della rilevazione: Mensile
Outbreak: Definition

- An increase in the occurrence of a complication or disease above the background rate
- One rare infection
  - e.g. malaria
- Many episodes of common infections
  - e.g. MRSA surgical site infections
Clusters that suggest healthcare transmission

- Similar cases on one unit
- Similar cases among similar patients
- Similar cases on a short time interval
- HCW and patients with same infection
Case definition

- Standard set of criteria for deciding if a person should be classified as suffering from the disease under investigation.

- Clinical and/or biological criteria, restrictions of time, place, person

- Simple, practical, objective

- Sensitivity versus specificity

- Several case definitions: confirmed, probable, possible
Examples: Case Definition

“A case of MDR-TB was defined as any patient whose clinical picture was consistent with TB, who had an *M. tuberculosis* isolate resistant to at least isoniazid, rifampin, streptomycin, and ethambutol, and who was diagnosed and treated for MDR-TB at Hospital A and/or Hospital B between October 1991 and July 1995.”

Moro ML et al, AIDS 1998
Case Finding

Use case definition to find other cases in the source population

- Large potential source population: discharge diagnoses, microbiology log books, emergency room visits, use of diagnostic technique

- Small population (unit of hospital): review charts of entire cohort
Confirm outbreak and diagnosis

More cases than expected?
- Surveillance data
- Surveys: hospitals, laboratories, physicians

Be cautious!
- Seasonal variations
- Changes in the organization/admission policies
- Diagnostic bias (new technique)
- Diagnostic errors (pseudo-outbreaks)
Search for similar outbreaks in the literature

**Infection.** 2011 Feb;39(1):29-34.

Worldwide Outbreak Database: the largest collection of nosocomial outbreaks.

*Vonberg RP, Weitzel-Kage D, Behnke M, Gastmeier P.*
### Outbreak Database

**Worldwide Database for Nosocomial Outbreaks**

**Beta Release**

Your query was: acinetobacter

183 Results of 2764 found. (Query date: 2011-11-28 19:09:41 (UTC+00:00:00))

#### Table of Outbreaks

<table>
<thead>
<tr>
<th>Ranking</th>
<th>PDF</th>
<th>Matchcode</th>
<th>Title</th>
<th>Author</th>
<th>Language</th>
<th>Publication Type</th>
<th>Study Type</th>
<th>Reference [RI]</th>
<th>Year</th>
<th>Articles Related [AR]</th>
<th>Further Outbreaks [FO]</th>
<th>Comments [CS]</th>
<th>URL [URI]</th>
</tr>
</thead>
</table>
Outbreak confirmed ✅

Adopt immediate control measures
- Isolation precautions
- Hand hygiene
- Reinforce standard hygienic measures
- Others

Decide if further investigation is needed
- Aetiological agent
- Mode of transmission
- Vehicle of transmission
- Source of contamination
- Population at risk
- Exposure causing illness
Rapid notification of alert & outbreaks in the Emilia-Romagna Region

• Since 2006
• **What** should be rapidly notified?
  – Single case of “rare” HCAIS
  – Isolation of unusual antimicrobial resistant bugs
  – Outbreaks and clusters of HAIs (hospitals, nursing homes, ambulatory)
• **How**?
  – By e-mail of Fax (since next year web-based system)
• **Why**?
  – Outbreaks are a small but significant part of HAIs: it is important to to be prepared and detect them rapidly
Since 2006, outbreaks in healthcare setting must be notified in the Emilia-Romagna region

### Emilia-Romagna/In un dossier le indicazioni agli

**Infezioni H sotto**

Attese in Regione 56-169 epidemie ogni anno

<table>
<thead>
<tr>
<th>N. ricoveri/anno</th>
<th>N. presidi ospedalieri in Regione</th>
<th>N. epidemie attese/anno in ogni presidio*</th>
<th>N. infezioni nell’ambito di epidemie o cluster epidemiici/anno**</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;50.000</td>
<td>2</td>
<td>5-18</td>
<td>252-474</td>
</tr>
<tr>
<td>30.001-50.000</td>
<td>4</td>
<td>3-13</td>
<td>161-345</td>
</tr>
<tr>
<td>20.001-30.000</td>
<td>8</td>
<td>2-8</td>
<td>103-236</td>
</tr>
<tr>
<td>5.001-20.000</td>
<td>9</td>
<td>0,5-5</td>
<td>35-137</td>
</tr>
<tr>
<td>&lt;5.000</td>
<td>5</td>
<td>0-1</td>
<td>2-34</td>
</tr>
<tr>
<td>Tot. Regione***</td>
<td>28</td>
<td>56-169</td>
<td>2.825-4.520</td>
</tr>
</tbody>
</table>

* Considerando una frequenza di 1-3/10.000 ricoveri e i ricoveri/anno.
** Considerando che si verifichino 5-8 infezioni ospedalieri/100 ricoveri e che il 10% di queste sia nell’ambito di epidemie o cluster epidemiici.
*** 564.918 ricoveri nel 2003.
Epidemiological investigation

**Objective:** To develop an hypothesis about the source and mechanism of transmission

**Methods:** Descriptive data – cases satisfying the “case definition criteria”

**TIME**
- Epidemic curve

**PLACE**
- Ward/Service
- Room/bed
- Operating Room

**PERSON**
- Age, gender, disease
- Exposures
- Invasive procedures

- Is it common source or person-to-person?
- Are cases aggregated by place of stay or treatment?
- Are cases sharing one or more characteristics?
Eighteen cases of infection were identified in the different phases of the investigation. Of these, five constitute a significant molecular cluster of infection. A P. aeruginosa strain with the same genetic fingerprint and sequence type (ST175) as clinical isolates strain was also isolated from a heavily contaminated triclosan soap dispenser.
Epi curve

An epi curve is a graphic depiction of the **number of outbreak cases by date of illness onset**. It is useful because it can provide information on the outbreak’s:

- Pattern of spread
- Magnitude
- Outliers
- Time trend
- Exposure and/or disease incubation period
Pattern of spread

Figure 1. Example of an epidemic curve from a common intermittent exposure source

- Shorter duration
- Sharp peak in epidemic curve
- Rapid resolution
  - May resolve without intervention

Figure 3. Example of a point source epidemic curve

North Carolina Center for Public Health Preparedness, Focus on Field Epidemiology
Estimation of time or period of exposure

Probable period of exposure
**Common source**

- **Intrinsic contamination (at production):** parenteral nutrition, disinfectants, plasma, immunoglobulins, creams, peritoneal liquids, etc.

- **Extrinsic contamination (in use):** disinfectants, contrast media, heparin, multidose vials, anesthetics, powder milk, endoscopes, haemodialysis, finger sticks, etc.
Transmission of Hepatitis C Virus in a Gynecological Surgery Setting

MARCO MASSARI, NICOLA PETROSILLO, GIUSEPPE IPPOLITO, LAURA Solfarosi, LUCIO BONAZZI, MASSIMO CLEMENTI, AND ALDO MANZIN

Divisione Malattie Infettive Arcispedale “Santa Maria Nuova” Azienda Ospedaliera, Reggio Emilia, 1 Istituto Nazionale per le Malattie Infettive, IRCCS “L. Spallanzani,” Rome, 2 Dipartimento Scienze Biomediche, University of Trieste, Trieste, and Istituto di Microbiologia, University of Ancona, Ancona, Italy

Received 15 November 2000/Returned for modification 2 February 2001/Accepted 30 May 2001

- 4 Hepatitis C cases in women in gynecology (all HCV type 1b)
- molecular analysis (sequential analysis) close match between the index case and the secondary cases
- all underwent surgery the same day
- multidose propofol
Person to person or persistent environmental source

- Hands of HCWs
- Carrier (S.aureus, Streptococco di gruppo A, Candida e Nocardia, Epatite B, Epatite C, HIV, Salmonella, Epatite A)
- Airborne (Measles, chickenpox, TB), and droplets (Adenovirus, influenza, parotitis, Mycoplasma pneumoniae, parvovirus, pertussis, rubella, RSV, SARS)
- Environmental (Legionella, aspergillo, Pseudomonas, Flavobacterium.....)
Verify hypothesis: further investigations/studies

- Microbiological investigation of suspected sources or vehicles of transmission
- Epidemiological analytical studies (case-control or cohort studies)
HOW OUTBREAKS CAN CONTRIBUTE TO PREVENTION OF NOSOCOMIAL INFECTION: ANALYSIS OF 1,022 OUTBREAKS

Petra Gastmeier, MD; Sabine Stamm-Balderjahn, MD; Sonja Hansen, MD; Frauke Nitzschke-Tiemann, MD; Irina Zuschneid, MD; Katrin Groneberg, MD; Henning Rüden, MD

<p>| TABLE 5 |</p>
<table>
<thead>
<tr>
<th>PERCENTAGE OF OUTBREAKS USING GENOTYPING METHODS AND ANALYTIC EPIDEMIOLOGIC STUDIES FOR INVESTIGATING OUTBREAKS ACCORDING TO YEAR OF PUBLICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of outbreaks</td>
</tr>
<tr>
<td>Genotyping methods</td>
</tr>
<tr>
<td>Case-control studies</td>
</tr>
<tr>
<td>Cohort studies</td>
</tr>
<tr>
<td>No genotyping methods and no case–control or cohort study</td>
</tr>
</tbody>
</table>

Infect Control Hosp Epidemiol 2005;26:357-361
The Clinical Microbiology Laboratory and Infection Control: Emerging Pathogens, Antimicrobial Resistance, and New Technology

Michael A. Pfaller and Loreen A. Herwaldt

From the Departments of Pathology and Internal Medicine, University of Iowa College of Medicine, Iowa City, Iowa

Table 3. Role of the laboratory in the epidemiological investigation of an outbreak of nosocomial infections.

<table>
<thead>
<tr>
<th>Investigative step</th>
<th>Laboratory participation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identify the problem</td>
<td>Laboratory surveillance</td>
</tr>
<tr>
<td>Form case definition</td>
<td>Communication (early warning)</td>
</tr>
<tr>
<td>Look for additional cases</td>
<td>Microbiological confirmation</td>
</tr>
<tr>
<td>Calculate rates</td>
<td>Identification</td>
</tr>
<tr>
<td></td>
<td>Susceptibility testing</td>
</tr>
<tr>
<td></td>
<td>Archive data on occurrences</td>
</tr>
<tr>
<td></td>
<td>Store isolates</td>
</tr>
<tr>
<td>Characterize the outbreak</td>
<td>Characterize outbreak-related isolates</td>
</tr>
<tr>
<td>Who</td>
<td>Type isolates</td>
</tr>
<tr>
<td>Where</td>
<td>Phenotypic methods</td>
</tr>
<tr>
<td>When</td>
<td>Molecular methods</td>
</tr>
<tr>
<td>What</td>
<td>Assess the number and distribution (clustering) of strains</td>
</tr>
<tr>
<td>Consider possible causes</td>
<td>Conduct supplementary studies</td>
</tr>
<tr>
<td>Define the mode of transmission</td>
<td>Obtain cultures of specimens from personnel, patients, and environment</td>
</tr>
<tr>
<td>Identify potential reservoirs</td>
<td>Select isolates from these cultures on basis of phenotypic characteristics</td>
</tr>
<tr>
<td>Identify potential vectors</td>
<td>Type selected phenotypically identical isolates to determine whether they match the outbreak strain</td>
</tr>
<tr>
<td>Control or terminate the outbreak</td>
<td>Adjust laboratory procedures to support control activities</td>
</tr>
<tr>
<td>Define and implement control measures</td>
<td>Continue laboratory surveillance</td>
</tr>
<tr>
<td>Evaluate the efficacy of control measures</td>
<td>Store isolates</td>
</tr>
<tr>
<td>Continue surveillance for new cases</td>
<td>Maintain communication</td>
</tr>
</tbody>
</table>

NOTE. Adapted in part from [1].
Infection control measures

**Hand hygiene**

**Intensify environmental hygienic measures**

**Compliance to asepsis protocols and promotion of disinfection and sterilization good practices**

**Specific measures** on the basis of the microorganisms and source of infection:

- elimination of contaminated products
- modification of organizational aspects of care
- identification and treatment of carriers
- promotion of specific & appropriate IC measures

**Verify the impact**
What should **not** be done

- Generalized microbiological screening with no prior hypothesis of the infection source
- Aspecific and generalized antimicrobial prophylaxis
- Not allow visitors and relatives entrance, if not strictly necessary
- Close the ward or hospital admission (except than if necessary to assure patient safety)
The ORION statement: guidelines for transparent reporting of outbreak reports and intervention studies of nosocomial infection

Sheldon P Stone, Ben S Cooper, Chris C Kibbler, Barry D Cookson, Jenny A Roberts, Graham F Medley, Georgia Duckworth, Rosalind Lai, Shah Ebrahim, Erwin M Brown, Phil J Wiffen, Peter G Davey

The quality of research in hospital epidemiology (infection control) must be improved to be robust enough to influence policy and practice. In order to raise the standards of research and publication, a CONSORT equivalent for these largely quasi-experimental studies has been prepared by the authors of two relevant systematic reviews, following consultation with learned societies, editors of journals, and researchers. The ORION (Outbreak Reports and Intervention Studies Of Nosocomial infection) statement consists of a 22 item checklist, and a summary table. The emphasis is on transparency to improve the quality of reporting and on the use of appropriate statistical techniques. The statement has been endorsed by a number of professional special interest groups and societies. Like CONSORT, ORION should be considered a “work in progress”, which requires ongoing dialogue for successful promotion and dissemination. The statement is therefore offered for further public discussion. Journals and research councils are strongly recommended to incorporate it into their submission and reviewing processes. Feedback to the authors is encouraged and the statement will be revised in 2 years.