

ORIGINAL ARTICLE

Pseudomonas aeruginosa and *Serratia marcescens* Contamination Associated with a Manufacturing Defect in Bronchoscopes

David L. Kirschke, M.D., Timothy F. Jones, M.D., Allen S. Craig, M.D.,
Patricia S. Chu, M.D., Glenda G. Mayernick, R.N., Jayesh A. Patel, M.D.,
and William Schaffner, M.D.

ABSTRACT

From the Epidemic Intelligence Service, Centers for Disease Control and Prevention, Atlanta (D.L.K.); the Tennessee Department of Health, Nashville (D.L.K., T.F.J., A.S.C.); the Vanderbilt University School of Medicine, Nashville (T.F.J., A.S.C., P.S.C., W.S.); and Skyline Medical Center, Nashville (G.G.M., J.A.P.). Address reprint requests to Dr. Schaffner at the Vanderbilt University School of Medicine, Medical Center North, Rm. A-1124, Nashville, TN 37232, or at william.schaffner@vanderbilt.edu.

N Engl J Med 2003;348:214-20.

Copyright © 2003 Massachusetts Medical Society.

BACKGROUND

Several outbreaks and pseudo-outbreaks of *Pseudomonas aeruginosa* and *Serratia marcescens* infections associated with bronchoscopy have been reported. We conducted an investigation of *P. aeruginosa* and *S. marcescens* isolates related to bronchoscopy at a community hospital.

METHODS

We reviewed the records of all bronchoscopic procedures at the community hospital from July to October 2001. Environmental samples were obtained. Pulsed-field gel electrophoresis (PFGE) was performed on isolates of *P. aeruginosa*.

RESULTS

From July 1 to October 31, 2001, 66 bronchoscopic procedures were performed in 60 patients, and 43 specimens were obtained for bacterial culture; 20 of the specimens (47 percent) were positive for *P. aeruginosa*. Six (30 percent) of the specimens that were positive for *P. aeruginosa* also yielded *S. marcescens*. All 20 *P. aeruginosa* isolates were associated with procedures performed with three of four new bronchoscopes from the same manufacturer. Contrary to manufacturing specifications, the biopsy-port caps on all four bronchoscopes were easily removable, and *P. aeruginosa* was cultured from the biopsy ports of the three implicated bronchoscopes. The PFGE patterns of *P. aeruginosa* isolates from the bronchoscopes, patients, and two environmental samples were indistinguishable. One patient was hospitalized with *P. aeruginosa* pneumonia 11 days after bronchoscopy. The manufacturer reported a design change instituted in 1997, and production problems may have resulted in the distribution of bronchoscopes that did not meet specifications.

CONCLUSIONS

We documented contamination of bronchoscopes with *P. aeruginosa* and *S. marcescens* and possible infection of patients at a community hospital as a result of the inadequate disinfection of bronchoscopes because of a manufacturing defect.

IN ADDITION TO VISUAL INSPECTION OF the airway, laser therapy, electrocautery, and placement of airway stents can now be done by means of flexible bronchoscopy¹; approximately 500,000 bronchoscopic procedures are performed annually in the United States.² One limitation to the use of bronchoscopes is that sterilization between procedures is not practical because autoclaving damages the instrument and ethylene oxide reprocessing requires an often unacceptable amount of time.³ Therefore, cleaning and high-level disinfection are routinely performed instead.^{4,5} However, even cleaning and disinfection have been a challenge because of the complex design of flexible bronchoscopes,⁶ prompting the publication of guidelines.⁷⁻¹¹ Several bronchoscope-related outbreaks and pseudo-outbreaks of *Pseudomonas aeruginosa* and *Serratia marcescens* infection have been reported,¹²⁻¹⁷ all of which resulted from some breach of the cleaning and disinfection guidelines.^{9,11,18}

In September 2001, an infection-control practitioner at a community hospital notified the Tennessee Department of Health of an increase in the number of *P. aeruginosa* and *S. marcescens* isolates associated with bronchoscopy. We report the results of the subsequent investigation.

METHODS

We reviewed laboratory reports of all *P. aeruginosa* and *S. marcescens* isolates at the community hospital during 2001. A case was defined by the isolation of *P. aeruginosa* or *S. marcescens* from a specimen obtained during bronchoscopy in a patient at the community hospital from July 1 to October 31, 2001. We reviewed the endoscopy records, which included the serial numbers of the bronchoscopes used, for all patients who underwent bronchoscopy during this period. We reviewed the medical records of all patients who underwent bronchoscopy during the study period to determine whether any were readmitted for infections caused by *P. aeruginosa* or *S. marcescens* during the month after the procedure.

Environmental samples were obtained from the bronchoscopes and other sites within the endoscopy suite. Specimens were obtained from the bronchoscopes by flushing them with sterile saline or by using moistened swabs. Swab specimens were obtained from the automated endoscope reprocessor and items used during procedures. In addition, 100-ml specimens of liquids were collected, including source water, rinse water, and disinfectant used

in the automated endoscope reprocessor and tap water and drain water from the cleaning sink. The hospital's endoscope-reprocessing procedures were reviewed, and the bronchoscopes were inspected.

Isolates of *P. aeruginosa* were compared with the use of pulsed-field gel electrophoresis (PFGE). Restriction-endonuclease digestion of bacterial chromosomes was performed with *Xba*I (New England Biolabs), and the relatedness of strains was examined with the use of Molecular Analyst software.¹⁹

We performed bivariate statistical analyses using chi-square tests calculated with Epi Info 2000 software.²⁰

RESULTS

The community hospital is a 203-bed facility with four pulmonologists who performed 267 bronchoscopy procedures in 2001. From July 1 to October 31, 2001, 66 bronchoscopic procedures were performed in 60 patients with eight different bronchoscopes owned by the hospital, and 43 specimens were obtained for bacterial culture. Of the 43 bacterial cultures, 20 specimens (47 percent) yielded *P. aeruginosa*. Six of the 20 specimens (30 percent) with *P. aeruginosa* also yielded *S. marcescens*.

Of the 20 patients with specimens positive for *P. aeruginosa*, 11 (55 percent) were male; the median age of these patients was 59 years (range, 24 to 88). Evaluation of pneumonia was the primary indication for bronchoscopy in the case of only four patients (20 percent). None of the 20 patients were discharged with a diagnosis of pneumonia caused by *P. aeruginosa* or *S. marcescens*.

Between July 1 and September 17, when the investigation began, four of the hospital's eight bronchoscopes had been used, but *P. aeruginosa* was isolated from specimens obtained from only two (bronchoscopes A and B). Both were new bronchoscopes of similar models (BF-1T160 and BF-160, respectively) produced by the same manufacturer (Olympus America).

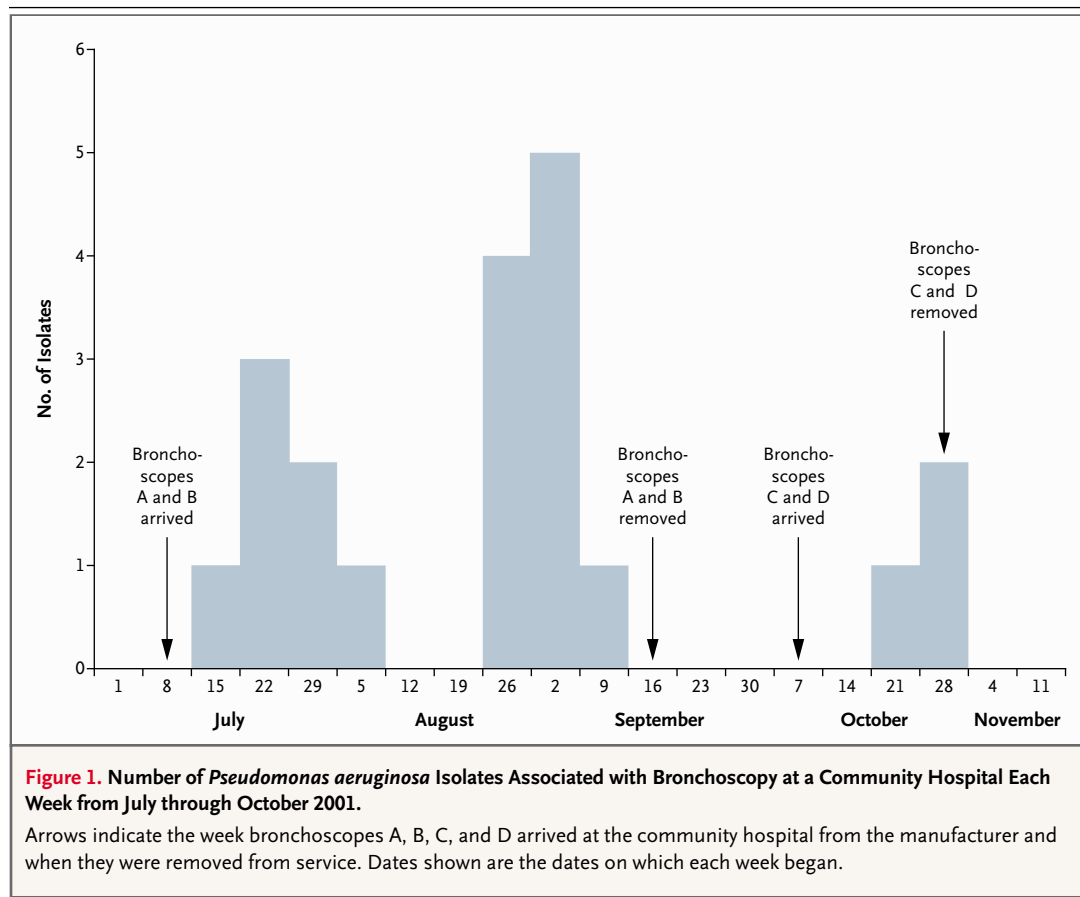
Bronchoscopes A and B had been received by the hospital on July 11, just eight days before the collection of the first specimen that was positive for *P. aeruginosa* (Fig. 1). They were first used on July 13 and July 24, respectively, and specimens positive for *P. aeruginosa* were obtained by the time of the third procedure performed with either bronchoscope. Of the 16 specimens collected for bacterial culture from patients during bronchoscopy with bronchoscope A, 12 (75 percent) were positive for

P. aeruginosa; 5 of 8 specimens (62 percent) collected from patients during bronchoscopy with bronchoscope B were positive for *P. aeruginosa*. Bronchoscopes A and B were removed from service on September 18, and no *P. aeruginosa* isolates were reported in specimens obtained during bronchoscopy during the following five weeks.

Inspection of bronchoscopes A and B revealed that the caps of the biopsy ports (Fig. 2) were not securely fastened and were easily removable, contrary to manufacturing specifications. The port caps were loose enough to be unscrewed with two fingers but not so loose that the problem was apparent to the bronchoscopy staff. When the threads of the biopsy ports and the inside of the caps of bronchoscopes A and B (Fig. 3) were swabbed, a dark green film was noted, and 9 of 12 swab specimens were positive for *P. aeruginosa* and *S. marcescens*. The other three swab specimens were positive for *P. aeruginosa* alone, including one specimen obtained after three cycles of cleaning and disinfection in the hospital's automated endoscope reprocessor.

On October 11, the community hospital received two new bronchoscopes (C and D) from the manufacturer, which were the same two models as bronchoscopes A and B. Bronchoscope C was used only twice. On reprocessing, it was noted that the biopsy-port cap was loose, and the bronchoscope was removed from service, but no specimen was collected from the biopsy port. *P. aeruginosa* was isolated from all three specimens collected for bacterial culture from patients who underwent bronchoscopy with bronchoscope D. The biopsy-port cap was found to be loose, and all five swab specimens of the biopsy-port cap yielded *P. aeruginosa*. Bronchoscope D was removed from service on October 31.

The four recent-model bronchoscopes with loose biopsy-port caps (bronchoscopes A, B, C, and D) were used for 40 procedures; 28 specimens were obtained for culture, and 20 were positive for *P. aeruginosa* (Table 1). We compared these bronchoscopes with four older-model bronchoscopes by the same manufacturer (bronchoscopes E, F, G, and H) that were in use during the study period and



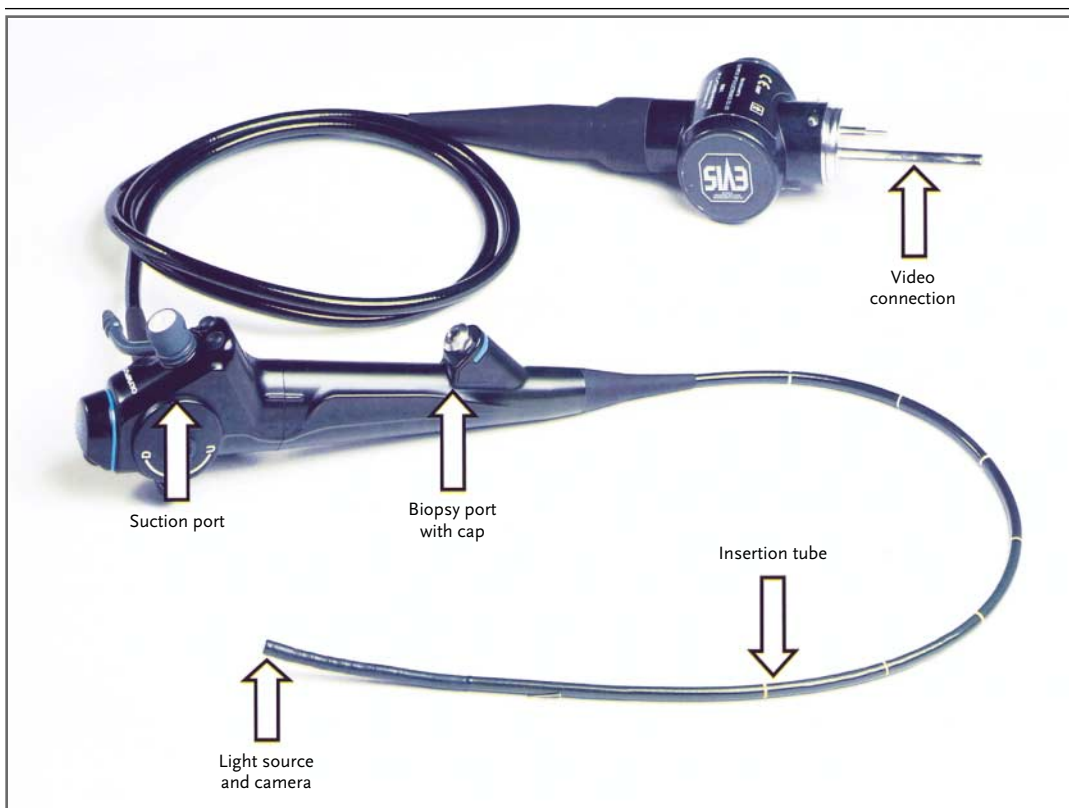


Figure 2. Bronchoscope.

The insertion tube has a single channel through which sterile saline can be injected by means of the biopsy port. A bronchoalveolar-lavage specimen can be recovered through the same channel by means of the suction port. The biopsy-port caps of the implicated bronchoscopes were found to be loose.

that were never noted to have loose or removable biopsy-port caps (Table 1). The risk that a specimen would be positive for *P. aeruginosa* was associated only with the use of recent-model bronchoscopes with the loose biopsy-port caps ($P < 0.001$).

The bronchoscopy-associated strain of *P. aeruginosa* was resistant only to gentamicin. Isolates of *P. aeruginosa* from 10 patients were available for PFGE; no *S. marcescens* isolates were available. The *P. aeruginosa* isolates from all 10 patients and from the biopsy-port caps of bronchoscopes A, B, and D were indistinguishable on PFGE (Fig. 4).

A total of 113 environmental samples were collected within the bronchoscopy suite; 61 were from bronchoscopes and 52 were from other environmental sources. Of the 52 environmental samples, 2 specimens (4 percent) were positive for *P. aeruginosa*. Both were from the sink trap where the bronchoscopes were rinsed before being placed in the

automated endoscope reprocessor. The PFGE patterns of the two environmental isolates matched the bronchoscopy-associated strain.

The bronchoscopes were routinely processed in an automated endoscope reprocessor (model MV-2, MediVators) with use of a 0.55 percent solution of ortho-phthalaldehyde (Cidex OPA, Advanced Sterilization Products). A representative of the manufacturer of the automated endoscope reprocessor reviewed the hospital's reprocessing procedures and indicated that they were satisfactory, except that the source water filter for the reprocessor had not been changed within the recommended six months. No strains of *P. aeruginosa* were isolated from either the source water or the filter.

A 50-year-old woman was readmitted 11 days after bronchoscopy with new pulmonary infiltrates in the right middle lobe. The specimen obtained during bronchoscopy was positive for *P. aeruginosa*.



Figure 3. Biopsy Port with Cap and Bushing Removed.

A biofilm was detected on the threads of the biopsy port and inside the cap; specimens obtained by swabbing these areas were positive for *Pseudomonas aeruginosa* and *Serratia marcescens*.

Table 1. Risk of Infection with *Pseudomonas aeruginosa* Associated with the Use of Recent-Model Bronchoscopes, as Compared with Older-Model Bronchoscopes.

Bronchoscope	No. of Procedures	No. of Cultures	<i>P. aeruginosa</i>	P Value
			Isolated from Culture no. (%)	
Recent-model bronchoscopes with loose biopsy-port caps				
A	17	16	12 (75)	<0.001
B	12	8	5 (62)	0.002
C	2	1	0	—
D	9	3	3 (100)	0.001
A, B, C, and D	40	28	20 (71)	<0.001
Older-model bronchoscopes (E, F, G, and H)*	26	15	0	—

* Older-model bronchoscopes served as the reference group.

On readmission, she had fever, leukocytosis, dyspnea, and increasing cough with darkening sputum. Culture of a sputum sample yielded *P. aeruginosa* with an antibiotic-susceptibility pattern similar to that of the epidemic strain. No isolates were available for PFGE. The pneumonia resolved.

DISCUSSION

A striking increase in the number of isolates of *P. aeruginosa* and *S. marcescens* from bronchoscopy specimens occurred at a community hospital from July through October 2001. One bronchoscopy-associated case of *P. aeruginosa* pneumonia was identified. The likelihood of positivity for *P. aeruginosa* or *S. marcescens* was associated only with the use of recent-model bronchoscopes that had loose biopsy-port caps. Strains of *P. aeruginosa* and *S. marcescens* were isolated from the biopsy ports of the implicated bronchoscopes. PFGE patterns linked the *P. aeruginosa* isolates from the patients to the isolates from the bronchoscopes.

Because the risk of a specimen's being positive for *P. aeruginosa* or *S. marcescens* was associated exclusively with the use of the recent-model bronchoscopes with the loose biopsy-port caps and because a case of bronchoscopy-associated pneumonia was identified, the manufacturer and the Food and Drug Administration were notified on September 18 and October 8, respectively. At that time, the Centers for Disease Control and Prevention indicated that no related outbreaks had been reported.

In 1997, the manufacturer changed the design of the biopsy port on at least 15 models of bronchoscopes that were still in use in 2001. Part of the new design involved changing the biopsy-port housing to a removable cap that was screwed on but fixed with adhesive. The manufacturer reported that failure to conform to production standards resulted in the distribution of bronchoscopes that did not meet manufacturing specifications. This might explain why problems with these models of bronchoscopes had not been reported previously. An alternative explanation is that infectious complications related to bronchoscopes often go unrecognized or unreported.^{9,21-23}

Persistent bacterial contamination of the biopsy port was probably not a result of a breach of the cleaning and disinfection guidelines, because the hospital's reprocessing procedures were determined to be satisfactory. In addition, contamination persisted even after three cycles of cleaning and disinfection in the automated reprocessor, and other bronchoscopes in use during the study period were not associated with positive cultures.

The loose biopsy-port caps most likely interfered with three important steps in reprocessing performed according to the current guidelines:

mechanical cleaning, high-level disinfection, and drying.⁷ Mechanical cleaning is necessary to remove the biofilm that can interfere with disinfection.^{24,25} Contaminated surfaces inside the hollow biopsy-port caps could not be cleaned mechanically. High-level disinfection requires an approved disinfectant to be in contact with a contaminated surface for a specified period of time.²⁶ The loose biopsy-port caps, which probably had air pockets when submerged, might have prevented effective contact between the disinfectant and the microorganisms. Finally, drying is recommended to prevent the growth of microorganisms with a predilection for moist environments.²⁷ The design of the caps probably prevented thorough drying of surfaces inside the caps.

The origin of the contaminating bacteria remains elusive. One postulated sequence of events is that the loose biopsy-port caps were contaminated in the sink when the bronchoscopes were cleaned before being placed in the automated endoscope reprocessor. Once within the biopsy-port caps, the bacteria were protected from the chemical-disinfection process. During subsequent use of the bronchoscopes, sterile saline was flushed through the biopsy ports, thereby becoming contaminated and further contaminating the bronchoscope channels and the patients' lower respiratory tracts. The contaminated lavage specimens were then suctioned back through the bronchoscope channels by means of the suction ports and collected for bacterial culture, yielding false positive results.

Antibiotic therapy was initiated in five patients (25 percent) after false positive culture results were reported. If these results reflected contaminated bronchoscopes rather than actual infections, the patients may have received unnecessary antibiotic treatment. Conversely, if patients were infected during the bronchoscopic procedures, the antibiotics may have prevented nosocomial illnesses.

After receiving our report, the manufacturer of the bronchoscopes initiated a recall of certain models. The voluntary recall, issued on November 30, 2001, affected 15 models of bronchoscopes, including the 2 models implicated in this investigation. The stated purpose was "to address a poten-

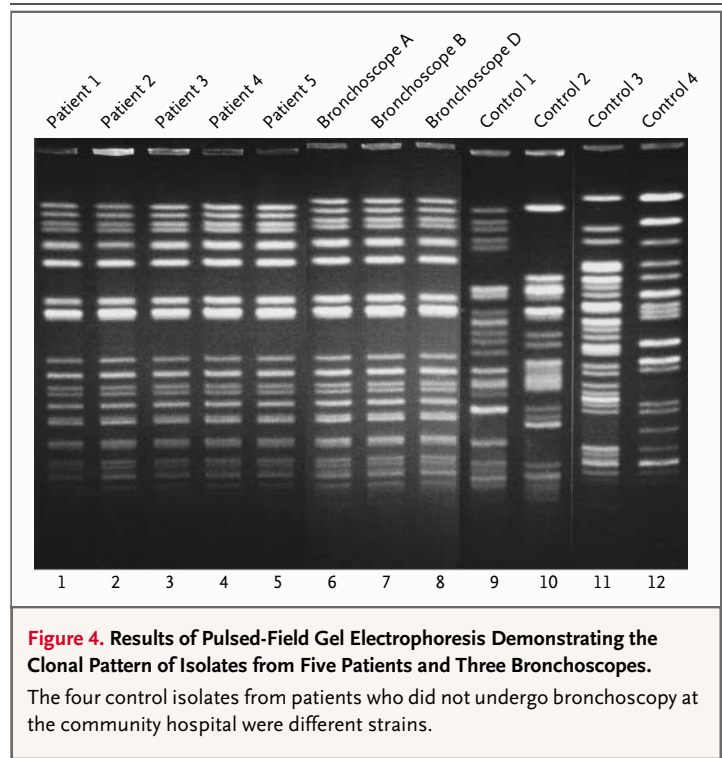


Figure 4. Results of Pulsed-Field Gel Electrophoresis Demonstrating the Clonal Pattern of Isolates from Five Patients and Three Bronchoscopes.

The four control isolates from patients who did not undergo bronchoscopy at the community hospital were different strains.

tial looseness of the biopsy-channel port housing [cap].” The recall reportedly involved an estimated 4700 bronchoscopes nationwide and was later expanded to include approximately 14,000 bronchoscopes worldwide. The manufacturer proposed modifying the bronchoscopes to resolve the problem with the caps. The recall received national media attention after an outbreak associated with the recalled models of bronchoscopes was reported at a hospital in another state, as described by Srinivasan et al.²⁸ Further microbiologic and epidemiologic surveillance is warranted to ensure that bronchoscopes modified as a result of the recall are not associated with further cases of false positive clinical specimens or infections.

We are indebted to Henrietta Hardin and the Tennessee Department of Health State Laboratory staff; to Patricia Coleman, Lynn King, and the community hospital pulmonologists and endoscopy staff; to Nita Lamb and the Vanderbilt University Medical Center infection-control practitioners for consultation and advice; to Walter E. Phillips, Ph.D.; and to Laura J. Fehrs, M.D.

REFERENCES

- Seijo LM, Sterman DH. Interventional pulmonology. *N Engl J Med* 2001;344:740-9.
- Owings MF, Kozak LJ. Ambulatory and inpatient procedures in the United States, 1996. Vital and health statistics. Series 13. No. 139. Hyattsville, Md.: National Center for Health Statistics, November 1998. (DHHS publication no. (PHS) 99-1710.)
- Favero MS, Bond WW. Chemical disinfection of medical and surgical materials. In: Block SS, ed. *Disinfection, sterilization, and preservation*. 4th ed. Philadelphia: Lea & Febiger, 1991:617-40.
- Rutala WA, Weber DJ. Disinfection of endoscopes: review of new chemical ster-

- ilants used for high-level disinfection. *Infect Control Hosp Epidemiol* 1999;20:69-76. [Erratum, *Infect Control Hosp Epidemiol* 1999;20:302.]
5. Muscarella LF. High-level disinfection or "sterilization" of endoscopes? *Infect Control Hosp Epidemiol* 1996;17:183-7.
 6. Bond WW. Endoscopy reprocessing: problems and solutions. In: Rutala WA, ed. *Disinfection, sterilization and antisepsis in health care*. Washington, D.C.: Association for Professionals in Infection Control and Epidemiology, 1998:151-63.
 7. Alvarado CJ, Reichelderfer M. APIC guideline for infection prevention and control in flexible endoscopy. *Am J Infect Control* 2000;28:138-55.
 8. Feigal DW Jr, Hughes JM. FDA and CDC public health advisory: infections from endoscopes inadequately reprocessed by an automated endoscope reprocessing system. Rockville, Md.: Food and Drug Administration, Center for Devices and Radiological Health, September 10, 1999. (Also available at <http://www.fda.gov/cdrh/safety/endorepress.html>.)
 9. Spach DH, Silverstein FE, Stamm WE. Transmission of infection by gastrointestinal endoscopy and bronchoscopy. *Ann Intern Med* 1993;118:117-28.
 10. Prakash UB. Does the bronchoscope propagate infection? *Chest* 1993;104:552-9.
 11. Ostrowsky B. Endoscopes — current practices and controversies in infection control. *Semin Infect Control* 2001;1:267-79.
 12. Sorin M, Segal-Maurer S, Mariano N, Urban C, Combet A, Rahal JJ. Nosocomial transmission of imipenem-resistant *Pseudomonas aeruginosa* following bronchoscopy associated with improper connection to the Steris System 1 processor. *Infect Control Hosp Epidemiol* 2001;22:409-13.
 13. Blanc DS, Parret T, Janin B, Raselli P, Francioli P. Nosocomial infections and pseudo-infections from contaminated bronchoscopes: two-year follow up using molecular markers. *Infect Control Hosp Epidemiol* 1997;18:134-6.
 14. Sammartino MT, Israel RH, Magnussen CR. *Pseudomonas aeruginosa* contamination of fiberoptic bronchoscopes. *J Hosp Infect* 1982;3:65-71.
 15. Kolmos HJ, Lerche A, Kristoffersen K, Rosdahl VT. Pseudo-outbreak of *Pseudomonas aeruginosa* in HIV-infected patients undergoing fiberoptic bronchoscopy. *Scand J Infect Dis* 1994;26:653-7.
 16. Vandenbroucke-Grauls CM, Baars AC, Visser MR, Hulstaert PF, Verhoef J. An outbreak of *Serratia marcescens* traced to a contaminated bronchoscope. *J Hosp Infect* 1993;23:263-70.
 17. Siegman-Igra Y, Inbar G, Campus A. An 'outbreak' of pulmonary pseudo-infection by *Serratia marcescens*. *J Hosp Infect* 1985;6:218-20.
 18. Weber DJ, Rutala WA. Lessons from outbreaks associated with bronchoscopy. *Infect Control Hosp Epidemiol* 2001;22:403-8.
 19. Molecular Analyst software, version 1.6. Hercules, Calif.: BioRad Laboratories, 1992.
 20. Dean AG, Arner TG, Sangam S, et al. Epi Info 2000, version 1.1: a database and statistics program for public health professionals for use on Windows 95, 98, NT, and 2000 computers. Atlanta: Centers for Disease Control and Prevention, 2001.
 21. Bronchoscopy-related infections and pseudo-infections — New York, 1996 and 1998. *MMWR Morb Mortal Wkly Rep* 1999;48:557-60.
 22. Wheeler PW, Lancaster D, Kaiser AB. Bronchopulmonary cross-colonization and infection related to mycobacterial contamination of suction valves of bronchoscopes. *J Infect Dis* 1989;159:954-8.
 23. Michele TM, Cronin WA, Graham NM, et al. Transmission of *Mycobacterium tuberculosis* by a fiberoptic bronchoscope: identification by DNA fingerprinting. *JAMA* 1997;278:1093-5.
 24. Davies DG, Parsek MR, Pearson JP, Iglewski BH, Costerton JW, Greenberg EP. The involvement of cell-to-cell signals in the development of a bacterial biofilm. *Science* 1998;280:295-8.
 25. Kolter R, Losick R. One for all and all for one. *Science* 1998;280:226-7.
 26. Rutala WA, Gergen MF, Weber DJ. Comparative evaluation of the sporicidal activity of new low-temperature sterilization technologies: ethylene oxide, 2 plasma sterilization systems, and liquid peracetic acid. *Am J Infect Control* 1998;26:393-8.
 27. Muscarella LF. Deja vu . . . all over again? The importance of instrument drying. *Infect Control Hosp Epidemiol* 2000;21:628-9.
 28. Srinivasan A, Wolfenden LL, Song X, et al. An outbreak of *Pseudomonas aeruginosa* infections associated with flexible bronchoscopes. *N Engl J Med* 2002;348:221-7.

Copyright © 2003 Massachusetts Medical Society.

CLINICAL PROBLEM-SOLVING SERIES

The *Journal* welcomes submissions of manuscripts for the Clinical Problem-Solving series. This regular feature considers the step-by-step process of clinical decision making. For more information, please see <http://www.nejm.org/hfa/articles.asp>.