

ORIGINAL ARTICLE

An Outbreak of *Pseudomonas aeruginosa* Infections Associated with Flexible Bronchoscopes

Arjun Srinivasan, M.D., Linda L. Wolfenden, M.D., Xiaoyan Song, M.D., Karen Mackie, R.N., Theresa L. Hartsell, M.D., Ph.D., Heather D. Jones, M.D., Gregory B. Diette, M.D., M.H.S., Jonathan B. Orens, M.D., Rex C. Yung, M.D., Tracy L. Ross, B.S., William Merz, Ph.D., Paul J. Scheel, M.D., Edward F. Haponik, M.D., and Trish M. Perl, M.D.

ABSTRACT

BACKGROUND

Endoscopes, including bronchoscopes, are the medical devices most frequently associated with outbreaks of nosocomial infections. We investigated an outbreak of *Pseudomonas aeruginosa* infections after bronchoscopic procedures.

METHODS

Microbiologic results were reviewed to determine the rates of recovery of *P. aeruginosa* from bronchoalveolar-lavage specimens. Environmental samples from endoscopes and the endoscopy suite were cultured. Medical records were reviewed to identify infections in the 14 days after a bronchoscopy.

RESULTS

The rate of recovery of *P. aeruginosa* from bronchoalveolar-lavage specimens obtained with use of endoscopy-suite bronchoscopes increased from 10.4 percent at base line to 31.0 percent during the outbreak (relative risk, 2.97; 95 percent confidence interval, 2.28 to 3.90). Cultures of samples from three bronchoscopes grew *P. aeruginosa*, whereas cultures of samples from the environment, instrument-cleaning machines, and gastrointestinal endoscopes did not. The three bronchoscopes had been part of a nationwide recall. A total of 414 patients underwent bronchoscopy during the outbreak, and there were 48 respiratory tract and bloodstream infections among 39 of these patients (9.4 percent). In 32 infections (66.7 percent), *P. aeruginosa* was confirmed as a potentially causative organism. Exposure to a potentially contaminated bronchoscope may have had a role in the death of three patients. The rate of recovery of *P. aeruginosa* returned to base line after the instruments were removed from service.

CONCLUSIONS

This large outbreak of *P. aeruginosa* infections related to bronchoscopy was apparently caused by a loose biopsy-port cap in the bronchoscopes. Instrument safety and surveillance methods for bronchoscopy must be improved, and better recall procedures are needed for medical devices.

From the Department of Hospital Epidemiology and Infection Control (A.S., X.S., K.M., T.M.P.), the Divisions of Infectious Diseases (A.S., T.M.P.), Pulmonary and Critical Care Medicine (L.L.W., G.B.D., J.B.O., R.C.Y., E.F.H.), and Nephrology (P.J.S.), Department of Medicine, and the Departments of Anesthesiology and Critical Care Medicine (T.L.H.) and Pathology (T.L.R., W.M.), Johns Hopkins Medical Institutions, Baltimore; and the Pulmonary–Critical Care Medicine Branch, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, Md. (H.D.J.). Address reprint requests to Dr. Srinivasan at the Office of Antibiotic Management, Johns Hopkins Hospital, 600 N. Wolfe St., Carnegie Bldg., Rm. 284, Baltimore, MD 21287-6284.

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ALTHOUGH INFECTIOUS COMPLICATIONS of flexible bronchoscopy are uncommon,^{1,2} nosocomial outbreaks related to bronchoscopy have been reported,³⁻¹⁰ and endoscopes, including bronchoscopes, are the medical devices most commonly linked to outbreaks.¹¹ At Johns Hopkins Hospital, between June 2001 and January 2002, the rate of isolation of *Pseudomonas aeruginosa* from bronchoalveolar-lavage specimens was three times as high as the usual rate. We investigated the cause of the increase and implemented control measures.

METHODS

SETTING

Johns Hopkins Hospital is a 1000-bed tertiary care hospital in Baltimore, where approximately 1000 flexible bronchoscopic procedures are performed annually. About 65 percent of these procedures include bronchoalveolar lavage, in which sterile saline is instilled into the lower airways and then aspirated to obtain specimens. Bronchoscopy is performed primarily in an endoscopy suite, where gastrointestinal endoscopy is also performed; endoscopy-suite bronchoscopes are also used in some intensive care units.

BRONCHOSCOPE CLEANING PROCEDURES

Bronchoscopes are cleaned by trained personnel in accordance with national guidelines¹² and the manufacturer's recommendations (Olympus America). Instruments are soaked in an enzymatic cleaner (Enzol, Advanced Sterilization Products) and then cleaned manually by wiping the outer surface and brushing the inner channel. Bronchoscopes then undergo high-level disinfection in an automated endoscope reprocessor (model DSD 91-ED, Dual Endoscope Disinfector, Olympus America) in which ortho-phthalaldehyde (Cidex OPA, Advanced Sterilization Products) is the liquid germicide. Finally, the channels are flushed with 70 percent alcohol and dried with pressurized air. Logbooks are used to record when the filters and solutions are changed in the reprocessors.

SURVEILLANCE

After a report of a cluster of infections with mucoid, antibiotic-resistant *P. aeruginosa* organisms in patients without known risk factors for the infections, microbiologic data were reviewed to determine the rates of recovery from bronchoalveolar-

lavage specimens of *P. aeruginosa*; *Serratia*, *Acinetobacter*, and *Klebsiella* species; *Stenotrophomonas maltophilia*; *Alcaligenes xylosoxidans*; *Staphylococcus aureus*; *Aspergillus* species; and mycobacteria.

MICROBIOLOGIC METHODS

Specimens were obtained from bronchoscopes and gastrointestinal endoscopes for culture in both a standard, anterograde manner and a retrograde manner that mimicked bronchoalveolar lavage. In the standard technique, approximately 50 ml of sterile saline was flushed through the distal, or biopsy, port of the instrument into a sterile cup. In the retrograde approach, roughly half this volume was then aspirated back through the endoscopes and collected in a sterile trap connected to the proximal, or sampling, port (the protocol is available as Supplementary Appendix 1 with the full text of this article at <http://www.nejm.org>). Samples were filtered through a 0.45- μ m cellulose nitrate membrane filter (Falcon filter, Becton Dickinson), which was placed on MacConkey agar.

Swabs of environmental surfaces in the endoscopy suite and storage wells of the automated endoscope reprocessors, along with samples of tap water, cleaning solutions, multidose medications, and solutions and water used in the automated endoscope reprocessor were sent for bacterial culture. Surface samples were obtained with the use of sterile cotton swabs (Culturette System, Becton Dickinson Microbiology Systems). All samples were plated onto MacConkey agar.

MOLECULAR TYPING

Pulsed-field gel electrophoresis (PFGE)¹³ (Bio-Rad Gen Path) was performed on available isolates. DNA was digested with *Spe*I (New England Biolabs), and gels were analyzed with Molecular Analyst Fingerprinting Plus software (Bio-Rad). Isolates were considered genetically related if their PFGE patterns differed by three or fewer bands.¹⁴

OUTCOMES

Patients potentially at risk were identified from a bronchoscopy data base.¹⁵ Medical records were reviewed to determine whether patients had colonization or infection that was potentially related to bronchoscopic procedures. Upper and lower respiratory tract and bloodstream infections were defined according to the criteria of the Centers for Disease Control and Prevention¹⁶ and were considered potentially attributable to bronchoscopy if they oc-

curred in the 14 days after a procedure. Patients who could be reached with certified letters and telephone calls were asked to return for evaluation and a sputum culture. Using a preestablished definition, we reviewed available information on any patient who died to determine what role exposure to a potentially contaminated bronchoscope might have had in the patient's death. The institutional review board at Johns Hopkins Hospital approved submission of the report for publication.

STATISTICAL ANALYSIS

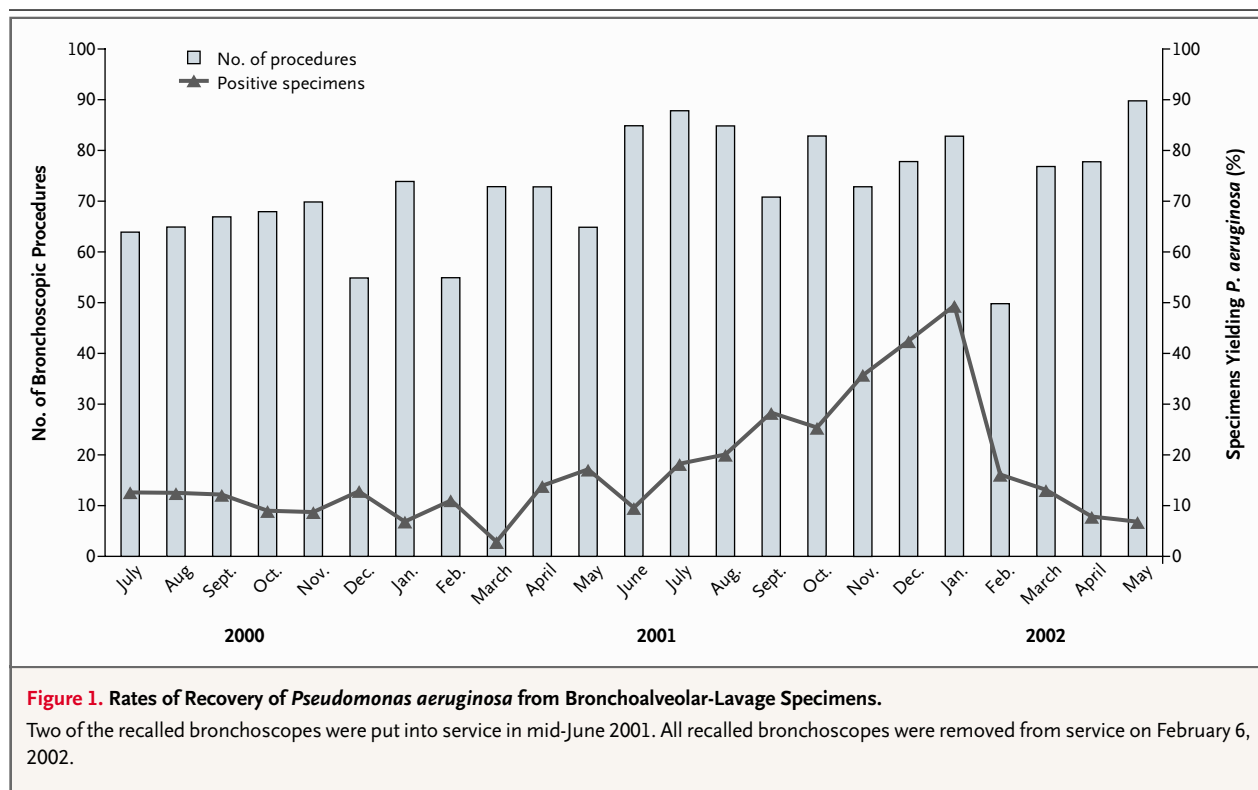
Data were analyzed with use of Stata software (version 7). To compare the incidence of *P. aeruginosa* in bronchoalveolar-lavage specimens obtained from July 2000 to May 2001 (the base-line period) with that during the outbreak, June 2001 to January 2002, we calculated the relative risk, 95 percent confidence intervals, and P values. Two-sided P values of less than 0.05 were considered to indicate statistical significance.

RESULTS

A total of 414 patients underwent 665 bronchoscopic procedures during the outbreak. The rate of re-

covery of *P. aeruginosa* from bronchoalveolar-lavage specimens obtained using endoscopy-suite bronchoscopes increased from a mean of 10.4 percent at base line to 31.0 percent during the outbreak (relative risk, 2.97; 95 percent confidence interval, 2.28 to 3.90) (Fig. 1). The frequency of recovery of *P. aeruginosa* from bronchoalveolar-lavage specimens obtained with bronchoscopes maintained in other hospital areas did not increase, nor did the rate of recovery of other pathogens from bronchoalveolar-lavage specimens. There were no significant differences in the frequency of risk factors for *P. aeruginosa* infection (immunosuppression, mechanical ventilation, or cystic fibrosis) between patients undergoing bronchoalveolar lavage during the base-line period and those undergoing the procedure during the outbreak period.

During the outbreak, 97 patients (23.4 percent) had a bronchoalveolar-lavage culture that grew *P. aeruginosa*. Twenty-one patients (5.1 percent) had had *P. aeruginosa* isolated from a respiratory tract specimen before undergoing bronchoscopy during the outbreak period, and 35 patients (8.5 percent) had a subsequent culture of a respiratory tract specimen, not obtained by bronchoalveolar lavage, that grew *P. aeruginosa*.



BRONCHOSCOPIC AND REPROCESSING PROCEDURES

Bronchoscopic and reprocessing procedures were observed during random, unannounced visits. No significant breaches in technique were observed. Examination of the maintenance records for the automated endoscope reprocessors demonstrated that cleaning solutions and filters had been changed according to recommendations.

ENDOSCOPIC AND ENVIRONMENTAL CULTURES

No cultures from bronchoscopes maintained outside the endoscopy suite, gastrointestinal endoscopes, the endoscopy suite itself, or automated endoscope reprocessors yielded *P. aeruginosa* (Table 1). Initially, cultures in which saline was flushed through the bronchoscopes did not grow *P. aeruginosa*. On reculturing, with both antero- and retrograde sampling, specimens from three bronchoscopes grew *P. aeruginosa* (models BFP40, BF160, and BFIT160, Olympus America): one antero- and two retrograde samples. One culture obtained from a swab of a biopsy-port cap grew *P. aeruginosa*. One bronchoscope remained contaminated despite gas sterilization with ethylene oxide.

TERMINATION OF THE OUTBREAK

The contaminated bronchoscopes were removed from service on February 6, 2002, and elective bronchoscopies were postponed. The rates of recovery of *P. aeruginosa* from bronchoalveolar-lavage specimens subsequently returned to base-line levels and remained stable (Fig. 1).

On further investigation, we learned that the contaminated bronchoscopes were subject to a national recall, issued in November 2001, because of "a customer complaint regarding a loosened bronchoscope biopsy port and microbial contamination of the port." In the light of this information, we examined the biopsy ports of the contaminated bronchoscopes and found that all were loose.

MOLECULAR TYPING

PFGE revealed three distinct *P. aeruginosa* strains (A, B, and C) from the three contaminated bronchoscopes (Fig. 2). One was contaminated with strain A, whereas the other two were contaminated with strains B and C. Another isolate, which differed by three bands from strain A (strain A2), was recovered from several patients but not from any bronchoscopes. Isolates from cultures of bronchoalveolar-lavage specimens were available from 48 patients,

Table 1. Results of Cultures of Specimens from Environmental Sources and Bronchoscopes.

Source and Type of Specimen	<i>Pseudomonas aeruginosa</i> Isolated on Culture
Washers (automated endoscope reprocessors)	
Water from wall-intake filters	No
Input water filters	No
Water from output filters	No
Rinse water	No
Disinfectant	No
Alcohol cups	No
Detergent cups	No
Drains	No
Condensation from lids	No
Treatment rooms	
Undated sterile water	No
Sink drains	No
Sink aerators	No
Bronchoscope equipment	
Connector tubing	No
Cap	No
Fluid from suction canister tubing	No
Tip of air hose	No
Cleaning room	
"Dirty" aerator sink	No
"Clean" aerator sink	No
Medication	
Open tube of surgical lubricant	No
Aliquot of lidocaine	No
Injectable lidocaine	No
Injectable saline solution	No
Gastrointestinal endoscopes	
Endoscopes 1, 2, 3, and 4	No
Colonoscopes 1, 2, and 3	No
Endoscopy-suite bronchoscopes	
Bronchoscopes 1, 2, and 3*	Yes
Bronchoscopes 4, 5, and 6	No
Bronchoscopes 7, 8, 9, and 10*	No

* These bronchoscopes had been recalled by the manufacturer in November 2001.

and 26 (54.2 percent) were genetically related to a strain recovered from the bronchoscopes. One of the four bloodstream isolates was related to a strain obtained from a bronchoscope. No isolates were available from respiratory tract specimens not obtained by bronchoalveolar lavage.

OUTCOMES

There were 48 infections among 39 of the 414 patients (9.4 percent) in the two weeks after bronchoscopy (7.2 percent of procedures), including 28 cases of pneumonia, 7 of bronchitis, 6 of sinusitis, 3 of

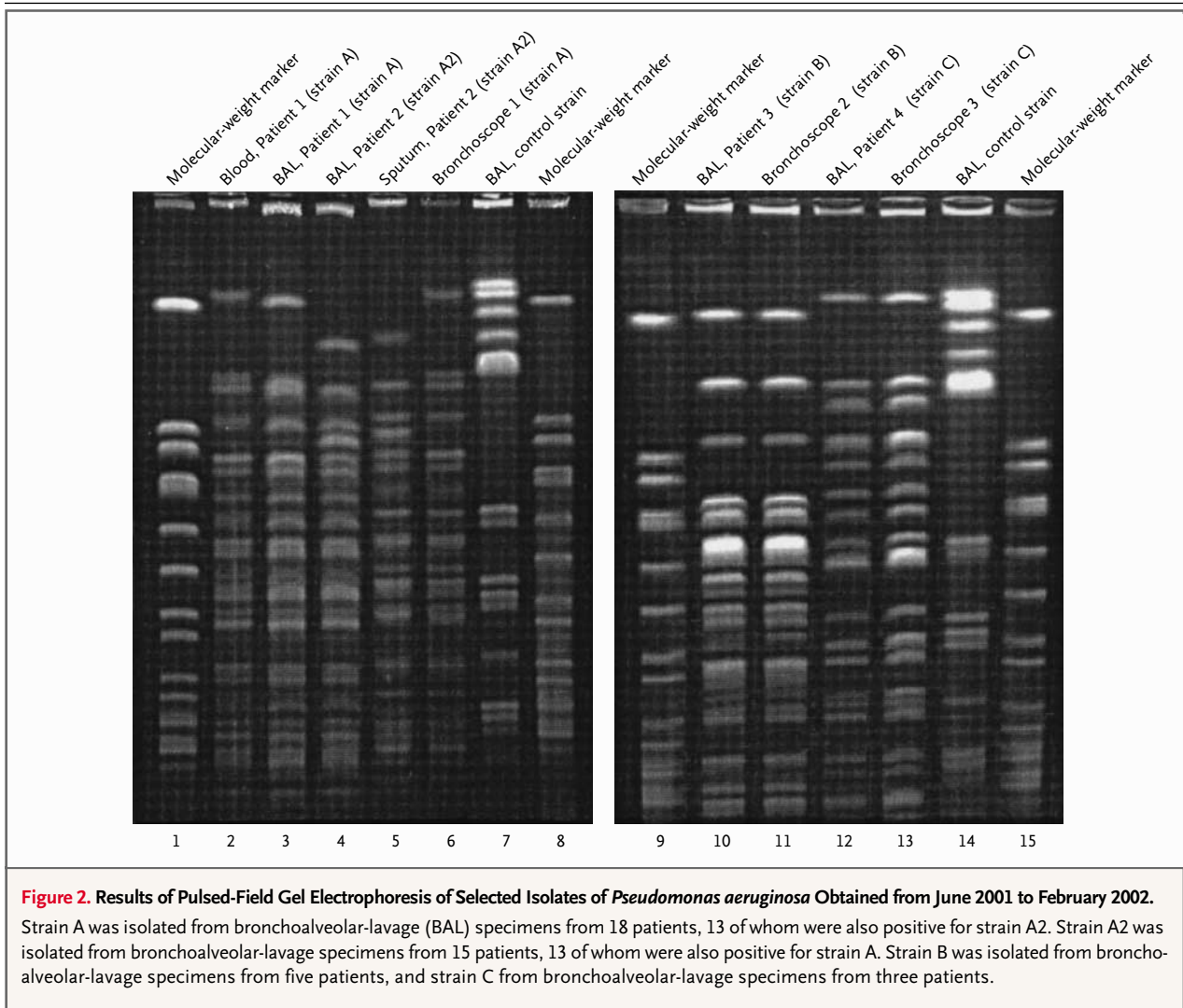


Figure 2. Results of Pulsed-Field Gel Electrophoresis of Selected Isolates of *Pseudomonas aeruginosa* Obtained from June 2001 to February 2002. Strain A was isolated from bronchoalveolar-lavage (BAL) specimens from 18 patients, 13 of whom were also positive for strain A2. Strain A2 was isolated from bronchoalveolar-lavage specimens from 15 patients, 13 of whom were also positive for strain A. Strain B was isolated from bronchoalveolar-lavage specimens from five patients, and strain C from bronchoalveolar-lavage specimens from three patients.

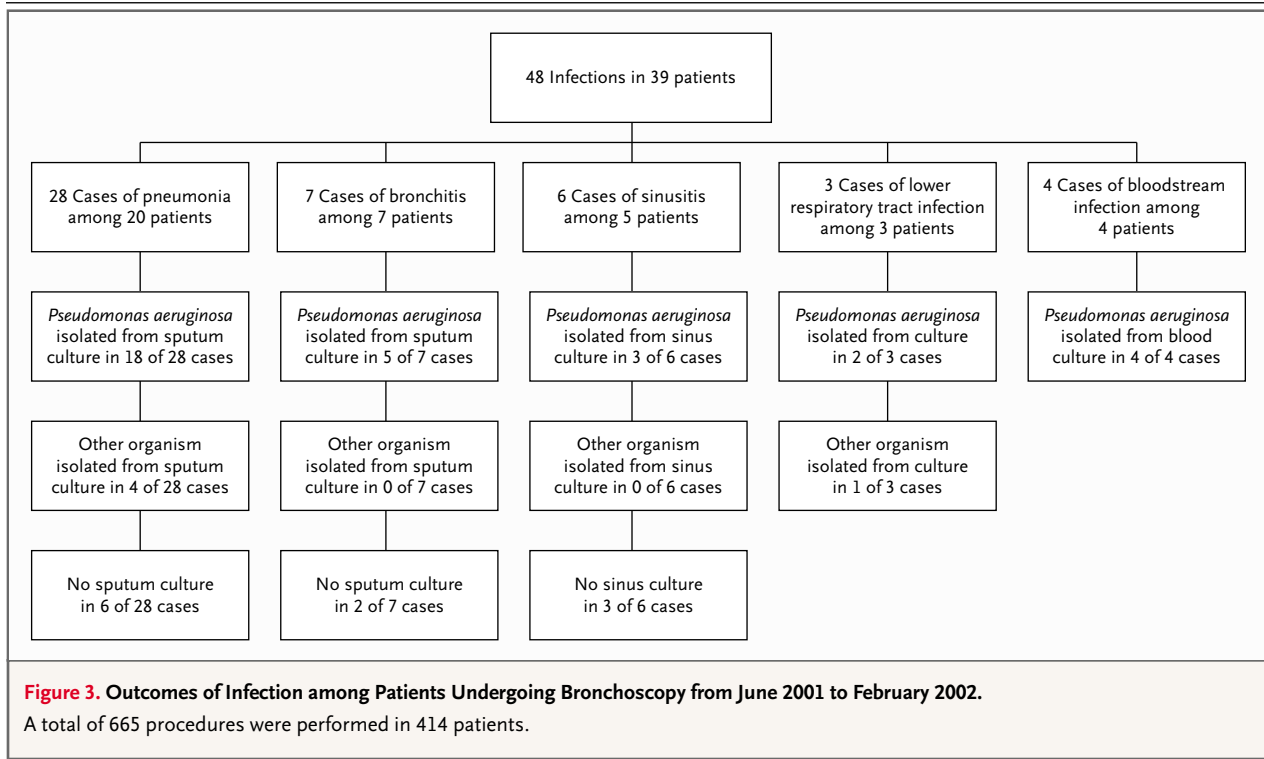
lower respiratory tract infection, and 4 bloodstream infections (Fig. 3). Some patients who underwent multiple procedures had multiple infections. In 5 of the 48 infections (0.8 percent of procedures), an organism other than *P. aeruginosa* was recovered, whereas in 32 infections (4.8 percent of procedures), *P. aeruginosa* was identified. Twelve of the patients were colonized with *P. aeruginosa* before undergoing bronchoscopy during the outbreak; however, because the isolates were not available for PFGE, we could not rule out the possibility that they had been infected with a new strain; hence, colonized patients were included in the outcomes.

On the basis of our definition, exposure to a potentially contaminated bronchoscope may have had a role in the death of three patients, all of whom were critically ill at the time of bronchoscopy.

Of the 414 patients, 101 (24.4 percent) returned for a follow-up evaluation. Eight had a sputum culture that grew *P. aeruginosa*, but PFGE demonstrated that only one of the organisms was related to a strain recovered from a bronchoscope.

DISCUSSION

We describe a large outbreak related to bronchoscopy, which involved 48 infections of the upper and lower respiratory tracts and bloodstream among 39 of 414 patients who underwent bronchoscopy (9.4 percent). In 66.7 percent of these infections, *P. aeruginosa* was recovered on culture. Furthermore, exposure to a potentially contaminated bronchoscope may have contributed to the deaths of three critically ill patients. A direct cause-and-effect rela-



tion, however, could not be determined, since patients who underwent procedures could not be definitively linked to the contaminated bronchoscopes.

As in the outbreak reported by Kirschke et al.,¹⁷ the contamination appeared to be related to a loose biopsy-port cap on the bronchoscopes, which may have sheltered organisms and thus rendered disinfection procedures ineffective. Several findings support this hypothesis: only bronchoscopes with loose biopsy ports were contaminated, none of the gastrointestinal endoscopes or bronchoscopes that were not implicated in the recall were contaminated, no serious breaches in technique were observed during bronchoscopic procedures or cleaning and reprocessing of the instruments, cultures of specimens obtained from the automated endoscope reprocessors and endoscopy suite did not grow *P. aeruginosa*, ethylene oxide sterilization failed to eradicate *P. aeruginosa* from one bronchoscope, and the outbreak ended with the removal of the recalled bronchoscopes, with no changes in reprocessing procedures. Because the source of the contamination was not traced to the environment, we believe that bronchoscopes became contaminated during procedures in patients who were colonized or infected with *P. aeruginosa*.

A major limitation of our investigation was our inability to link the contaminated bronchoscopes to specific patients. We were thus unable to determine whether exposure to a contaminated bronchoscope was associated with either the recovery of *P. aeruginosa* from bronchoalveolar-lavage specimens or post-bronchoscopy infections. In addition, except for one bloodstream isolate, no isolates from patients who had *P. aeruginosa* infections after bronchoscopy were available for molecular typing. Because no isolates were available to rule out the possibility that a new strain had been acquired, we included previously colonized patients in the outcomes. This approach may have falsely elevated the number of post-procedural infections. Furthermore, we were unable to determine all the potential clinical effects of this outbreak, since we could not ascertain how many patients received unnecessary courses of antibiotics to treat supposed infections, which actually reflected contamination of the bronchoalveolar-lavage fluid by the bronchoscope (pseudoinfections). Finally, in some cases the data necessary to determine a patient's outcome were not available.

Outbreaks such as this one have led patients and physicians to question the safety of bronchos-

copy — a concern that is receiving heightened attention with the increased focus on patient safety.¹⁸ Our findings heighten this concern because of the duration of the outbreak and the number of patients involved. This outbreak emphasizes the challenges that new forms of technology present with respect to adequate reprocessing of instruments and the importance of appropriate instrument design to adequate disinfection, since a loose part may have been the cause of the contamination. It remains to be seen whether the use of instruments such as sheathed bronchoscopes¹⁹ will protect patients from infections due to contaminated instruments. In the meantime, perhaps new standards should be developed to test and review the design of instruments with respect to disinfection before these instruments are used in patients.

Our findings arouse concern about the adequacy of nationwide recalls of medical devices. Currently, the Food and Drug Administration relies on manufacturers “to take full responsibility for product recalls, including follow-up checks to assure that recalls are successful.”²⁰ In the case of this recall, the manufacturer initially sent letters to facilities in which the bronchoscopes were used. When the initial effort was not sufficient, letters were sub-

sequently sent to individual physicians. A federal mandate that recall notices be sent to all physicians who may use a device could have shortened the duration of the outbreak we studied, decreasing the number of patients at risk. Such a measure might help ensure that future recalls are handled expeditiously and thus optimize the safety of medical equipment.

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