Contaminated mouth swabs caused a multi-hospital outbreak of Pseudomonas aeruginosa infection

Bjørn G. Iversen*
Department of Infectious Disease Epidemiology, Norwegian Institute of Public Health, Oslo, Norway

Doctoral dissertation on 23 September 2009 at the University of Oslo, Oslo, Norway

Pseudomonas aeruginosa is a gram-negative, obligate aerobic rod-shaped bacterium with minimal nutritional requirements. It is often found in moist environments and can cause infections in immunocompromised or otherwise-susceptible hosts (1, 2). Numerous outbreaks have been associated with faulty or unclean medical equipment or products (3–9) and with personnel and environmental reservoirs (10–16), as well as with cross-contamination within the hospital (13, 17, 18).

Hospital-acquired infections are costly for society, because of patient suffering and are partly preventable. Pseudomonas spp. are ranked among the top 10 causes of bacteraemias in hospitals (19–24). Medical devices have often caused outbreaks.

In late February 2002, the Norwegian Institute of Public Health (NIPH) was alerted to a possible increase in the number of Pseudomonas infections in the clinical wards of Norwegian hospitals, especially in intensive care units (ICUs). Infection control personnel in different hospitals had vague impressions of seeing more Pseudomonas infections than normal. On 8 March 2002, investigators at St. Olav’s Hospital in Trondheim, Norway, discovered genotypically identical strains of Pseudomonas aeruginosa in patient samples from two hospitals in different regions, and 10 days later, they discovered a genotypically identical strain from a third hospital in yet another region. A national outbreak investigation was launched.

The outbreak strain of Pseudomonas aeruginosa was traced to a mouth swab called Dent-O-Sept. This is a clean, non-sterile, moist sponge-on-a-stick produced in Norway, which according to the Norwegian text on the wrap is an antiseptic single-use swab for mouth hygiene (Fig. 1).

The research originates from the results of the outbreak investigation. From it, four areas were explored: (1) the outbreak investigation; (2) the contamination of the medical device involved; (3) theories for causality of the outbreak; and (4) the epidemiology of invasive P. aeruginosa infection.

Paper I (25) describes the outbreak investigation of P. aeruginosa infections, in particular how a nationwide, multicentre investigation was organised and conducted. The team work and combination of epidemiological and microbiological methods were essential in finding the cause and stopping the outbreak. A total of 231 patients from 24 hospitals were identified with the outbreak strain of P. aeruginosa; 71 of them died while hospitalised, and for 34 the Pseudomonas infection probably contributed to the patients’ deaths. Genotypically identical strains of the bacterium were isolated from patients, several batches of the Dent-O-Sept swab and from the production plant. We concluded that susceptible patient groups should use only documented quality-controlled, high-level disinfected products and items in the oropharynx.

Paper II (26) describes the investigation of the swabs, the moisturising liquid and the production facility. A total of 76 swabs from 12 different batches produced over a period of 30 weeks were contaminated with the outbreak strain of P. aeruginosa. Many swabs were also contaminated with other microbes. More than 250 of 1,565 examined swabs were contaminated with one or more microbial species. A system audit revealed serious breaches of production regulations. Biofilm formation in the wet part of the production was proposed as the most plausible explanation for the continuous contamination of the swabs. The legal requirements for microbiological purity of medical devices in Class 1 are not optimal.

Paper III (27) explores the theories for causality of the outbreak of P. aeruginosa infections. Applying various theories for causality and responsibility from different fields, such as science, philosophy and law on the actors and acts involved in the outbreak helped elucidating their roles and responsibilities, especially legal theories and counterfactual reasoning. We concluded that many factors contributed to causing the outbreak, but that contamination of a medical device in the production facility was the major necessary condition. The reuse of the medical device in hospitals contributed primarily to the size of the outbreak. In addition, there were many errors in the chain from the production of the swabs,
through purchasing and storage systems in the health care institutions to the use of the swabs and reporting of defective devices. The unintended error by its producer – and to a minor extent by the hospital practice – was mainly due to non-application of relevant knowledge and skills, and appears to constitute professional negligence. Due to factors outside the discourse of causality, no one was criminally charged for the outbreak.

Paper IV (28) investigates the epidemiology of invasive \textit{P. aeruginosa} infection in Norway. Although \textit{P. aeruginosa} usually does not cause infection in healthy persons, it frequently does in patients with certain underlying diseases, and in patients with disrupted barriers, especially in the ICU. Invasive \textit{P. aeruginosa} infection is a rare disease with an incidence rate of 3.16 per 100,000 person-years at risk or 0.20 per 1,000 hospital stays, but very serious for those contracting it with a 30-day case fatality rate of 33%. Patients with malignant neoplasms of lymphoid and haematopoietic tissue and other diseases of blood and blood-forming organs have the highest risk of infection. Prudent antibiotic use is one possible explanation for much lower rates of infection in Norway compared with all other published studies.

\textbf{Lessons learned}

Medical devices, moist equipment and solutions and moist environments are frequently associated with outbreaks with \textit{P. aeruginosa} and related moisture-prone bacteria. Lack of adherence to standard precautions for infection control and prevention by hospital personnel contributes to the propagation of these outbreaks.

Biofilm formation is possibly the more common of the two distinct modes of behaviour for bacteria; the other being the planktonic mode (29–31). Bacterial biofilms are less sensitive to disinfection and make it more difficult to eradicate. Not abiding by the production regulations, e.g. the requirement to have quality assurance systems including an effective microbiological control system, made the contamination possible in the production process.

Outbreak investigations are essential to detect causes of an outbreak and to gain experience in order to prevent their recurrence. Investigating large, multicentre outbreaks is resource demanding and necessitates a defined network structure where everyone knows their role and qualifications and try upmost to cooperate. Expertise in a variety of fields is essential. Molecular finger-printing techniques to identify the outbreak strain of the microbe and discriminate against other strains have become an indispensable part of most outbreak investigations.

This outbreak has necessitated a reassessment of the guidelines for preventing infection in critically ill and otherwise-susceptible patients. Oropharyngeal colonisation is important for the development of ventilator-associated pneumonia, and oral care may prevent pneumonia, but few have addressed whether oral products other than ventilators or nebuliser equipment need to be sterile or subjected to high-level disinfection for this patient group. We conclude that sterility is not necessary for such products, but only items for which the manufacturer can document that quality control and high-level disinfection have been performed (including tap water and moist products) should be used in the oropharynx for susceptible patient groups.

\textbf{Conflict of interest and funding}

There is no conflict of interest in the present study for the author. All primary costs were covered by the health care institutions and national bodies involved. Costs for genotyping of \textit{Pseudomonas aeruginosa} was refunded by the Norwegian Ministry of Health.

\textbf{References}

1. Arnow PM, Flaherty JP. Nonfermative gram-negative bacilli. In: Mayhall CG, ed. Hospital epidemiology and infection control. Philadelphia: Lippincott Williams & Wilkins; 1999. p. 431-51.
2. Pollack M. \textit{Pseudomonas aeruginosa}. In: Mandell GL, Bennett JE, Dolin R, eds. Principles and practice of infectious diseases. Philadelphia: Churchill Livingstone; 2000. p. 2310-35.
3. Stephenson JR, Heard SR, Richards MA, Tabaqchali S. Gastrointestinal colonization and septicemia with \textit{Pseudomonas aeruginosa} due to contaminated thymol mouthwash in immunocompromised patients. J Hosp Infect 1985; 6: 369–78.
4. Becke VE, Lorenzoni NM. \textit{Pseudomonas aeruginosa} outbreak in a neonatal intensive care unit: a possible link to contaminated hand lotion. Am J Infect Control 1995; 23: 396–8.
5. Silva CV, Magalhaes VD, Pereira CR, Kawagoe Y, Ikura C, Ganc AJ. Pseudo-outbreak of \textit{Pseudomonas aeruginosa} and \textit{Serratia marcescens} related to bronchoscopes. Infect Control Hosp Epidemiol 2003; 24: 195–7.
6. Srivivasa A, Wolfenden LL, Song X, Mackie K, Hartsell TL, Jones HD et al. An outbreak of \textit{Pseudomonas aeruginosa}
infections associated with flexible bronchoscopes. N Engl J Med 2003; 348: 221–7.
7. Cobben NA, Drent M, Jonkers M, Wouters EF, Vaneechoutte M, Stobberringh EE. Outbreak of severe Pseudomonas aeruginosa respiratory infections due to contaminated nebulizers. J Hosp Infect 1996; 33: 63–70.
8. Schelenz S, French G. An outbreak of multidrug-resistant Pseudomonas aeruginosa infection associated with contamination of bronchoscopes and an endoscope washer-disinfector. J Hosp Infect 2000; 46: 23–30.
9. Millership SE, Patel N, Chattopadhyay B. The colonization of patients in an intensive treatment unit with gram-negative flora: the significance of the oral route. J Hosp Infect 1986; 7: 226–35.
10. Foca M, Jakob K, Whittier S, Della LP, Factor S, Rubenstein D et al. Endemic Pseudomonas aeruginosa infection in a neonatal intensive care unit. N Engl J Med 2000; 343: 695–700.
11. Bukholm G, Tannaes T, Kjelsberg AB, Smith-Erichsen N. An outbreak of carbapenem-resistant Pseudomonas aeruginosa in a urology ward. Clin Microbiol Infect 2003; 9: 938–43.
12. Broder MS, Deresiewicz T, Fass RR, Mitchell D, Mower WR, Steigerwald DL et al. An outbreak of Pseudomonas aeruginosa associated with increased risk of patient death in an intensive care unit. J Infect Dis 1999; 180: 352–8.
13. Lytikainen O, Golovanova V, Kolho E, Ruutu P, Sivonen A, Tiittanen L et al. Outbreak caused by tobramycin-resistant Pseudomonas aeruginosa in a bone marrow transplantation unit. Scand J Infect Dis 2001; 33: 445–9.
14. Bukholm G, Tannaes T, Kjelsberg AB, Smith-Erichsen N. An outbreak of multidrug-resistant Pseudomonas aeruginosa associated with increased risk of patient death in an intensive care unit. J Hosp Infect 1996; 33: 63–70.
15. Schelenz S, French G. An outbreak of multidrug-resistant Pseudomonas aeruginosa infection associated with contamination of bronchoscopes and an endoscope washer-disinfector. J Hosp Infect 2000; 46: 23–30.
16. Miller SE, Patel N, Chattopadhyay B. The colonization of patients in an intensive treatment unit with gram-negative flora: the significance of the oral route. J Hosp Infect 1986; 7: 226–35.
17. Foca M, Jakob K, Whittier S, Della LP, Factor S, Rubenstein D et al. Endemic Pseudomonas aeruginosa infection in a neonatal intensive care unit. N Engl J Med 2000; 343: 695–700.
18. Pena C, Dominguez MA, Pujol M, Verdaguer R, Gudiol F, Ariza J. An outbreak of carbapenem-resistant Pseudomonas aeruginosa in a urology ward. Clin Microbiol Infect 2003; 9: 938–43.
19. Bukholm G, Tannaes T, Kjelsberg AB, Smith-Erichsen N. An outbreak of multidrug-resistant Pseudomonas aeruginosa associated with increased risk of patient death in an intensive care unit. J Infect Dis 1999; 180: 352–8.
20. Broder MS, Deresiewicz T, Fass RR, Mitchell D, Mower WR, Steigerwald DL et al. An outbreak of Pseudomonas aeruginosa associated with increased risk of patient death in an intensive care unit. J Infect Dis 1999; 180: 352–8.
21. Javaloyas M, García-Somoza D, Gudiol F. Epidemiology and prognosis of bacteremia: a 10-y study in a community hospital. Scand J Infect Dis 2002; 34: 436–41.
22. Scheckler WE, Bobula JA, Beamsley MB, Hadden ST. Bloodstream infections in a community hospital: a 25-year follow-up. Infect Control Hosp Epidemiol 2003; 24: 936–41.
23. Weinstein MP, Reller LB, Murphy JR, Lichtenstein KA. The clinical significance of positive blood cultures: a comprehensive analysis of 500 episodes of bacteremia and fungemia in adults. In: Laboratory and epidemiologic observations. Rev Infect Dis 1983; 5: 35–53.
24. Diekema DJ, Pfaller MA, Jones RN, Doern GV, Winokur PL, Gales AC et al. Survey of bloodstream infections due to gram-negative bacilli: frequency of occurrence and antimicrobial susceptibility of isolates collected in the United States, Canada, and Latin America for the SENTRYPseudomonas aeruginosa infection caused by contaminated mouth swabs. Clin Infect Dis 2007; 44: 794–801.
25. Iversen BG, Jacobsen T, Eriksen HM, Bukholm G, Melbye KK, Nygard K et al. An outbreak of Pseudomonas aeruginosa infection caused by contaminated mouth swabs. Clin Infect Dis 2007; 44: 794–801.
26. Iversen BG, Eriksen HM, Bo G, Hagestad K, Jacobsen T, Engeset E et al. Pseudomonas aeruginosa contamination of mouth swabs during production causing a major outbreak. Ann Clin Microbiol Antimicrob 2007; 6: 3.
27. Iversen BG, Hofmann B, Aavitsland P. Questions on causality and responsibility arising from an outbreak of Pseudomonas aeruginosa infections in Norway. Emerg Themes Epidemiol 2008; 5: 22.
28. Iversen BG, Brantsaeter AB, Aavitsland P. Nationwide study of invasive Pseudomonas aeruginosa infection in Norway: importance of underlying disease. J Infect 2008; 57: 139–46.
29. Hall-Stoodley L, Stoodley P. Biofilm formation and dispersal in: Laboratory and epidemiologic observations. Rev Infect Dis 1999; 29: 595–607.
30. Dunne WM, Jr. Bacterial adhesion: seen any good biofilms lately? Clin Microbiol Rev 2002; 15: 155–66.
31. Donlan RM, Costerton JW. Biofilms: survival mechanisms of clinically relevant microorganisms. Clin Microbiol Rev 2002; 15: 167–93.