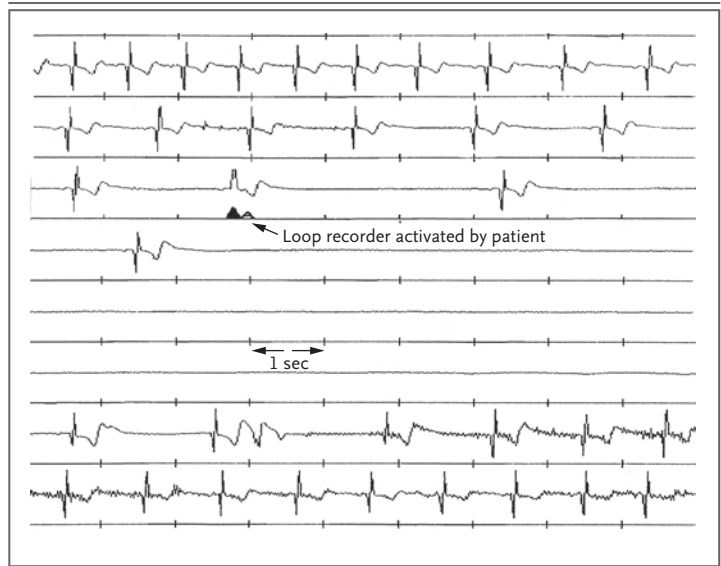


activity and mostly occurred while he was sitting down. He collapsed again several weeks later, while sitting for a meal at a wedding. Repeat EEG with simultaneous ECG revealed a localized, epileptogenic disturbance in the left anterior temporal region. Temporal-lobe epilepsy was diagnosed, and he was treated with oxcarbazepine. He remains asymptomatic at 1 year of follow-up.

Ictal bradycardia is a rare manifestation of epileptic seizures. Autonomic modifications may result because of ictal discharges in the region of the structures of the central autonomic network. There is limited evidence of a preferential left temporal-lobe onset.<sup>1</sup> Most patients are male and 60 years of age or older.<sup>2</sup> This pattern of epilepsy may induce central or obstructive apneas as well as malignant arrhythmias and is linked to sudden unexpected death in patients with epilepsy.<sup>3</sup> Temporal-lobe epilepsy may present with feelings of panic and impending doom, palpitations, diaphoresis, dyspnea, and paresthesias. Hence, it is easily misdiagnosed as an anxiety attack.<sup>4</sup> The discovery of a major arrhythmia without EEG monitoring may lead to an incorrect diagnosis of primary cardiac disease and treatment with cardiac pacing.

Cardiac pacemakers may be indicated in symptomatic ictal bradycardia or asymptomatic bradycardia lasting more than 5 seconds. However, cardiac pacemakers have not been proved to reduce the incidence of sudden unexpected death among patients with epilepsy.<sup>3</sup> Physician awareness, patient education, and effective seizure control are of prime importance in preventing ictal asystole and potential sudden unexpected death among patients with epilepsy.



**Figure 1. Reading from a Loop Recorder Showing a Prolonged Pause of 25 Seconds after a Sinus Bradycardia.**

The patient reported feeling dizzy several minutes before the loop was activated.

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## Reports of Esophageal Cancer with Oral Bisphosphonate Use

**TO THE EDITOR:** Between the time of the initial marketing of alendronate in October 1995 through mid-May 2008, the Food and Drug Administration (FDA) received reports of 23 patients in the United States receiving a diagnosis of esophageal cancer, with alendronate (Fosamax, Merck) as the suspect drug (in 21 patients) or the concomitant drug (in 2 patients). No similar U.S. reports for other oral bisphosphonates were retrieved from the FDA's

database for adverse-event reporting. Eight deaths were reported. Of the 23 patients, 18 (78%) were women; the median age was 74.0 years (mean, 71.8; based on 19 patients). Among the 14 patients with dose information, 8 were reported to have taken alendronate at a dose of 10 mg per day; 5 were reported to have taken 70 mg per week; and 1 was reported to have taken alendronate "once per week." The median time from alendronate use to diag-

nosis was 2.1 years (range, 0.5 to 10.0; mean, 3.0; based on 16 patients). Information about risk factors was not provided for all patients, but one patient took alendronate despite having Barrett's esophagus, a precursor of esophageal adenocarcinoma. The predominant site mentioned was the distal esophagus (in six patients), with gastric involvement in some cases. Histologic analysis showed adenocarcinoma in seven patients and squamous-cell carcinoma in one patient.

Thirty-one patients from Europe and Japan were reported as having received a diagnosis of esophageal cancer after using alendronate (the suspect drug in 21 of the patients). Risedronate (Actonel, Procter & Gamble), ibandronate (Boniva, Roche), etidronate (Didronel, Procter & Gamble), or a combination thereof were suspect drugs in six cases, and bisphosphonates were concomitant drugs in four cases. Six deaths were reported. Twenty-two patients (71%) were women; the median age was 68.5 years (mean, 68.5; based on 25 patients). For the 20 patients with dose information, 2 were reported to have taken risedronate, 1 at a dose of 5 mg per day and 1 at a dose of 35 mg per week, respectively; 9 were reported to have taken alendronate at a dose of 10 mg per day; 8 were reported to have taken alendronate at a dose of 70 mg per week; and 1 was reported to have taken a single 150-mg tablet of ibandronate each month after years of etidronate use. The median time from drug exposure to diagnosis was 1.3 years (range, 0.3 to 8.0; mean, 2.2; based on 21 patients). Information on risk factors was not provided for all patients. Barrett's esophagus, mentioned for three patients, appeared to be di-

agnosed near the date of diagnosis of esophageal cancer and after alendronate use. The distal esophagus was affected in eight patients (with gastric involvement in four). Six patients had adenocarcinoma, and five had squamous-cell carcinoma.

Esophagitis has been associated with oral bisphosphonates, usually when the drugs are not taken according to directions.<sup>1-3</sup> Crystalline material similar to ground alendronate tablets has been found on biopsy in patients with erosive esophagitis,<sup>4,5</sup> and persistent mucosal abnormalities have been noted in some of these patients,<sup>4</sup> suggesting a potential for carcinogenic effects. Physicians should avoid prescribing oral bisphosphonates to patients with Barrett's esophagus. Studies should include oral bisphosphonates as possible risk factors for esophageal cancer.

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The views expressed are those of the author and do not necessarily represent the official position of the Food and Drug Administration.

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