Editor's Note: Authors are invited to respond to Correspondence that cites their previously published work. Those responses appear after the related letter. In cases where there is no response, the author of the original article declined to respond or did not reply to our invitation.

Link Between Short Sleep and Obesity in Humans

A Matter of Age?

To the Editor:

I read with great interest the article by Calvin et al (July 2013).¹ The authors found that people whose sleep was restricted to approximately 5 h per night over an 8-day period consumed on average 822 more calories per day than people who slept approximately 7 h per night.¹ This outcome is in-line with previous study findings. For instance, when sleep-deprived for one night, young adults chose greater portion sizes under both fasting and sated conditions than they do after one night of normal sleep.² However, in contrast to previous findings,^{3,4} Calvin et al¹ did not observe any differences in activity energy expenditure or circulating concentrations of leptin and ghrelin. Based on their findings, the authors conclude that short sleep duration, if habitual, may contribute to the high and rising prevalence of obesity in our modern societies. However, one methodologic issue of their study requires a more detailed discussion. Although the sleep groups did not differ in terms of age, their participants' ages ranged from 18 to 40 years.¹ During aging—also covering the age period between 18 and 40 years—total sleep time, sleep efficiency, percentage of slow-wave sleep, percentage of rapid eye movement sleep, and rapid eye movement sleep latency all significantly decrease.⁵ With this in mind, it cannot be definitively discounted, especially in light of the small sample sizes (sleep deprivation group, $n = 8$ vs sleep control group, $n = 9$), that the participants' heterogeneous age masked the effect of sleep restriction on activity energy expenditure and circulating concentrations of leptin and ghrelin.

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Response

To the Editor:

We thank Dr Benedict for his interest and thoughtful comments regarding our study¹ and the potential role of age in the modification of the response to sleep deprivation. Dr Benedict points out that in contrast to the work of others,^{2,3} we found no change in energy expenditure or in the level of hormones leptin and ghrelin and suggests that confounding by age be considered as a potential explanation.

We indeed found no change in activity energy expenditure or circulating levels of leptin and ghrelin after 8 nights of restricted sleep. These findings are consistent with the work of Nedeltcheva et al,⁴ who also found no changes in total energy expenditure and its components or in leptin or ghrelin levels over a 14-day period of restricted sleep. Their findings and ours are in contrast to other studies that used 24 h of continuous wakefulness² or 2 nights of restricted sleep.³ On the other hand, Buxton et al⁵ found that sleep restriction and circadian misalignment over a 3-week period decreased leptin and increased ghrelin levels when food intake was fixed. We suggest that one simple synthesis of these apparently conflicting data may be that acute sleep restriction promotes caloric intake, lowering ghrelin levels, and that subclinical fat gain secondary to positive energy balance attenuates the initial decrease in leptin level.

We agree with Dr Benedict that age-related changes in sleep parameters may be clinically important, although we are not aware of data specifically pertaining to the role of age in modifying the relationship between sleep duration and energy balance. The present study inclusion criteria were age 18 to 40 years, and the study

actually included individuals between the ages of 18 and 33 years, which would seem to make confounding by age less likely. Furthermore, we note that the average age in our study (24 years in the sleep-deprived group, 25 years in the control group) seems reasonably close to the average age in the study by Benedict et al² (23 years) and Spiegel et al³ (22 years). We hope that future studies will carefully consider age and aging when examining the metabolic effects of sleep restriction.

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Hyperimmune IV Immunoglobulin Treatment of 2009 Influenza A(H1N1)

To the Editor:

We read the article by Hung et al¹ in this issue of *CHEST* (see page 464) on hyperimmune IV immunoglobulin (H-IVIG) treatment for 2009 influenza A(H1N1) with great interest. They

concluded that "treatment of severe A(H1N1) infection with H-IVIG within 5 days of symptom onset was associated with a lower viral load and reduced mortality."¹ Use of immunoglobulin treatment seems to be a new treatment of H1N1 influenza. It is mentioned as an additional therapy to the standard antiviral treatment.² The present report showed a good clinical outcome: clearance of symptoms. However, the concern is on the adverse effect and long-term outcome of using H-IVIG treatment. Because the present report is based on a limited number of patients, some uncommon adverse effects of using H-IVIG (such as anaphylaxis, hypotension, and rash³) might not be detected. Additionally, the issue of cost-effectiveness of this new therapeutic option should be further assessed.

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Response

To the Editor:

We thank Drs Joob and Wiwanitkit for their comments on our article on hyperimmune IV immunoglobulin (H-IVIG) treatment.¹ Based on the prospective, multicenter, randomized, double-blind nature of our study and the effect of the H-IVIG on the viral load and cytokines, we believe that this study is important in the management of patients with severe 2009 influenza A(H1N1) infection in which no effective treatment other than supportive care is available. The 17 patients who underwent H-IVIG treatment in this study showed no adverse effects of anaphylaxis, hypotension, or rash, with excellent long-term outcome upon follow-up for the 12 patients who survived. As mentioned in the "Discussion," the safety of the H-IVIG is further improved by fractionation with additional pathogen reduction steps. Nevertheless, we agree with Drs Joob and Wiwanitkit that a future study of a larger scale based upon this study on H-IVIG would be necessary to determine the cost-effectiveness of this new therapeutic option.