Management of Fibromyalgia

To the Editor: Dr. Leventhal’s review of fibromyalgia treatment (1) fails to indicate that long-term studies have not shown useful benefit from fibromyalgia treatment. Somewhat surprisingly, he omits from his review our multicenter, 7-year study on fibromyalgia outcomes among 538 patients who were seen in the clinics of fibromyalgia experts and who were exposed to many of the treatments labeled as effective in Leventhal’s review (2). It appears useful to repeat our study conclusions: “Patients with established fibromyalgia, seen in rheumatology centers in which there was a special interest in the disease, and who were not followed up for as long as 7 years, had markedly abnormal scores for pain, functional disability, fatigue, sleep disturbance, and psychological status, and these values did not change substantially over time.”

In knowing what works, it is important to understand what is meant by “working.” Dr. Leventhal does not define terms that he uses, such as “benefit,” “improvement,” “effective,” and “effectiveness.” Except for an occasional perfunctory use of the word “clinically,” he does not distinguish between statistical and clinical significance. Having worked in fibromyalgia research for many years (2, 3), I suggest that an effective treatment must produce a sustained improvement of at least 20%. It is fundamentally wrong to extrapolate short-term data to long-term outcomes.

In his discussion of causes and mechanisms of fibromyalgia, Dr. Leventhal ignores a huge body of literature linking psychological abnormality and psychosocial distress to the production and maintenance of fibromyalgia symptoms. To do this is to terribly distort the reality of fibromyalgia.

If treatments do not work in a sustained and useful way, they should not be used (4). Physicians, with their treatments and beliefs, can be responsible for creating and sustaining illness, as in the case of the growing fibromyalgia epidemic (5).

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References

To the Editor: I commend Dr. Leventhal (1) for an overall superb review of fibromyalgia management and Annals for providing a prominent position for this topic.

Fibromyalgia is universally encountered in internal medicine practices and is often misunderstood and misdiagnosed. I wish to raise a few points about the prominence placed by Dr. Leventhal on tramadol as an effective agent for fibromyalgia. No mention is made of the substantial side-effect profile of this medication, whereas other therapeutic agents discussed in the paper are presented in a balanced fashion. Recently, I attended a gathering of rheumatology colleagues to discuss analgesic medicine. There was near-universal rejection of tramadol as a drug of choice in the management of fibromyalgia because of its expense and side-effect profile. Clearly, as most of my colleagues agreed, there is a limited subset of patients for whom tramadol is appropriate; Dr. Leventhal, however, presents it as the analgesic of choice for fibromyalgia. In all fairness to the author, he does note that “tramadol was found to be as effective as acetaminophen with codeine in elderly patients with various chronic painful conditions, including fibromyalgia.” Left out is the vast cost differential between tramadol and acetaminophen with codeine. Many managed care formularies have noted this and have appropriately excluded tramadol from their list of reimbursable medications. Because the paper was supported by an “unrestricted educational grant from Ortho-McNeil Pharmaceutical,” such an omission becomes understandable. Although unimpeachable in every other way, this paper must be considered an “informational” (paid advertisement presented as factual information) for tramadol. The cursory reader is lead to believe that tramadol is the proven best analgesic for fibromyalgia. This is clearly not the case.

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Reference
McNeil Pharmaceutical. Tramadol (Ultram) is marketed by Ortho-McNeil. Enough said.

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Reference

To the Editor: Leventhal (1) states in the abstract of his paper that trigger-point injections of analgesics may be helpful in the management of pain associated with fibromyalgia. In the Conclusion section of the paper, however, he mentions “tender point injections.” “Tender points” and “trigger points” are distinct clinical entities (2, 3), although the two phenomena may coexist in the same patient and overlap syndromes can occur (2). “Tender points” are areas of tenderness occurring in muscle, muscle–tendon junctions, bursa, or fat pads. Tender points are considered characteristic of fibromyalgia, especially when they occur in a widespread manner (2). On the other hand, “trigger points” are defined as areas of muscle that are painful to palpation and are characterized by the presence of taut bands and the generation of a referral pattern of pain. They typically occur in a more restricted regional pattern and are indicative of the myofascial pain syndrome (2).

I recommend that the two phrases be distinguished because fibromyalgia and the myofascial pain syndrome are two different clinical conditions that require different treatment plans.

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References

To the Editor: The essence of a peer-reviewed journal is an unbiased, scientific appraisal of data, vetted by the editors and reviewers. Review articles with therapy recommendations should be held to a higher standard than reporting of scientific experiments. Therefore, Leventhal’s review on fibromyalgia (1) is deeply disturbing. The existence of a definite clinical disease is not the issue. The repeated recommendations for the use of tramadol are.

In the review, the efficacy of tramadol in fibromyalgia is supported by five references (references 65 through 69). Only one is from a genuine peer-reviewed journal, and that is an abstract. None of the other four journals do I consider genuine peer-reviewed journals. Furthermore, two of the other four reports appear in supplements, which are often sponsored by a pharmaceutical company and are disclaimed by the journal editors.

Mentioned at the end of the review is the grant support from Ortho-McNeil Pharmaceutical, the manufacturer of tramadol. Moreover, the discussion of tramadol omits the fact that the drug is an opiate-like agent and a controlled substance. Some writers consider the drug to have substantial addiction potential and want it reclassified as a class II narcotic.

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Reference

In response: Dr. Wolfe is surprised that I did not mention his study (1), but my review focused on controlled trials. Although Wolfe and colleagues’ study yielded important information, the authors stated that they did not test specific treatments in fibromyalgia and that the patients’ conditions may have worsened over time had the patients not sought conventional treatment. Additionally, concern should be raised on how information on treatment failures at tertiary care centers gathered by fibromyalgia experts translates to patient responses in community settings.

Dr. Wolfe indicates that I do not define “what works” and that it is “fundamentally wrong to extrapolate short-term data to long-term outcomes.” This is a problem common to therapeutic trials for most chronic conditions. I agree that uniform criteria for improvement must be established for fibromyalgia clinical trials. Up to this point, however, this has not occurred. As a review of the available literature, my paper relied on definitions of improvement as given by the researchers and as approved by the journals publishing these studies. I endorse the idea that an organization such as the American College of Rheumatology establish and validate uniform criteria for improvement in fibromyalgia. I acknowledged in my review that in fibromyalgia, “pharmacologic therapies show only limited success. . . .”

Dr. Wolfe states that physicians who attempt to treat patients with fibromyalgia are “responsible for creating . . . illness.” The purpose of my review was to help clinicians distinguish therapeutic interventions that have been evaluated scientifically from those for which the experience is anecdotal. Until evidence shows that all patients meeting the clinical definition of fibromyalgia are malingered or feigning their suffering, and until there are better suggestions on how to help these patients, we must help them by using agents evaluated in a controlled fashion.

Given the increasing industry support for medical research, I understand Dr. Huppert’s and Mr. Muilenburg’s sensitivity to pharmaceutical company influences. I do not, however, believe I expressed more enthusiasm for tramadol than for other interventions requiring further study. Tramadol is the only currently available agent, marketed as an oral “analgesic,” shown to be effective in fibromyalgia. Ortho-McNeil Pharmaceutical was unaware that my review was being prepared. Honoraria received by my division from pharmaceutical companies for speaking engagements are used to help offset secretarial costs incurred by manuscript preparation. It is unfortunate that my review does not coincide with Huppert and colleagues’ experience, as expressed in their discussion.

Finally, I hope that Mr. Muilenburg’s opinions are not influenced by any incentive to limit access to medications he considers “too expensive.”

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Reference

Time and Medicine

To the Editor: The 4 January issue on “Time and Medicine” was thought-provoking. I wish, however, that someone had thought to include, perhaps as a quotation, the following comments from an address given by my revered teacher, the late Philip A. Tumulty, and published as “The Art of Healing” (1):

“From a purely practical standpoint, these special characteristics of patients lead to but one conclusion regarding the practice of clinical medicine—it is simply not possible to give excellent care to patients in a quick, easy or offhand fashion, or through the agency of some aid or substitute. . . . Time personally spent with the patient is the most essential ingredient of excellence in clinical practice. There are simply no short cuts and no substitutions. . . . There must be time to assay the patient’s intellectual and psychological elements; time to meticulously gather each piece of clinical evidence from the history and physical examination; time to analyze these data and to add to them other helpful...”

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Reference
Auscultation through a Shirt

To the Editor: Time pressures have increased recently, but is it standard practice for internists to listen to the lungs and heart through the patient’s shirt? (See the cover and the interior photographs in the American College of Physicians–American Society of Internal Medicine’s recent brochures, “Resources for Internists 2000” and “Report of the Executive Vice President, Fiscal Year 1998/1999”.) Is the remainder of the physical examination also done through clothing?

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Cholangiocarcinoma and AIDS-Related Sclerosing Cholangitis

To the Editor: Primary sclerosing cholangitis, chronic parasitic infection of the biliary ducts, and X-linked immunodeficiency are well-known risk factors for cholangiocarcinoma (1, 2). We report cholangiocarcinoma in a patient with AIDS-related sclerosing cholangitis.

A 38-year-old homosexual man with AIDS was hospitalized for rapidly progressive jaundice and fever. He had a history of cytomegalovirus retinitis and AIDS-related sclerosing cholangitis that had developed 5 and 3 years before admission, respectively. When sclerosing cholangitis developed, the patient was severely immunodepressed (CD4+ cell count, 5 cells/mm3). The patient has been asymptomatic since undergoing endoscopic sphincterotomy 3 years ago. On admission, abdominal ultrasonography showed important bilateral dilatation of the intrahepatic bile ducts caused by a 2-cm tumor located in the upper part of the common hepatic duct. Endoscopic retrograde cholangiopancreatography showed an intraluminal polyoid mass (type II in the Bismuth classification), and biopsies identified cholangiocarcinoma. The preoperative CA19-9 level was 1783 IU/L. We attempted radical surgery because of the limited extension of the tumor, the good condition of the patient, and a relatively high CD4+ cell count during highly active antiretroviral therapy (170 cells/mm3). Complete tumor resection and hepaticojunostomy, the CA19-9 level decreased to 116 IU/L. The patient was well 2 months after surgery.

Highly active antiretroviral therapy has been associated with dramatically improved long-term survival in patients with AIDS (3); this increased survival, however, allows new pathologic conditions to emerge. Biliary cancer remains uncommon in patients with AIDS: the primary types of cancer are Kaposi sarcoma and malignant lymphoma (1). No correlation has been found between those cancers and AIDS-related sclerosing cholangitis, a frequent cause of cholestasis among HIV-infected patients (4). Further follow-up of patients with AIDS-related sclerosing cholangitis who are receiving highly active antiretroviral therapy is warranted to determine whether these patients have an increased risk for cholangiocarcinoma.

Because an early diagnosis is needed to attempt complete surgical resection of the tumor, screening procedures (such as...
abdominal ultrasonography and assessment of CA19-9 level) should be encouraged in this setting.

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References

The Cadaveric Option

To the Editor: Bone marrow transplant nephropathy (1) is a radiation-induced syndrome similar to the hemolytic uremic syndrome that occurs 6 to 12 months after bone marrow transplantation (BMT). Because some patients require maintenance dialysis, renal transplantation might offer the best therapeutic option. Four cases of immunologic tolerance to renal allografts after BMT from the same donor have been reported (2). We report immunologic tolerance to cadaveric renal allografts after BMT.

A 26-year-old woman underwent allogeneic BMT with bone marrow from her HLA-identical sister for acute myeloblastic leukemia (M2 FAB classification) in first complete remission. The conditioning regimen included cyclophosphamide (120 mg/kg of body weight), unfractionated total-body irradiation (10 Gy), and cyclosporine. Methotrexate and methylprednisolone were continued by day 180 because no signs of GVHD were present. Complete donor chimerism was documented. One year after BMT, the patient developed BMT nephropathy (1). Treatment with plasmapheresis, aspirin, and vincristine was unsuccessful, and long-term hemodialysis was initiated. A renal graft from her HLA-identical sister was not available. After 29 months of dialysis, the patient received a 3-HLA-mismatched cadaveric renal allograft. The immunosuppressive regimen included steroids, cyclosporine, and mycophenolate mofetil. The post-transplantation course was uneventful. Fourteen months later, the patient is healthy and has normal function of both grafts. She is receiving only mycophenolate.

Actively acquired tolerance to alloantigens in animal models was first reported by Billingham and colleagues in 1953 (3). Several cases of acquired specific immunologic tolerance to organ allografts after BMT have been reported in humans since then (2). For patients with BMT nephropathy, renal transplantation from the same HLA-identical bone marrow donor is the best option because of specific immunologic unresponsiveness, even in the absence of immunosuppressive treatment (4). Unfortunately, this kind of renal graft is not always available; a cadaveric allograft may therefore be a promising solution.

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References

Isotretinoin in Respiratory Papillomatosis

To the Editor: Retinoids can reduce the risk for second primary tumors of the head and neck and may reverse dysplasia of the aerodigestive tract mucosa, a premalignant condition. An 81-year-old nonsmoking woman was referred for consideration of isotretinoin therapy for severe tracheal dysplasia associated with recurrent papillomatosis. Over the previous two decades, she had required 113 surgical procedures to clear her upper airway of rapidly recurring papillomas; her disease had progressed despite therapy with cyclophosphamide and recombiant human interferon-α. She began receiving isotretinoin, 2 mg/kg of body weight per day Monday through Friday for 3 months. The dosage was then decreased to 1 mg/kg per day Monday through Friday for 9 months. Therapy was well tolerated except for mild xerodema and pruritus. During the year of isotretinoin therapy, the patient underwent only two resections of papillomas; in contrast to her condition at most of her previous procedures, the patient did not present with near-total airway obstruction. No evidence of dysplasia was noted during the first resection; the second procedure was a laser photoablation. The patient is currently receiving maintenance therapy with isotretinoin, 40 mg/d (total dosage), Monday through Friday.

Few reports of retinoid treatment given as postsurgical adjuvant therapy to patients with respiratory papillomatosis suggest a potential benefit. Neither Avidano and Singleton (1) nor Bell and colleagues (2) could demonstrate activity in patients who received isotretinoin. Eicher and colleagues (3), however, reported a case similar to ours, in which the patient responded successfully to retinoid therapy.

Prolonged isotretinoin therapy in modest doses may be an effective adjunct to surgical resection of aggressive papillomatosis of the aerodigestive tract that does not respond to interferon therapy. In such a setting, we suggest that reasonable end points might be a reduction in the number and frequency of surgical procedures, as well as reversal of dysplasia.

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References

 Interruption of the Inferior Vena Cava in a Patient with Hirschsprung Disease

To the Editor: A 47-year-old man was admitted with dyspnea (New York Heart Association class III), edema in both legs, and micturition that had been occurring twice a night. He had had Hirschsprung disease since childhood. Chest radiography, computed tomography, and magnetic resonance imaging showed dilatedazygos and hemiazygous veins. Magnetic resonance imaging demonstrated a weak flow in the inferior vena cava. Insertion of the inferior vena cava to the right atrium was interrupted, indicating a rare form of continuation syndrome of theazygos vein. Angiography of the inferior vena cava clearly demonstrated an interruption of this vein immediately before the right atrium

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Hirschsprung disease is frequently associated with the Down syndrome, in which there is a deletion in chromosome 21 (1, 2). Undine, Waardenburg, Goldberg-Sprinhtzen, Smith-Lemli-Opitz, and Bardet-Biedl syndromes. Cardiac abnormalities, such as a defect of the ventricular septum, persistent patent ductus arteriosus, tetralogy of Fallot, and defects of the endocardium, have been reported in patients with Hirschsprung disease. Other reports have described Hirschsprung disease combined with teratoma (3), agenesis of one hand (4), and intestinal obstruction caused by a mucosal web according to fibromuscular and neuronal dysplasia (5). The interrupted inferior vena cava can be combined with cardiac or visceral abnormalities, such as asplenia (the Ivemark syndrome) and polysplenia syndromes. Our patient had Hirschsprung disease plus angiographically validated high interruption of the inferior vena cava at the insertion to the right atrium; the latter is a rare finding even by itself. 

Venous blood flow from the liver was directed through the inferior vena cava and ascending lumbar veins into the dilated azygos and hemiazygos veins.

Richard Lower: Anatomist and Physiologist

To the Editor: Dr. Felts is to be commended for his review of the life and accomplishments of Richard Lower (1). After publication of Dr. Lower’s observations about transfusion, Jean Denis, physician to Louis XIV, repeated Lower’s dog studies. On 15 June 1667, Denis gave the first of five heterologous transfusions to different persons (2). He obtained blood from the carotid artery of a lamb and thus did not, as noted by Dr. Felts, perform “the first transfusion between humans.” After another transfusion, given to a paid “robust” volunteer, the subject reported he felt stronger than before the transfusion (3). Arthur Coga, Dr. Lower’s patient, was also paid (20 shillings), bled, and then given about 270 mL of sheep blood. Samuel Pepys recorded that after the transfusion, Mr. Coga “did this day give … an oration in Latin . . . finding himself much better since the transfusion.”

Finally, in December 1667, Denis twice gave calf blood to a 34-year-old man who was reputed to have run naked through the streets of Paris and was considered “mad.” He had a hemolytic reaction after the second transfusion: “His pulse rose, we observed plentiful sweat . . . he complained of great pains in his kidneys . . . he was ready to choke.” After sleeping, he awoke to make a “great glass full of urine the color as black as if it had been mixed with the soot of chimneys” (4). Transfusion subsequently was banned by the French Parliament, the Royal Society, and the Pope in 1679. Nevertheless, heterologous transfusion was done as late as 1882 (5). Dr. F. Dedolph of St. Paul, Minnesota, gave 250 mL of sheep blood to a patient (with probable von Willebrand disease) after 12 days of uncontrolled bleeding. The transfusion could have provided up to 1000 U of factor VIII clotting activity and may well have corrected the patient’s platelet functional defect. Dr. Dedolph’s final comment was “Full recovery.”

To the Editor: The recent article by Sofair and Kaldjian (1) serves as an important reminder of the U.S. experience with forced eugenic sterilization programs. We believe it is important to mention the role that psychiatrists played in those programs. The authors state that their review of the American Journal of Psychiatry revealed no editorials on the topic of euthanasia. In our review of the entire contents of the Journal between 1930 and 1948, we found two editorials and a presidential address that discuss euthanasia. The presidential address, published in the July 1931 issue of the Journal (2) and titled “The Feeble-Minded Problem,” warns that the rate of feeble-mindedness is increasing “alarmingly.” The address calls for immediate action to stem the tide and concludes, “I believe the time has arrived when we should, as an Association, again most strongly express our approval of the procedure of sterilization as an effective effort to reduce the number of the defective population of our countries.”

The most infamous editorial was printed in the July 1942 issue of the Journal. This editorial commented on a series of articles in the same issue that debated the merits of euthanasia for the severely mentally disabled (both articles take for granted the need for eugenic sterilization). In the first of the two articles, Dr. Foster Kennedy recommends euthanasia for children who “should never have been born—nature’s mistakes” (3). The editorial that follows, titled “Euthanasia,” agrees with Kennedy’s position and states that the role of the psychiatrist should be to convince the parents that they are doing a disservice to their children by keeping them alive and that euthanasia is the most humane solution (4).

In addition to these editorials, the American Journal of Psychiatry published many articles in support of euthanasia throughout the 1930s, 1940s, and 1950s, consistent with the fact that psychiatrists were at the forefront of the U.S. eugenic sterilization movement.

Eugenic Sterilization and a Nazi Analogy

To the Editor: Dr. Felts is to be commended for his review of the life and accomplishments of Richard Lower (1). After publication of Dr. Lower’s observations about transfusion, Jean Denis, physician to Louis XIV, repeated Lower’s dog studies. On 15 June 1667, Denis gave the first of five heterologous transfusions to different persons (2). He obtained blood from the carotid artery of a lamb and thus did not, as noted by Dr. Felts, perform “the first transfusion between humans.” After another transfusion, given to a paid “robust” volunteer, the subject reportedly felt stronger than before the transfusion (3). Arthur Coga, Dr. Lower’s patient, was also paid (20 shillings), bled, and then given about 270 mL of sheep blood. Samuel Pepys recorded that after the transfusion, Mr. Coga “did this day give . . . an oration in Latin . . . finding himself much better since the transfusion.”

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To the Editor: The recent article by Sofair and Kaldjian (1) serves as an important reminder of the U.S. experience with forced eugenic sterilization programs. We believe it is important to mention the role that psychiatrists played in those programs. The authors state that their review of the American Journal of Psychiatry revealed no editorials on the topic of euthanasia. In our review of the entire contents of the Journal between 1930 and 1948, we found two editorials and a presidential address that discuss euthanasia. The presidential address, published in the July 1931 issue of the Journal (2) and titled “The Feeble-Minded Problem,” warns that the rate of feeble-mindedness is increasing “alarmingly.” The address calls for immediate action to stem the tide and concludes, “I believe the time has arrived when we should, as an Association, again most strongly express our approval of the procedure of sterilization as an effective effort to reduce the number of the defective population of our countries.”

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In addition to these editorials, the American Journal of Psychiatry published many articles in support of euthanasia throughout the 1930s, 1940s, and 1950s, consistent with the fact that psychiatrists were at the forefront of the U.S. eugenic sterilization movement.
Epidemiologic Relation between HIV and Invasive Pneumococcal Disease in San Francisco County, California

To the Editor: Nuorti and colleagues (1) reported on the epidemiology of invasive pneumococcal disease in HIV-infected patients in San Francisco. They found that this population had a high incidence of invasive pneumococcal infections. Even more important, they observed a significant reduction in pneumococcal disease among patients with AIDS, probably as a result of the wider use of highly active antiretroviral therapy.

In our institution, we noted a significant reduction in the number of HIV-infected patients among all patients with bacteremic pneumococcal infections: 38 of 198 (19.2%) in 1994–1996 and 25 of 224 (11.2%) in 1997–1999 (P = 0.02). As occurred in our study (2), Nuorti and colleagues found that the mortality rate did not differ between patients with and those without HIV infection; this could be due to the relatively younger age of HIV-infected patients.

Although the authors conducted a detailed study of serotypes, they did not mention the problem of antibiotic resistance, which is increasing worldwide and in certain populations, such as persons with HIV infection (3). We can extrapolate from Nuorti and colleagues’ Table 4 that serotypes 6, 9, 14, 19, and 23 (which more commonly show penicillin and multiple-antibiotic resistance [4]) were more prevalent in patients with AIDS (50 of 103 [48.5%]) than in patients without HIV infection (49 of 135 [36.3%]) (P = 0.05).

In our experience, HIV-infected patients have a higher prevalence of penicillin-resistant strains than do patients without HIV infection. Thus, among 681 adults seen at our institution in 1988–1998 with bacteremic pneumococcal infection, 43.0% of 93 HIV-infected patients and 29.1% of 558 patients without HIV infection had penicillin-resistant strains (minimal inhibitory concentration of penicillin ≥ 0.12 μg/mL) (P = 0.007).

In summary, the epidemiologic data reported by Nuorti and colleagues (1) reported important information about the epidemiology of invasive pneumococcal disease from population-based laboratory data collected in San Francisco County, California, from October 1994 to June 1997. They described a statistically significant decreasing trend in the incidence of pneumococcal disease in persons with AIDS, with the most substantial decrease occurring from 1996 to 1997. For comparison, we analyzed data from the Adult and Adolescent Spectrum of HIV Disease (ASD) Project of person-time from January 1994 through December 1998; these data were collected from more than 100 inpatient and outpatient facilities in 18 U.S. cities and 1 city in Puerto Rico (2). Data were weighted to a standardized AIDS population on the basis of national AIDS data.

We observed a nonsignificant decrease in the incidence of invasive pneumococcal disease—from 4.1 cases per 1000 person-years during 1996 to 3.3 cases per 1000 person-years during 1997. The incidence of invasive pneumococcal disease did not decline significantly during the 5-year period (P > 0.2) (Figure). Trends in San Francisco County may differ from the 11-city ASD data because of differences between HIV-infected populations in the two surveillance systems. Compared with the HIV-infected population in San Francisco County, the ASD population had 10% more women, 29% fewer white persons, 11% more African Americans, and 16% fewer injection drug users. Use of preventive strategies, including pneumococcal polysaccharide vaccine and highly active antiretroviral therapy, may also differ between San Francisco County and other areas.

Pneumococcal disease remains an important cause of preventable illness and death in HIV-infected persons. Continued surveillance will be important to better assess the impact of the increased use of highly active antiretroviral therapy on the incidence of invasive pneumococcal disease in patients with AIDS.

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References
However, the notion that dizziness is purely a geriatric disease is misguided and may delay a physician’s approach to proper diagnosis and treatment. Many factors are relevant, but the authors did not mention a common causation.

In 1992 and 1993, I described the “beauty parlor stroke syndrone” in elderly women, with subsequent demonstration of vertebral artery flow reduction at the atlanto-occipital and atlanto-axial junction by hyperextension and rotation movements (2). Distinct hemodynamic changes of slow flow, reversal of flow, and altered perfusion with regional hypovolemia, in the absence of neurologic symptoms, arise with hyperextension maneuvers (3). Patients identified with the congenital biological marker of hypoplasia display a unique vulnerability and are most at risk. This observation has been estimated to occur in 40% of the population. These persons also had a higher incidence of posterior-circulation silent infarctions. This mechanical change is not influenced by age or medication, has been confirmed by other investigators (4), and can be seen at all ages. Consequently, it would have been more informative for Tinetti and coworkers to correlate neurologic examination findings of presence or absence of the Babinski response and magnetic resonance imaging findings of posterior infarction in their cohort. It should be noted that women made up 72% of their participants.

Finally, I concur with Dr. Drachman’s admonition for caution: “This geriatric syndrome requires—and deserves—careful attention to sort out the underlying diagnoses and most often to treat successfully” (5).

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References

Cocaine-Induced Acute Cytologic Hepatitis in HIV-Infected Patients with Nonactive Viral Hepatitis

To the Editor: Cocaine hepatotoxicity is well documented, but there are few data on effects of nonparenteral cocaine use (1-3). We report intranasal cocaine-induced acute hepatitis in three HIV-infected patients with viral hepatitis.

The patients were seropositive for hepatitis B virus (patient 1) and hepatitis C virus (patients 2 and 3) and had no signs of liver dysfunction. Acute cytolytic hepatitis occurred a few days after intranasal intake of cocaine. In patients 2 and 3, hepatitis was associated with hepatomegaly, fever, stiffness, and sweat. The Table summarizes the findings on laboratory tests. Liver biopsy was not done in any patient. Within a few days, clinical and biological signs of hepatitis improved in all patients.

Alcohol and hepatotoxic agents were ruled out. Although the patients had nonactive chronic viral hepatitis, findings on viral hepatitis tests remained unchanged during the hepatitis episode. Moreover, rapid decreases in results of hepatitis tests indicated that viral hepatitis activation is an unlikely cause of the hepatitis. Although no toxicology screening was performed, we believe that cocaine induced the acute liver injury.

After intravenous administration of cocaine, aminotransferase levels increased (to approximately 10 000 IU/L) (4); in the most severe cases of cocaine-induced hepatic disease, hepatitis is associated with rhabdomyolysis (2). In our three patients, aminotransferase levels increased to very high values even though the cocaine had been taken intranasally. Unlike in other cases reported in the literature, the hepatotoxicity in our patients was the sole illness.

Infection with HIV does not seem to be a risk factor because our patients’ immunologic status was not deficient when hepatitis developed. Moreover, no recent publications have reported hepatitis related to cocaine use in HIV-infected patients.

Hepatotoxicity must be considered a serious complication of cocaine use even when cocaine is taken intranasally. Intake of cocaine must be investigated in patients presenting with transient and unexplained increases in liver enzyme levels, especially in patients with viral hepatitis or HIV infection.

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References

Table. Laboratory Test Results before Intranasal Intake of Cocaine and at Presentation with Hepatitis*

| Variable | Patient 1 | | Patient 2 | | Patient 3 | | Few Days | | Summarizes | | Background | | 
|---|---|---|---|---|---|---|---|---|---|---|
| | Before | Presentation | At | Presentation | Before | Presentation | At | Presentation | Few Days | after | Presentation | 
| Alanine aminotransferase level, IU/L | 33 | 1205 | 30 | 617 | 346 | 7 | 1007 | 206 | | | 
| Aspartate aminotransferase level, IU/L | 33 | 851 | 28 | 340 | 137 | 23 | 1669 | 44 | | | 
| γ-Glutamyltransferase level, IU/L | 33 | 196 | 12 | 270 | 450 | 5000 | 5600 | <400 | <400 | <400 | 
| Alkaline phosphatase level, IU/L | 52 | 138 | 86 | 324 | 378 | 76 | 519 | 76 | | | 
| CD4 count, cells/mm³ | 400 | 622 | 510 | 1236 | 1102 | 450 | | | | | 
| Viral load, RNA copies/mL | 5000 | 5600 | <400 | <400 | 450 | | | | | | 
| Antibodies to hepatitis A virus (IgG/IgM) | +/- | ND | +/- | ND | -/- | ND | -/- | -/- | -/- | -/- | 
| Antibodies to HCV | -/- | -/- | ND | -/- | -/- | ND | -/- | -/- | -/- | -/- | 
| HCV RNA | ND | ND | ND | ND | ND | ND | ND | ND | ND | ND | 
| Antibodies to HBV core antigen | ND | ND | ND | ND | ND | ND | ND | ND | ND | ND | 
| Antibodies to HBV surface | ND | ND | ND | ND | ND | ND | ND | ND | ND | ND | 
| Hepatitis B surface antigen | +/− | +/− | +/− | +/− | +/− | +/− | +/− | +/− | +/− | +/− | +/− | 
| HBV DNA | +/− | +/− | +/− | +/− | +/− | +/− | +/− | +/− | +/− | +/− | +/− | 
| Cytomegalovirus (IgG/IgM) | +/− | ND | +/− | ND | -/− | ND | -/− | -/− | -/− | -/− | -/− | 

* Patient 1 was a 35-year-old man; patient 2 was a 39-year-old man; patient 3 was a 22-year-old woman. + = positive; = negative; HBV = hepatitis B virus; HCV = hepatitis C virus; ND = not done.

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Parvovirus B19–Related Anemia in an HIV-Infected Patient: Rapid Control after Production of Neutralizing Antibodies during Highly Active Antiretroviral Therapy

To the Editor: Patients with AIDS cannot generate neutralizing antibodies against parvovirus B19 (1). Consequently, these patients can develop high-level parvovirus viremia, which is treated with repeated courses of intravenous immunoglobulin (IVIG). We describe an HIV-infected patient who mounted a primary immune response against parvovirus B19 after starting highly active antiretroviral therapy.

A 31-year-old man was referred to our clinic because of recently diagnosed HIV infection. The hemoglobin level was 61 g/L, the CD4⁺ cell count was 0.02 cells × 10⁹/L, and the HIV RNA level on polymerase chain reaction (PCR) was 14 700 copies/mL. Serum parvovirus IgG and IgM were not detected. Bone marrow biopsy showed pure erythrocyte aplasia with giant and dysplastic pronormoblasts. Serum PCR for parvovirus B19 had strongly positive results.

The patient underwent transfusion with 5 units of packed red blood cells and started treatment with stavudine, lamivudine, and nelfinavir. He received IVIG (total dose, 2 g/kg of body weight). Results of testing for serum parvovirus IgG were positive on the last day of IVIG therapy (Figure). Twenty-four and 45 days after the first IVIG infusion, the patient was negative for serum parvovirus IgG and IgM and the hemoglobin level decreased to 68 g/L. The patient received three units of packed red blood cells and a second 5-day course of IVIG. Three weeks later, the patient was positive for serum parvovirus IgG and IgM.

In our case, the first detection of serum parvovirus IgG was probably due to the exogenous infusion of immunoglobulins. The serum parvovirus IgM detected 12 weeks after antiretroviral therapy started was most likely produced by the patient because commercial immunoglobulins lack substantial amounts of parvovirus IgM. After this first IgM detection, serum was consistently positive for parvovirus IgG and IgM during a follow-up period of 6 months. Production of parvovirus IgM and IgG occurred along with an increase in CD4⁺ cell count from 0.02 to 0.46 × 10⁹ cells/L. Our report strongly suggests that highly active antiretroviral therapy can reconstitute the ability of HIV-infected patients to produce neutralizing parvovirus antibodies.

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Reference

Correction: Misaligned Table

In Table 3 of a recent review on cyclooxygenase-2 inhibitors (1), several rows are misaligned. On page 140, the row ending “430” should be aligned with the row beginning “Celecoxib group” on page 141; the row ending “784” should be aligned with the row beginning “Not reported”; the row ending “736” should be aligned with the row beginning “1 symptomatic ulcer”; and the row ending “1427” should be aligned with the row beginning “150 endoscopic ulcers.”

Reference

Correction: End-of-Life Care Paper

The recent paper written for the American College of Physicians–American Society of Internal Medicine End-of-Life Care Consensus Panel on intractable terminal suffering (1) was incorrectly identified as a “Position Paper.” The paper should have appeared under the heading “Academia and Clinic,” as was done for the other papers in the series on end-of-life care. The views expressed in this paper do not represent official College policy.

Reference