

merit; improving patient outcomes is the ultimate reason for the existence of our profession. However, its current practical application seems plagued with difficulties.

I agree that to restore public confidence, we do need to work harder in policing ourselves. Most medical specialties currently require periodic retesting to maintain certification. This should assure minimum competency in terms of knowledge. Although not perfect, a process-based system evaluating conformance to established standards of care is at least manageable from a logistic standpoint and does not penalize physicians who care for difficult patients.

Stephen Clement, MD

Major, Medical Corp
Department of the Army
Walter Reed Army Medical Center
Washington, DC 20307-5001

Disclaimer: The opinions and assertions stated here are those of the author and do not represent the views of the Department of the Army or the Department of Defense.

References

1. Brook RH. Health care reform is on the way: Do we want to compete on quality? *Ann Intern Med.* 1994;120:84-6.
2. Topol EJ, Califf RM. Scorecard cardiovascular medicine: its impact and future directions. *Ann Intern Med.* 1994;120:65-70.
3. Lichtman SW, Pisarska K, Berman ER, Pestone M, Dowling H, Offenbacher E, et al. Discrepancy between self-reported and actual caloric intake and exercise in obese subjects. *N Engl J Med.* 1992;327:1893-8.
4. Fulop G, Reinhardt J, Strain JJ, Paris B, Miller M, Fillit H. Identification of alcoholism and depression in a geriatric medicine outpatient clinic. *J Am Geriatr Soc.* 1993;41:737-41.
5. Sobolski JC, Kolesar JJ, Kornitzer MD, De Backer GG, Mikes Z, Dramaix MM, et al. Physical fitness does not reflect physical activity patterns in middle-aged workers. *Med Sci Sports Exerc.* 1988;20:6-13.

In response: I agree with Dr. Clement that, unless publicly released data on quality are accurate, untoward events may occur. In particular, physicians who perceive that outcome-based systems do not adequately adjust for sickness at the time of treatment may stop caring for sick patients to improve their performance profiles. One solution is to build severity adjustment models that "overadjust" for sickness (that is, give physicians who care for sicker patients extra credit in terms of expected mortality).

Patients' habits that affect outcome, such as smoking (1), weight (2), and even exercise, can be measured and included as adjusters in outcome models. Because self-reports would be anonymous, confidential, and not used for determining eligibility for life or health insurance, patient responses should not be biased.

Finally, I did not intend to leave the impression that outcome data are the only or even the best ways to compare health plans or physicians. Process comparisons are often preferable and have been useful for comparing plans on quality of prenatal care (3), use of hysterectomy (4), and treatment of myocardial infarction (5). Process measures are better for these purposes because they are more directly under the control of the physician or plan and can be measured contemporaneously. By contrast, it might take 10 years to judge a surgeon by the hernia recurrence rate. Furthermore, for example, only a few cases need to be reviewed to determine whether physicians differ in their use of influenza vaccine in the elderly. Many more persons must be included to determine whether differences occurred in the pneumonia death rate because physicians failed to provide a medically indicated influenza vaccination. Only process measures for which good scientific evidence supports a relation to outcome should be included in quality scorecards. Otherwise, we may encourage the use of processes that will not improve or protect a person's health and that will result in a distortion of our investment in health care.

Robert H. Brook, MD, ScD

University of California, Los Angeles, Center for the Health Sciences
Los Angeles, CA 90024

References

1. Stewart AL, Brook RH, Kane RL. Conceptualization and Measurement of Health Habits for Adults in the Health Insurance Study. Vol. I, Smoking. Santa Monica, CA: RAND; 1979. R-2374/1-HEW.
2. Stewart AL, Brook RH, Kane RL. Conceptualization and Measurement of Health Habits for Adults in the Health Insurance Study. Vol. II, Overweight. Santa Monica, CA: RAND; 1980. R-2374/2-HEW.
3. Murata PJ, McGlynn EA, Siu AL, et al. Quality measures for prenatal care. A comparison of care in six health plans. *Arch Fam Med.* 1994;3:41-9.
4. Bernstein SJ, McGlynn EA, Siu AL, Roth CP, Sherwood MJ, Keesey JW, et al. The appropriateness of hysterectomy. A comparison of care in seven health plans. Health Maintenance Organization of Quality of Care Consortium. *JAMA.* 1993;269:2398-402.
5. Carlisle DM, Siu AL, Keeler EB, McGlynn EA, Kahn KL, Rubenstein LV, et al. HMO vs fee-for-service care of older persons with acute myocardial infarction. *Am J Public Health.* 1992;82:1626-30.

Enterovirus in the Chronic Fatigue Syndrome

To the Editor: The chronic fatigue syndrome is a recurring illness of unknown cause characterized by incapacitating fatigue and a range of symptoms and laboratory findings suggestive of hypothalamic dysfunction (1-3). Rare patients who have died from other acute causes have had cellular infiltrates in the hypothalamus (4). The syndrome usually follows a flu-like illness, and circumstantial evidence has implicated enteroviruses (1). We therefore examined the central nervous system of a woman with the syndrome who died from suicide for the presence of enterovirus.

In June 1992, a 30-year-old woman who had met all criteria for the syndrome for 5 years was brought to the hospital after attempted suicide and died of complications. Immediately after death, tissue was removed from the brain, heart, skeletal muscle, lungs, and spleen and was stored at -80°C . The brain samples were from the frontal, temporal, parietal, and occipital cortices and from the mid-brain, hypothalamus, and brain stem. Control samples were obtained from four patients who died of cerebrovascular diseases and from four age- and sex-matched patients who had committed suicide during severe depression over the next 2 months.

Ribonucleic acid (RNA) from the tissues was prepared for analysis by polymerase chain reaction (PCR). The RNA samples were prepared and amplified using oligonucleotide primers.

No enteroviral sequences were detected in any of the control tissues. Positive PCR sequences were detected in the muscle,

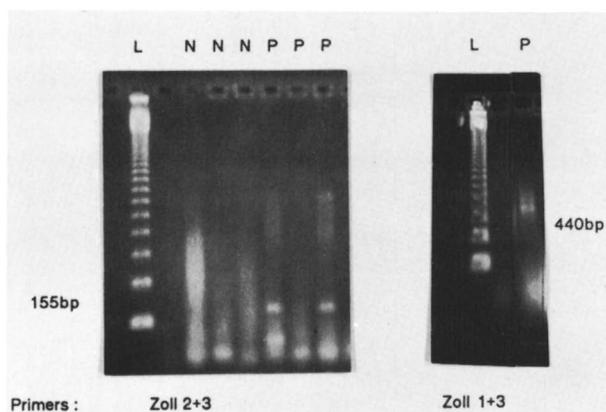


Figure 1. Polymerase chain reaction products isolated from hypothalamic samples of a patient with the chronic fatigue syndrome and three controls. The agarose gels were stained with ethidium bromide and were visualized in ultraviolet light. **Left.** The results with Zoll primers 2+3 (positive band is 155 base pairs). **Right.** The results with Zoll primers 1+3 (440 base pairs). Lane N shows three hypothalamic samples from controls. Lane P shows independent RNA preparations and polymerase chain reactions carried out on the hypothalamus of the patient with the chronic fatigue syndrome. Lane L = 123 base pair DNA ladder.

heart, and brain samples from the hypothalamus and brain stem region of our patient with the syndrome (Figure 1). Sequence analyses on the PCR products were compatible with exogenous virus and not with contamination. The results showed an enterovirus with an 83% similarity to Coxsackievirus B3. Although the findings may represent chance occurrence, they further support the possibility that hypothalamic dysfunction exists in the pathogenesis of the syndrome. Also, they suggest that the chronic fatigue syndrome may be mediated by enterovirus infection and that persistent symptoms may reflect selective persistence in affected organs.

Frances McGarry, BSc
John Gow, PhD
Peter O. Behan, MD
Southern General Hospital
Glasgow G51 4TF
Scotland

References

1. Bakheit AM, Behan PO, Watson WS, Morton JJ. Abnormal arginine-vasopressin secretion and water metabolism in patients with postviral fatigue syndrome. *Acta Neurol Scand.* 1993;87:234-8.
2. Bakheit AM, Behan PO, Dinan TG, Gray CE, O'Keane V. Possible upregulation of hypothalamic 5-HT receptors in patients with the postviral fatigue syndrome. *Br Med J.* 1992;304:1010-2.
3. Demitrik MA, Dale JK, Straus SE. Evidence for impaired activation of the hypothalamic-pituitary-adrenal axis in patients with chronic fatigue syndrome. *J Clin Endocrinol Metab.* 1991;73:1224-34.
4. Crowley N, Nelson M, Stouin S. Epidemiological aspects of an outbreak of encephalomyelitis at the Royal Free in the summer of 1955. *J Hygiene.* 1957;55:116.

Microsporidia and HIV-related Diarrhea

To the Editor: The recent article by Rabeneck and colleagues (1) questioning the association between chronic diarrhea and intestinal microsporidiosis raises several concerns: Were the *Enterocytozoon bienewsi*-infected asymptomatic patients more likely to develop diarrhea than the pathogen-negative patients (2)? Why and how was transmission electron microscopy used for quantitation? Was there a difference in the degree of parasite maturation or pattern of mucosal infection between the groups? Was there a difference in the large-bowel burden of *E. bienewsi* (4) compared with that of the small bowel?

The histopathologic findings are important because mucosal damage generally parallels parasite burden and the severity of diarrhea (3). Because light microscopy of plastic sections can readily detect all microsporidial stages (3) and more accurately assess parasite burden. Further, despite that electron micrographs showed "abundant organisms," no light microscopic diagnoses were made prospectively, and only 36% were made retrospectively. This fact is in striking contrast to the observations of others (3).

That none of the infections were correlated with diarrhea is surprising. Support for a pathogenic role for *Microsporidia* is based on its identification, often as the sole pathogen, in several hundred patients worldwide with characteristic histopathologic and functional abnormalities, including impaired D-xylose absorption and weight loss (3). Self-limiting acute diarrhea and *Microsporidia* infection were recently reported in patients with and those without human immunodeficiency virus infection (Presented at the Microsporidiosis and Cryptosporidiosis in Immunodeficient Patients Meeting, Ceske Budejovice, Czech Republic, 1993). Moreover, albendazole therapy for the second intestinal microsporidia, *Septata intestinalis*, leads to resolution of symptoms, clearance of organisms, and reversal of histopathologic abnormalities, fulfilling three of Koch's postulates (5).

Intestinal microsporidiosis is probably a common infection in humans that can exist latently, and the authors are to be congratulated for unearthing evidence of such a condition. However, based on the available data, their implication that microsporidiosis is not a cause of intestinal disease seems unwarranted.

Jan Marc Orenstein, MD, PhD
George Washington University Medical Center
Washington, DC 20037

Debra Benator, MD
Washington Hospital Center
Washington, DC 20010

Donald P. Kotler, MD
St. Luke's-Roosevelt Hospital Center
New York, NY 10025

References

1. Rabeneck L, Gyorkey F, Genta R, Gyorkey P, Foote LW, Risser JM. The role of *Microsporidia* in the pathogenesis of HIV-related chronic diarrhea. *Ann Intern Med.* 1993;119:895-9.
2. Eeffinck Schattenkerk JK, van Gool T, van Ketel RJ, Bartelmsman JF, Kuiken C, Terpstra WJ, et al. Clinical significance of small-intestinal microsporidiosis in HIV-1-infected individuals. *Lancet.* 1991;337:895-8.
3. Orenstein JM. Microsporidiosis in the acquired immunodeficiency syndrome. *J Parasitol.* 1991;77:843-64.
4. Gourley WK, Swedo JL. Intestinal infection by microsporidia *Enterocytozoon bienewsi* of patients with AIDS: an ultrastructural study of the use of human mitochondria by a protozoan [Abstract]. *Lab Invest.* 1988;58:35A.
5. Orenstein JM, Dieterich DT, Lew EA, Kotler DP. Albendazole as a treatment for disseminated microsporidiosis due to *Septata intestinalis* in AIDS patients. *AIDS.* 1994. (In press).

In response: With respect to the clinical course of *E. bienewsi*-infected men, after a mean of 15 months of follow-up, the 18 men with chronic diarrhea retained this pattern, and 2 of the 13 asymptomatic men developed intermittent diarrhea (unpublished data). Histologic findings varied from normal architecture to almost complete effacement of the villous architecture (unpublished data). We do not agree with Orenstein and colleagues' statement correlating parasite burden and the severity of diarrhea. Such a correlation requires a valid and reliable method for assessing parasite burden, which is not currently available. Classifying the degree of mucosal damage on the basis of one or more small biopsy fragments assumes that the lesion is not patchy. We are aware of only one study of the topographic distribution of intestinal microsporidiosis (1) and were unfamiliar with the earlier published abstract describing large-bowel infection with *E. bienewsi* (2).

We agree that plastic embedding is the best method to process specimens for light microscopy, but we used electron microscopy because of its ready availability. As Orenstein and colleagues (1) previously stated, the detection of microsporidia by light microscopy in slides prepared from paraffin-embedded tissues is difficult because "*E. bienewsi* organisms are not reliably detected in paraffin sections using a variety of cytochemical stains" (1). Because the pathologist experiences a learning curve, we decided to learn to recognize organisms on slides from patients known to have microsporidia that was previously diagnosed by electron microscopy. We recognize the shortcomings of attempting to quantify intensity of infection (or parasite burden) using electron microscopy, as stated in our article (3).

From our evidence, we cannot conclude that a relation between diarrhea and *Microsporidia* does not exist, but only that we did not detect any such relation. It seems likely that, as with many other parasites, a relation exists between the intensity of infection and clinical illness (in this case, diarrhea).

Linda Rabeneck, MD, MPH
Robert M. Genta, MD
Houston Veterans Affairs Medical Center
Houston, TX 77030

References

1. Orenstein JM, Tenner M, Kotler DP. Localization of infection by the microsporidian *Enterocytozoon bienewsi* in the gastrointestinal tract of AIDS patients with diarrhea. *AIDS.* 1992;6:195-7.
2. Gourley WK, Swedo JL. Intestinal infection by microsporidia *Enterocytozoon bienewsi* of patients with AIDS: an ultrastructural study of the use of human mitochondria by a protozoan [Abstract]. *Lab Invest.* 1988;58:35A.

3. Rabeneck L, Gyorkey F, Genta RM, Gyorkey P, Foote LW, Risser JM. The role of *Microsporidia* in the pathogenesis of HIV-related diarrhea. *Ann Intern Med.* 1993;119:895-9.

The Birth of a Common Procedure

To the Editor: I enjoyed the quotation from Banting and Best that appeared in your 1 January 1994 issue (p. 70). It occurred to me that many housestaff physicians regularly do a procedure for which Werner Forssmann (along with Courmand and Richards) received the Nobel prize in 1956.

Forssmann was a 26-year-old intern at a community hospital on the outskirts of Berlin at the time. When the article was published, he was a surgical resident in the department of Ferdinand Sauerbruch at the Charité in Berlin. The two-page article caused such a furor that Sauerbruch, a man of more bravado than insight, fired poor Forssmann only to rehire him after the hubbub died down. He re-fired him later.

I thought that younger readers might be interested in this story and have inserted a few paragraphs translated from Forssmann's original German:

In cases of shock, such as those engendered by sudden cardiac standstill, or during anesthetic emergencies and poisonings, it may be desirable to deliver medications directly to the heart itself. In such patients, injections of drugs into the heart may be life saving. Nevertheless, intracardiac puncture is a dangerous procedure for several reasons, including injury to the coronary arteries and its branches, pericardial tamponade, injury to the diaphragm, and pneumothorax. Thus, the administration of intracardiac medications is a measure of last resort, which results in loss of time and opportunity. For these reasons, I considered a new method to approach the heart in a less dangerous fashion, namely the catheterization of the right heart from the venous system.

Experiments on a cadaver were productive. I was able to catheterize any vein in the antecubital fossa and was able to regularly reach the right ventricle, before encountering resistance. Subsequent dissection showed the catheter, which was also palpable, present in the cephalic or basilic vein, extending through the subclavian and innominate veins, to the superior vena cava and into the right heart itself. I next undertook experiments on a living subject, namely on myself. I first convinced a colleague to puncture a vein in my right antecubital fossa with a large needle. I next advanced a well-oiled ureteral catheter size 4 Charriere in diameter through the needle into the vein. The catheter allowed itself to be advanced with trivial ease to 35 cm. Because my friend objected to our proceeding with these experiments further, we broke them off even though I felt perfectly well. One week later, I tried again alone. I anesthetized my own left antecubital fossa and because I was not able to manipulate the needle by myself, I constructed a "cut down" and advanced the catheter along its full 65 cm length. From surface estimates, I reasoned that the catheter tip would be at the level of the heart.

I documented the position of the catheter with roentgenograms that I obtained by standing in front of the fluoroscope while observing the catheter in a mirror held by a nurse. In conclusion, I would like to

point out the utility of this technique in providing new opportunities to research the metabolic activities and the actions of the heart (1).

Friedrich C. Luft, MD
Franz Volhard Clinic
Berlin, Germany

Reference

1. Forssmann W. Catheterization of the right heart. *Klinische Wochenschrift.* 1929;No. 45:2085-7.

An Aid for Caregivers of Patients with Dementia

To the Editor: The potential psychiatric and physical symptoms experienced by caregivers of patients with dementia are highlighted by Baumgarten and colleagues (1). Many personal interactions outside the home environment can result in anxiety and embarrassment to both the caregiver and the patient (2). The caregiver of one of my patients provided a novel solution.

A 67-year-old woman, accompanied by her husband, came to the Urgent Care Center with abdominal pain. No past medical records were available. It became increasingly difficult to document the patient's presenting problem until her husband took from his shirt pocket a card that he had made with the word "Alzheimer's" on it. After I saw the card, he returned it to his pocket. This maneuver took about 5 seconds and was not perceived by his wife.

This simple, inexpensive tool prevented embarrassment to the patient and her caregiver. The card not only simplified the consultation but many other aspects of their lives.

James A. Levine, MD, PhD
Mayo Clinic
Rochester, MN 55905

References

1. Baumgarten M, Hanley JA, Infante-Rivard C, Battista RN, Becker R, Gauthier S. Health of family members caring for elderly patients: a longitudinal study. *Ann Intern Med.* 1994;120:126-32.
2. O'Connor DW, Pollitt PA, Roth M, Brook CP, Reiss BB. Problems reported by relatives in a community study of dementia. *Br J Psychiatry.* 1990;156:835-41.

Correction: Mechanical Ventilation Weaning Using Gastric pH

In a recent issue of *Annals*, a critical sentence was omitted from Mohsenifar and colleagues' response (1) to a series of letters to the Editor on weaning patients from mechanical ventilation using gastric pH. The last sentence of the last paragraph should read as follows: "Most of the commonly used tests have good sensitivity and negative predictive values, therefore, they predict true successes and true failures. Of importance, however, they have a high false-positive rate (even in Tobin's paper) which, unfortunately, results in failed extubation."

Reference

1. Mohsenifar Z, Koerner SK, Lewis MI. Weaning patients from mechanical ventilation using gastric pH [Letter]. *Ann Intern Med.* 1994; 120:439.