Warning: The Short Days of Winter May Be Hazardous to Your Health

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Almost all living organisms have evolved biological rhythms linked to the day-night or light-dark cycles of the sun. The impact of such rhythms that follow the time of day and season of the year on a variety of physiological functions in humans has been recognized for a long time. The internal oscillator, or control station regulating the body’s circadian clock, is the suprachiasmatic nucleus (SCN), a tiny (70 000 neurons) structure situated in the hypothalamus. Located above the optic chiasm, the SCN processes external signals, such as ambient light and inputs from the brain, to regulate a variety of cyclical functions, including body temperature, sleep/wake cycles, and secretion of hormones such as serum cortisol, melatonin, thyroxin, and vasopressin. Ambient light can entrain the SCN, which then modulates physiological and pathophysiological processes. In fact, like modulated parasystole, a burst of light striking the photoreceptors in the morning can advance the SCN cycle, whereas a burst in the evening can delay the phase-response curve. In humans, the SCN sets the intrinsic 24-hour cycle accurately to average \( \approx 24 \) hours and 11 minutes.4

In addition to daily modulation by the SCN, seasonal fluctuations in body rhythms occur. For example, plasma L-tryptophan and competing amino acids are significantly lower in the spring, changes that parallel seasonal variations in the prevalence of violent suicide and depression.5 The seasonal affective disorder syndrome (SADS) is a well-established entity characterized by depression during the winter months. Psychiatrists have treated SADS patients by exposing them to artificial light for 2 hours each morning to simulate an earlier sunrise.6 We have known for a number of years that circadian fluctuations affect, and perhaps orchestrate, a variety of pathophysiological states. The onset of myocardial infarction, sudden cardiac death, and stroke are all increased from 6 AM to 12 noon. These responses may be related, in part, to increased sympathetic activity after getting out of bed, with subsequent catecholamine interaction with platelets and atherosclerotic plaque pathophysiology.7 Circadian variations also have been observed for several hemodynamic and cardiovascular events, including blood pressure, coronary artery flow, and heart rate. In addition, circadian alterations in platelet response to aggregating stimuli, plasma fibrinogen, coagulation factor concentration, and intrinsic fibrinolytic activity have been documented. Increased morning hematocrit levels may contribute.8

Changing electrophysiological conditions accompany the greater frequency of morning sudden death, which may be due to ventricular fibrillation.9 A morning peak in ventricular tachyarrhythmias can be detected by therapy delivered with implantable cardioverter-defibrillators.10 Maximal shortening of ventricular effective refractory period occurs in the early morning hours, along with a morning peak in defibrillation threshold and failed first shock frequency.12 Weekly death trends have been reported. In New Zealand, patients surviving myocardial infarction showed an increased incidence in symptom onset during the weekend and on Monday for surviving patients and a Saturday high for sudden death patients.13 Myocardial infarction frequency has been shown to peak on Mondays14,15 and during the winter.14 A recent study found an increase in the number of deaths occurring in the United States during the first week of the month.16 Although the influence of the time of day can be explained by known physiological changes, day-of-the-week and week-of-the-month peaks may be due more to environmental work/play influences.

Data from several recent studies have focused on the seasonal impact on cardiovascular mortality. Sheth et al17 analyzed 159 884 deaths from acute myocardial infarction and 136 157 deaths from stroke in the Canadian mortality database from 1980 to 1982 and 1990 to 1992. They found that acute myocardial infarction deaths were highest in January and lowest in September, producing a relative risk difference of 18.6%. This seasonal variation in acute myocardial infarction between winter and summer increased with age from 5.8% for \(<65\) years old to 15.8% for \(>85\) years old. Stroke mortality peaked in January, with a trough in September and a relative risk difference of 19.9%, again showing an increase in seasonal variation with age. The authors suggested that environmental factors accompanying the cold weather may play a major role in triggering these acute cardiovascular events or determining their outcome.

In this issue of Circulation, Kloner et al18 analyzed 222 265 reports from the monthly death certificate data in Los Angeles County for death due to coronary artery disease from 1985 through 1996. The mean number of deaths was 33% higher in December and January than between June and September. When deaths were plotted by year, there was a decrease from 1985 to 1996, but the shape of the curve was
maintained. Monthly mortality correlated inversely with temperature. However, during December and January, there was an increase in deaths that peaked around the holiday season and then fell. These deaths could not be explained solely on the basis of the daily temperature, which is generally mild in Los Angeles at that time. The minimum daily temperature remained relatively flat, and maximum temperature showed minor fluctuations during these times. The authors suggested that factors other than temperature, such as superimposed respiratory infections, behavioral changes around the holiday time, including increased food, salt, and alcohol consumption, and emotional and psychological stress, contributed to the increase in deaths in December and the fall after January 1.

In the Antiarrhythmics Versus Implantable Defibrillators (AVID) study,19 vital status was obtained for 4467 registered patients with sustained ventricular arrhythmias or unexplained syncope through the National Death Index as of December 31, 1996. Of these patients, 735 died, among whom 137 were discharged with an ICD, 425 received antiarrhythmic drugs, 66 received both, and 107 received neither. In this population, there was no difference in the pattern of death among the days of the week, but mortality from Thanksgiving to New Year’s Day increased to 15%, versus 11% expected (P=0.002). There was no significant difference among the treatment groups (ICD, drugs, both, or neither). The pattern of increased holiday mortality was evident in subgroup analysis for patients in both warmer and colder parts of the United States, suggesting that the increase in mortality related to the holiday season was not due to cold temperature. The authors concluded that the increased mortality may have been related to increased seasonal physical and emotional stress.

Thus, these 3 studies, as well as others not mentioned, all point to an increased mortality during the winter season. Except for the Canadian study, the other 2 reports fairly well exclude temperature as an important variable and suggest that the holiday season, with its overindulgence of emotions, food, and beverages, may contribute. Although these factors certainly may play a role, an interesting animal study suggests that those issues may be insufficient to explain the seasonal differences. Scherlag et al20 studied the incidence of sudden death in 184 dogs after ligation of the left anterior descending coronary artery. Forty-six sudden deaths from ventricular tachyarrhythmias 13 to 22 hours after coronary artery ligation occurred between November and February (42%), compared with only 6% in July and August. Surviving dogs (n=138) underwent an electrophysiology study, during which a greater number showed inducible sustained monomorphic ventricular tachycardia during winter compared with summer months. The authors speculated that increased sympathetic tone or catecholamine levels were responsible. Certainly, excessive emotional, gustatorial, or alcoholic intake was not a likely factor in canine sudden deaths. Additional support for minimizing the impact of holiday season activities comes from numerous studies on the sudden infant death syndrome that also show increased winter mortality.21

In Australia/New Zealand, the same winter influences occur, although seasons are reversed compared with the United States.13 Enquaselassie et al,22 using data from a community-based register of heart disease (WHO MONICA Project), demonstrated that coronary events, both fatal and nonfatal, were 20% to 40% more likely to occur in winter (June through August) and spring (September through November) than at other times of the year. Coronary deaths were more likely to happen on cold days and to a much lesser extent on warmer days. No differences were found between patterns of sudden and nonsudden deaths. Winter dominance of sudden infant death syndrome deaths also exists in New Zealand.23 Knowing seasonal mortality data on the equator and North and South Poles would be of interest.

The 1 constant in all these observations is the impact of winter, whether in the northern or southern hemisphere, in animals, or in young or older humans. And, of course, the 1 constant of winter is decreased daylight hours. As stated in the beginning of this editorial, such changes are perceived by the SCN, which then signals a myriad of physiological and possibly pathophysiological processes.

Although romanticists may argue that the heart influences the head, scientists have well established that the reverse also occurs. Skinner,24 Lown,25 and others elegantly demonstrated that the brain modulated the cardiac electrophysiological milieu to affect the generation of cardiac arrhythmias. Leor et al26 documented an increase in sudden cardiac death after the 1994 Los Angeles earthquake. This modulation, via the autonomic nervous system, hormone release, and a variety of other possible pathways, offers a potential mechanism by which the chronobiological rhythms, controlled by the SCN, could affect cardiovascular events, including sudden and nonsudden death, on a daily, weekly, or yearly basis (Figure). Naturally, this conclusion is speculative, and not all the data fit the curves of the figure. A recent study from the Lille- WHO MONICA study attributed alterations in coronary morbidity and mortality to meteorological variables, showing a linear relationship with temperature but a V-shaped relationship with atmospheric pressure.27 Others28,29 have described increased coronary mortality with heat. Certainly, stressful temperatures, either high or low, can have an additional impact.

But the conclusion that the short days of winter are related to increased cardiovascular mortality offers a hypothesis to test that, if true, opens new approaches for investigating and potentially reducing deaths from coronary and perhaps other
vascular diseases. One could envision future coronary care units using morning light treatments to lessen the hazards of winter cardiovascular mortality!

Acknowledgments
This work was supported in part by the Herman C. Kranert Fund and by grant HL-52323 from the National Heart, Lung, and Blood Institute of the National Institutes of Health.

References

Key Words: Editorials, circadian rhythm, myocardial infarction, mortality
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Circulation. 1999;100:1590-1592
doi: 10.1161/01.CIR.100.15.1590

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