patients. Chest 2002; 121:1070–1078

To the Editor:

Dr. Bennett’s letter warned of the risk of deep venous thrombosis (DVT) as a complication of treatment with megestrol acetate among nursing home patients. We agree that DVT is an established risk of this treatment, but we believe there are good reasons why our experience2 is different than the one he previously reported.

We would like to point out that Bennett’s observation2 was retrospective and without a randomized control group, and that only 18 patients were at risk (patients who received megestrol acetate over a specific 9-month period at a nursing home). Although DVT developed in six patients, two patients were at especially high risk since one patient had endometrial cancer and another patient had a recent fracture. Because the study was initiated when a cluster of DVT episodes were observed, we believe that projecting incidence in the nursing home population is questionable. Also, reporting DVT incidence per 100,000 patient-years is misleading when the summed observation period for all patients receiving megestrol acetate was approximately 7 years.

Furthermore, of the at-risk patients, one was not ambulatory, three had presence of arrhythmia, two had suffered stroke, and three had coronary artery disease. The average age of the patients with DVT was 80 years.

Moreover, Dr. Bennett’s study is in apparent conflict with that of Yeh et al.,3 who specifically studied nursing home patients for weight and quality-of-life measures. None of the 36 patients treated with megestrol acetate in their study acquired DVT.

The average age of our patients was 67 years, and all were ambulatory. Our intervention was limited to 56 days; most of Dr. Bennett’s nursing home residents experienced DVT after > 50 days of treatment.

Although Dr. Bennett’s article is thought provoking, it hardly refutes the safety findings of our study, where no patient was reported to have DVT in our randomized, prospective, and much larger patient population (72 receiving megestrol acetate and 73 receiving placebo).

Based on our study, we believe the benefits of short-term administration of megestrol acetate in underweight patients with COPD might outweigh the risks. We believe that future trials will prove that megestrol acetate can be an important component in the management of the underweight COPD patient.

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Relationships Between Insomnia and Sleep-Disordered Breathing

To the Editor:

I read with interest the article by Krakov et al (December 2001)1 on the prevalence of insomnia symptoms (ISs) in patients with sleep-disordered breathing (SDB). The study showed that insomnia complaints were common in SDB patients, but it remained unclear why some patients with repeated apneas had insomnia whereas others did not. I report here the prevalence of different subtypes of insomnia in SDB patients. The finding is useful in understanding the relationship between SDB and insomnia.

I analyzed the data of 150 consecutive patients referred to our laboratory because of suspected obstructive sleep apnea (OSA).2 ISs were reported using a Likert-scale to four statements: “I have a hard time getting to sleep” (IS-1); “I wake up during the night and have a hard time getting back to sleep” (IS-2); “I wake up repeatedly during the night” (IS-3); and “I wake up too early in the morning and can’t get back to sleep” (IS-4). Responses of “often” and “almost always” were considered presence of insomnia complaints.

OSA according to the international classification of sleep disorders was diagnosed in 119 patients3 who had an apnea-hypopnea index (AHI) ≥ 5 events per hour. The 119 subjects were predominately male (105 male and 14 female patients) and 44.6 ± 10.4 years of age (mean ± SD). The mean body mass index was 27.5 ± 5.0 and AHI was 37.3 ± 26.5. The most frequent IS was IS-3 (33%), followed by IS-4 (21%), IS-2 (16%), and IS-1 (9%). Subjects with and without ISs were similar in demographics, daytime sleepiness, and AHI. However, patients with difficulty initiating sleep (IS-1, IS-2, or IS-4) had significantly lower AHI (26.7 ± 24.6) than subjects with frequent awakenings (IS-3 only) [45.0 ± 26.1] and those with no insomnia [40.4 ± 26.3] (F = 4.5; degrees of freedom = 2, 116; p = 0.01).

The most common IS in SDB patients was frequent awakening, while a significant proportion of subjects had difficulty initiating sleep. It appears that repeated apnea is not the single factor that can account for the ISs in SDB patients, particularly in those with difficulty initiating sleep. Individual vulnerability to develop insomnia needs to be addressed.4,5

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To the Editor:

We concur with Chung’s conclusion, “Individual vulnerability to insomnia [in patients with sleep-disordered breathing (SDB)] needs to be addressed,” and our data also showed a statistically significant higher apnea-hypopnea index (AHI) in those without insomnia compared to those with insomnia. A tempting explanation, then, for SDB plus insomnia (“complex insomnia”) in our sample would be their greater self-reported psychiatric distress and ruminations and anxiety about sleep in contrast to SDB-induced respiratory compromise and resultant sleep fragmentation. We believe this conclusion has validity but is also an incomplete model for several reasons.

First, conclusions drawn from polysomnography using AHI may be undermined by the lack of advanced respiratory monitoring (e.g., esophageal manometry [EM], nasal cannula pressure transducer [NCPT]), which detects subtle breathing disturbances such as respiratory effort-related arousals (RERAs) that fragment sleep in ways similar to apneas and hypopneas. In our study or in the study by Chung, it may be misleading to suggest that one group has more apneas or hypopneas without accounting for a broader respiratory disturbance index (apnea plus hypopnea plus RERAs) that might more accurately reflect pathology. In fact, we reported that RERAs may be the predominant type of respiratory event among insomniacs with comorbid SDB. Therefore, we speculate that meaningful statistical analyses cannot be conducted from these studies with the use of AHI as it is currently configured.

Second, in our clinical practice and research experience, approximately 80% of patients reporting insomnia for > 6 months also have SDB, which has led us to assume that the disorders termed psychophysiological insomnia (PPI) and SDB reflect two overlapping pathophysiology of sleep fragmentation. However, when these two disorders occur together, resultant sleep fragmentation may produce an impairment continuum, comprising symptoms of pathologic sleepiness (hypersomnia) on one end and pathologic sleeplessness (insomnia) on the other end (Fig. 1). A typical SDB presentation with recurrent awakenings

![Complex insomnia hypothesis](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21987/)

**Figure 1.** Complex insomnia hypothesis. A patient may initially acquire SDB and/or PPI for many reasons. The pathophysiology of either or both disorders produces sleep fragmentation. Repeated exposure to sleep fragmentation might lead to instability of the upper airway, which in turn could result in sleep respiratory events such as RERAs, hypopneas, or apneas. These SDB events provoke greater sleep fragmentation in the form of arousals, awakenings, and increased stage 1 NREM sleep, which further feeds the cycle by promoting more upper-airway collapsibility, increased sleep respiratory events, and subsequent sleep fragmentation. Finally, sleep fragmentation induces an impairment continuum of symptoms, with pathologic sleepiness on one end and pathologic sleeplessness on the other. Clinically, some patients present with a static set of symptoms (typical sleep apnea patient) whereas others (complex insomnia patient) may move along the continuum in a dynamic fashion, experiencing different symptom clusters (sleepiness or sleeplessness) according to time and circumstances.

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