Mortality and Sleep Apnea
The Trouble with Looking Backward

Recently, two retrospective studies have addressed the issue of mortality in patients with sleep apnea syndrome (SAS). Their appearance in this journal has provided the readers of Chest with seemingly contrasting impressions on the natural history of this disorder; this merits further comment.

A study by Gonzalez-Rothi and coworkers1 spanning the years of 1978-1986 compared the five-year mortality of 91 patients with documented SAS with that of 35 control patients of similar age and body habitus who had normal sleep tracings. Complete follow-up was obtained on all patients in this study which included deaths, causes, time, and circumstances of death, as well as morbidity variables. Although SAS patients in this study had significant sleep-disordered breathing (mean apnea-hypopnea indices of 42), their five-year mortality, as assessed by Kaplan-Meier life table analysis, was no different than that of the control subjects. Moreover, none of the SAS patients died during sleep. Although SAS patients had more vehicular mishaps than control subjects, none died as a result of a motor vehicle accident. The authors concluded that their findings did not support (either statistically or by simple numerical trend) the hypothesis that SAS patients have increased mortality, or for that matter, that they are at increased risk of dying during sleep. The findings thus leave the reader to either concur with the authors’ conclusions or to consider the possibility of a “type 2” statistical error (insufficient numbers to detect statistically significant differences in mortality between the two groups) in their analysis.

An earlier study by He and coworkers,1 spanning the same eight-year period, included male patients over age 15 with documented SAS. If of an initial group of 706 patients studied, follow-up information was obtained in only 385 patients (55 percent of the total sample), and it was from the latter proportion of the group upon which the data analyses were based. The results of multiple life table analyses of combinations of subgroups by these investigators showed that SAS patients with apnea indices greater than 20 who were younger than 50 years old had a higher mortality than patients with apnea indices less than 20. An increased mortality rate that could be directly related to the magnitude of the sleep apnea index was not present in the subgroup of patients over age 50, however. Patients with SAS who were treated with either tracheostomy or nasal CPAP (but not uvulopalatopharyngoplasty) in this study had significantly better overall survival than untreated patients, irrespective of pre-therapy apnea index.

The findings by He and coworkers, thus, leave the reader to conclude that if sleep apnea is present and untreated, then the greater the number of sleep disordered breathing events one has, the more likely one is to die—provided one is older than 15 and younger than 50 years of age. The reader would then be pressed to ask “But, to die of what?” and further, “Why die of SAS if one is younger than if one is older?” when SAS is epidemiologically more prevalent in middle aged, and older men? To satisfy the reader’s concept of direct causality between the severity of sleep apnea and increased mortality, a pathophysiologically plausible explanation for this relationship should be able to withstand a testable hypothesis: if people with SAS have recurrent nocturnal hypoxemia, episodic pulmonary hypertension, and associated cardiac arrhythmias, then they should die during sleep. A corollary to that hypothesis is that since SAS is more prevalent in older men, who are also more likely to suffer from underlying cardiac and respiratory disease, if one is older and one has more severe apnea, then one should have an increased chance of mortality. The reader is then left wondering why more older men with higher apnea indices in the study by He and coworkers did not die. By neither providing causes/circumstances of death, nor comparisons of mortality between SAS patients and a control population of patients without SAS, any inferences to be made from this study regarding causality and the natural history of SAS are therefore posed with potential shortcomings.

As an explanation of the findings of He et al of increased mortality in the younger SAS patients, it might also be tempting for the reader to hypothesize that many of their patients might have been Pickwickian, since this disorder (which is also associated with sleep-disordered breathing and apneas) tends to manifest earlier in life and is well known to be associated with high mortality.45 Were this the case, a different
conclusion might have been reached by this study—young Pickwickian patients with presumably more severe baseline daytime hypoxemia, chronic hypercarbia, and cor pulmonale are more likely to die if they have higher numbers of sleep apneas and oxygen desaturations per night. That definitive treatments which ameliorate obstructive apneas, such as tracheostomy and nasal CPAP as He and coworkers found, might also improve survival (even in a group of Pickwickian patients) would also fit with this hypothesis.

The exclusion by He et al of 321 patients from their analysis because of failure to respond to a follow-up questionnaire and their analysis of multiple subgroups also deserves attention. The fact that these investigators found no statistically significant differences in two of three demographic variables (body mass index and apnea index) between questionnaire responders and nonresponders does not justify omission of these patients from their analysis and neither does it completely exonerate their study from the hazards of selection and response bias. As regards the analysis of multiple subgroups according to arbitrary age and apnea index ranges, it should be well recognized that the exploration of multiple subsets of the original sample in any analysis will often result in a positive finding by chance alone if enough subgroups are sampled, even when that finding may be unrelated to causality.

Ultimately, the reader, though puzzled, can be left with only one incontrovertible feeling: that these two studies are troubled by retrospection. While one suffers from possibly insufficient numbers to secure sufficient statistical certainty, the larger one falls victim to the absence of a control group and to the pitfalls of response and selection bias, as well as to incomplete documentation of causality. Both studies are probably valid in that they are timely and raise important questions about the natural history of sleep apnea syndrome, but the conclusions of neither should be accepted until they can be validated prospectively. A task of such epidemiologic magnitude would call for randomized multicenter cooperative longitudinal studies which included both symptomatic and asymptomatic at-risk patients to be done. It would then be reasonable for the reader to conclude that the trouble with looking backward is not so much what is seen, but whether we recognize it for what it is when it is time to turn around and face forward.

R. J. Gonzalez-Rothi, M.D., F.C.C.P.; and A. Jay Block, M.D., F.C.C.P.
Gainesville, FL

References
1. Gonzalez-Rothi RJ, Foresman GA, Block AJ. Do patients with sleep apnea die in their sleep? Chest 1988; 94:531-38

Alphabet Soup Reheated

I am reviewing the most recent issue of Chest as I write this editorial. I began my review in a spirit of equanimity, tranquility, and good will, but at the moment my head is pounding, my palms are sweaty and I feel frustrated and bewildered. All this has occurred and I have read only the first four articles!

The abstracts of the four articles contain the following abbreviations: LVSWI, CPPV, APRV, CPAP, and MAI. However, the abstracts are only a foretaste of that which is yet to come. In the discussion of the first article, I discovered abbreviations which did not appear in the abstract, including PCWF, EDVI, and LVEF. I have in front of me a listing of abbreviations in the manual for authors and editors published by the American Medical Association, which urges authors to use “abbreviations in the text, titles, illustrations, legends and tables.” However, none of the abbreviations cited above appears in this guide. Now I turn to the “Uniform Requirements for Manuscripts” prepared by a distinguished international panel of editors. Once again, my good intentions are frustrated since the abbreviations in Chest do not appear in this guide.

Determined, therefore, to “go it alone,” I return to the articles and discover that I can feel confident and all-knowing, but only for a paragraph or two. Ordinarily, the explanations of what the letters represent appear in Material and Methods. Thus, by the time that I get to the discussion and conclusions, I have forgotten what the abbreviations stand for and I am back to biting my nails.

The current fad of alphabet soup, ie, the use of abbreviations for phrases or terms which appear repeatedly in an article, has a reasonable rationale. A rapidly increasing number of excellent manuscripts are worthy of publication in our periodical; therefore, I share with editors of other scholarly journals the need to conserve page space. Secondly, reading convenience is enhanced if one need not scan lengthi