Human Health

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Key Findings

The following bulleted points summarize the main findings of this chapter:

- Warmer temperatures lead to a net decrease in temperature-related mortality, including deaths associated with cardiovascular disease, respiratory disease, and strokes. The evidence of this benefit comes from research conducted in every major country of the world.
- In the United States the average person who died because of cold temperature exposure lost in excess of 10 years of potential life, whereas the average person who died because of hot temperature exposure likely lost no more than a few days or weeks of life.
- Some 4,600 deaths are delayed each year as people in the U.S. move from cold northeastern states to warm southwestern states. Between 3 and 7% of the gains in longevity experienced by the

U.S. population over the past three decades is due simply to people moving to warmer states.

- Cold-related deaths are far more numerous than heat-related deaths in the United States, Europe, and almost all countries outside the tropics. Coronary and cerebral thrombosis account for about half of all cold-related mortality.
- Global warming is reducing the incidence of cardiovascular diseases related to low temperatures and wintry weather by a much greater degree than it increases the incidence of cardiovascular diseases associated with high temperatures and summer heat waves.
- The adverse health impacts of cold temperatures, especially with respect to respiratory health, are more significant than those of high temperatures in many parts of the world, including Spain, Canada, Shanghai, and Taiwan. In the subtropical island of Taiwan, for example, researchers found low minimum temperatures were the strongest risk

factor associated with outpatient visits for respiratory diseases.

- A vast body of scientific examination and research contradict the claim that malaria will expand across the globe and intensify as a result of CO₂-induced warming.
- Concerns over large increases in vector-borne diseases such as dengue as a result of rising temperatures are unfounded and unsupported by the scientific literature, as climatic indices are poor predictors for dengue disease.
- While climatic factors largely determine the geographical distribution of ticks, temperature and climate change are not among the significant factors determining the incidence of tick-borne diseases.
- The ongoing rise in the air's CO₂ content is not only raising the productivity of Earth's common food plants but also significantly increasing the quantity and potency of the many healthpromoting substances found in their tissues, which are the ultimate sources of sustenance for essentially all animals and humans.
- Atmospheric CO₂ enrichment positively impacts the production of numerous health-promoting substances found in medicinal or "health food" plants, and this phenomenon may have contributed to the increase in human life span that has occurred over the past century or so.
- There appears to be little reason to expect any significant CO₂-induced increases in human-health-harming substances produced by plants as the atmosphere's CO₂ concentration continues to rise.

Introduction

Carbon dioxide (CO₂) does not seriously affect human health until the CO₂ content of the air reaches approximately 15,000 ppm (Luft *et al.*, 1974; Schaefer, 1982), more than 37 times greater than the current concentration of atmospheric CO₂. There is no reason to be concerned about any direct adverse human health consequences of the ongoing rise in the air's CO₂ content now or in the future, as even extreme model projections do not indicate anthropogenic activities will raise the air's CO_2 concentration above 1,000 to 2,000 ppm.

Nevertheless, IPCC contends rising CO_2 concentrations are causing several *indirect* threats to human health, which they project will worsen as the air's CO_2 concentration rises in the future. According to a draft from the Working Group II contribution to IPCC's *Fifth Assessment Report*,

The most important effect of climate change is that it will exacerbate current risks to health *[very high confidence]*. In recent decades, climate change has contributed to levels of ill-health (*likely*). If climate change continues as projected in scenarios in the next few decades, the major increases of ill-health compared to no climate change will occur through:

Greater incidence of injury, disease, and death due to more intense heat waves, storms, floods, and fires. [*very high confidence*]

Increased risk of under-nutrition resulting from diminished food production in poor regions. [*high confidence*]

Increased risks of food- and water-borne diseases and vector-borne infections. [high confidence]

... positive effects will be out-weighed, worldwide, by the magnitude and severity of the negative effects of climate change. [*high confidence*] ((IPCC-II, 2013a, Chapter 11, Human Health, p. 3; italics in original, bold removed and formatting changed).

We should note before going on that IPCC's assignment of "confidence" levels to each of these claims is purely a rhetorical device and not based on any statistical tests. (Idso *et al.*, 2013) Placing these expressions of opinion in italics and brackets doesn't make any of these dubious or untrue statements any more credible or true.

In a draft Technical Summary of the same document, Working Group II claims, "The health of human populations is sensitive to shifts in weather patterns and other aspects of climate change [*very high confidence*] and "There is emerging evidence of non-linearities in response (such as greater-thanexpected mortality due to heat waves) as climates become more extreme" (IPCC-II, 2013b, Technical Summary, p. 16; italics in original, bold removed).

As shown in the material presented in this chapter, however, IPCC's view of the impacts of rising temperatures and atmospheric CO_2 on human

health is simply wrong. Numerous peer-reviewed studies demonstrate a warmer planet is beneficial to humanity, as warmer temperatures in all parts of the world lead to decreases in temperature-related mortality. The medical literature shows warmer temperatures and a smaller difference between daily high and low temperatures, as occurred during the twentieth and early twenty-first centuries, reduce mortality rates due to cardiovascular and respiratory disease and stroke occurrence.

Similarly, the research is quite clear that climate has exerted only a minimal influence on recent trends in vector-borne diseases such as malaria, dengue fever, and tick-borne diseases. Other factors, many of them related to economic and technological setbacks or progress and not to weather, are far more important factors determining the transmission and prevalence of such diseases.

Finally, IPCC entirely overlooks several positive effects of rising levels of atmospheric CO_2 on human health. Carbon dioxide fertilization, for example, has been shown to enhance certain health-promoting substances in plants, such as antioxidants, vitamin C, and fatty acids, and promote the growth of plants such as St. John's wort used for the treatment of a variety of illnesses. In this way, global warming portends great health benefits for humans. IPCC makes no mention of these benefits.

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7.1 Hot vs. Cold Weather

• Warmer temperatures lead to a net decrease in temperature-related mortality, including deaths associated with cardiovascular disease, respiratory disease, and strokes. The evidence of this benefit comes from research conducted in every major country of the world.

According to IPCC, rising atmospheric carbon dioxide concentrations cause global warming, and this temperature increase will lead to greater human mortality. However, examination of pertinent real-world data reveals warmer temperatures lead to a decrease in temperature-related deaths, and this phenomenon represents one of the many indirect benefits of atmospheric CO_2 enrichment that IPCC has long downplayed and ignored.

As illustrated in the research described below, it is abundantly clear unseasonable cold temperatures cause far more health-related maladies and deaths than do unseasonable warm temperatures.

7.1.1 Asia

Behar (2000) studied sudden cardiac death (SCD) and acute myocardial infarction (AMI) in Israel, concentrating on the role temperature may play in the incidence of these health problems. Behar notes "most of the recent papers on this topic have concluded that a peak of SCD, AMI and other cardiovascular conditions is usually observed in low temperature weather during winter." He cites an Israeli study by Green et al. (1994), which reported between 1976 and 1985 "mortality from cardiovascular disease was higher by 50% in mid-winter than in mid-summer, both in men and women and in different age groups," even though summer temperatures in the Negev, where much of the work was conducted, often exceed 30°C and winter temperatures typically do not drop below 10°C. Behar concludes these results "are reassuring for populations living in hot countries."

Several researchers have examined the relationship between temperature and human health in Shanghai, China. Kan *et al.* (2003), for example, investigated the association between temperature and daily mortality from 1 June 2000 to 31 December 2001, finding a V-like relationship between total mortality and temperature that had a minimum mortality risk at 26.7°C. Above this optimum temperature, they observe, "total mortality increased

by 0.73% for each degree Celsius increase; while for temperatures below the optimum value, total mortality decreased by 1.21% for each degree Celsius increase." The net effect of a warming in Shanghai, China, therefore, would likely be reduced mortality on the order of 0.5% per degree Celsius increase in temperature, or perhaps more, since the warming of the past few decades has been primarily manifested in increases in daily minimum temperatures, with much smaller increases at the high end of the temperature spectrum. Hence, the recovery of Earth from the global chill of the Little Ice Age has had a positive effect on the health of the people of Shanghai that should continue into the foreseeable future if the planet continues to warm.

Tan et al. (2007) used a multivariate analysis "to investigate the relationships between mortality and heat wave intensity, duration, and timing within the summer season, along with levels of air pollution," for the exceptional heat waves of 1998 and 2003. "For heat waves in both summers," the researchers write, "mortality was strongly associated with the duration of the heat wave." Whereas the heat wave of 2003 was of much greater duration than the heat wave of 1998 (19 days in 2003 vs. 11 days in 1998), the mortality experienced in 2003 was much less than that experienced in 1998 (6.3 deaths/heat day in 2003 vs. 13.3 deaths/heat day in 1998). Tan et al. write, "since the meteorological conditions and pollution levels for the two heat waves were alike, we conclude that improvements in living conditions in Shanghai, such as increased use of air conditioning [1.35/household in 2003 vs. 0.69/household in 1998], larger living areas [13.8 m²/person in 2003 vs. 9.7 m²/person in 1998], and increased urban green space, along with higher levels of heat awareness and the implementation of a heat warning system, were responsible for the lower levels of human mortality in 2003 compared to 1998."

Kan *et al.* (2007) examined the association between Diurnal Temperature Range (DTR, defined as daily maximum temperature minus daily minimum temperature) and human mortality, using daily weather and mortality data from Shanghai over the period 1 January 2001 to 31 December 2004 via a semi-parametric generalized additive model after controlling for covariates including time trend, day of week, temperature, humidity, and outdoor air pollution levels. For cold days (below 23°C), "a 1°C increase of the 3-day moving average of DTR corresponded to 1.41%, 1.76% and 1.47% increases in total non-accidental, cardiovascular and respiratory mortality," respectively, whereas for warm days (above 23°C), "an increase of 1°C DTR corresponded to 1.13%, 1.91% and 0.54% increases in total non-accidental, cardiovascular and respiratory mortality."

Kan *et al.* say their data suggest "even a slight increase in DTR is associated with a substantial increase in mortality." In addition, they note over the past century global warming has been characterized by "the daily minimum temperature increasing at a faster rate ... than the daily maximum, resulting in a decrease in the DTR for many parts of the world." Their results suggest that in addition to the reduction in human mortality typically provided by the increase in daily mean temperature, the accompanying decrease in DTR also should have been tending to reduce human mortality.

Ma *et al.* (2011) analyzed weather data from the Shanghai Meteorological Bureau to investigate the impact of heat waves and cold spells on hospital admissions in Shanghai, China. They defined a heat wave as a period of at least seven consecutive days with daily maximum temperature above 35.0°C and daily average temperatures above the 97th percentile during the study period. They defined a cold spell as a period of at least seven consecutive days with daily maximum temperature and daily average temperatures below the 3rd percentile during the study period. For one heat wave (24 July to 2 August, 2007) and one cold spell (28 January to 3 February, 2008), they obtained daily hospital admission data for these periods from the Shanghai Health Insurance Bureau.

The four researchers report the number of excess (above normal) hospital admissions during the eightday heat wave was 352—driven by a 2% increase in all-cause admissions, an 8% increase in admissions due to cardiovascular problems, and a 6% increase in admissions related to respiratory problems. During the 10-day cold spell there were 3,725 excess admissions, driven by 38%, 33%, and 32% increases in admissions due to all-cause, cardiovascular, and respiratory problems, respectively. Ma *et al.* conclude "the cold spell seemed to have a larger impact on hospital admission than the heat wave in Shanghai."

Cheng and Kan (2012) employed a generalized additive model with penalized splines to analyze mortality, air pollution, temperature, and covariate data over the period 1 January 2001 through 31 December 2004 in Shanghai, focusing on particulate matter of diameter 10 μ m or less (commonly referred to as PM₁₀) and ozone (O₃). Cheng and Kan report they "did not find a significant interaction between air pollution and higher temperature [>85th percentile days]," but "the interaction between PM₁₀ and extreme low temperature [<15th percentile days] was statistically significant for both total and cause-specific mortality." Compared to normal temperature days (15th-85th percentile), they found a $10-\mu g/m^3$ increase in PM₁₀ on extreme low temperature days led to all-cause mortality rising from 0.17% to 0.40%. They add, "the interaction pattern of O₃ with low temperature was similar," noting their finding of "a stronger association between air pollution and daily mortality on extremely cold days confirms those of three earlier seasonal analyses in Hong Kong, Shanghai and Athens," citing Touloumi *et al.* (1996), Wong *et al.* (1999, 2001), and Zhang *et al.* (2006).

Wang *et al.* (2013) write, "a large change in temperature within one day may cause a sudden change in the heart rate and circulation of elderly people, which all may act to increase the risk of cardiopulmonary and other diseases, even leading to fatal consequences." They further note, "it has been shown that a rise of the minimum temperature has occurred at a rate three times that of the maximum temperature during the twentieth century over most parts of the world, which has led to a decrease of the diurnal temperature range (Karl *et al.*, 1984, 1991)."

Wang *et al.* evaluated the short-term effect of diurnal temperature range (DTR) on emergency room (ER) admissions among elderly adults in Beijing. As they describe it, "after controlling the long-time and seasonal trend, weather, air pollution and other confounding factors, a semi-parametric generalized additive model (GAM) was used to analyze the exposure-effect relationship between DTR and ER admissions among elderly adults with different lag structures from 2009 to 2011 in Beijing," where they "stratified groups by age and gender."

The nine researchers report "significant associations were found between DTR and four major causes of daily ER admissions among elderly adults in Beijing." They state "a 1°C increase in the 8-day moving average of DTR (lag 07) corresponded to an increase of 2.08% in respiratory ER admissions and 2.14% in digestive ER admissions," and "a 1°C increase in the 3-day and 6-day moving average of DTR (lag 02 and lag 05) corresponded to a 0.76% increase in cardiovascular ER admissions, and a 1.81% increase in genitourinary ER admissions, respectively." They add, "people aged 75 years and older were associated more strongly with DTR than the 65-74 age group."

Guo *et al.* (2012) note knowledge of the health effects of extreme temperatures on mortality comes mainly from developed countries, particularly from regions with temperate climates, and they say "few

studies have been conducted in developing countries, particularly in tropical regions." They used a Poisson regression model combined with a distributed lag non-linear model to examine the nonlinear and delayed effects of temperature on cause-specific and age-specific mortality, employing data from 1999 to 2008 for Chiang Mai, Thailand (18°47'N, 98°59'E), with a population of 1.6 million people. Controlling for season, humidity, ozone, and particulate matter (PM₁₀) pollution, the three researchers found "both hot and cold temperatures resulted in immediate increase in all mortality types and age groups," but "the hot effects on all mortality types and age groups were short-term, while the cold effects lasted longer." The cold effects were greater, with more people dying from them than from the effects of heat.

Lindeboom et al. (2012) write, "while the association of weather and mortality has been well documented for moderate climate zones, little is known about sub-tropical zones, particularly Bangladesh." They aimed "to assess the short-term relationship of temperature and rainfall on daily mortality after controlling for seasonality and timetrends." Working with daily mortality and weather data for the period 1983-2009 pertaining to Matlab, Bangladesh, where a rigorous health and demographic surveillance system (HDSS) has been operational since 1966, Lindeboom et al. applied time series Poisson regression with cubic spline functions that allowed for lagged effects of weather on mortality, controlling for time trends and seasonal patterns.

The four researchers report "mortality in the Matlab surveillance area shows overall weak associations with rainfall, and stronger negative association with temperature." They determined there was "a 1.4% increase in mortality with every 1°C decrease in mean temperature at temperatures below 29.2°C," but only "a 0.2% increase in mortality with every 1°C increase in mean temperature." In addition, they note the "elderly, aged 60 years and above, seem to be most affected at lower temperatures, with a 5.4% increase in mortality with every 1°C decrease in temperature below 23°C." Lindeboom et al. further report the Bangladesh Meteorological Department data on minimum and maximum temperatures observed in 1950-2010 "showed an increasing trend," but they note the increase was faster for minimum temperature, as opposed to maximum temperature.

Wu *et al.* (2013) note "numerous studies have reported the association between ambient temperature and mortality," but "few multi-city studies have been conducted in subtropical regions in developing countries." They first assessed the health effects of temperature on mortality in four subtropical cities of China (Changsha, Kunming, Guangzhou, and Zhuhai) by means of a "double threshold-natural cubic spline" distributed lag non-linear model at different temporal lags. They used the combined results to conduct a meta-analysis to estimate the overall cold and hot effects on mortality at different lag days. The 11 researchers report a U-shaped relationship between temperature and mortality was found in the four cities, indicating "mortality is usually lowest around a certain temperature and higher at lower or higher temperatures," as they say also was found by Alberdi et al. (1998), Huynen et al. (2001), Curriero et al. (2002), O'Neill et al. (2003), Armstrong (2006), Laaidi et al. (2006), and Kan et al. (2007). In addition, "the hot effect peaked at the current day, and then diminished with lag days; whereas "the cumulative cold effect increased gradually with lag days, with the highest effect at lag 0-27."

Although "both low and high temperatures were associated with increased mortality in the four subtropical Chinese cities," Wu *et al.* state the "cold effect was more durable and pronounced than the hot effect."

Yang et al. (2013) examined the effects of Diurnal Temperature Range (DTR) on human mortality rates, as well as whether the effects were different for different individual characteristics, such as gender, age, and education level. This was accomplished using daily meteorological data for the period 1 January 2003 through 31 December 2010 obtained from the China Meteorological Data Sharing System, which included daily mean temperature plus minimum and maximum temperatures collected from a single station located in the heart of the urban area of Guangzhou City (the largest metropolis in Southern China), along with individual data for all 189.379 registered deaths that occurred over the same time period, which they obtained from the Guangzhou Center for Disease Control and Prevention.

They found "a linear DTR-mortality relationship, with evidence of increasing mortality with DTR increase," where "the effect of DTR occurred immediately and lasted for four days," such that over that time period, a 1°C increase in DTR was associated with a 0.47% increase in non-accidental mortality. They also found "the elderly, females and residents with less education have been identified as more vulnerable to rapid temperature change within a single day." In addition, they report there was a joint adverse effect with temperature "when mean temperature was below 22°C, indicating that high DTR enhanced cold-related mortality." In light of their findings, the eight researchers speculate the expected "decrease in DTR in future climate scenarios might lead to two benefits: one from decreasing the adverse effects of DTR [which is reduced due to greater warming at night than during the day], and the other from decreasing the interaction effect with temperature [which is expected to rise with greenhouse warming]."

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7.1.2 Europe

The early studies of Bull (1973) and Bull and Morton (1975a, b) in England and Wales demonstrate even normal changes in temperature are typically associated with inverse changes in death rates, especially in older people. That is, when temperatures rise, death rates fall, whereas when temperatures fall, death rates rise. In addition, at the lower end of the temperature range, Bull and Morton (1978) report, "there are more deaths the longer the 'run of days,' while at the higher end of the temperature range the reverse is true"; i.e., "the longer the 'run' the fewer the deaths," suggesting people adapt more readily to extreme heat than to extreme cold. Such findings have been echoed in many studies across Europe.

Keatinge and Donaldson (2001) analyzed the effects of temperature, wind, rain, humidity, and sunshine during high pollution days in the greater London area over the period 1976–1995 to determine which weather and/or pollution factors have the biggest influence on human mortality. They observed simple plots of mortality rate versus daily air temperature revealed a linear increase as temperatures fell from 15°C to near 0°C. Mortality rates at temperatures above 15°C, however, were "grossly alinear," as they describe it, showing no trend. Days with high SO₂, CO, or PM₁₀ (particulate matter of diameter less than 10µm) concentrations were colder than average, but a multiple regression analysis revealed none of these pollutants was associated with a significant increase in mortality among people 50 years of age or older. Only low temperatures were found to have a significant effect on immediate mortality (one day after a temperature perturbation) and long-term mortality (up to 24 days after a temperature perturbation), with the net increase in

mortality over the 24 days following a one-day fall in temperature amounting to 2.77 daily deaths per million people per degree Celsius temperature drop. Keatinge and Donaldson conclude "the large, delayed increase in mortality after low temperature is specifically associated with cold and is not due to associated patterns of wind, rain, humidity, sunshine, SO_2 , CO, or smoke."

How does cold kill? The two scientists say "cold causes mortality mainly from arterial thrombosis and respiratory disease, attributable in turn to coldinduced hemoconcentration and hypertension [in the first case] and respiratory infections [in the second case]." McGregor (2005) notes "anomalous cold stress can increase blood viscosity and blood pressure due to the activation of the sympathetic nervous system which accelerates the heart rate and increases vascular resistance (Collins et al., 1985; Jehn et al., 2002; Healy, 2003; Keatinge et al., 1984; Mercer, 2003; Woodhouse et al., 1993)," adding, "anomalously cold winters may also increase other risk factors for heart disease such as blood clotting or fibrinogen concentration, red blood cell count per volume and plasma cholesterol." Keatinge and Donaldson conclude although "increases in mortality due to cold weather are large in many temperate regions ... effective protection against personal cold exposure virtually prevents excess winter mortality," even in places as cold as Siberia.

In a study explicitly considering personal cold exposure, Gemmell (2001) analyzed the answers of 858 respondents to pertinent health and housing questions put to them in the second sweep of the "West of Scotland Twenty-07 Study" conducted in 1991. This effort indicated "over and above socioeconomic factors and house conditions. inadequate home heating is associated with poor health in those aged 55-60." Gemmell notes, for example, "respondents who reported feeling cold in winter 'most of the time' were over three times more likely to suffer from a limiting condition and almost five times as likely to report 'fair' or 'poor' self assessed health," leading him to conclude "living in a cold house will almost certainly exacerbate existing conditions and may lead to early mortality." Gemmell suggests "affordable efficient methods of home heating could help reduce the number of people living in homes that are detrimental to their health."

Carson *et al.* (2006) analyzed London mortality and meteorological data for four periods of the twentieth century they "selected to avoid times of war and influenza pandemics: 1900–1910, 1927–1937, 1954–1964, and 1986–1996." They found "an increase in risk at low temperatures in each period, but the strength of association gradually declined over the century ... from a 2.5% increase in mortality for each degree-C fall in temperature below 15°C in 1900–1910 to approximately a 1.2% increase in mortality per degree-C fall in temperature in 1986– 1996." At the other end of the temperature spectrum, their analyses "also provided some indication of heatrelated mortality in the earlier periods of analysis, but not in 1954–1964 or 1986–1996."

These results suggest cold is a more effective killer than heat. In addition, they suggest the deadly effects of both extreme cold and extreme heat have been muted with the passage of time, "despite the aging of the population and a progressive increase in the prevalence of cardiorespiratory disease, as Carson *et al.* add, "which would otherwise tend to increase susceptibility" to temperature-induced death.

Another implication of their study results, Carson *et al.* write, is "the decline in vulnerability to cold and heat is most readily explained by beneficial changes relating to increasing wealth." Some of the items they mention are improvements in health care, nutrition, and housing; increased car ownership; climate-controlled transportation and shopping facilities; and improved clothing fabrics, although they say, "we cannot quantify or even identify all of the modifying factors that have contributed to this reduced susceptibility." Finally, they say "it is reasonable to conclude that a similar modification of risk will occur among populations in other settings, particularly in low- and middle-income countries, as they grow richer."

According to Christidis et al. (2010), "the IPCC AR4 states with very high confidence that climate change contributes to the global burden of disease and to increased mortality," citing the contribution of Confalonieri et al. (2007) to that document. In an effort to evaluate this very-high-confidence contention of IPCC, Christidis et al. extracted the numbers of daily deaths from all causes from death registration data supplied by the UK Office of National Statistics for men and women 50 years of age or older in England and Wales for the period 1976-2005, which they divided by daily estimates of population "obtained by fitting a fifth order polynomial to midyear population estimates, to give mortality as deaths per million people." They then compared the death results with surface air temperature data that showed a warming trend during the same three-decade period of 0.47°C per decade. In addition, they employed a technique called optimal detection, which they describe as "a formal statistical methodology" that can be used to estimate the role played by human adaptation in the temperature-related changes in mortality they observed.

As expected, during the hottest portion of the year, warming led to increases in death rates, whereas during the coldest portion of the year warming led to decreases in death rates. The three scientists report if no adaptation had taken place, there would have been 1.6 additional deaths per million people per year due to warming in the hottest part of the year over the period 1976-2005, but there would have been 47 fewer deaths per million people per year due to warming in the coldest part of the year, for a livessaved to life-lost ratio of 29.4, representing a huge net benefit of the warming experienced in England and Wales over the three-decade period of warming. When adaptation was included in the analysis, as was the case in the data they analyzed, they found there were only 0.7 death per million people per year due to warming in the hottest part of the year, but a decrease of fully 85 deaths per million people per year due to warming in the coldest part of the year, for a phenomenal lives-saved to live-lost ratio of 121.4. Such observations indicate IPCC's "very-highconfidence" conclusion is woefully wrong. Warming is highly beneficial to human health, even without any overt adaptation to it. And when adaptations are made, warming is incredibly beneficial in terms of lengthening the human lifespan.

In France, Laaidi *et al.* (2006) conducted an observational population study in six regions between 1991 and 1995 to assess the relationship between temperature and mortality in areas of widely varying climatic conditions and lifestyles, including urban (Paris), oceanic (Finistere), semi-continental (Coted'Or), or mountain (the Hautes-Alpes) climates and two types of Mediterranean climate, one relatively mild and sheltered (the Alpes-Maritimes) and the other more extreme and windy (the Herault). Daily death and cause-of-death data were provided by the Epidemiological Centre on the Medical Causes of Death, part of the country's National Institute for Health and Medical Research.

Laaidi *et al.* report "mean daily counts of deaths showed an asymmetrical V-like or U-like pattern with higher mortality rates at the time of the lowest temperatures experienced in the area than at the time of the highest temperatures," noting "between these two peaks, there is a critical temperature threshold, referred to as the thermal optimum, where mortality rates are minimal." This relationship varied somewhat between the two sexes and among different age groups and causes of death. In all cases, however, they found "more evidence was collected showing that cold weather was more deadly than hot weather." These findings, the researchers say, are "broadly consistent with those found in earlier studies conducted elsewhere in Europe (Kunst *et al.*, 1993; Ballester *et al.*, 1997; Eurowinter Group, 1997; Keatinge *et al.*, 2000a,b; Beniston, 2002; Muggeo and Vigotti, 2002), the United States (Curriero *et al.*, 2002) and South America (Gouveia *et al.*, 2003)." They also say their findings "give grounds for confidence in the near future," stating even a 2°C warming over the next half century "would not increase annual mortality rates."

Diaz et al. (2005) examined the effect of extreme winter temperature on mortality in Madrid, Spain for people older than 65, using data from 1,815 winter days over the period 1986-1997, during which time 133,000 deaths occurred. They found daily T_{max} was more closely correlated with mortality than was daily T_{min}, because, as they describe it, "very low Tmin mostly occur during stagnation episodes. characterized by very cold nights and sunny days, with a typical temperature range of between 15°C and 20°C," while "most of the days with very low Tmax occur under cloudy conditions, with very limited temperature ranges of around 5°C," so "human exposure to low temperatures during these days is longer than that occurring during the stagnation days associated with a very low Tmin." In addition, they note, "Tmin is usually recorded around 7 a.m., when very little human activity occurs outdoors, while Tmax is usually recorded at around 4 p.m."

Diaz et al. determined that as Tmax dropped below 6°C, which they describe as an unusually cold day (UCD), "the impact on mortality also increased significantly." They also found the impact of UCDs increased as the winter progressed, with the first UCD of the season producing an average of 102 deaths/day at a lag of eight days and the sixth UCD producing an average of 123 deaths/day at a lag of eight days. This behavior suggests, in their words, "acclimatisation does not occur, with every cold spell enhancing the pathologies produced in previous spells." Consequently, whereas they report "the impact of heat waves is reduced as they occur during a certain season, suggesting an acclimatisation to heat," just the opposite occurs in the case of recurring cold, which becomes ever more deadly with each new occurrence.

Fernandez-Raga *et al.* (2010) obtained from Spain's National Meteorological Institute data from weather stations situated in eight of the provincial capitals in the Castile-Leon region—a plateau in the northwestern part of the country that includes nine provinces "with low a population density that can be considered as ageing." The data covered the period 1980-1998, and they obtained contemporary mortality data from the country's National Institute for Statistics for deaths associated with cardiovascular. respiratory, and digestive system diseases.

Analyses of the monthly averaged data revealed a number of interesting results. First, for all three of the disease types studied, Fernandez-Raga *et al.* found "the death rate is about 15% higher on a winter's day than on a summer's day," which they describe as "a result often found in previous studies,"



Figure 7.1.2.1. Monthly deaths in the Castile-Leon region of Spain attributable to cardiovascular disease. Adapted from Fernandez-Raga *et al.* (2010).

citing Fleming et al. (2000), Verlato et al. (2002), Grech et al. (2002), Law et al. (2002), and Eccles (2002). Second, in a finding that helps explain the first, the three researchers discovered when monthly averaged human death rates were plotted against monthly averages of daily mean, maximum, and minimum air temperature, the results nearly always took the form of a U-shaped concave parabola. And for all three disease types, they found all three temperatures (daily mean, maximum, and minimum) at which minimum death rates occurred—which they refer to as ideal or comfort temperatures-were within about 1–7°C of the maximum values typically reached by those three types of temperature, and they were anywhere from 14-24°C away from their minimum values. Consequently, the ideal or comfort temperatures always were very close to (and sometimes nearly identical to) the maximum values reached by the mean, maximum, and minimum temperatures experienced in the region, and they were much more removed from the minimum values of those three temperature parameters, as illustrated in Figure 7.1.2.1, which relates death rates due to cardiovascular diseases to mean air temperature.

The data of Figure 7.1.2.1 clearly demonstrate the people of the Castile-Leon region of Spain are much more likely to die from a cardiovascular disease in the extreme cold of winter than in the extreme heat of summer. The same holds true with respect to dying from respiratory and digestive system diseases.

Referencing the Fourth Assessment Report of

IPCC, Wichmann et al. (2011) write "temperature, a key climate change indicator, is expected to increase substantially in the Northern Hemisphere, with potentially grave implications for human health." Concerned about what that might mean for their homeland, the five Danish researchers investigated the association between the daily three-hour maximum apparent temperature (which reflects the physiological experience of combined exposure to humidity and temperature) and deaths due to cardiovascular disease (CVD), cerebrovascular disease (CBD), and respiratory disease (RD) in the nation's capital. Copenhagen, over the period 1999-2006.

During the warm half of the year (April– September), Wichmann *et al.* found a rise in temperature had an inverse or protective effect with respect to CVD mortality (a 1% decrease in death in response to a 1°C increase in apparent temperature). This finding is unusual but also has been observed in Dublin, Ireland, as reported by Baccini *et al.* (2008, 2011). Wichmann *et al.* found no association with RD and CBD mortality. At the other end of the thermal spectrum, during the cold half of the year, all three associations were inverse or protective. This finding, according to the researchers, is "consistent with other studies (Eurowinter Group, 1997; Nafstad *et al.*, 2001; Braga *et al.*, 2002; O'Neill *et al.*, 2003; Analitis *et al.*, 2008)."

Whereas many observers (including IPCC) continue to emphasize the primarily negative impact

of summer heat waves on human death rates in lowand mid-latitude regions of Earth, essentially neglecting to report what happens there during winter cold spells, Wichmann *et al.*'s summer results tell a dramatically different story that is likely typical of higher latitudes. They also portray what tends to happen nearly everywhere in winter, noting during that cold part of the year "only protective effects [of warming] were observed."

Matzarakis *et al.* (2011) developed a relationship between heat stress and all-cause mortality in the densely populated city of Vienna (Austria), using a human biometeorological index known as the physiologically equivalent temperature or PET, which "describes the thermal situation by the air temperature of a reference environment, in which the core and the skin temperature is the same as in the complex outdoor environment." This reference environment is defined as "a room with a wind velocity < 0.1 m/sec, a vapor pressure of 12 hPa and a mean radiation temperature that equals the air temperature," as described in more detail by Mayer and Hoppe (1987).

Based on data from 1970–2007, and after adjusting the long-term mortality rate to account for temporal variations in the size of the population of Vienna, temporal changes in life expectancy, and the changing age structure of Vienna's population, the three researchers found a significant relationship between heat stress and mortality. Over this 38-year period, "some significant decreases of the sensitivity were found, especially in the medium heat stress levels," they report.

With respect to the cause of this decrease in heat stress sensitivity, Matzarakis *et al.* state in the final sentence of their abstract, these decreases in sensitivity "could indicate active processes of longterm adaptation to the increasing heat stress." In the discussion section of their paper, they write such sensitivity changes "were also found for other regions," citing Davis *et al.* (2003), Koppe (2005), Tan *et al.* (2007), and Donaldson and Keatinge (2008). In the conclusion of their paper, they refer to these changes as "positive developments."

Vocks *et al.* (2001) statistically evaluated the influence of various meteorological variables on the intensity of clinical symptoms (itching) caused by the skin disease atopic eczema in the high-mountain area of Davos, Switzerland for the period 1983–1989. Itching intensity was found to be inversely correlated with air temperature, air pressure, and water vapor pressure, such that an increase in any of these variables decreased the severity of itching. Examination of the three variables during periods of

abrupt and/or prolonged change, on the order of several weeks to months, substantially improved the correlations. Such findings suggest future warming, whether local, regional, or global, will bring a measure of relief from itching to sufferers of atopic eczema.

In Germany, Laschewski and Jendritzky (2002) analyzed daily mortality rates in Baden-Wurttemberg (10.5 million inhabitants) over the 30-year period 1958-1997 to determine the sensitivity of the population of this moderate climatic zone to long- and short-term episodes of heat and cold. Their research indicates mortality shows "a marked seasonal pattern with a minimum in summer and a maximum in winter." With respect to short-term exposure to heat and cold, they found "cold spells lead to excess mortality to a relatively small degree, which lasts for weeks," and "the mortality increase during heat waves is more pronounced, but is followed by lower than average values in subsequent weeks." The authors say the latter observation suggests people who died from short-term exposure to heat possibly "would have died in the short term anyway."

With respect to this short-term mortality displacement in the case of heat-related deaths, it is worth noting Laschewski and Jendritzky's data demonstrate it is merely a displacement of deaths and not an overall increase. They found, for example, the mean duration of above-normal mortality for the 51 heat episodes that occurred from 1968 to 1997 was 10 days, with a mean increase in mortality of 3.9%, after which there was a mean decrease in mortality of 2.3% for 19 days. Hence, the net effect of the two perturbations was an overall decrease in mortality of 0.2% over the full 29-day period. This is additional evidence cold spells are more deadly than heat waves. Hence, global warming should be expected to confer significant benefits upon mankind in both the shortand long-term, for in both situations, cold kills but heat heals, especially in the long term, which is what global warming projections are all about.

Focusing on the Czech Republic, Kysely and Huth (2004) calculated deviations of the observed number of deaths from the expected number of deaths for each day of the year for the period 1992–2000. They found "the distribution of days with the highest excess mortality in a year is clearly bimodal, showing a main peak in late winter and a secondary one in summer." Regarding the smaller number of summer heat-wave-induced deaths, they also found "a large portion of the mortality increase is associated with the harvesting effect, which consists in short-term shifts in mortality and leads to a decline in the number of deaths after hot periods (e.g. Rooney et al., 1998; Braga et al., 2002; Laschewski and Jendritzky, 2002)." For the Czech Republic, they report, "the mortality displacement effect in the severe 1994 heat waves can be estimated to account for about 50% of the total number of victims." As they describe it, "people who would have died in the short term even in the absence of oppressive weather conditions made up about half of the total number of deaths." Hence, not only is the overall number of deaths typically smaller in the warmest part of the year than in the coldest time of the year in the Czech Republic, approximately half of the heat-related excess deaths associated with the severe 1994 heat waves likely would have occurred even without the unseasonable heat, as they were merely normal deaths simply hastened by unseasonably warm temperatures.

Kysely and Plavcova (2012) write, "there is much concern that climate change may be associated with large increases in heat-related mortality," but "growing evidence has been emerging that the relationships between temperature extremes and mortality impacts are nonstationary," and "most of these studies point to declining heat-related mortality in developed countries, including the US, Australia, the UK, the Netherlands and France (Davis *et al.*, 2002, 2003a, 2003b; Bi and Walker, 2001; Donaldson *et al.*, 2003; Garssen *et al.*, 2005; Carson *et al.*, 2006; Fouillet *et al.*, 2008; Sheridan *et al.*, 2009)." This is true, they note, despite "aging populations and prevailing rising trends in temperature extremes."

Most of the studies cited above were conducted in developed countries; the two Czech researchers note "much less is understood about temporal changes in the impacts of temperature extremes in developing (low- and middle-income) countries and in regions that have undergone (or are undergoing) a transition from the developing to the developed world," They note "post-communist Central and Eastern Europe is one such region, where pronounced changes have occurred over the past 20 years." They examined "temporal changes in mortality associated with spells of large positive temperature anomalies (hot spells) in extended summer season in the population of the Czech Republic (Central Europe) during 1986–2009."

Kysely and Plavcova found declining mortality trends in spite of rising temperature trends, just the opposite of what IPCC claims will occur in response to global warming. The Czech scientists add, "the finding on reduced vulnerability of the population remains unchanged if possible confounding effects of within-season acclimatization and mortality displacement are taken into account," and "neither does it depend on the changing age structure of the population, since similar (and slightly more pronounced) declines in the mortality impacts are found in the elderly (age group 70+ years) when examined separately."

Kysely and Plavcova write, "recent positive socioeconomic development following the collapse of communism in 1989 is the likely primary cause of the declining impacts of hot spells," and "other important factors have been enhanced media coverage and better public awareness of heat-related risks." They also note their key result "supports the idea that the adverse health effects of heat are largely preventable (e.g., Matthies and Menne, 2009)," ultimately concluding "climate change may have relatively little influence on heat-related deaths, particularly if the recent warming trend is viewed as an early manifestation of anthropogenic climate change." They continue, "it appears that changes in other factors that influence vulnerability of a population are dominant instead of temperature trends and that the level of adaptability to high ambient temperatures may be large."

Huynen et al. (2001) evaluated the impact of heat waves and cold spells on mortality rates of people of all ages throughout the Netherlands for the 19-year period 1 January 1979 through 31 December 1997. During heat waves they found a mean excess mortality of 39.8 deaths per day, whereas during cold spells they found a mean excess mortality of 46.6 deaths per day. These numbers indicate a typical coldspell day kills at a rate 17% greater than a typical heat-wave day. They also report the heat waves of the period they studied ranged from six to 13 days in length, whereas the cold spells lasted from nine to 17 days, making the average cold spell approximately 37% longer than the average heat wave. Adjusting for this duration differential makes the number of deaths per cold spell in the Netherlands fully 60% greater than the number of deaths per heat wave. Also, excess mortality continued for the entire month after the cold spells, leading to even more deaths, whereas in the case of heat waves, there appeared to be mortality deficits in the following month, suggesting "some of the heat-induced increase in mortality can be attributed to those whose health was already compromised" or "who would have died in the short term anyway." That conclusion also was reached by Kunst et al. (1993), Alberdi et al. (1998), Eng and Mercer (1998), and others mentioned in this section. It is highly likely, therefore, that the 60% greater death toll calculated for Dutch cold spells compared to Dutch heat waves is a vast underestimate of the

true differential killing power of these two temperature extremes.

In a letter to the editor of *Epidemiology*, the senior and second authors of the Huynen *et al.* paper discussed whether global climate change reduces thermal stress in the Netherlands (Martens and Huynen, 2001). Based on the predictions of nine GCMs for an atmospheric CO_2 concentration of 550 ppm in the year 2050—taken to imply a 50% increase in Dutch heat waves and a 67% drop in Dutch cold spells—they calculated a total mortality decrease of approximately 1,100 people per year for the country at that point in time.

In a multiregional study, Keatinge et al. (2000a) examined heat- and cold-related mortality in north Finland, south Finland, southwest Germany, the Netherlands, Greater London, north Italy, and Athens, Greece, in people aged 65-74. For each of these regions, they determined the 3°C temperature interval of lowest mortality and then evaluated mortality deviations from that base level as temperatures rose and fell by increments of 0.1°C. As they describe their findings, "all regions showed more annual cold related mortality than heat related mortality." Over the seven regions studied, annual cold-related deaths were nearly 10 times greater than annual heat-related deaths. Moreover, Keatinge et al. note the very successful adjustment of the populations in their study to widely different summer temperatures "gives grounds for confidence that they would adjust successfully, with little increase in heat related mortality, to the global warming of around 2°C predicted to occur in the next half century." They say their data suggest "any increases in mortality due to increased temperatures would be outweighed by much larger short term declines in cold related mortalities." For the entire population of Europe. therefore, even a 2°C increase in temperature, if it were to occur, would be a climate change for the better.

In a major assessment of cold-weather effects on mortality in Europe, Analitis *et al.* (2008) state, "in recent years, the effects of meteorologic factors on health have attracted renewed interest because of the observed and predicted climate change, which is expected to result in a general rise in temperature." This development, they write, has led to a "recent focus on heat-wave episodes," which may have fostered the perception cold-related mortality is not as important a public health concern as heat-related mortality.

Analitis *et al.* analyzed short-term effects of cold weather on mortality in 15 European cities: Athens,

Greece; Barcelona, Spain; Budapest, Hungary; Dublin, Ireland; Helsinki, Finland; Ljubljana, Slovenia; London, United Kingdom; Milan, Italy; Paris, France; Prague, Czech Republic; Rome, Italy; Stockholm, Sweden; Turin, Italy; Valencia, Spain; and Zurich, Switzerland. They assessed the effects of minimum apparent temperature on cause- and agespecific daily mortality over the cold half of the year (October–March), using data from 1990–2000 they analyzed via "Poisson regression and distributed lag models, controlling for potential confounders."

The international team of scientists—from Finland, Greece, Ireland, Italy, Slovenia, Spain, and Sweden—found "a 1°C decrease in temperature was associated with a 1.35% increase in the daily number of total natural deaths and a 1.72%, 3.30% and 1.25% increase in cardiovascular, respiratory, and cerebrovascular deaths, respectively." In addition, they report "the increase was greater for the older age groups," and the cold effect "persisted up to 23 days, with no evidence of mortality displacement." Analitis *et al.* conclude their results "add evidence that cold-related mortality is an important public health problem across Europe and should not be overlooked by public health authorities because of the recent focus on heat-wave episodes."

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7.1.3 North America

Goklany and Straja (2000) examined trends in United States death rates over the period 1979–1997 due to excessive hot and cold weather. They report there were no trends in deaths due to either extreme heat or cold in the entire population or, "more remarkably," as they say, in the older, more-susceptible age groups, those aged 65 and over, 75 and over, and 85 and over. Deaths due to extreme cold in these older age groups exceeded those due to extreme heat by as much as 80% to 125%. With respect to the absence of trends in death rates attributable to either extreme heat or cold, Goklany and Straja say this "suggests that adaptation and technological change may be just as important determinants of such trends as more obvious meteorological and demographic factors."

Davis et al. (2002) studied changes in the impact of high temperatures on daily mortality rates over a period of four decades in six major metropolitan areas along a north-south transect in the eastern United States. They found few significant weather-mortality relationships for any decade or demographic group in the three southernmost cities examined, where warmer weather is commonplace. In the three northernmost cities, however, there were statistically significant decreases in population-adjusted mortality rates during hot and humid weather between 1964 and 1994. The authors write, "these statistically significant reductions in hot-weather mortality rates suggest that the populace in cities that were weathersensitive in the 1960s and 1970s have become less impacted by extreme conditions over time because of improved medical care, increased access to air conditioning, and biophysical and infrastructural They further note, "this analysis adaptations." counters the paradigm of increased heat-related mortality rates in the eastern US predicted to result from future climate warming."

Davis et al. (2003) evaluated "annual excess mortality on days when apparent temperatures-an index that combines air temperature and humidityexceeded a threshold value for 28 major metropolitan areas in the United States from 1964 through 1998." They found "for the 28-city average, there were 41.0 \pm 4.8 excess heat-related deaths per year (per standard million) in the 1960s and 1970s, 17.3 ± 2.7 in the 1980s, and 10.5 ± 2.0 in the 1990s." Analyzing these results together with various types of ancillary data, they conclude, "this systematic desensitization of the metropolitan populace to high heat and humidity over time can be attributed to a suite of technologic, infrastructural, and biophysical adaptations, including availability of air conditioning." increased Consequently, because "all-causes mortality during heat stress events has declined despite increasingly stressful weather conditions in many urban and suburban areas ... heat-related mortality in the United States seems to be largely preventable at present." The technology and infrastructure advancements made possible by the economic progress of the past few decades have more than compensated for the increasing heat stress during this period of what IPCC describes as "unprecedented" global warming.

Davis *et al.* (2004) examined the seasonality of mortality due to all causes, using monthly data for 28 major U.S. cities from 1964 to 1998, then calculated the consequences of a future 1°C warming of the conglomerate of those cities. At all locations studied, they report "warmer months have significantly lower

mortality rates than colder months." They calculate "a uniform 1°C warming results in a net mortality decline of 2.65 deaths (per standard million) per metropolitan statistical area." Since the annual death rate of about 9,500 deaths (per standard million) is so much larger, however, the "death benefits" of the warming are extremely small—a reduction in the annual number of deaths of less than 0.03%, which also pales in comparison to the nearly 20% reduction in annual mortality that has occurred as a consequence of technological advancements experienced between the 1960s–1970s and the 1990s.

The primary implication of Davis *et al.*'s findings, in their words, "is that the seasonal mortality pattern in US cities is largely independent of the climate and thus insensitive to climate fluctuations, including changes related to increasing greenhouse gases."

O'Neill et al. (2005) assessed the influence of air pollution and respiratory epidemics on empirical associations between apparent temperature, which "represents an individual's perceived air temperature," and daily mortality in Mexico's largest and third-largest cities: Mexico City and Monterrey, respectively. They report, "the effects of cold weather on all-age mortality were similar in Monterrey and Mexico City." When considering the entire temperature spectrum, they found "in Mexico City, the 7-day temperature mortality association has a hockey stick shape with essentially no effect of higher temperatures," whereas in Monterrey the function they fit to the data "shows a U-shape," with "a higher mortality risk at both ends of the distribution," although the effect is much weaker at the hightemperature end of the plot than at the lowtemperature end, and the absolute value of the slope of the mortality vs. temperature relationship is smaller across the high-temperature range of the data.

Most interesting, perhaps, was the researchers' finding that "failure to control for respiratory epidemics and air pollution resulted in an overestimate of the impact of hot days by 50%," whereas "control for these factors had little impact on the estimates of effect of cold days." They note "most previous assessments of effects of heat waves on hot days have not controlled for air pollution or epidemics." In other words, the death-dealing effects of heat waves typically are not adjusted for concurrent effects of air pollution and respiratory epidemics, which often account for as much as half of the deaths attributed to hot temperatures; these two confounding factors do not appear to impact assessments of the effect of cold temperatures on deaths.

A prime example of the failure to account for concurrent air pollution effects on mortality occurred in the aftermath of the European heat wave of 2003. In analyzing the impact of air pollutants present during that episode in the United Kingdom, Stedman (2004) found 21–38% of the total excess deaths claimed to be due to high temperatures were actually the result of elevated concentrations of ozone and PM_{10} (particulate matter of diameter less than 10µm). Likewise, Fischer *et al.* (2004) determined 33–50% of the deaths attributed to the same heat wave in the Netherlands were caused by concurrent high ozone and PM_{10} concentrations. This factor is often unaccounted for in mortality-related studies of heat waves.

Deschenes and Moretti (2009) analyzed the relationship between weather and mortality, based on "data that include the universe of deaths in the United States over the period 1972-1988," in which they "match each death to weather conditions on the day of death and in the county of occurrence." This "highfrequency data and the fine geographical detail," they write, allow them "to estimate with precision the effect of cold and hot temperature shocks on mortality, as well as the dynamics of such effects." Most notably, the data allowed them to detect the existence or absence of a "harvesting effect." whereby the temperature-induced deaths are or are not subsequently followed by a drop in the normal death rate, which could compensate for the prior extreme temperature-induced deaths.

The two researchers say their results "point to widely different impacts of cold and hot temperatures on mortality." They discovered "hot temperature shocks are indeed associated with a large and immediate spike in mortality in the days of the heat wave," but "almost all of this excess mortality is explained by near-term displacement." As a result, "in the weeks that follow a heat wave, we find a marked decline in mortality hazard, which completely offsets the increase during the days of the heat wave," so "there is virtually no lasting impact of heat waves on mortality."

In the case of cold temperature days, they also found "an immediate spike in mortality in the days of the cold wave," but "there is no offsetting decline in the weeks that follow," so "the cumulative effect of one day of extreme cold temperature during a thirtyday window is an increase in daily mortality by as much as 10%." In addition, they write, "this impact of cold weather on mortality is significantly larger for females than for males," but "for both genders, the effect is mostly attributable to increased mortality due to cardiovascular and respiratory diseases."

Deschenes and Moretti state "the aggregate magnitude of the impact of extreme cold on mortality in the United States is large," noting it "roughly corresponds to 0.8% of average annual deaths in the United States during the sample period." They estimate "the average person who died because of cold temperature exposure lost in excess of ten years of potential life," whereas the average person who died because of hot temperature exposure likely lost no more than a few days or weeks of life.

Interestingly, Deschenes and Moretti report many people in the United States have taken advantage of these evident facts by moving "from cold northeastern states to warm southwestern states." Based on their findings, for example, they calculate "each year 4,600 deaths are delayed by the changing exposure to cold temperature due to mobility," and "3% to 7% of the gains in longevity experienced by the U.S. population over the past three decades are due to the secular movement toward warmer states in the West and the South, away from the colder states in the North."

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7.1.4 Other Regions

In Brazil, Gouveia *et al.* (2003) extracted daily counts of deaths from all causes except violent deaths and neonatal deaths up to one month of age, from Sao Paulo's mortality information system for the period 1991–1994. They analyzed this data for the effects of temperature on the age groups of less than 15 years (children), 15–64 years (adults), and 65 years or older (elderly), determining "change points" at which heat and cold effects started.

Interestingly, the authors found the change points for both heat- and cold-induced deaths were identical: 20°C. For each 1°C increase above this value for a given and prior day's mean temperature, they observed a 2.6% increase in deaths from all causes in children, a 1.5% increase in deaths from all causes in adults, and a 2.5% increase in deaths from all causes in the elderly. For each 1°C decrease below the 20°C change point, the effect was greater, with increases in deaths from all causes in children, adults, and the elderly registering 4.0%, 2.6%, and 5.5%, respectively. These cooling-induced death rates were 54%, 73%, and 120% greater than those attributable to warming.

Bi *et al.* (2008) used correlation and autoregressive integrated moving average regression analyses to derive relationships between various aspects of weather and mortality in the general population and elderly (65 years of age and older) of Brisbane, Australia, which they describe as having a subtropical climate, over the period 1986–1995. They found "death rates were around 50–80 per 100,000 in June, July, and August [winter], while they were around 30–50 per 100,000 in the rest of the year, including the summer," and "this finding applied both to the general population and to the elderly population, and to deaths from various causes."

In discussing their finding that "more deaths occurred in the winter than during other seasons of the year, although winter in Brisbane is very mild," the researchers note "it is understandable that more deaths would occur in winters in cold or temperate regions, but even in a subtropical region, as indicated in this study, a decrease in temperatures (in winters) may increase human mortality." The evidence continues to grow for extremes of cold leading to the deaths of many more people than extremes of heat, in both cold and warm climates.

Xu *et al.* (2013) preface their work by stating, "previous studies have found that high and cold temperatures increase the risk of childhood diarrhea," but much less is known about whether the within-day variation of temperature (i.e., the daily maximum minus minimum, or diurnal temperature range, DTR) has any effect on it. They write, "a Poisson generalized linear regression model combined with a distributed lag non-linear model was used to examine the relationship between diurnal temperature range and emergency department admissions for diarrhea among children under five years in Brisbane [Australia] from 1st January 2003 to 31st December 2009."

The six scientists found "a statistically significant relationship between diurnal temperature range and childhood diarrhea," such that "a 1°C increase in diurnal temperature range was associated with a 3% increase of Emergency Department Admissions for childhood diarrhea." They conclude, "as climate change continues. DTRs are likely to become more variable," and as a result, "the incidence of childhood diarrhea may increase." Other research suggests this is likely not to be the case: Karl et al. (1984, 1991) have shown during most of twentieth century global warming, daily minimum temperatures rose at a rate fully three times greater than daily maximum temperature over most of the world. DTRs actually declined over this period and must have led to significant decreases in emergency department admissions for diarrhea among children under five years of age, representing yet another positive health benefit of global warming.

Mrema *et al.* (2012) state "weather and climate changes are associated with a number of immediate and long-term impacts on human health that occur directly or indirectly, through mediating variables," but "few studies to date have established the empirical relationship between monthly weather and mortality in sub-Saharan Africa." Working with mortality data obtained from the Rufiji (Tanzania) Health and Demographic Surveillance System (RHDSS) for the period 1999 to 2010, Mrema *et al.* employed time-series Poisson regression models to estimate the association between monthly temperature—which ranges from 27.9 to 34.4°C in this tropical region—and mortality, adjusted for long-term trends, in three age groups (0–4, 5–59, 60+).

The four Tanzanian researchers report "mortality in all age groups peaked up at the mid of the year," which is "the time when the temperature is relatively lower compared to other periods of the year in Rufiji." If the monthly average temperature drops to a value of 24° C from the threshold, they state, "mortality will increase by 80.7%, 65.7% and 74% in age groups 0–4, 5–59 and over 60, respectively." Mrema *et al.* note "Rufiji's population is accustomed to a tropical climate and, like any other population, is exposed to cold temperatures relative to its average climate." Hence even in a warm, tropical region, relative cold kills far more people than relative heat.

Egondi *et al.* (2012) state, "many studies have established a link between weather (primarily temperature) and daily mortality in developed countries," but "little is known about this relationship in urban populations in sub-Saharan Africa." They employed mortality data from the Nairobi Urban Health and Demographic Surveillance System (NUHDSS) along with time-series models "to study the relationship between daily weather and mortality for a population of approximately 60,000 during the period 2003–2008."

"Overall," the six scientists report, "there are seasonal fluctuations in mortality, with the highest rates of death occurring during periods of relative cold." They also note "mortality risk over the year rises from the lowest mortality risk by about 40% in the 0-4 age group and by about 20% for all ages" in response to a drop in temperature. In addition, "the effects of low temperatures on mortality can last for days," and therefore, "although the world will get warmer in the future, the low temperature-related mortality is likely to remain an important concern." Such findings further demonstrate a change in the weather or shifting of the seasons to cooler conditions, rather than an equivalent increase in warmth, is typically the more deadly of the two types of temperature evolution, even in relatively warm places.

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7.1.5 Multiple Regions

Studying North Carolina (USA); South Finland, comprising all of Finland except the northern provinces of Oulu and Lapland; and Southeast England, comprising Greater London, Essex, Kent. Sussex, Hampshire, Surrey, Berkshire, Oxfordshire, Buckinghamshire, and Bedfordshire, Donaldson et al. (2003) determined the mean daily May-August 3°C temperature band in which deaths of people aged 55 and above were at a minimum. They compared the numbers of heat- and cold-related deaths at temperatures above and below this optimum temperature interval for each region and determined how heat-related deaths in the three areas changed between 1971 and 1997 in response to the 1.0°C temperature rise experienced in North Carolina over this period, starting from an initial temperature of 23.5°C; the 2.1°C temperature rise experienced in Southeast England, starting from an initial temperature of 14.9°C; and the unchanging 13.5°C temperature of South Finland.

Donaldson *et al.* report the 3°C temperature band at which mortality was at its local minimum was lowest for the coldest region (South Finland), highest for the warmest region (North Carolina), and in between for the "in between" region (Southeast England), indicating the populations of these three regions are somewhat acclimated to their respective thermal climates. They also found cold-related mortality was greater than heat-related mortality in each region. With respect to changes in heat-related mortality from 1971 to 1997, they determined for the coldest of the three regions (South Finland, where there was no change in temperature over the study period), heat-related deaths per million inhabitants in the 55-and-above age group declined from 382 to 99. In somewhat warmer Southeast England, where it warmed by 2.1°C over the study period, heat-related deaths per million of the at-risk age cohort declined, but only from 111 to 108. And in the warmest of the three regions (North Carolina, where mean daily May–August temperature rose by 1.0°C over the study period), corresponding heat-related deaths also fell from 228 to a mere 16 per million.

Such findings imply first that people can adapt to both warmer and cooler climates to some degree. Beyond that, local cooling tends to produce many more deaths than does local warming in all three of the areas studied. As for the dramatic decline in the number of heat-related deaths over a period of warming in the hottest area of the study (North Carolina), Donaldson et al. attribute this phenomenon to "the increase of air conditioning in the South Atlantic region of the U.S.A.," where they note "the percentage of households with some form of air conditioning in that region rose from 57% in 1978 to 72% in 1997." With respect to the declining heatrelated deaths in the other two regions, they say, "the explanation is likely to lie in the fact that both regions shared with North Carolina an increase in prosperity, which could be expected to increase opportunities for avoiding heat stress."

In a review article touching on multiple aspects of temperature-related deaths, Keatinge and Donaldson (2004) report "cold-related deaths are far more numerous than heat-related deaths in the United States, Europe, and almost all countries outside the tropics," noting coronary and cerebral thrombosis account for about half of all cold-related mortality. In describing the mechanisms behind this cold temperature-death connection, they say cold stress causes an increase in arterial thrombosis "because the blood becomes more concentrated, and so more liable to clot during exposure to cold." The sequence of events, as they describe it, is as follows: "the body's first adjustment to cold stress is to shut down blood flow to the skin to conserve body heat," which "produces an excess of blood in central parts of the body," and to correct for this effect, "salt and water are moved out from the blood into tissue spaces," leaving behind "increased levels of red cells, white cells, platelets and fibrinogen" that lead to increased viscosity of the blood and a greater risk of clotting. In addition, cold stress "tends to suppress immune

responses to infections," and respiratory infections typically "increase the plasma level of fibrinogen," which also "contributes to the rise in arterial thrombosis in winter."

Keatinge and Donaldson note "cold spells are closely associated with sharp increases in mortality rates," and "deaths continue for many days after a cold spell ends." On the other hand, "increased deaths during a few days of hot weather are followed by a lower than normal mortality rate," because "many of those dying in the heat are already seriously ill and even without heat stress would have died within the next 2 or 3 weeks."

Keatinge and Donaldson state, "since heat-related deaths are generally much fewer than cold-related deaths, the overall effect of global warming on health can be expected to be a beneficial one." As an example, and even including the heat-harvesting of naturally expected deaths, they report "the rise in temperature of 3.6°F expected over the next 50 years would increase heat-related deaths in Britain by about 2,000 but reduce cold-related deaths by about 20,000." Keatinge and Donaldson conclude, "the overall effect of global warming on health can be expected to be a beneficial one."

Hajat et al. (2005) analyzed the history of heatwave-related deaths in three cities of contrasting wealth (defined as gross national income per capita)-Delhi (India), Sao Paulo (Brazil), and London (England)-based on daily numbers of nonviolent deaths derived from mortality registries for the four-year period January 1991 to December 1994, examining "time-series of daily mortality data in relation to daily ambient temperature using Poisson models and adjusting for season, relative humidity, rainfall, particulate air pollution, day of the week and holidays," and using "unconstrained public distributed lag models to identify the extent to which heat-related [death] excesses were followed by The latter phenomenon deficits." (mortality displacement) arises when people who die during heat waves would have died shortly thereafter even in the absence of the elevated warmth.

For each city, an increase in all-cause mortality was observed for same- and previous-day temperatures greater than 20°C, with excess deaths being greatest in Delhi and smallest in London. In Delhi, the excess of deaths persisted for three weeks, whereas in London it prevailed for only two days and was followed by deficits that led to the sum of the two effects being zero by day 11. In Sao Paulo, as might have been expected, the pattern of deaths was intermediate between these two extremes. Summed over the course of 28 days, the risk of death associated with heat stress was 2.4% per degree greater than 20°C in Delhi, 0.8% in Sao Paulo, and negative 1.6% in London. These findings led Hajat *et al.* to conclude, "populations in low-income countries where life-threatening infections are still common may have the greatest vulnerability to the effects of heat," and "those most susceptible to heat are likely to remain susceptible if there is not due attention paid to infectious disease, diarrheal illness, and other major causes of early mortality in these poor populations."

Byremo *et al.* (2006) studied the effects of temperature on atopic eczema, "a chronic inflammatory skin disease characterized by itching, lesions and lichenification," especially at "the flexure sites of the major joints of the upper and lower extremities." The pain and itching associated with the disease, as they describe it, "may cause depressive symptoms, social isolation and reduced self-perception," lowering the quality of life in children and their caretakers. They report epidemiological studies suggest climate influences the disease's prevalence, noting "atopic eczema has been reported worldwide to be positively associated with latitude and negatively with temperature (Weiland *et al.*, 2004)."

Byremo et al. transported 30 children, 4 to 13 years of age with severe atopic eczema, from their homes in Norway to the Canary Islands, where they stayed for four weeks before returning, and 26 similarly infected children of the same age group staved at home in Norway the entire time. All were evaluated for various disease characteristics at the start of the study, at the conclusion of the group-of-30's four-week period of stay in the Canary Islands, and three months after the 30 children left the islands to return home to Norway. The specific disease parameters employed in the evaluation were the Scoring of Atopic Dermatitis, the Children's Dermatology Life Quality Index, skin colonization by Staphylococcus aureus, and pharmacological skin treatment.

Noting temperatures during the children's stay in the Canary Islands were much higher than those in Norway, Byremo et al. report the children's time in the warmer climate significantly reduced the severity of atopic eczema, and the youths improved in severity of eczema, quality of life, and bacterial skin culture, which was reflected in a reduction in the use of topical and steroids. antihistamines, topical antibiotics. These positive changes were observed at the conclusion of the four-week stav in the Canary Islands as well as back home in Norway three months later. The researchers state the four weeks spent in the

Canary Islands "led to a lasting improvement for the children," whereas "the control group did not show similar improvement."

Although greater exposure to sunlight and the effect of regularly bathing in seawater, such as the children did at the Canary Islands, likely played positive roles in reducing the severity of their atopic eczema, the results of this study are harmonious with the worldwide negative correlation that prevails between eczema and temperature, suggesting global warming may prove beneficial to people unfortunate enough to suffer from it.

According to Young and Kakinen (2010), "Arctic populations, especially indigenous people, could be considered as 'vulnerable,' because their health status generally shows disparities when compared to the national or more southern populations," and "it is not known if the harsh climate, and especially cold temperatures, could be a contributing or causative factor of the observed health inequalities." To shed some light on this subject, they determined "mean January and July temperatures ... for 27 Arctic regions based on weather station data for the period 1961– 1990 and their association with a variety of health outcomes assessed by correlation and multiple linear regression analyses."

The two researchers report mean January temperature correlated negatively with several health outcomes, including infant mortality rate, agestandardized mortality rates (all causes, respiratory, cancer, injuries), perinatal mortality rate, and tuberculosis incidence rate, but it correlated positively with life expectancy. That is to say, as mean January temperature rose, life expectancy at birth rose as well, whereas the undesirable health metrics (such as mortality and disease incidence) declined. They report, "for every 10°C increase in mean January temperature, the life expectancy at birth among males increased by about six years," whereas "infant mortality rate decreased by about four deaths per thousand live births." Young and Kakinen conclude the cold climate of the Arctic is "significantly associated with higher mortality" and "should be recognized in public health planning," noting "within a generally cold environment, colder climate results in worse health."

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7.2 Cardiovascular Disease

• Global warming is reducing the incidence of cardiovascular diseases related to low temperatures and wintry weather by a much greater degree than it increases the incidence of cardiovascular diseases associated with high temperatures and summer heat waves.

According to IPCC, global warming will pose numerous challenges to human health, including premature death due to heat-induced cardiovascular problems. This section examines the results of studies that dealt with this important subject in the past decade or so.

Enquselassie *et al.* (1993) investigated the effects of extremes of temperature and rainfall, as well as intermediate levels, on the number of coronary events, both fatal and nonfatal, reported in the Hunter Region of New South Wales, Australia, located on the east coast of the country about 150 km north of Sydney, for the five-year period 1 July 1985 to 30 June 1990. "Daily temperature and rainfall," they write, "were taken as indicators of acute effects of weather and the month when an event occurred was used to indicate longer-term or seasonal effects."

Regarding seasonal effects, Enquselassie *et al.* report "fatal coronary events and non-fatal definite myocardial infarction were 20–40% more common in winter and spring than at other times of year." As to daily temperature effects, they found "rate ratios for deaths were significantly higher for low temperatures," noting "on cold days coronary deaths were up to 40% more likely to occur than at moderate temperatures." Effects of humidity and rainfall were negligible. The authors conclude their data "support the theory of increased risk of coronary mortality when temperatures are unusually low," and "avoiding temperature extremes could contribute to reduction in annual peaks in coronary events," which occur during the colder part of the year.

Thanks to Norwegian law, which requires all deaths be examined by a physician who diagnoses cause and reports it on the death certificate, Nafstad *et al.* (2001) were able to examine the effects of temperature on mortality due to all forms of cardiovascular disease for citizens of the country's capital over the period 1990 to 1995. Their analysis showed the average daily number of cardiovascular-related deaths was 15% higher in the winter months (October–March) than in the summer months (April–September), leading them to conclude "a milder climate would lead to a substantial reduction in average daily number of deaths."

Research in Israel conducted by Green *et al.* (1994) revealed that between 1976 and 1985, mortality from cardiovascular disease was higher by 50% in mid-winter than in mid-summer, both in men and in women, as well as in different age groups. Summer temperatures in the Negev, where much of the work was conducted, often exceeded 30°C, whereas winter temperatures typically did not drop below 10°C. These findings have been substantiated by several other Israeli studies, including those reviewed by Behar (2000), who wrote "most of the recent papers on this topic have concluded that a peak of sudden cardiac death, acute myocardial infarction and other cardiovascular conditions is usually observed in low temperature weather during winter."

Evidence of a seasonal variation in cardiacrelated mortality also has been noted in the relatively mild climate of southern California in the United States. In a study of all 222,265 death certificates issued by Los Angeles County for deaths caused by coronary artery disease from 1985 through 1996, Kloner et al. (1999) found death rates in December and January were 33% higher than those observed in June through September. Likewise, based on a study of the Hunter region of New South Wales, Australia, which covered 1 July 1985 to 30 June 1990, Enquselassie et al. (1993) determined "fatal coronary events and non-fatal definite myocardial infarction were 20-40% more common in winter and spring than at other times of year." With respect to daily temperature effects, they found "rate ratios for deaths were significantly higher for low temperatures," noting "on cold days coronary deaths were up to 40% more likely to occur than at moderate temperatures."

Hajat and Haines (2002) set out to determine whether the number of cardiovascular-related doctor visits by the elderly bore a similar relationship to cold temperatures. Based on data obtained between January 1992 and September 1995 for registered patients aged 65 and older from several practices in London, England, they found the number of general practitioner consultations was higher in the coolseason months (October–March) than in the warmseason months (April–September) for all cardiovascular diseases.

In a study of both "hot" and "cold" cities in the United States-where Atlanta, Georgia; Birmingham, Alabama; and Houston, Texas comprised the "hot" group, and Canton, Ohio; Chicago, Illinois; Colorado Springs, Colorado; Detroit, Michigan; Minneapolis-St. Paul, Minnesota; New Haven, Connecticut; Pittsburgh, Pennsylvania; and Seattle and Spokane, Washington comprised the "cold" group-Braga et al. (2002) determined both the acute effects and lagged influence of temperature on cardiovascularrelated deaths. They found in the hot cities neither hot nor cold temperatures had much impact on mortality related to cardiovascular disease (CVD). In the cold cities, on the other hand, both high and low temperatures were associated with increased CVD deaths. The effect of cold temperatures persisted for days, whereas the effect of high temperatures was restricted to the day of the death or the day before. For all CVD deaths, the hot-day effect was five times smaller than the cold-day effect. In addition, the hotday effect included some "harvesting," where Braga et al. observed a deficit of deaths a few days later, which they did not observe for the cold-day effect.

Gouveia *et al.* (2003) determined the number of cardiovascular-related deaths in adults aged 15–64 years of age in Sao Paulo, Brazil over the period 1991–1994 increased by 2.6% for each 1°C decrease in temperature below 20°C, while they found no evidence for heat-induced deaths due to temperatures rising above 20°C. In the elderly (65 years of age and above), a 1°C warming above 20°C led to a 2% increase in deaths, but a 1°C cooling below 20°C led to a 6.3% increase in deaths, more than three times as many cardiovascular-related deaths due to cooling than to warming in the elderly.

For the period 1974–1999, McGregor *et al.* (2004) obtained data on ischaemic heart disease (IHD) and temperature for five English counties aligned on a north-south transect (Tyne and Wear,

West Yorkshire, Greater Manchester, West Midlands, and Hampshire) and analyzed them for relationships between the two parameters. They determined "the seasonal cycles of temperature and mortality are inversely related," and "the first harmonic accounts for at least 85% (significant at the 0.01 level) of the variance of temperature and mortality at both the climatological and vearly time scales." They also report "years with an exaggerated mortality peak are associated with years characterized by strong temperature seasonality," and "the timing of the annual mortality peak is positively associated with the timing of the lowest temperatures." McGregor et al. explain, "frequent exposure to cold causes a rise in IHD risk factors (Lloyd, 1991) through increasing blood pressure and viscosity, vasoconstriction, heart rate and angina (Morgan and Moran, 1997)."

Chang et al. (2004) analyzed data from the World Health Organization (WHO) Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception (WHO, 1995) to determine the effects of monthly mean temperature on rates of hospitalization for arterial stroke and acute myocardial infarction (AMI) among young women aged 15-49 from 17 countries in Africa, Asia, Europe, Latin America, and the Caribbean. These efforts revealed "among young women from 17 countries, the rate of hospitalized AMI, and to a lesser extent stroke, was higher with lower mean environmental air temperature." They report, "on average, a 5°C reduction in mean air temperature was associated with a 7 and 12% increase in the expected hospitalization rates of stroke and AMI, respectively." They also note "the findings of an inverse association between mean air temperature and hospitalization rate of AMI in this study are in agreement with several other studies," citing Douglas et al. (1990), Douglas et al. (1991), Mackenbach et al. (1992). Douglas et al. (1995). Seto et al. (1998), Danet et al. (1999), and Crawford et al. (2003). Finally, they note, "lagging the effects of temperature suggested that these effects were relatively acute, within a period of a month."

Bartzokas *et al.* (2004) "examined the relationship between hospital admissions for cardiovascular (cardiac in general including heart attacks) and/or respiratory diseases (asthma etc.) in a major hospital in Athens [Greece] and meteorological parameters for an 8-year period." Over the year, "there was a dependence of admissions on temperature" and low temperatures were "responsible for a higher number of admissions," they found. Specifically, "there was a decrease of cardiovascular or/and respiratory events from low to high values [of

temperature], except for the highest temperature class in which a slight increase was recorded."

Nakaji et al. (2004) evaluated seasonal trends in deaths in Japan due to various diseases, using nationwide vital statistics from 1970 to 1999 and recorded weather data, specifically, mean monthly temperature. The nine researchers note Japan has "bitterly cold winters," and their analysis indicates the numbers of deaths due to infectious and parasitic diseases including tuberculosis, respiratory diseases including pneumonia and influenza, diabetes, digestive diseases, and cerebrovascular and heart diseases rise to a maximum during that cold time of year. Of the latter two categories, they found peak mortality rates due to heart disease and stroke were one-and-a-half to two times greater in winter (January) than at the time of their yearly minimums (August and September). They conclude, in order "to reduce the overall mortality rate and to prolong life expectancy in Japan, measures must be taken to reduce those mortality rates associated with seasonal differences." They also note, "it has long been recognized that cold temperature acts as a trigger for coronary events," and "major infectious diseases are epidemic in winter."

Hence, to achieve the scientists' stated objectives, it is necessary to bring about a "reduction in exposure to cold environments," as they put it, which is precisely what global warming does, and what it does best by warming more in winter than in summer, as Nakaji *et al.* demonstrate to be the case in Japan, where winter warming over the past 30 years was twice as great as it was during the rest of the year.

In Sao Paulo, Brazil, where 12,007 deaths were observed from 1996 to 1998, Sharovsky et al. (2004) investigated "associations between weather (temperature, humidity and barometric pressure), air pollution (sulfur dioxide, carbon monoxide, and inhalable particulates), and the daily death counts attributed to myocardial infarction." Their efforts revealed "a significant association of daily temperature with deaths due to myocardial infarction (p < 0.001), with the lowest mortality being observed at temperatures between 21.6 and 22.6°C." For all practical purposes, however, their data showed little variation in death rates from 18°C to just over 25°C, with the latter representing the typical upper limit of observed temperature in Sao Paulo, which is located on the Tropic of Capricorn at an altitude of 800 m. As mean daily temperature dropped below 18°C, however, death rates rose in essentially linear fashion to attain a value at 12°C (the typical lower limit of observed temperature in Sao Paulo) more than 35%

greater than the minimum baseline value registered between 21.6 and 22.6°C.

Sharovsky *et al.* say their findings "demonstrated a strong association between daily temperature and myocardial infarction in Sao Paulo, Brazil," which suggests "an acclimatization of the population to the local climate occurs and that myocardial infarction deaths peak in winter not only because of absolute low temperature but possibly secondary to a decrease relative to the average annual temperature." This indeed must be true, for deaths due to heart attacks are consistently greater in winter than in summer, as they write, "across many regions of the world (Marshall *et al.*, 1998; Douglas *et al.*, 1991; Seto *et al.*, 1998; Sheth *et al.*, 1999)."

Kovats *et al.* (2004) analyzed patterns of temperature-related hospital admissions and deaths in Greater London during the mid-1990s. For the three-year period 1994–1996, cardiovascular-related deaths were approximately 50% greater during the coldest part of the winter than during the peak warmth of summer, whereas respiratory-related deaths were nearly 150% greater in the depths of winter cold than at the height of summer warmth. Also, with respect to heat waves, the mortality impact of the notable heat wave of 29 July to 3 August 1995 was so tiny it could not be discerned among the random scatter of plots of three-year-average daily deaths from cardiovascular and respiratory problems versus day of year.

In a review article published in the *Southern Medical Journal*, Keatinge and Donaldson (2004) begin with a clear declaration of the relative dangers of heat and cold for human mortality, writing, "coldrelated deaths are far more numerous than heatrelated deaths in the United States, Europe, and almost all countries outside the tropics, and almost all of them are due to common illnesses that are increased by cold."

Keatinge and Donaldson report coronary and cerebral thrombosis account for about half of all coldrelated deaths, and respiratory diseases account for approximately half of the rest. They say cold stress causes an increase in arterial thrombosis "because the blood becomes more concentrated, and so more liable to clot during exposure to cold." As they describe it, "the body's first adjustment to cold stress is to shut down blood flow to the skin to conserve body heat," which "produces an excess of blood in central parts of the body," and to correct for this effect, "salt and water are moved out from the blood into tissue spaces," leaving behind "increased levels of red cells, white cells, platelets and fibrinogen" that lead to increased viscosity of the blood and a greater risk of clotting.

As to respiratory-related deaths, the British scientists report the infections that cause them spread more readily in cold weather because people "crowd together in poorly ventilated spaces when it is cold." In addition, they say "breathing of cold air stimulates coughing and running of the nose, and this helps to spread respiratory viruses and bacteria." The "train of events leading to respiratory deaths," they continue, "often starts with a cold or some other minor infection of the upper airways," which "spreads to the bronchi and to the lungs," whereupon "secondary infection often follows and can lead to pneumonia." They also note cold stress "tends to suppress immune responses to infections," and respiratory infections typically "increase the plasma level of fibrinogen, and this contributes to the rise in arterial thrombosis in winter."

Keatinge and Donaldson also note "cold spells are closely associated with sharp increases in mortality rates," and "deaths continue for many days after a cold spell ends." On the other hand, they report, "increased deaths during a few days of hot weather are followed by a lower than normal mortality rate," because "many of those dying in the heat are already seriously ill and even without heat stress would have died within the next 2 or 3 weeks."

With respect to the implications of global warming for human mortality, Keatinge and Donaldson state "since heat-related deaths are generally much fewer than cold-related deaths"—and, it should be noted, consist primarily of deaths that typically would have occurred shortly even without excess heat—"the overall effect of global warming on health can be expected to be a beneficial one." They report, "the rise in temperature of 3.6°F expected over the next 50 years would increase heat-related deaths in Britain by about 2,000 but reduce cold-related deaths by about 20,000."

Keatinge and Donaldson concluded, "even in climates as warm as southern Europe or North Carolina [USA], cold weather causes more deaths than hot weather." They report "global warming will reduce this at first," but "the improvement is not likely to continue without action to promote defenses against cold." They report "people in regions with mild winters become careless about cold stress, protect themselves less effectively against cold, and generally have more winter deaths than people in colder regions," noting "climatic warming therefore calls for action to control cold stress as well as heat stress," and stating if appropriate precautions are taken, "rising temperatures could reduce overall mortality rates." Consequently, they conclude, "the overall effect of global warming on health can be expected to be a beneficial one."

McGregor (2005) noted "anomalous cold stress can increase blood viscosity and blood pressure due to the activation of the sympathetic nervous system which accelerates the heart rate and increases vascular resistance (Collins et al., 1985: Jehn et al., 2002: Healy, 2003; Keatinge et al., 1984; Mercer, 2003; Woodhouse et al., 1993)," while further noting "anomalously cold winters may also increase other risk factors for heart disease such as blood clotting or fibrinogen concentration, red blood cell count per volume and plasma cholesterol." He conducted an analysis to determine whether there was any association between the level of IHD mortality in three English counties (Hampshire, West Midlands, and West Yorkshire) and the winter-season North Atlantic Oscillation (NAO), which exerts a fundamental control on the nature of winter climate in Western Europe, focusing on the winters of 1974-1975 through 1998–1999.

McGregor found "generally below average monthly and all-winter IHD mortality is associated with strong positive values of the monthly or winter climate index which indicates the predominance of anomalously warm moist westerly flows of air over England associated with a positive phase of the NAO." At the other extreme, he found "winters with elevated mortality levels ... have been shown to be clearly associated with a negative NAO phase and anomalously low temperatures," adding "the occurrence of influenza ... helps elevate winter mortality above that of summer."

Carder et al. (2005) used generalized linear Poisson regression models to investigate the relationship between outside air temperature and deaths due to all non-accident causes in the three largest cities of Scotland (Glasgow, Edinburgh, and Aberdeen) between January 1981 and December 2001. They observed "an overall increase in mortality as temperature decreases," which "appears to be steeper at lower temperatures than at warmer temperatures," while "there is little evidence of an increase in mortality at the hot end of the temperature range." They also report "the observed relation between cold temperature and mortality was typically stronger among the elderly," and "cold temperature effects on mortality persist with lag periods of beyond two weeks." The seven scientists found, for temperatures below 11°C, a 1°C drop in the daytime mean temperature on any one day was associated with an increase in cardiovascular-caused mortality of 3.4% over the following month. At any season of the year a decline in air temperature in the major cities of Scotland leads to increases in deaths due to cardiovascular causes, whereas there is little or no such increase in mortality associated with heat waves.

Cagle and Hubbard (2005) examined the relationship between temperature and cardiac-related deaths in King County, Washington (USA) over the period 1980-2000 using Poisson regression analysis, based on information provided by the Washington State Department of Health on out-of-hospital deaths of all adults over the age of 54, plus historical meteorological data obtained from the National Climate Data Center for the Seattle-Tacoma International Airport. They determined there was an average of 2.86 cardiac-related deaths per day for all days when the maximum temperature fell within the broad range of 5-30°C. For days with maximum temperatures less than 5°C, the death rate rose by 15% to a mean value of 3.30, whereas on days with maximum temperatures greater than 30°C, death rates did not rise at all, actually dropping by 3% to a mean value of 2.78. In addition, "the observed association between temperature and death rate is not due to confounding by other meteorological variables," and "temperature continues to be statistically significantly associated with death rate even at a 5-day time lag."

Cagle and Hubbard describe a number of human haematological changes that occur upon exposure to cold, including a decrease in blood plasma volume (Bass and Henschel, 1956; Chen and Chien, 1977; Fregley, 1982; Collins et al., 1985) that is accompanied by "a sympathetic nervous system reflex response to cold-induced stress (LeBlanc et al., 1978; Collins et al., 1985; LeBlanc, 1992)" and "an increase in packed cell volume due to increased numbers of red cells per unit volume (Keatinge et al., 1984), increased platelet counts and platelet volume (Finkel and Cumming, 1965; Keatinge et al., 1984), increased whole blood viscosity (Keatinge et al., 1984), increased serum lipid levels (Keatinge et al., 1984; Woodhouse et al., 1993; Neild et al., 1994), and increased plasma fibrinogen and factor VII clotting activity values (Keatinge et al., 1984; Woodhouse et al., 1994)." These haemodynamic and vasoconstrictive factors combine "to produce what Muller et al. (1994) refer to as 'acute risk factors' that may trigger a cardiac event." Vasoconstriction and concomitant increases in central blood volume and systolic blood pressure, for example, "put additional workload on the heart which may lead to increased arrhythmias (Amsterdam et al., 1987), decreased thresholds for angina and abnormal myocardial

contractions (De Lorenzo *et al.*, 1999), as well as increasing the risk of dislodging a vulnerable plaque which could lead to thrombosis (Muller *et al.*, 1994)," which "may occur through increased cardiac filling pressure and stroke volume which in turn increases cardiac oxygen requirements while lessening cardiac access to oxygen (Muza *et al.*, 1988; De Lorenzo *et al.*, 1999)." In addition, the Washington researchers report "greater blood viscosity also works to increase the load on the heart through greater resistance to flow (Frisancho, 1993) and increasing blood pressure (Keatinge *et al.*, 1984)."

Tam et al. (2009) employed daily mortality data for the years 1997 to 2002, obtained from the Hong Kong Census and Statistics Department, to examine the association between diurnal temperature range (DTR = daily maximum temperature minus dailyminimum temperature) and cardiovascular disease among the elderly (people aged 65 and older). They report "a 1.7% increase in mortality for an increase of 1°C in DTR at lag days 0-3" and describe these results as being "similar to those reported in Shanghai." The four researchers state "a large fluctuation in the daily temperature-even in a tropical city like Hong Kong-has a significant impact on cardiovascular mortality among the elderly population." In addition, the DTR has declined significantly over many parts of the world as mean global temperature has risen over the past several decades (Easterling et al., 1997), perhaps another reason why colder temperatures are a much greater risk to human life than are warmer temperatures.

Working in the nine urban districts of Shanghai, China, Cao et al. (2009) used time-series and casecrossover approaches to assess the relationship between DTR and coronary heart disease (CHD) deaths that occurred between 1 January 2001 and 31 December 2004, based on mortality data for elderly (66 years of age or older) people, obtained from the Shanghai Municipal Center of Disease Control and Prevention, and temperature data they obtained from a fixed-site station in the Xuhui District of Shanghai. They adjusted the data to account for the mortality impacts of long-term and seasonal trends in CHD mortality, day of week, temperature, relative humidity, and concomitant atmospheric concentrations of PM₁₀, SO₂, NO₂, and O₃, which they from the Shanghai Environmental obtained Monitoring Center. They found "a 1°C increase in DTR (lag = 2) corresponded to a 2.46% increase in CHD mortality on time-series analysis, a 3.21% increase on unidirectional case-crossover analysis. and a 2.13% increase on bidirectional case-crossover analysis," and "the estimated effects of DTR on CHD mortality were similar in the warm and cool seasons." The seven scientists conclude their "data suggest that even a small increase in DTR is associated with a substantial increase in deaths due to CHD."

Employing a generalized additive statistical model that blends the properties of generalized linear models with additive models. Bayentin et al. (2010) analyzed the standardized daily hospitalization rates for ischemic heart disease (IHD) and their relationship with climatic conditions up to two weeks prior to the day of admission-controlling for time trends, day of the season, and gender-to determine the short-term effects of climate conditions on the incidence of IHD over the 1989-2006 time period for 18 health regions of Quebec. The authors report, "a decline in the effects of meteorological variables on IHD daily admission rates was observed over the period of 1989-2006." This observation, they write, "can partly be explained by the changes in surface air temperature," which they describe as warming "over the last few decades," as is further described by Bonsal et al. (2001) and Zhang et al. (2000) for the twentieth century portion of the study's duration. In addition, they note, "winters have been steadily warmer" while "summers have yet to become hotter for most regions," another beneficial characteristic of the warming experienced over most of the planet throughout the latter part of the twentieth century (Easterling et al., 1997). The six scientists also report what they call their "counter-intuitive finding," that "cold temperatures resulted in a protective effect for women except for most Northern regions."

Toro *et al.* (2010) note "several studies have demonstrated that cardiovascular mortality has a seasonal distribution (Arntz *et al.*, 2000; Weerasinghe *et al.* 2002; Nakaji *et al.*, 2004; Kloner, 2006)" and "the relationship between cold weather and ischemic heart disease mortality is well established (Vuori, 1987; Gyllerup *et al.*, 1993; Gyllerup, 2000)." They state "cold temperature may be an important factor in bringing on the onset of life-threatening cardiac events, even in regions with relatively mild winters," citing Cagle and Hubbard (2005).

Working with data on 7,450 cardiovascularrelated deaths that occurred in Budapest, Hungary between 1995 and 2004, where the deceased were "medico-legally autopsied," Toro *et al.* sought potential relationships between daily maximum, minimum, and mean temperature, air humidity, air pressure, wind speed, global radiation, and daily numbers of the heart-related deaths.

The six Hungarian scientists report and restate

their primary finding numerous times throughout their paper, writing, "both the maximum and the minimum daily temperatures tend to be lower when more death cases occur in a day," "on the days with four or more death cases, the daily maximum and minimum temperatures tend to be lower than on days without any cardiovascular death events," "the largest frequency of cardiovascular death cases was detected in cold and cooling weather conditions," "we found a significant negative relationship between temperature and cardiovascular mortality," "the analysis of 6-hour change of air pressure suggests that more acute or chronic vascular death cases occur during increasing air pressure conditions (implying cold weather fronts)." "we found a high frequency of cardiovascular death in cold weather," "a significant negative relationship was detected between daily maximum [and] minimum temperature[s] and the number of sudden cardiovascular death cases," and "a significant negative correlation was detected between daily mean temperature and cardiovascular mortality." In a summary statement regarding their work, Toro et al. write, "with these analyses, we confirmed the results of other studies (Donaldson et al., 1998; Gyllerup, 2000; Mercer, 2003) that mortality was in inverse relation to air temperature."

Bhaskaran et al. (2010) explored the short-term relationship between ambient temperature and risk of heart attacks (myocardial infarction) in England and Wales by analyzing daily time series data from 15 metropolitan areas. The data covered 84,010 hospital admissions from 2003-2006. They found a broadly linear relationship between temperature and heart attacks that was well characterized by log-linear models without a temperature threshold, such that each 1°C reduction in daily mean temperature was associated with a 2.0% cumulative increase in risk of myocardial infarction over the current and following 28 days. They also report heat had no detrimental effect, as an increased risk of myocardial infarction at higher temperatures was not detected. They found adults aged 75-84 and those with previous coronary heart disease seemed more vulnerable to the effects of cold than other age groups (P for interaction 0.001 or less in each case), whereas those taking aspirin were less vulnerable (P for interaction 0.007).

Kysely *et al.* (2011) write, "in the Czech Republic, mortality associated with heat waves (Kysely, 2004; Kysely and Kriz, 2008) and cold spells (Kysely *et al.*, 2009) has been examined," but they note, "previous studies were based on different definitions and approaches which did not allow for a comparative analysis.

Working with a nationwide database of daily mortality records that cover the 21-year period 1986-2006—which, in their words, "encompasses seasons with the hottest summers on record (1992, 1994, 2003) as well as several very cold winters (1986/87, 1995/96, 2005/06)"-Kysely et al. compared the effects of hot and cold periods on cardiovascular mortality using analogous definitions for heat waves and cold spells based on quantiles of daily average temperature anomalies and did not incorporate any location-specific threshold, while excluding periods characterized by epidemics of influenza and acute respiratory infections that occur primarily in winter and are also responsible for many deaths. The four Czech scientists report "both hot and cold spells are associated with significant excess cardiovascular mortality," but "the effects of hot spells are more direct (unlagged) and typically concentrated in a few days of a hot spell, while cold spells are associated with indirect (lagged) mortality impacts persisting after a cold spell ends." Although they report "the mortality peak is less pronounced for cold spells," they determined "the cumulative magnitude of excess mortality is larger for cold than hot spells."

With respect to gender differences, the researchers found a "much larger excess mortality of females in hot spells and more lagged effects in females than males associated with cold spells." With respect to age, they report "effects of hot spells have a similar temporal pattern in all age groups but much larger magnitude in the elderly," whereas in the case of cold spells, "relative excess mortality is largest in the middle-aged population (25–59 years)."

Kysely *et al.* (2011) conclude, "in the context of climate change, substantial reductions in cold-related mortality are very likely in mid-latitudinal regions, particularly if the increasing adaptability of societies to weather is taken into account (cf. Christidis *et al.*, 2010)," and "it is probable that reductions in cold-related mortality will be more important than possible increases in heat-related mortality."

Lim *et al.* (2012) state, "with the increasing concern directed at climate change, temperaturerelated environment variables have been studied as risk factors for cardiovascular and respiratory diseases, especially in European, Australian, and US cities," noting "in addition to heat or cold waves, diurnal temperature range (DTR) has been suggested as a predictor of mortality (Curriero *et al.*, 2002) and was, in fact, found to be a risk factor for human health." Focusing on the four largest cities of Korea the populations of which ranged from 2.5 to 9.8 million (Seoul, Incheon, Daegu, and Busan)— Lim *et al.* obtained daily hospital admission information pertaining from the countrywide database of the Korea National Health Insurance Corporation, which covers 97% of Korea's population. They assessed the effects of increasing DTR on hospital admissions for the most common cardiovascular and respiratory diseases in those four cities for the period 2003–2006, employing two statistical approaches: "a Poisson generalized linear model (GLM) and a temperature-matched case-crossover (CC) design (Basu *et al.*, 2005)."

According to the three South Korean researchers, the data showed "the area-combined effects of DTR on cardiac failure and asthma were statistically significant," and the DTR effects on asthma admissions were greater for the elderly (75 years or older) than for the non-elderly group. "In particular," they write, "the effects on cardiac failure and asthma were significant with the percentage change of hospital admissions per 1°C increment of DTR at 3.0% and 1.1%, respectively."

Because the global warming of the past several decades has been associated with a decrease in DTR (global warming is predominantly caused by an increase in daily minimum temperature), it likely has helped to significantly reduce hospital admissions for cardiac failure and asthma in the larger cities of Korea and around the world. Lim et al. note DTR effects on nonaccidental, cardiovascular, and respiratory mortality or emergency admissions have been studied in a number of Asian countries, citing Cao et al. (2009), Chen et al. (2007), Kan et al. (2007), Liang et al. (2008), Liang et al. (2009), Lim et al. (2012), Shinkawa et al. (1990), Song et al. (2008), and Tam et al. (2009). Each of these studies, Lim et al. note, "reported a 1 to 2% increase in mortality risk per 1°C increase of DTR."

Wanitschek *et al.* (2013) note "previous studies reported an association of cold weather conditions with an excess incidence of acute coronary syndromes (ACS) according to hospital discharge reports (Eurowinter Group, 1997; Spencer *et al.*, 1998; Danet *et al.*, 1999; Kloner *et al.*, 1999; Dilaveris *et al.*, 2006)." However, they write, "whether these epidemiologic facts also translate into a significantly different rate of acute coronary angiographies between two consecutive winters characterized by a dramatic temperature increase is less clear."

Noting the 2005/2006 winter was very cold, whereas the 2006/2007 winter was extraordinarily warm, Wanitschek *et al.* studied the cases of patients who were suffering acute myocardial infarctions and had been referred to the University Clinic of Internal

Medicine III (Cardiology) at Innsbruck Medical University, Tyrol, Austria, for coronary angiography (CA). They compared the patients' risk factors and inhospital mortality rates between these two consecutive winters, the latter of which was 7.5°C warmer than the former. The two winters saw nearly identical CA cases (987 vs. 983). According to the six Austrian researchers, 12.9% of the CA cases in the colder winter were acute, while 10.4% of the cases in the warmer winter were acute. Diagnoses of STEMI (ST Elevation Myocardial Infarction) as an indication of acute CA were 74.in the colder winter 0 vs. 62.7% in the warmer. Wanitschek et al. conclude. "the average temperature increase of 7.5°C from the cold to the warm winter was associated with a decrease in acute coronary angiographies, in particular due to a lower incidence of STEMI referred for primary percutaneous intervention."

Vasconcelos et al. (2013) studied the healthrelated effects of a daily human-biometeorological index known as the Physiologically Equivalent Temperature or PET, which is based on the input parameters of air temperature, humidity, mean radiant temperature, and wind speed, as employed by Burkart et al. (2011), Grigorieva and Matzarakis (2011), and Cohen et al. (2012), focusing their attention on Lisbon and Oporto Counties in Portugal over the period 2003-2007. The five Portuguese researchers report there was "a linear relationship between daily mean PET, during winter, and the risk of myocardial infarction, after adjustment for confounding factors," thus confirming "the thermal environment, during winter, is inversely associated with acute myocardial infarction morbidity in Portugal." They observed "an increase of 2.2% of daily hospitalizations per degree fall of PET, during winter, for all ages." In Portugal and many other countries where low winter temperatures "are generally under-rated compared to high temperatures during summer periods," Vasconcelos et al. conclude cold weather is "an important environmental hazard" that is much more deadly than the heat of summer.

These several studies clearly demonstrate global warming is beneficial to humanity, reducing the incidence of cardiovascular diseases related to low temperatures and wintry weather by a much greater degree than it increases the incidence of cardiovascular diseases associated with high temperatures and summer heat waves.

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7.3 Respiratory Disease

• The adverse health impacts of cold temperatures, especially with respect to respiratory health, are more significant than those of high temperatures in many parts of the world, including Spain, Canada, Shanghai, and Taiwan. In the subtropical island of Taiwan, for example, researchers found low minimum temperatures were the strongest risk factor associated with outpatient visits for respiratory diseases.

According to IPCC, global warming will pose numerous challenges to human health, including the potential for an excess of deaths. This section examines the results of a number of studies conducted over the past decade or so that deal with this important subject as it applies to respiratory diseases. The studies show the excess death hypothesis from respiratory causes is 180 degrees out of phase with reality.

Hajat and Haines (2002) set out to determine whether the well-documented relationship between cold temperatures and respiratory mortality in the elderly extends to the number of visits by the elderly to general practitioners. They employed additive models to regress time-series of daily numbers of general practitioner consultations by the elderly against temperature. The consultation data they employed included visits to the doctor for asthma, lower respiratory diseases other than allergic rhinitis as obtained for registered patients aged 65 and older from several London practices between January 1992 and September 1995.

Hajat and Haines found the mean number of consultations was higher in cool-season months (October–March) than in warm-season months (April–September) for all respiratory diseases. At mean temperatures below 5°C, the relationship between respiratory disease consultations and temperature was linear, and stronger at a time lag of six to 15 days—a 1°C decrease in mean temperature below 5°C was associated with a 10.5% increase in all respiratory disease consultations.

Keatinge and Donaldson (2001) obtained similar results in their study of the effects of temperature on mortality in people over 50 years of age in the greater London area over the period 1976–1995. Simple plots of mortality rate versus daily air temperature revealed a linear increase in mortality as the air temperature fell from 15°C to near 0°C. Mortality rates at temperatures above 15°C, on the other hand, were, in their words, "grossly alinear," showing no trend. Low temperatures were shown to have a significant effect on both immediate (one day after the temperature perturbation) and long-term (up to 24 days after the temperature perturbation) mortality rates. Why are cold temperatures so deadly? Keatinge and Donaldson say it is because "cold causes mortality mainly from arterial thrombosis and respiratory disease, attributable in turn to cold-induced hemoconcentration and hypertension and respiratory infections."

Nafstad et al. (2001) studied the association between temperature and daily mortality in citizens of Oslo, Norway over the period 1990 to 1995. Because Norwegian law requires all deaths be examined by a physician, who diagnoses the cause of death and reports it on the death certificate, the authors were able to categorize and examine the effects of temperature on mortality specifically associated with respiratory diseases. The results showed the mean daily number of respiratory-related deaths was considerably higher in winter (October-March) than in summer (April-September). Winter deaths associated with respiratory diseases were 47% more numerous than summer deaths. Nafstad et al. conclude, "a milder climate would lead to a substantial reduction in average daily number of deaths."

Braga et al. (2002) conducted a time-series analysis of both the acute and lagged influence of temperature and humidity on mortality rates in 12 U.S. cities, finding no clear evidence for a link between humidity and respiratory-related deaths. With respect to temperature, they found respiratoryrelated mortality increased in cities with more variable temperature. This phenomenon, they write, "suggests that increased temperature variability is the most relevant change in climate for the direct effects of weather on respiratory mortality." This finding bodes well for a potentially warmer world, for Robeson (2002) has clearly demonstrated, based on a 50-year study of daily temperatures at more than 1,000 U.S. weather stations, that temperature variability declines with warming, and at a very substantial rate, so this aspect of a warmer world also would lead to a reduction in respiratory-related deaths.

Gouveia *et al.* (2003) extracted daily counts of deaths from all causes, except violent deaths and neonatal deaths (up to one month of age), from Sao Paulo, Brazil's mortality information system for the period 1991–1994 and analyzed them for effects of temperature within three age groups: less than 15 years of age (children), 15–64 years old (adults), and more than 64 years old (elderly). This exercise revealed the change points (the temperatures above and below which temperature begins to impact mortality) for both heat- and cold-induced deaths were identical, at 20°C. For each 1°C increase above

this value for a given and prior day's mean temperature, Gouveia *et al.* observed a 2.6% increase in deaths from all causes in children, a 1.5% increase in deaths from all causes in adults, and a 2.5% increase in deaths from all causes in the elderly. For each 1°C decrease below the 20°C change point, the cold effect was greater, with increases in deaths from all causes in children, adults, and the elderly registering 4.0%, 2.6%, and 5.5%, respectively. These cooling-induced death rates are 54%, 73%, and 120% greater than those due to warming.

Findings with respect to respiratory-induced deaths were similar. Death rates due to a 1°C cooling were twice as great as death rates due to a 1°C warming in adults, and 2.8 times greater in the elderly.

Nakaji et al. (2004) evaluated seasonal trends in deaths due to various diseases in Japan, using nationwide vital statistics from 1970 to 1999 and concurrent mean monthly air temperature data. They found the numbers of deaths due to diabetes, digestive diseases, cerebrovascular and heart diseases, infectious and parasitic diseases including tuberculosis, and respiratory diseases including pneumonia and influenza all rise to a maximum during the coldest time of the year. Hence, the team of nine scientists concludes, "to reduce the overall mortality rate and to prolong life expectancy in Japan, measures must be taken to reduce those mortality rates associated with seasonal differences." Consequently, to achieve the scientists' stated objectives, it is necessary to bring about a "reduction in exposure to cold environments," as they put it.

Bartzokas *et al.* (2004) "examined the relationship between hospital admissions for cardiovascular (cardiac in general including heart attacks) and/or respiratory diseases (asthma etc.) in a major hospital in Athens [Greece] and meteorological parameters for an 8-year period." Over the whole year, they found, "there was a dependence of admissions on temperature," and low temperatures were "responsible for a higher number of admissions." Specifically, "there was a decrease of cardiovascular or/and respiratory events from low to high values [of temperature], except for the highest temperature class in which a slight increase was recorded."

Kovats *et al.* (2004) studied patterns of temperature-related hospital admissions and deaths in Greater London during the mid-1990s. For the three-year period 1994–1996, they found respiratory-related deaths were nearly 150% greater in the depth of winter cold than at the height of summer

warmth. They also found the mortality impact of the heat wave of 29 July to 3 August 1995 (which boosted daily mortality by just over 10%) was so tiny it could not be discerned among the random scatter of plots of three-year-average daily deaths from cardiovascular and respiratory problems versus day of year. Similarly, in a study of temperature effects on mortality in three English counties (Hampshire, West Midlands, and West Yorkshire), McGregor (2005) found "the occurrence of influenza ... helps elevate winter mortality above that of summer."

Carder et al. (2005) used generalized linear Poisson regression models to investigate the relationship between outside air temperature and deaths due to all non-accident causes in the three largest cities of Scotland (Glasgow, Edinburgh, and Aberdeen) between January 1981 and December 2001. The authors observed "an overall increase in mortality as temperature decreases," which "appears to be steeper at lower temperatures than at warmer temperatures," and "there is little evidence of an increase in mortality at the hot end of the temperature range." They also state "the observed relation between cold temperature and mortality was typically stronger among the elderly," and "cold temperature effects on mortality persist with lag periods of beyond two weeks." Specifically, "for temperatures below 11°C, a 1°C drop in the daytime mean temperature on any one day was associated with an increase in respiratory mortality of 4.8% over the following month."

Noting "in temperate regions, respiratory disease adds greatly to the workload in general practice facilities and hospitals during the winter," partly because of increases in cases of "bronchiolitis in young children caused by infection with respiratory syncytial virus (RSV)," Donaldson (2006) studied the effect of annual mean daily air temperature on the length of the yearly RSV season. He used weekly data on laboratory reports of RSV isolation by the Health Protection Agency and National Health Service hospital laboratories in England and Wales for 1981-2004, along with meteorological data from four surface stations (Ringway, Squires Gate, Malvern, and Rothamsted) that "are representative of a roughly triangular area of the United Kingdom enclosed by Preston, London, and Bristol."

Reporting "climate change may be shortening the RSV season," Donaldson found "the seasons associated with laboratory isolation of respiratory syncytial virus (for 1981–2004) and RSV-related emergency department admissions (for 1990–2004) ended 3.1 and 2.5 weeks earlier, respectively, per 1°C

increase in annual central England temperature (P = 0.002 and 0.043, respectively)." Consequently, since "no relationship was observed between the start of each season and temperature," he reports, "the RSV season has become shorter." He concludes, "these findings imply a health benefit of global warming in England and Wales associated with a reduction in the duration of the RSV season and its consequent impact on the health service."

According to Frei and Gassner (2008), from 1926 to 1991, hay fever prevalence in Switzerland rose from just under 1% of the country's population to just over 14%, but from 1991 to 2000 it simply fluctuated about a mean value on the order of 15%. In addition, the authors write, "several studies show that no further increase in asthma, hay fever and atopic sensitization in adolescents and adults has been observed during the 1990s and the beginning of the new century," citing Braun-Fahrlander et al. (2004) and Grize et al. (2006). To see what effect changes in pollen production might have had on this trend in respiratory ailments, Frei and Gassner analyzed daily average concentrations of birch and grass pollen monitored by the country's National Pollen Network at Basel for the period 1969-2007, at Locarno for 1989–2007, and at Zurich for 1982–2007.

The two researchers report "the pollen exposure has been decreasing in Basel since the beginning of the 1990s," and "in Locarno, most of the pollen species also show a decreasing trend," while in Zurich, "most of the pollen types have been increasing," although "some of the pollen counts of this station (grass, stinging nettle, mugwort and ragweed) have been decreasing in the period 1982– 2007." In addition, they state the length of the pollen season has recently tended "to get shorter."

Frei and Gassner write, "parallel to the increasing hay fever rate, the pollen amounts of birch and grass were increasing from 1969 to 1990," but "subsequently, the pollen of these plant species decreased from 1991 to 2007." They say this finding "is more or less consistent with the changes of the hay fever rate that no longer increased during this period and even showed a tendency to decrease slightly." Nearly identical findings were presented a year later (Frei, 2009). Although some have claimed rising temperatures and CO_2 concentrations will lead to more pollen and more hay fever (Wayne *et al.*, 2002), the analyses of Frei (2009) and Frei and Gassner (2008) suggest that is not true of Switzerland.

Jato *et al.* (2009) collected airborne samples of Poaceae pollen "using Hirst-type volumetric traps" in four cities in Galicia (Northwest Spain)—Lugo, Santiago, Vigo, and Ourense—noting "the global climate change recorded over recent years may prompt changes in the atmospheric pollen season (APS). The subjected the data "to Spearman's correlation test and regression models, in order to detect possible correlations between different parameters and trends." They calculated the APS "using ten different methods, in order to assess the influence of each on survey results." The Poaceae family (composed chiefly of herbaceous grasses), Jato *et al.* write, "is the most diverse and prolific herbaceous plant family in urban areas," and "its pollen is considered a major aeroallergen, causing symptoms in over 80% of pollen allergy sufferers in Europe (D'Amato *et al.*, 2007)."

The four researchers report "all four cities displayed a trend towards lower annual total Poaceae pollen counts, lower peak values and a smaller number of days on which counts exceeded 30, 50 and 100 pollen grains/m³." The percentage decline in annual pollen grain counts between 1993 and 2007 in Lugo was approximately 75%, and in Santiago the decline was 80%, as best as can be determined from the graphs of the researchers' data. In addition, they write, "the survey noted a trend towards delayed onset and shorter duration of the APS." Thus, even though there was a "significant trend towards increasing temperatures over the months prior to the onset of the pollen season," according the Spanish scientists, Poaceae pollen became far less of a negative respiratory health factor in the four Galician cities over the decade and a half of their study.

Miller *et al.* (2012) say "there is concern that climate change may affect hay fever and other allergic conditions by impacting pollen amount, pollen allergenicity, pollen season, and plant and pollen distribution," because "allergy and atopic disease rates are rising, and global warming has been implicated as a possible cause." They note, "concomitant with climate change over the time course of many of these studies are changes in air pollution levels, economic factors, and lifestyle," and they conducted a study to clarify the situation by separating these potentially confounding factors.

Miller *et al.* extracted annual prevalence data for frequent otitis media (defined as three or more ear infections per year), respiratory allergy, and nonrespiratory seizures in children from the U.S. National Health Interview Survey for 1998 to 2006. They also obtained average annual temperatures for the same period from the U.S. Environmental Protection Agency. They performed "complex samples logistic regression analyses" to identify possible correlations between annual temperature and each of the three disease conditions, while controlling for age and sex.

The three researchers-from the David Geffen School of Medicine at the University of California at Los Angeles, Harvard Medical School, and Brigham and Women's Hospital in Boston-report the regression analysis found "annual temperature did not influence the prevalence of frequent otitis media." "annual temperature did not influence prevalence of respiratory allergy," and "annual temperature and sex did not influence seizure prevalence." Miller et al. conclude their findings "may demonstrate that average temperature is not likely to be the dominant cause of the increase in allergy burden or that larger changes in temperatures over a longer period are needed to observe this association." They conclude, "in the absence of more dramatic annual temperature changes, we do not expect prevalence of otitis media to change significantly as global warming may continue to affect our environment."

Xu et al. (2013) state "childhood asthma is a major global health issue, affecting more than 300 million people worldwide (Baena-Cagnani and Badellino, 2011)," and it "is regarded as a national health priority in several countries," citing Asher et al. (1995, 2006). They studied the relationship between diurnal temperature range (DTR) and the incidence of childhood asthma in Brisbane. Australia. For the study, "a Poisson generalized linear model combined with a distributed lag non-linear model was used to examine the relationship between DTR and emergency department admissions for childhood asthma in Brisbane from January 1st 2003 to December 31st 2009," and daily maximum and minimum temperatures in Brisbane for the same time period were retrieved from the Australian Bureau of Meteorology. Each day's DTR was calculated as the difference between its maximum and minimum temperatures.

The six scientists report "childhood asthma increased above a DTR of 10°C" and "was the greatest for lag 0–9 days, with a 31% increase in [hospital] emergency department admissions per 5°C increment of DTR," further noting, "male children and children aged 5–9 years appeared to be more vulnerable to the DTR effect than others." Since daily minimum temperatures have nearly always risen faster than have daily maximum temperatures in most locations around the globe whenever various regions have warmed, the study's results indicate the decrease in DTR under global warming should lead to a decline in the number of cases of childhood asthma.

Ge et al. (2013) also investigated respiratory
health and DTR. They write, "respiratory tract infection (RTI) is among the most common acute diseases worldwide, leading to considerable morbidity, complications, and days lost from work and school," citing Mourtzoukou and Falagas (2007). They report the DTR "has been identified as an independent risk factor for coronary heart disease (Cao *et al.*, 2009; Tam *et al.*, 2009), stroke (Shinkawa *et al.*, 1990; Kyobutungi *et al.*, 2005; Chen *et al.*, 2007), and chronic obstructive pulmonary disease (Song *et al.*, 2008)."

The researchers collected numbers of daily emergency-room visits for RTI at one of the largest medical establishments in Shanghai, China (Huashan Hospital) between 1 January 2008 and 30 June 2009, along with DTR data and data pertaining to possible confounding air pollutants (PM₁₀, SO₂, and NO₂). After making appropriate statistical analyses, the scientists determined increasing DTRs were closely associated with daily emergency-room visits for RTIs, such that "an increase of 1°C in the current-day and in the 2-day moving average DTR corresponded to a 0.94% and 2.08% increase in emergency-room visits for RTI, respectively."

Lin et al. (2013) state "high temperatures have garnered considerable attention in Europe and the U.S. because of their short-term adverse health impacts." However, they add, several studies have reported "the adverse health effects of cold temperatures may be more significant than those of high temperatures in Spain, Canada, Shanghai and Taiwan (Gomez-Acebo et al., 2010; Lin et al., 2011; Ma et al., 2011; Martin et al., 2012; Wang et al., 2012)," and "mortality risk associated with low temperatures is likely underestimated when studies fail to address the prolonged effect of low temperature (Martin et al., 2012; Mercer, 2003)." Working with data on daily area-specific deaths from all causes. circulatory diseases, and respiratory diseases, Lin et al. developed relationships between each of these cause-of-death categories and a number of coldtemperature related parameters for 2000-2008.

The five researchers discovered "mortality from [1] all causes and [2] circulatory diseases and [3] outpatient visits of respiratory diseases has a strong association with cold temperatures in the subtropical island, Taiwan." In addition, they found "minimum temperature estimated the strongest risk associated with outpatient visits of respiratory diseases."

The several studies described above clearly indicate a warmer world would be a much better world, especially with respect to the respiratory health of the world's citizens.

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7.4 Stroke Occurrence

According to IPCC, global warming will pose numerous challenges to human health, including the potential for an excess of deaths. This section examines the results of a number of studies conducted over the past decade or so that deal with this subject as it applies to strokes.

Feigin et al. (2000) conducted what they call "the first truly population-based study on the relationship between stroke occurrence and weather parameters in Russia," working within the city of Novosibirsk, Siberia, which has one of the highest stroke incidence rates in the world. Based on analyses of 2,208 patients with sex and age distributions similar to those of Russia as a whole, they found a statistically significant association between stroke occurrence and low ambient temperature over the period 1982-1993. In the case of ischemic stroke (IS), which accounted for 87% of all stroke types, they determined "the risk of IS occurrence on days with low ambient temperature [was] 32% higher than that on days with high ambient temperature." Given what they describe as "the highly significant association observed between low ambient temperature ($< -2.0^{\circ}$ C) and IS occurrence (P = 0.02), together with the proportion of days with such temperature in the region during a calendar year (41.3%)," they conclude the "very high stroke incidence in Novosibirsk, Russia may partially be explained by the highly prevalent cold factor there." They suggest the implementation of "preventive measures in [the] region, such as avoiding low temperature."

Hong et al. (2003) investigated the association

between the onset of ischemic stroke and prior episodic decreases in temperature in 545 patients who suffered strokes in Incheon, Korea from January 1998 to December 2000. They report "decreased ambient temperature was associated with risk of acute ischemic stroke," with the strongest effect being seen on the day after exposure to cold weather, further noting "even a moderate decrease in temperature can increase the risk of ischemic stroke." They also found "risk estimates associated with decreased temperature were greater in winter than in the summer," which suggests "low temperatures as well as temperature changes are associated with the onset of ischemic stroke." Finally, they explain the reason for the 24- to 48-hour lag between exposure to cold and the onset of stroke "might be that it takes some time for the decreasing temperature to affect blood viscosity or coagulation," which is also suggested by the work of Keatinge et al. (1984), who found blood viscosity and the plasma fraction of platelets began to increase one hour after cold exposure and did not reach a peak until sometime bevond six hours later.

Nakaji *et al.* (2004) evaluated seasonal trends in deaths due to various diseases in Japan using nationwide vital statistics from 1970 to 1999 together with mean monthly temperature data. They note Japan has "bitterly cold winters," and their analysis indicates the number of deaths due to cerebrovascular disease rises to a maximum during that cold time of year. They found the peak mortality rate due to stroke was two times greater in winter (January) than at the time of its yearly minimum (August and September). The team of nine scientists say it is necessary to bring about a "reduction in exposure to cold environments," as they put it.

Chang *et al.* (2004) analyzed data from the World Health Organization (WHO) Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception (WHO, 1995) to determine the effects of monthly mean temperature on rates of hospitalization for arterial stroke and acute myocardial infarction among women aged 15–49 from 17 countries in Africa, Asia, Europe, Latin America, and the Caribbean. Among these women, a 5°C reduction in mean air temperature was associated with a 7% increase in the expected hospitalization rate due to stroke, and this effect was relatively acute, within a period of about a month, the scientists write.

Each spring, Asian dust storm (ADS) events originating in the deserts of Mongolia and China transport great quantities of fine particulate matter of 10μ m diameter (PM₁₀) to populated cities of East Asia, including Taipei, Taiwan, where the tiny particles have the potential to affect people's lives in a very big way. In an attempt to assess one aspect of this phenomenon, Yang et al. (2005) identified 54 ADS events that affected Taipei from 1996 to 2001, and they evaluated the impacts of these events on hospital admissions for primary intracerebral hemorrhagic stroke (PIH), ischemic stroke (IS), as well as the conglomerate of strokes of all types. The scientists found associations between dust storms and total stroke admissions and PIH and IS admissions were prominent three days after ADS events, with the relative risk for total stroke admissions being 1.05, that for IS admissions being 1.04, and that for PIH admissions being 1.15, with the latter finding being deemed statistically significant. For this particular stroke category, they additionally determined risk of stroke rose by 2.67% for each 10 µg/m³ increase in PM₁₀ concentration above the normal mean value of 55.43 $\mu g/m^3$.

With respect to how the ongoing rise in the air's CO₂ content might impact this phenomenon, Chapter 1 of this volume discusses the well-documented increase in plant water use efficiency that results from increases in atmospheric CO2 concentration. This benefit should allow more plants to grow in the arid source regions of the Asian dust clouds, which will help to stabilize the soil and decrease its susceptibility to wind erosion, thereby reducing the severity of ADS events. Second, the propensity for elevated CO₂ concentrations to increase moisture contents of soils beneath plant canopies as a consequence of CO₂induced reductions in plant transpiration also should lead to greater ground cover and reduced wind erosion. Third, the ability of extra CO_2 in the atmosphere to enhance the growth of cryptobiotic soil crusts should stabilize the surface of the soil. And fourth, as noted by Zavaleta et al. (2003), global warming itself may increase soil moisture contents in water-limited regions by hastening plant senescence and thereby reducing the period of time over which transpiration-driven soil water losses occur.

If the air's CO_2 content continues to rise, even in the face of further warming, there should be a gradual reduction in the number of PM_{10} -induced strokes in the populace of Taipei, Taiwan, as well as in other places affected by Asian and other dust storms.

Gill *et al.* (2012) write, "in the past two decades, several studies reported that meteorologic changes are associated with monthly and seasonal spikes in the incidence of aneurysmal subarachnoid hemorrhage (aSAH)," and "analysis of data from large regional databases in both hemispheres has revealed increased seasonal risk for aSAH in the fall, winter and spring,"

citing Chyatte *et al.* (1994), Lejeune *et al.* (1994), Langmayr *et al.* (1995), Feigin *et al.* (2001), Abe *et al.* (2008), and Beseoglu *et al.* (2008). Gill *et al.* identified the medical records of 1,175 patients at the Johns Hopkins Hospital in Baltimore, Maryland (USA) who were admitted with a radiologically confirmed diagnosis of aSAH between 1 January 1991 and 1 March 2009. The researchers employed Poisson regression "to model the risk of a patient presenting with aSAH based on maximum ambient temperature (MAT), average relative humidity (ARH), and atmospheric pressure, clustering by season of the year to control for the previously reported relationship between season and aSAH presentation."

The six scientists report both "a one-day decrease in temperature and colder daily temperatures were associated with an increased risk of incident aSAH," and "these variables appeared to act synergistically" and were "particularly predominant in the fall, when the transition from warmer to colder temperatures occurred." Gill *et al.* add their study "is the first to report a direct relationship between a temperature decrease and an increased risk of aSAH," and "it also confirms the observations of several reports of an increased risk of aSAH in cold weather or winter," citing Lejeunne *et al.* (1994), Jakovljevic *et al.* (1996), and Nyquist *et al.* (2001).

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7.5 Malaria

• A vast body of scientific examination and research contradict the claim that malaria will expand across the globe and intensify as a result of CO₂-induced warming.

According to IPCC, ""If climate change continues as projected in scenarios in the next few decades, the major increases of ill-health compared to no climate change will occur through ...increased risks of foodand water-borne diseases and vector-borne infections. *[high confidence]" (IPCC-II, 2013).* Chapter 11, Human Health, Working Group II, *IPCC Fifth Assessment Report,* dated March 28, 2013, p. 3, italics in original, bold removed). This section investigates the reliability of IPCC's claim with respect to malaria.. According to the results of a vast body of scientific examination and research on this topic, there is little support for IPCC's claims. The next two sections will address the related claims regarding dengue fever and tick-borne diseases.

In a research report in *Science*, Rogers and Randolph (2000) note "predictions of global climate change have stimulated forecasts that vector-borne diseases will spread into regions that are at present too cool for their persistence." There are, however, several problems with this scenario.

According to Reiter (2000), claims that malaria resurgence is the product of CO_2 -induced global warming ignore other important factors and disregard known facts. A historical analysis of malaria trends, for example, reveals this disease was an important cause of illness and death in England during a period of colder-than-present temperatures throughout the Little Ice Age. Its transmission began to decline only in the nineteenth century, during a warming phase, when, according to Reiter, "temperatures were already much higher than in the Little Ice Age." In short, malaria was prevalent in Europe during some of

the coldest centuries of the past millennium, and it has only recently undergone widespread decline, when temperatures have been warming, Clearly, there are other factors at work that are more important than temperature. Such factors include the quality of public health services, irrigation and agricultural activities, land use practices, civil strife, natural disasters, ecological change, population change, use of insecticides, and the movement of people (Reiter, 2000; Reiter, 2001; Hay *et al.*, 2002).

Nevertheless, concerns have lingered about the possibility of widespread future increases in malaria due to global warming. These concerns are generally rooted in climate models that typically use only one, or at most two, climate variables in making their predictions of the future distribution of the disease over Earth, and they generally do not include any of the non-climatic factors listed in the preceding paragraph. When more variables are included, a lessworrisome future is projected. In one modeling study, for example, Rogers and Randolph (2000) employed five climate variables and obtained very different results. Briefly, they used the present-day distribution of malaria to determine the specific climatic constraints that best define that distribution, after which the multivariate relationship they derived from this exercise was applied to future climate scenarios derived from state-of-the-art climate models, in order to map potential future geographical distributions of the disease.

Their study revealed very little change: a 0.84% increase in potential malaria exposure under the "medium-high" scenario of global warming and a 0.92% decrease under the "high" scenario. Rogers and Randolph explicitly state their quantitative model "contradicts prevailing forecasts of global malaria expansion" and "highlights the use of multivariate rather than univariate constraints in such applications."

Hay *et al.* (2002) investigated long-term trends in meteorological data at four East African highland sites that experienced significant increases in malaria cases over the past couple of decades, reporting "temperature, rainfall, vapour pressure and the number of months suitable for *P. falciparum* transmission have not changed significantly during the past century or during the period of reported malaria resurgence." Thus these factors could not be responsible for the observed increases in malaria cases. Likewise, Shanks *et al.* (2000) examined trends in temperature, precipitation, and malaria rates in western Kenya over the period 1965–1997, finding no linkages among the variables.

Small et al. (2003) examined trends in a climatedriven model of malaria transmission between 1911 and 1995, using a spatially and temporally extensive gridded climate dataset to identify locations in Africa where the malaria transmission climate suitability index had changed significantly over this time interval. After determining areas of change, they more closely examined the underlying climate forcing of malaria transmission suitability for those localities. They found malaria transmission suitability did indeed increase because of climate change in specific locations of limited extent, but in Southern Mozambique, the only region for which climatic suitability consistently increased, the cause of the increase was increased precipitation, not temperature. Small et al. state, "climate warming, expressed as a systematic temperature increase over the 85-year period, does not appear to be responsible for an increase in malaria suitability over any region in Africa." They conclude "research on the links between climate change and the recent resurgence of malaria across Africa would be best served through refinements in maps and models of precipitation patterns and through closer examination of the role of nonclimatic influences," the great significance of which also has been demonstrated by Reiter et al. (2003) for dengue fever, another important mosquitoborne disease.

Zhou et al. (2004) employed a nonlinear mixedregression model study that focused on the numbers of monthly malaria outpatients of the past 10-20 years in seven East African highland sites and their relationships to the numbers of malaria outpatients during the previous time period, seasonality, and climate variability. They state, "for all seven study sites, we found highly significant nonlinear, synergistic effects of the interaction between rainfall and temperature on malaria incidence, indicating that the use of either temperature or rainfall alone is not sensitive enough for the detection of anomalies that are associated with malaria epidemics." Githeko and Ndegwa (2001), Shanks et al. (2002), and Hay et al. (2002) reached the same conclusion. In addition, climate variability-not just temperature or not just warming—contributed less than 20% of the temporal variance in the number of malaria outpatients, and at only two out of the seven sites studied.

Zhou *et al.* conclude "malaria dynamics are largely driven by autoregression and/or seasonality in these sites," and "the observed large among-site variation in the sensitivity to climate fluctuations may be governed by complex interactions between climate and biological and social factors." The latter include

"land use, topography, *P. falciparum* genotypes, malaria vector species composition, availability of vector control and healthcare programs, drug resistance, and other socioeconomic factors," including "failure to seek treatment or delayed treatment of malaria patients, and HIV infections in the human population," which they say have "become increasingly prevalent."

In a major review of the potential impacts of global warming on vector-borne diseases, Rogers and Randolph (2006) focus on recent upsurges of malaria in Africa, asking, "Has climate change already had an impact?" They demonstrate "evidence for increasing malaria in many parts of Africa is overwhelming, but the more likely causes for most of these changes to date include land-cover and land-use changes and, most importantly, drug resistance rather than any effect of climate," noting "the recrudescence of malaria in the tea estates near Kericho, Kenya, in East Africa, where temperature has not changed significantly, shows all the signs of a disease that has escaped drug control following the evolution of chloroquine resistance by the malarial parasite."

They explain, "malaria waxes and wanes to the beat of two rhythms: an annual one dominated by local, seasonal weather conditions and a *ca*. 3-yearly one dominated by herd immunity," noting "effective drugs suppress both cycles before they can be expressed," but "this produces a population which is mainly or entirely dependent on drug effectiveness, and which suffers the consequence of eventual drug failure, during which the rhythms reestablish themselves, as they appear to have done in Kericho."

Two more review papers on the subject followed two years later. In the first, Zell *et al.* (2008) write, "it is assumed that global warming is forced by the anthropogenic release of 'greenhouse gases,'" and a further "consistent assumption" has been a consequent "increased exposure of humans to tropical pathogens and their vectors." They also note "there is dissent about this hypothesis (Taubes, 1997; Reiter, 2001; Hay *et al.*, 2002; Reiter *et al.*, 2003; Randolph, 2004; Zell, 2004; Halstead, 2008)," and they explore it in more detail, examining the pertinent literature and describing "those mechanisms that have led to an increase of virus activity in recent years."

Based on their review, the three German researchers report "only very few examples point toward global warming as a cause of excess viral activity." Instead, they determined "coupled ocean/ atmosphere circulations and continuous anthropogenic disturbances (increased populations of humans and domestic animals, socioeconomic instability, armed conflicts, displaced populations, unbalanced ecosystems, dispersal of resistant pathogens etc.) appear to be the major drivers of disease variability," and "global warming at best contributes."

In the second 2008 paper (Reiter, 2008), Paul Reiter—who works with the Insects and Infectious Disease Unit of the Institut Pasteur in Paris, France writes, "man-made climate change has become a defining moral and political issue of our age," noting "speculations on its potential impact often focus on infectious diseases, and on malaria in particular," and "predictions are common that in the coming decades, tens—even hundreds—of millions more cases will occur in regions where the disease is already present, and that the vectors and the pathogens will move to higher latitudes and altitudes," infecting even more people.

In analyzing these claims, Reiter first discusses the mathematical models employed in this endeavor, after which he discusses common misconceptions and the nature of malaria in temperate regions. In the latter discussions he mentions such items as ecological change, new farm crops, new rearing practices, urbanization and mechanization, human living conditions, and medical care. Then, in a discussion of malaria in the tropics, he considers stable endemic malaria. unstable endemic malaria. birth rate, forest clearance, agriculture, movement of people, urbanization, insecticide resistance, resistance to drugs, degradation of the health infrastructure, and war and civil strife. He then treats three additional topics: Highland malaria in the tropics, Kenva Highlands, and New Guinea Highlands.

Reiter concludes, "simplistic reasoning on the future prevalence of malaria is ill-founded; malaria is not limited by climate in most temperate regions, nor in the tropics, and in nearly all cases, 'new' malaria at high altitudes is well below the maximum altitudinal limits for transmission." He further states, "future changes in climate may alter the prevalence and incidence of the disease, but obsessive emphasis on 'global warming' as a dominant parameter is indefensible; the principal determinants are linked to ecological and societal change, politics and economics." Reiter's conclusions have been borne out in additional studies of the subject.

Jackson *et al.* (2010) say "malaria is one of the most devastating vector-borne parasitic diseases in the tropical and subtropical regions of the world," noting it affects more than 100 countries. According to the World Health Organization, Africa carries the highest infection burden of any continent, with nearly

200 million cases reported in 2006, and the Centers for Disease Control and Prevention estimates between 700,000 and 2.7 million people each year die from the dreaded disease (Suh *et al.*, 2004). In addition, Jackson *et al.* report "the African region bears 90% of these estimated worldwide deaths," and "threequarters of all malaria related deaths are among African children," citing Breman (2001). They opine, "malaria could be greatly affected by the influence of climate change," such as global warming.

The five U.S. researchers linked reported malaria cases and deaths from the years 1996 to 2006, obtained from the World Malaria Report (2008) for 10 countries in western Africa (Benin, Burkina Faso, Cote d'Ivoire, Gambia, Ghana, Liberia, Mali, Senegal, Sierra Leone, and Togo) with corresponding climate data from the U.S. National Oceanic and Atmospheric Administration's National Climatic Data Center. They searched for transitive relationships between the weather variables and malaria rates via spatial regression analysis and tests for correlation. Jackson et al. report their analyses showed "very little correlation exists between rates of malaria prevalence and climate indicators in western Africa." This result, as they describe it, "contradicts the prevailing theory that climate and malaria prevalence are closely linked and also negates the idea that climate change will increase malaria transmission in the region."

Stern et al. (2011) examined trends in temperature and malaria for the Highlands of East Africa, which span Rwanda, Burundi, and parts of Kenya, Tanzania, and Uganda, to resolve controversies over whether the area has warmed and malaria has become more prevalent. For temperature, the authors used three time series obtained from the Climatic Research Unit (CRU) for four locations. Temperature data for Kericho extend through 2009, but only through 2006 for the Highlands. For malaria, the researchers used a data set on malaria cases through May 2010 at a hospital in Kericho, Kenya, and data from more than 5,200 surveys on the prevalence of malaria though 2009 in the Highlands. They report temperature has increased significantly in the region, yet "malaria in Kericho and many other areas of East Africa has decreased during periods of unambiguous warming." Their paper does not attempt an explanation for the divergence in these trends.

In a model-based study, Nkurunziza and Pilz (2011) employed Bayesian generalized additive models (GAMs) to assess the impact of an increase in temperature on malaria transmission in Burundi. Overall, the two researchers write, "the results of the GAMs show that an increase in the maximum temperature will cause an increase in minimum temperature," and "the increase in the latter will result in a decreasing maximum humidity, leading to a decrease in rainfall." These results, the writers continue, "suggest that an increased temperature will result in a shortening of the life span of mosquitoes (due to decreasing humidity) and decrease in the capacity of larva production and maturation (due to decreasing rainfall)." Thus, "the increase in temperature will not result in an increased malaria transmission in Burundi," which is "in good agreement with some previous works on the topic," citing as examples WHO, WMO, UNEP (2003), Lieshout et al. (2004), and Thomas (2004). In a final statement on the matter, Nkurunziza and Pilz note that in regions with endemic malaria transmission, such as Burundi, "the increase in temperature may lead to unsuitable climate conditions for mosquitoes survival and, hence, probably to a decreasing malaria transmission."

In another model-based study, Béguin et al. (2011) quantified the independent effects of climate and socioeconomic factors on the historical and projected future global distribution of malaria. The authors also provide estimates of the factors' separate and combined contributions to the populations at risk of malaria. Specifically, they estimated populations at risk of malaria (PAR) based on climatic variables, population growth, and GDP per capita (GDP_{pc}). GDP_{pc} is an approximation for per-capita income ("income" for short) for 1990, 2010, and 2050, based on sensitivity analyses for the following three scenarios: (1) a worst-case scenario, in which income declines to 50% of its 2010 values by 2050; (2) a "growth reduction" scenario, in which income declines by 25% in 2030 and 50% in 2050, relative to the A1B scenario; and (3) a scenario in which income stavs constant at 2010 values.

The PAR was derived from information on the presence or absence of *P. vivax* malaria in 1990 based on a logistic model for malaria presence that used three parameters: the mean temperature of the coldest month, the mean precipitation of the wettest month during the period 1961–1990, and the square root of income. Accordingly, the PAR does not directly reflect the health impacts of malaria. Secular technological change was ignored in this study. The results are presented in Table 7.5.1.

The authors observe, "under the A1B climate scenario, climate change has much weaker effects than GDP_{pc} increase on the geographic distribution of malaria." This result is consistent with the few studies that have considered the impact of climate change and

Model type	Population at Risk 2030 [billions]	Population at Risk 2050 [billions]
Socioeconomic changes only (no climate change)	3.52	1.74
Socioeconomic and climatic changes (A1B scenario)	3.58 [3.55–3.60]	1.95 [1.93–1.96]
Socioeconomic changes and CC (slower growth scenario)	3.82 [3.39–3.84]	3.42 [3.28–3.45]
No growth scenario , only CC	4.61 [4.54-4.67]	5.20 [5.11-5.25]
Pessimistic growth scenario and CC	5.18 [5.07–5.30]	6.27 [6.19–6.32]

 Table 7.5.1. Effects of Climate and Socioeconomic Factors on the Projected Future Global Distribution of Malaria.

 From Béguin *et al.* (2011).

socioeconomic factors on malaria. (See, e.g., Tol and Dowlatabadi, 2001; Bosello *et al.*, 2006). With respect to malaria, therefore, climate change is a relatively minor factor compared to economic development.

Kuhn *et al.* (2003) state, "there has been much recent speculation that global warming may allow the reestablishment of malaria transmission in previously endemic areas such as Europe and the United States." In particular, they note "the British Chief Medical Officer's recent report [*Getting Ahead of the Curve: A Strategy for Combating Infectious Diseases* (*Including Other Aspects of Health Protection*), Department of Health (2002), London] asserted that 'by 2050 the climate of the UK may be such that indigenous malaria could become re-established."" To investigate the robustness of this hypothesis, they analyzed the determinants of temporal trends in malaria deaths within England and Wales in 1840– 1910.

With respect to temperature changes over the period of study, Kuhn *et al.* report "a 1°C increase or decrease was responsible for an increase in malaria deaths of 8.3% or a decrease of 6.5%, respectively," which explains "the malaria epidemics in the 'unusually hot summers' of 1848 and 1859." Nevertheless, the long-term near-linear temporal decline in malaria deaths over the period of study, the researchers write, "was probably driven by nonclimatic factors," among which they identify increasing livestock populations (which tend to divert mosquito biting from humans), decreasing acreages of marsh wetlands (where mosquitoes breed), as well as "improved housing, better access to health care and

medication, and improved nutrition, sanitation, and hygiene." They also note the number of secondary cases arising from each primary imported case "is currently minuscule," as demonstrated by the absence of any secondary malaria cases in the UK since 1953.

Although simplistic model simulations may suggest the increase in temperature predicted for Britain by 2050 is likely to cause an 8-14% increase in the potential for malaria transmission, Kuhn et al. say "the projected increase in proportional risk is clearly insufficient to lead to the reestablishment of endemicity." They note "the national health system ensures that imported malaria infections are detected and effectively treated and that gametocytes are cleared from the blood in less than a week." For Britain, therefore, they conclude "a 15% rise in risk might have been important in the 19th century, but such a rise is now highly unlikely to lead to the reestablishment of indigenous malaria," because "socioeconomic and agricultural changes" have greatly altered the cause-and-effect relationships of the past.

Hulden and Hulden (2009) analyzed malaria statistics collected in Finland from 1750 to 2008 via correlation analyses between malaria frequency per million people and all variables that have been used in similar studies throughout other parts of Europe, including temperature data, animal husbandry, consolidation of land by redistribution, and household size. They report "malaria was a common endemic disease in Finland in the 18th and 19th centuries and prevalent in the whole country" and "mortality during malaria epidemics usually varied between 0.85 and 3%." Thereafter, however, they found "malaria declined slowly in Finland without any deliberate counter-measures," such that "the last epidemic in Helsinki occurred in 1902" and "during the 1930s malaria was close to extinction." Over the entire period, "malaria frequency decreased from about 20,000–50,000 per 1,000,000 people to less than 1 per 1,000,000 people," they report.

When malaria was still common in the country. they did find "high peaks in malaria followed high temperatures in June-July," but overriding this within-year temperature response over the long term, "both highs and lows in malaria frequency [were] declining independently of temperature trends." The two Finnish researchers conclude, "indigenous malaria in Finland faded out evenly in the whole country during 200 years with limited or no counter measures or medication," making that situation "one of the very few opportunities where natural malaria dynamics can be studied in detail." Their study indicates "malaria in Finland basically was a sociological disease and that malaria trends were strongly linked to changes in the human household size and housing standard."

Childs et al. (2006) present a detailed analysis of malaria incidence in northern Thailand based on a quarter-century monthly time series (January 1977 through January 2002) of total malaria cases in the country's 13 northern provinces. Over this time period, when IPCC claims the world warmed at a rate and to a level unprecedented over the prior one to two millennia, Childs et al. report there was an approximately constant rate of decline in total malaria incidence (from a mean monthly incidence in 1977 of 41.5 cases per hundred thousand people to 6.72 cases per hundred thousand people in 2001). This decrease was due primarily to a reduction in cases positive for Plasmodium falciparum (mean monthly incidence in 1977 and 2001 of 28.6 and 3.22 cases per 100.000 people, respectively) and secondarily to a reduction in cases positive for P. vivax (mean monthly incidence in 1977 and 2001 of 12.8 and 3.5 cases per 100,000 people, respectively). Consequently, noting "there has been a steady reduction through time of total malaria incidence in northern Thailand, with an average decline of 6.45% per year," they say this result "reflects changing agronomic practices and patterns of immigration, as well as the success of interventions as vector control programs, such improved availability of treatment and changing drug policies."

Haque *et al.* (2010) analyzed monthly malaria case data for the malaria endemic district of Chittagong Hill Tracts in Bangladesh from January 1989 to December 2008, looking for potential relationships between malaria incidence and various climatic parameters (rainfall, temperature, humidity, sea surface temperature, and the El Niño-Southern Oscillation), as well as the normalized difference vegetation index (NDVI), a satellite-derived measure of surface vegetation greenness. The six scientists report, "after adjusting for potential mutual confounding between climatic factors there was no evidence for any association between the number of malaria cases and temperature, rainfall and humidity," and "there was no evidence of an association between malaria cases and sea surface temperatures in the Bay of Bengal and NINO3." Instead, they found "the best leading indicator of the number of malaria cases was NDVI at a lag of 0-3 months, and that NDVI was negatively associated with malaria cases," such that "each 0.1 increase in monthly NDVI was associated with a 30.4% decrease in malaria cases." Haque et al. write, "it seems counterintuitive that a low NDVI, an indicator of low vegetation greenness, is associated with increases in malaria cases," since the primary vectors of the disease in Bangladesh are associated with forests. In light of this surprising result, they state their study "draws attention again to the complex nature of the relationship between malaria and climate," which in the case of the highlands of Bangladesh appears to be nonexistent.

Paaijmans *et al.* (2012) state "the development rate of parasites and pathogens within vectors typically increases with temperature," and, therefore, "transmission intensity is generally assumed to be higher under warmer conditions." However, they note, "development is only one component of parasite/pathogen life history," adding, "there has been little research exploring the temperature sensitivity of other traits that contribute to transmission intensity."

Paaiimans et al. examined prior "standard assumptions" and explored the resulting implications "for our understanding of the effects of temperature on disease transmission" on the rodent malaria Plasmodium yoelii and the Asian malaria vector Anopheles stephensi. The three U.S. researchers found "vector competence (the maximum proportion of infectious mosquitoes, which implicitly includes parasite survival across the incubation period) tails off at higher temperatures, even though parasite development rate increases." Moreover, "the standard measure of the parasite incubation period (i.e., time until the first mosquitoes within a cohort become infectious following an infected blood-meal) is incomplete because parasite development follows a cumulative distribution, which itself varies with

temperature." Finally, "including these effects in a simple model dramatically alters estimates of transmission intensity and reduces the optimum temperature for transmission." Paaijmans *et al.* conclude their results "challenge current understanding of the effects of temperature on malaria transmission dynamics," and they note their findings imply "control at higher temperatures might be more feasible than currently predicted." Therefore, in regard to "the possible effects of climate warming," they conclude "increases in temperature need not simply lead to increases in transmission."

Russell (2009), a professor in the Department of Medicine of the University of Sydney (Australia) and founding director of its Department of Medical Entomology, reports, "during the past 10 years, there has been increasing concern for health impacts of global warming in Australia, and continuing projections and predictions for increasing mosquitoborne disease as a result of climate change." He writes, these claims "are relatively simplistic, and do not take adequate account of the current or historic situations of the vectors and pathogens, and the complex ecologies that might be involved." Russell reviewed the consequences of these several inadequacies for malaria, dengue fever, the arboviral arthritides (Ross River and Barmah Forest viruses), and the arboviral encephalitides (Murray Valley encephalitis and Kunjin viruses) within the context of predictions of climate change modeled by Australia's Commonwealth Scientific and Industrial Research Organisation (CSIRO) and the Intergovernmental Panel on Climate Change (IPCC).

The abstract of Russell's paper begins with a question: "Will warming climate increase the risk or prevalence of mosquito-borne disease in Australia, as has been projected in a number of scientific publications and governmental reports?" His conclusion provides the answer: "there might be some increases in mosquito-borne disease in Australia with a warming climate, but with which mosquitoes and which pathogens, and where and when, cannot be easily discerned." He concludes, "of itself, climate change as currently projected, is not likely to provide great cause for public health concern with mosquito-borne disease in Australia."

Tuchman *et al.* (2003) took leaf litter from *Populus tremuloides* (Michaux) trees that had been grown out-of-doors in open-bottom root boxes located within open-top aboveground chambers maintained at atmospheric CO_2 concentrations of either 360 or 720 ppm for an entire growing season, incubated the leaf litter for 14 days in a nearby

stream, and fed the incubated litter to four species of detritivorous mosquito larvae to assess its effect on their development rates and survivorship. They report larval mortality was 2.2 times higher for Aedes albopictus (Skuse) mosquitos that were fed leaf litter that had been produced in the high-CO₂ chambers than it was for those fed litter that had been produced in the ambient-air chambers. In addition, they found larval development rates of Aedes triseriatus (Say), Aedes aegypti (L.), and Armigeres subalbatus (Coquillett) were slowed by 78%, 25%, and 27%, respectively, when fed litter produced in the high-CO₂ as opposed to the ambient- CO_2 chambers, so mosquitoes of these species spent 20, 11, and 9 days longer in their respective larval stages when feeding on litter produced in the CO₂-enriched as compared to the ambient-CO₂ chambers. The researchers suggest "increases in lignin coupled with decreases in leaf nitrogen induced by elevated CO₂ and subsequent lower bacterial productivity [on the leaf litter in the water] were probably responsible for [the] decreases in survivorship and/or development rate of the four species of mosquitoes."

Concerning the significance of these findings, Tuchman *et al.* write, "the indirect impacts of an elevated CO_2 atmosphere on mosquito larval survivorship and development time could potentially be great," because longer larval development times could result in fewer cohorts of mosquitoes surviving to adulthood. With fewer mosquitoes, there should be lower levels of mosquito-borne diseases.

Zell (2004) states many people "assume a correlation between increasing disease incidence and global warming." However, he concludes after studying the issue in considerable depth, "the factors responsible for the emergence/reemergence of vectorborne diseases are complex and mutually influence each other." As an example of this complexity, he notes, "the incidence and spread of parasites and arboviruses are affected by insecticide and drug resistance, deforestation, irrigation systems and dams, changes in public health policy (decreased resources of surveillance, prevention and vector control), demographic changes (population growth, migration, urbanization), and societal changes (inadequate housing conditions, water deterioration, sewage, waste management)." Therefore, he continues, "it may be over-simplistic to attribute emergent/reemergent diseases to climate change and sketch the menace of devastating epidemics in a warmer world." Zell states, "variations in public health practices and lifestyle can easily outweigh changes in disease biology," especially those that might be caused by

global warming.

Nabi and Qader (2009) considered the climatic conditions that impact the spread of malariatemperature, rainfall, and humidity-and the host of pertinent nonclimatic factors that play important roles in its epidemiology: the presence or absence of mosquito control programs, the availability or nonavailability of malaria-fighting drugs, changing resistances to drugs, the quality of vector control, changes in land use, the availability of good health services. human population growth, human migrations, international travel, and standard of living. The two researchers report "global warming alone will not be of a great significance in the upsurge of malaria unless it is accompanied by a deterioration in other parameters like public health facilities, resistance to anti-malarial drugs, decreased mosquito control measures," etc. They say "no accurate prediction about malaria can truly be made," because "it is very difficult to estimate what the other factors will be like in the future." They do note, however, mosquito-borne diseases were a major public health problem in the United States from the 1600s to the mid-1900s, "with occasional epidemics." By the middle of the twentieth century, however, "malaria disappeared from the country along with the other mosquito borne diseases like Dengue and Yellow fever," and "this decline was attributed to overall improvements in living conditions and better public health measures." These factors have kept these diseases at bay throughout the latter half of the twentieth century as well, even though that period included what climate alarmists describe as "unprecedented global warming."

Nabi and Qader conclude "as public health workers, it would be more justifiable for us to exert our efforts on these other [non-climatic] parameters for the eradication and control of malaria."

Gething *et al.* (2010) observe, based on "model predictions" it is "reported widely in global climate policy debates that climate change is adding to the present-day burden of malaria and will increase both the future range and intensity of the disease," citing IPCC (2007) and the U.S. Environmental Protection Agency (2010). Noting "it has long been known that the range of malaria has contracted through a century of economic development and disease control (Hay *et al.*, 2009)," when "global temperature increases have been unequivocal," Gething *et al.* explore this seeming incongruity by comparing "an evidence-based map of contemporary malaria endemicity (Hay *et al.*, 2009)" with "the most reliable equivalent for the pre-intervention era, around 1900 (Lysenko *et al.*,

1968)," when malaria was "at its assumed historical peak," thereby providing a comparison of "the magnitude of observed changes in range and endemicity to those proposed to occur in response to climate change."

The six scientists—from the Spatial Ecology and Epidemiology Group, the Malaria Public Health and Epidemiology Group, and the Centre for Tropical Medicine of the UK's University of Oxford, plus the Departments of Biology and Geography and the Emerging Pathogens Institute of the United States' University of Florida-report "comparison of the historical and contemporary maps revealed that endemic/stable malaria is likely to have covered 58% of the world's land surface around 1900 but only 30% by 2007." They report, "even more marked has been the decrease in prevalence within this greatly reduced range, with endemicity falling by one or more classes in over two-thirds of the current range of stable transmission." They write, "widespread claims that rising mean temperatures have already led to increases in worldwide malaria morbidity and mortality are largely at odds with observed decreasing global trends in both its endemicity and geographic "the combined natural and extent." Rather, anthropogenic forces acting on the disease throughout the twentieth century have resulted in the great majority of locations undergoing a net reduction in transmission between one and three orders of magnitude larger than the maximum future increases proposed under temperature-based climate change scenarios."

Gething *et al.* conclude there has been "a decoupling of the geographical climate-malaria relationship over the twentieth century, indicating that non-climatic factors have profoundly confounded this relationship over time." They note "non-climatic factors, primarily direct disease control and the indirect effects of a century of urbanization and economic development, although spatially and temporally variable, have exerted a substantially greater influence on the geographic extent and intensity of malaria worldwide during the twentieth century than have climatic factors." As for the future, they conclude climate-induced effects "can be offset by moderate increases in coverage levels of currently available interventions."

The many findings described above make it clear a vast body of scientific examination and research contradict the claim that malaria will expand across the globe and intensify as a result of CO₂-induced warming.

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7.6 Dengue Fever

• Concerns over large increases in vector-borne diseases such as dengue as a result of rising temperatures are unfounded and unsupported by the scientific literature, as climatic indices are poor predictors for dengue disease.

According to Ooi and Gubler (2009), "dengue/dengue hemorrhagic fever is the most important vector-borne viral disease globally," with more than half the world's population living in areas deemed to be at risk of infection. Also, they note, "many voices have raised concern that global warming is likely to increase the geographic distribution of the dengue mosquito vectors and the frequency and magnitude of dengue epidemics." Such concerns, as evidenced by the papers discussed below, are ill-founded.

In a major review of mosquito-borne diseases by one of the world's premier authorities on the subject, Reiter (2001) analyzed the history of malaria and dengue fever in an attempt to determine whether the incidence and range of influence of these diseases would indeed increase in response to CO_2 -induced global warming. This review indicates the natural history of these vector-borne diseases is highly complex, and the interplay of climate, ecology, vector biology, and a number of other factors defies definition by the simplistic analyses utilized in models that generate predictions of future geographical changes in these diseases under various global warming scenarios.

That there has in fact been a resurgence of these diseases in parts of the world is true; but, as Reiter notes, it is "facile to attribute this resurgence to climate change." This he shows via a number of independent analyses that clearly demonstrate factors associated with politics, economics, and human activity are the principal determinants of the spread of these diseases. He describes these factors as being "much more significant" than climate in promoting disease expansion.

Two years later, Reiter took up the subject again, this time with 19 other scientists as coauthors (Reiter *et al.*, 2003). They began by noting "it has frequently been stated that dengue, malaria, and other mosquitoborne diseases will become common in the United States as a result of global warming (Watson *et al.*, 1996; Jetten and Focks, 1997; Patz *et al.*, 1998; Watson *et al.*, 1998)." The Intergovernmental Panel on Climate Change had played a key role in promoting this claim, but Reiter and his colleagues had acquired solid evidence to prove IPCC was simply wrong on this point.

In the summer of 1999, toward the end of a significant dengue outbreak in "los dos Laredos"-Laredo, Texas, USA (population 200,000) and Nuevo Laredo, Tamaulipas, Mexico (population 290,000)the team of scientists conducted a seroepidemiologic survey to examine factors affecting dengue transmission in the two cities, located adjacent to each other on opposite sides of the Rio Grande and experience, according to the team, "massive crossborder traffic across three multi-lane bridges." They report "the incidence of recent cases, indicated by immunoglobulin M antibody serosurvey, was higher in Nuevo Laredo [16.0% vs. 1.3%], although the vector, Aedes aegypti, was more abundant in Laredo [91% vs. 37%]." Reiter et al. determined "environmental factors that affect contact with mosquitoes, such as air-conditioning and human behavior, appear to account for this paradox."

They found, for example, "the proportion of dengue infections attributable to lack of airconditioning in Nuevo Laredo [where only 2% of the homes had central air-conditioning compared to 36% of the homes in Laredo] was 55%," which means 55% of the cases of dengue in Nuevo Laredo would not have occurred if all households there had had airconditioning. Reiter et al. conclude, therefore, "if the current warming trend in world climates continues, air-conditioning may become even more prevalent in the United States, in which case, the probability of dengue transmission [there] will likely decrease." Likewise, if the economy of Mexico continues to grow, the use of air-conditioners likely will increase there as well, which likely would lead to even greater decreases in the occurrence of dengue fever in that country.

In a major review of the general subject of infectious diseases in a warming world, Roland Zell (2004) of the Institute for Virology and Antiviral Therapy at the Fredrich Schiller University in Jena, Germany, reviewed what was known about the

putative link some scientists were postulating-and a host of climate alarmists were championingbetween global warming and the spread of infectious diseases. Noting many people "assume a correlation between increasing disease incidence and global warming," he states that after studying the issue in considerable depth, he must conclude "the factors responsible for the emergence/reemergence of vectorborne diseases are complex and mutually influence each other." He notes "the incidence and spread of parasites and arboviruses are affected by insecticide and drug resistance, deforestation, irrigation systems and dams, changes in public health policy (decreased resources of surveillance, prevention and vector control), demographic changes (population growth, migration, urbanization), and societal changes (inadequate housing conditions, water deterioration, sewage, waste management)." Therefore, he continues, "it may be over-simplistic to attribute emergent/re-emergent diseases to climate change and sketch the menace of devastating epidemics in a warmer world." He reiterates "variations in public health practices and lifestyle can easily outweigh changes in disease biology."

Kyle and Harris (2008) note "dengue is a spectrum of disease caused by four serotypes of the most prevalent arthropod-borne virus affecting humans today," and "its incidence has increased dramatically in the past 50 years," to where "tens of millions of cases of dengue fever are estimated to occur annually, including up to 500,000 cases of the life-threatening dengue hemorrhagic fever/dengue shock syndrome." In an effort to better understand this increase, they conducted a thorough review of the pertinent scientific literature, exploring "the human, mosquito, and viral factors that contribute to the global spread and persistence of dengue, as well as the interaction between the three spheres, in the context of ecological and climate change."

With respect to the status of dengue fever within the context of global warming, they found "there has been a great deal of debate on the implications of global warming for human health," but "at the moment, there is no consensus." However, "in the case of dengue," they report, "it is important to note that even if global warming does not cause the mosquito vectors to expand their geographic range, there could still be a significant impact on transmission in endemic regions," because "a 2°C increase in temperature would simultaneously lengthen the lifespan of the mosquito and shorten the extrinsic incubation period of the dengue virus, resulting in more infected mosquitoes for a longer period of time." Nevertheless, they state there are "infrastructure and socioeconomic differences that exist today and already prevent the transmission of vector-borne diseases, including dengue, even in the continued presence of their vectors," citing Reiter (2001). It thus appears whatever advantages rising temperatures may confer upon the dengue virus vector, they can be more than overcome by proper implementation of modern vector control techniques.

In another review of the scientific literature, Wilder-Smith and Gubler (2008) note "the past two decades saw an unprecedented geographic expansion of dengue," reporting "each year an estimated 50 to 100 million dengue infections occur, with several hundred thousand cases of dengue hemorrhagic fever and about twenty thousand deaths." They too state, "global climate change is commonly blamed for the resurgence of dengue," but they add, "there are no good scientific data to support this conclusion." Wilder-Smith and Gubler reviewed what was known about the problem and pieced together a logical conclusion.

With respect to the occurrence of dengue infections, the two researchers report, "climate has rarely been the principal determinant of [their] prevalence or range," and "human activities and their impact on local ecology have generally been much more significant." They cite as contributing factors "urbanization, deforestation, new dams and irrigation systems, poor housing, sewage and waste management systems, and lack of reliable water systems that make it necessary to collect and store water," further noting "disruption of vector control programs, be it for reasons of political and social unrest or scientific reservations about the safety of DDT, has contributed to the resurgence of dengue around the world." In addition, they write "large populations in which viruses circulate may also allow more co-infection of mosquitoes and humans with more than one serotype of virus," which would appear to be borne out by the fact that "the number of dengue lineages has been increasing roughly in parallel with the size of the human population over the last two centuries." Most important, perhaps, is "the impact of international travel," of which they say "humans, whether troops, migrant workers, tourists, business travelers, refugees, or others, carry the virus into new geographic areas," and these movements "can lead to epidemic waves." The two researchers conclude, "population dynamics and viral evolution offer the most parsimonious explanation for the observed epidemic cycles of the disease, far more than climatic factors."

Russell (2009)-a professor in the Department of Medicine of the University of Sydney and founding director of its Department of Medical Entomologyreports, "during the past 10 years, there has been increasing concern for health impacts of global warming in Australia, and continuing projections and predictions for increasing mosquito-borne disease as a result of climate change." He notes these claims "are relatively simplistic, and do not take adequate account of the current or historic situations of the vectors and pathogens, and the complex ecologies that might be involved." He reviewed the consequences of these inadequacies for malaria, dengue fever, the arboviral arthritides (Ross River and Barmah Forest viruses) and the arboviral encephalitides (Murray Valley encephalitis and Kunjin viruses) within the context of predictions of climate changes modeled by Australia's Commonwealth Scientific and Industrial Research Organisation (CSIRO) and the Intergovernmental Panel on Climate Change (IPCC).

The abstract of Russell's paper begins with a question: "Will warming climate increase the risk or prevalence of mosquito-borne disease in Australia, as has been projected in a number of scientific publications and governmental reports?" His conclusion provides the answer: "there might be some increases in mosquito-borne disease in Australia with a warming climate, but with which mosquitoes and which pathogens, and where and when, cannot be easily discerned." He concludes, "of itself, climate change as currently projected, is not likely to provide great cause for public health concern with mosquito-borne disease in Australia."

Russell *et al.* (2009) report similar findings. The team of scientists note "dengue has emerged as a leading cause of morbidity in many parts of the tropics," and "Australia has had dengue outbreaks in northern Queensland." In addition, they report, "substantial increases in distribution and incidence of the disease in Australia are projected with climate change," or, more specifically, "with increasing temperatures." Russell *et al.* explored the soundness of these projections by reviewing the history of dengue in Australia.

This work showed the dengue vector (the *Aedes aegypti* mosquito) "was previously common in parts of Queensland, the Northern Territory, Western Australia and New South Wales," and it had, "in the past, covered most of the climatic range theoretically available to it," adding "the distribution of local dengue transmission has [historically] nearly matched the geographic limits of the vector." This being the case, they conclude the vector's current absence from

much of Australia "is not because of a lack of a favorable climate." Thus, they reason "a temperature rise of a few degrees is not alone likely to be responsible for substantial increases in the southern distribution of A. aegypti or dengue, as has been recently proposed." Instead, they note, "dengue activity is increasing in many parts of the tropical and subtropical world as a result of rapid urbanization in developing countries and increased international travel, which distributes the viruses between countries." Instead of futile attempts to limit dengue transmission by controlling the world's climate, therefore, the medical researchers recommend "well resourced and functioning surveillance programs, and effective public health intervention capabilities, are essential to counter threats from dengue and other mosquito-borne diseases."

Johansson et al. (2009) write, "the mosquitoborne dengue viruses are a major public health problem throughout the tropical and subtropical regions of the world," and "changes in temperature and precipitation have well-defined roles in the transmission cycle and may thus play a role in changing incidence levels." Since "the El Niño Southern Oscillation (ENSO) is a multiyear climate driver of local temperature and precipitation world wide," and "previous studies have reported varying degrees of association between ENSO and dengue incidence," they looked for relationships between ENSO, local weather, and dengue incidence in Puerto Rico (1986–2006), Mexico (1985–2006), and Thailand (1983-2006) using wavelet analysis as a tool to identify time- and frequency-specific associations.

The three researchers report they "did not find evidence of a strong, consistent relationship in any of the study areas," and Rohani (2009), who wrote a Perspective piece on their study, states the three researchers found "no systematic association between multi-annual dengue outbreaks and El Niño Southern Oscillation." Thus, as stated in the "Editors' Summary" of Johansson *et al.*'s paper, their findings "provide little evidence for any relationship between ENSO, climate, and dengue incidence."

Shang *et al.* (2010) used logistic and Poisson regression models to analyze biweekly, laboratory-confirmed dengue cases in Taiwan at their onset dates of illness from 1998 to 2007, in order to "identify correlations between indigenous dengue and imported dengue cases (in the context of local meteorological factors) across different time lags." The researchers write, "the occurrence of indigenous dengue was significantly correlated with temporally-lagged cases

of imported dengue (2-14 weeks), higher temperatures (6–14 weeks), and lower relative humidity (6–20 weeks)," and "imported and indigenous dengue cases had a significant quantitative relationship in the onset of local epidemics." The six Taiwanese researchers conclude, "imported dengue cases are able to initiate indigenous epidemics when appropriate weather conditions are present," or as they state in another place, "imported dengue are able to serve as an initial facilitator, or spark, for domestic epidemics." They suggest "early detection and case management of imported cases through timely surveillance and rapid laboratory-diagnosis may avert large scale epidemics of dengue/dengue hemorrhagic fever," while noting "meteorology alone does not initiate an epidemic." Finally, they state, "an increase in viremic international travelers has caused global dengue hemorrhagic fever case numbers to surge in the past several decades."

Ooi and Gubler (2009a) examined "the history of dengue emergence" in order to determine "the major drivers for the spread of both the viruses and mosquito vectors to new geographic regions." The two researchers note "frequent and cyclical epidemics are reported throughout the tropical world, with regular importation of the virus via viremic travelers into both endemic and non-endemic countries." They state, "there is no good evidence to suggest that the current geographic expansion of the dengue virus and its vectors has been or will be due to global warming." Instead, they conclude, "the magnitude of movement of the human population and trade materials, uncontrolled and poorly planned expansion of urban centers and the lack of effective disease prevention in dengue-endemic regions have served to produce conditions ideal for dengue virus transmission and have been the principal drivers of epidemic dengue for the past three decades," citing Gubler (1998, 2004), Gubler et al. (2001), and Ooi and Gubler (2009b).

In another review paper, Dr. Paul Reiter of the Insects and Infectious Disease Unit of the Institut Pasteur in Paris writes, "it is widely stated that the incidence of vector-borne diseases will increase if global temperatures increase" (Reiter, 2010a); and while admitting temperature and rainfall do indeed "play a role" in the transmission of such diseases, he states, "many other factors are involved," citing a paper he wrote at the turn of the century (Reiter, 2001). In revisiting this subject, Reiter (2010a) reviewed the scientific literature, distilling the essence of the then-current state of knowledge pertaining to the potential for yellow fever and dengue transmission throughout modern-day Europe.

The review revealed "the introduction and rapidly expanding range of *Aedes albopictus* in Europe is an iconic example of the growing risk of the globalization of vectors and vector-borne diseases," and "the history of yellow fever and dengue in temperate regions confirms that transmission of both diseases could recur, particularly if *Aedes aegypti*, a more effective vector, were to be re-introduced." He states "conditions are already suitable for transmission."

In light of Reiter's findings, can we expect to face the problem of the two deadly diseases suddenly reappearing and racing across Europe, especially if the climate begins to warm again? Actually, it would not be incredibly surprising if that were to happen even if the climate were to cool, for Reiter concludes, "a more urgent emerging problem is the quantum leap in the mobility of vectors and pathogens that has taken place in the past four decades, a direct result of the revolution of transport technologies and global travel," as described in his recently published article (Reiter, 2010b).

Carbajo *et al.* (2012) report "dengue cases have increased during the last decades, particularly in nonendemic areas, and Argentina was no exception in the southern transmission fringe." Although temperature rise has been blamed for this geographical expansion of the disease, they write, "human population growth, increased travel and inefficient vector control may also be implicated." Thus, they evaluated the relative contributions of geographic, demographic, and climatic variables to the recent spread of the disease.

Carbajo *et al.* divided their study into two halves—a first decade that included the reemergence of the disease, and a second decade that included several epidemics—in which "annual dengue risk was modelled by a temperature-based mechanistic model as annual days of possible transmission," and "the spatial distribution of dengue occurrence was modelled as a function of the output of the mechanistic model, climatic, geographic and demographic variables for both decades."

They found dengue spatial occurrence "was positively associated with days of possible transmission, human population number, population fall and distance to water bodies." When considered separately, the researchers write, "the classification performance of demographic variables was higher than that of climatic and geographic variables." Thus, although useful in estimating annual transmission risk, Carbajo *et al.* conclude temperature "does not fully describe the distribution of dengue occurrence at the country scale," and "when taken separately, climatic variables performed worse than geographic or demographic variables," while acknowledging "a combination of the three types was best for this task."

These several observations indicate concerns over large increases in vector-borne diseases such as dengue as a result of rising temperatures are unfounded and unsupported by the scientific literature, as climatic indices are poor predictors for dengue disease.

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7.7 Tick-Borne Diseases

• While climatic factors largely determine the geographical distribution of ticks, temperature and climate change are not among the significant factors determining the incidence of tick-borne diseases.

Randolph and Rogers (2000) state tick-borne encephalitis (TBE) "is the most significant vectorborne disease in Europe and Eurasia," having "a case morbidity rate of 10–30% and a case mortality rate of typically 1–2% but as high as 24% in the Far East." The disease is caused by a flavivirus (TBEV), which is maintained in natural rodent-tick cycles; humans may be infected with it if bitten by an infected tick or by drinking untreated milk from infected sheep or goats.

Early discussions on the relationship of TBE to global warming predicted the disease would expand its range and become more of a threat to humans in a warmer world. However, Randolph and Rogers note, "like many vector-borne pathogen cycles that depend on the interaction of so many biotic agents with each other and with their abiotic environment, enzootic cycles of TBEV have an inherent fragility," so "their continuing survival or expansion cannot be predicted from simple univariate correlations."

Confining their analysis to Europe, Randolph and Rogers first matched the present-day distribution of TBEV to the present-day distributions of five climatic variables: monthly mean, maximum, and minimum temperatures, plus rainfall and saturation vapor pressure, "to provide a multivariate description of present-day areas of disease risk." They applied this understanding to outputs of a general circulation model of the atmosphere that predicted how these five climatic variables may change in the future.

The results indicate the distribution of TBEV might expand both north and west of Stockholm, Sweden in a warming world. For most other parts of Europe, however, the two researchers say "fears for increased extent of risk from TBEV caused by global climate change appear to be unfounded." They report, "the precise conditions required for enzootic cycles of TBEV are predicted to be disrupted" in response to global warming, and the new climatic state "appears to be lethal for TBEV." This finding, they write, "gives the lie to the common perception that a warmer world will necessarily be a world under greater threat from vector-borne diseases." In the case of TBEV, they report the predicted change "appears to be to our advantage."

Noting "it is often suggested that one of the most important societal consequences of climate change may be an increase in the geographic distribution and transmission intensity of vector-borne disease," Estrada-Peña (2003) evaluated the effects of various abiotic factors on the habitat suitability of four tick species that are major vectors of livestock pathogens in South Africa. They report "vear-to-vear variations in the forecasted habitat suitability over the period 1983-2000 show a clear decrease in habitat availability, which is attributed primarily to increasing temperature in the region over this period." In addition, when climate variables were projected to the year 2015, Estrada-Peña found "the simulations show a trend toward the destruction of the habitats of the four tick species," just the opposite of what is often predicted about this disease.

Zell (2004) also has noted many people "assume a correlation between increasing disease incidence and global warming." He reviewed the scientific literature pertaining to the subject and determined "the factors responsible for the emergence/ reemergence of vector-borne diseases are complex and mutually influence each other." He cites as an example of this complexity, "the incidence and spread of parasites and arboviruses are affected by insecticide and drug resistance, deforestation, irrigation systems and dams, changes in public health policy (decreased resources of surveillance, prevention and vector control), demographic changes (population growth, migration, urbanization), and societal changes (inadequate housing conditions, water deterioration, sewage, waste management)."

Zell says "it may be over-simplistic to attribute emergent/re-emergent diseases to climate change and sketch the menace of devastating epidemics in a warmer world." Indeed, he concludes, "variations in public health practices and lifestyle can easily outweigh changes in disease biology."

Sarah Randolph (2010) of the University of Oxford's Department of Zoology in the United Kingdom examined the roles played by various factors that may influence the spread of tick-borne diseases. She begins by noting many vector-borne diseases "have shown marked increases in both distribution and incidence during the past few decades, just as human-induced climate change is thought to have exceeded random fluctuations." She adds, "this coincidence has led to the general perception that climate change has driven disease emergence." However, she notes, "climate change is the inevitable backdrop for all recent events," most of which no one would otherwise consider attributing to changes in the planet's temperature.

After describing some of the outbreaks of tickborne disease in Europe over the past couple of decades, Randolph states "the inescapable conclusion is that the observed climate change alone cannot explain the full heterogeneity in the epidemiological change, either within the Baltic States or amongst Central and Eastern European countries," citing Sumilo *et al.* (2007). Instead, she writes, "a nexus of interrelated causal factors—abiotic, biotic and human—has been identified," and "each factor appears to operate synergistically, but with differential force in space and time, which would inevitably generate the observed epidemiological heterogeneity."

Many of these factors, she continues, "were the unintended consequences of the fall of Soviet rule and the subsequent socio-economic transition (Sumilo *et al.*, 2008b)," among which she cites "agricultural reforms resulting in changed land cover and land use, and an increased reliance on subsistence farming; reduction in the use of pesticides, and also in the emission of atmospheric pollution as industries collapsed; increased unemployment and poverty, but also wealth and leisure time in other sectors of the population as market forces took hold."

Randolph concludes "there is increasing evidence from detailed analyses that rapid changes in the incidence of tick-borne diseases are driven as much, if not more, by human behavior that determines exposure to infected ticks than by tick population biology that determines the abundance of infected ticks," as per Sumilo *et al.* (2008a) and Randolph *et al.* (2008). She ends her analysis by stating, "while nobody would deny the sensitivity of ticks and tickborne disease systems to climatic factors that largely determine their geographical distributions, the evidence is that climate change has not been the most significant factor driving the recent temporal patterns in the epidemiology of tick-borne diseases."

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7.8 Effects of CO₂

Among the lesser-known findings about CO_2 enrichment of the air is that several health-promoting substances are often enhanced in plants growing at higher CO_2 concentrations. As discussed in the subsections below, these enhancements portend great benefits for human health, and they represent an important reality the IPCC assessment reports ignore.

7.8.1 Antioxidants

Oxidation is a chemical process that occurs naturally in plants, animals, and humans. Although the process is vital for life, it also can produce free radicals, including reactive oxygen species (ROS), in a series of chain reactions that lead to cell damage and cell death. In humans, oxidative stress has been linked to cardiovascular disease, cancer, neurodegenerative disorders, and other chronic diseases. Nature's way of responding to the threats posed by such radicals is to neutralize and inhibit their reactions via complex systems of multiple types of antioxidants.

Plants, animals, and humans each harbor defense systems comprised of various types of antioxidants, including vitamin A, vitamin C, and vitamin E, and enzymes such as catalase, superoxide dismutase, and various peroxidases. Inadequate levels of antioxidants, or inhibition of antioxidant enzymes, can lead to oxidative stress.

The following subsections examine the impact of rising atmospheric CO₂ on antioxidant compounds and enzymes found in plants, illustrating major benefits it provides for both plants and humans. With respect to plants, higher levels of atmospheric CO₂ tend to reduce oxidative stress, resulting in a reduction in antioxidant enzyme activity because fewer such enzymes are needed to counter the stress. As a result, plants are able to direct more of their limited resources into the production of other plant tissues or processes essential to their continued growth and development. In some cases, such resources are invested into the production and enhancement of antioxidative compounds, and these compounds are known to provide health benefits to animals and humans.

7.8.1.1 Benefits to Plants

Environmental stresses induced by exposure to pollutants, drought, intense solar radiation, and high air or water temperatures generate highly reactive oxygenated compounds that damage plants. Ameliorating these stresses typically involves the production of antioxidant enzymes that scavenge and detoxify the highly reactive oxygenated compounds. When stresses are present, concentrations and/or activities of antioxidants in plants are generally observed to be high so as to counter the effects of the stress. A number of researchers have examined the impact of atmospheric CO₂ enrichment on this relationship, the results of which are discussed below.

In a study of two soybean genotypes, Pritchard et al. (2000) report three months' exposure to twiceambient CO₂ concentrations reduced the activities of superoxide dismutase and catalase by an average of 23 and 39%, respectively. Likewise, Polle et al. (1997) show two years of atmospheric CO_2 enrichment reduced the activities of several key antioxidative enzymes, including catalase and superoxide dismutase, in beech seedlings. And Schwanz and Polle (1998) demonstrate this phenomenon can persist indefinitely, for they discovered similar reductions in these same enzymes

in mature oak trees that had been growing near natural CO_2 -emitting springs for 30 to 50 years.

The standard interpretation of these results is the observed reductions in the activities of antioxidative enzymes under CO_2 -enriched conditions imply plants exposed to higher-than-current atmospheric CO_2 concentrations experience less oxidative stress and thus have a reduced need for antioxidant protection. This conclusion further suggests " CO_2 -advantaged" plants will be able to funnel more of their limited resources into the production of other plant tissues or processes essential to their continued growth and development.

On the other hand, when oxidative stresses do occur under high CO₂ conditions, the enhanced rates of photosynthesis and carbohydrate production resulting from atmospheric CO₂ enrichment generally enable plants to better deal with such stresses by providing more of the raw materials needed for antioxidant enzyme synthesis. Thus, when CO₂enriched sugar maple seedlings were subjected to an additional 200 ppb of ozone, Niewiadomska et al. (1999) report ascorbate peroxidase, which is the first line of enzymatic defense against ozone, significantly increased. Likewise, Schwanz and Polle (2001) note poplar clones grown at 700 ppm CO₂ exhibited a much greater increase in superoxide dismutase activity upon chilling induction than clones grown in ambient air. In addition, Lin and Wang (2002) found activities of superoxide dismutase and catalase were much higher in CO₂-enriched wheat than in ambiently grown wheat following the induction of water stress.

Baczek-Kwinta and Koscielniak (2003) grew two hybrid maize (Zea mays L.) genotypes-KOC 9431 (chill-resistant) and K103xK85 (chill-sensitive)from seed in air of either ambient (350 ppm) or elevated (700 ppm) CO₂ concentration (AC or EC, respectively), after which the plants were exposed to air of 7°C for 11 days and then recovered in ambient air of 20°C for one day. Throughout this period, a number of physiological and biochemical parameters were measured on the plants' third fully expanded leaves. Among their many findings, the researchers note, "EC diminished the rate of superoxide radical formation in leaves in comparison to the AC control." In addition, "electrolyte leakage from the [leaf membrane] tissue, a parameter reflecting membrane injury, was significantly lower in samples of plants subjected to EC than AC." Finally, they discovered enrichment of the air with CO₂ successfully inhibited the decrease in the maximal quantum efficiency of photosystem 2, both after chilling and during the one-day recovery period. Lumping these positive effects of elevated CO_2 together, the two scientists conclude, "the increase in atmospheric CO_2 concentration seems to be one of the protective factors for maize grown in cold temperate regions."

In a study focusing solely on temperature, Yu et al. (2004a) investigated how global warming might affect crop reactive oxygen species (ROS) scavenging activities and chelating capacities, the latter of which may inhibit radical-mediated oxidative chain reactions by stabilizing transition metals required to catalyze the formation of the first few radicals needed to initiate the radical reactions (Nawar, 1996). In one of the few studies to broach this subject, Wang and Zheng (2001) examined the effects of a group of day/night temperature combinations on the antioxidant activities of the juice of two strawberry varieties, finding, in the words of Yu et al., "the highest day/night temperature resulted in fruits with the greatest phenolic content as well as antioxidant activities." Encouraged by this finding, Yu et al. (2004a) decided to explore the subject further in a study of winter wheat.

Yu et al. examined and compared flour extracts of three hard winter wheat varieties grown at five locations in Colorado for their radical scavenging properties, chelating capacities, and total phenolic contents. Although they found no statistically significant correlations, the scientists report "a correlation coefficient of 0.890 (P = 0.110) was detected for the chelating activity of Akron flour and the total hours of the growth location exceeding 32°C during the 6-week grain-filling period." Thus, although no firm conclusions could be drawn from the results of their study, in contrast to the study of Wang and Zheng (2001), Yu et al.'s findings are intriguing enough to lead them to state, "more research is needed to clarify how varieties and growing conditions alter the antioxidant properties of wheat, wheat flour and bran."

A different set of authors, Yu *et al.* (2004b), note "oxidative stress is potentially experienced by all aerobic life when exposed to UV-B radiation," and "elevated CO₂ can enhance the capacity of plants to resist stress-induced oxidative damage," citing Ren *et al.* (2001), who worked with terrestrial plants. Yu *et al.* set out to see whether this was also true of marine plants, focusing their attention on phytoplankton, which they describe as "the single most important ecosystem on our planet."

They grew the marine microalgae *Platymonas subcordiformis* (Wille) Hazen in the laboratory at ambient levels of atmospheric CO₂ concentration and

UV-B radiation flux density, and at elevated levels of 5,000 ppm CO₂ and UV-B radiation characteristic of that anticipated to result from a 25% stratospheric ozone depletion under clear sky conditions in summer. By itself, and by these means, the five researchers determined the elevated UV-B treatment significantly decreased microalgal dry weight, photosynthetic rate, chlorophyll a and carotenoid contents. The elevated CO_2 treatment by itself enhanced dry weight and photosynthetic rate, and chlorophyll a content and carotenoid content exhibited no major differences compared with those of ambient UV-B and ambient CO₂. They also report elevated UV-B by itself significantly increased the production of the toxic superoxide anion and hydrogen peroxide, as well as malonyldialdehyde, an end product of lipid peroxidation, whereas elevated CO_2 by itself did just the opposite. In addition, in the treatment consisting of both elevated UV-B and elevated CO₂, the concentrations of these three substances were lower than those observed in the elevated UV-B and ambient CO₂ treatment. Finally, they note elevated CO₂ decreased the levels of several antioxidative enzymes found in the microalgae, reflecting their reduced need for detoxification of reactive oxygen species in the elevated CO₂ treatment.

Yu *et al.* write their results suggest "CO₂ enrichment could reduce oxidative stress of reactive oxygen species to *P. subcordiformis*, and reduce the lipid peroxidation damage of UV-B to *P. subcordiformis.*" They also state, "CO₂ enrichment showed a protective effect against the oxidative damage of UV-B-induced stress," and therefore, "elevated CO₂ can be [in] favor of enhancing the capacity of stress resistance." Put more simply, they conclude, "we have shown that algae grown under high CO₂ would better overcome the adverse impact of environmental stress factor[s] that act via generation of activated oxygen species."

Plants cultured *in vitro* are know to typically suffer from a number of physiological and biochemical impairments, such that upon transfer to *ex vitro* conditions they often experience severe oxidative stress. Carvalho *et al.* (2005) conducted an analysis of the extent to which this stress might be alleviated by a nominal doubling of the air's CO₂ content. They evaluated the damage done to the large subunit of rubisco in grapevine (*Vitis vinifera* L.) plantlets while exposed to *in vitro* conditions and the degree to which that damage was ameliorated by atmospheric CO₂ enrichment during subsequent exposure to *ex vitro* conditions. The *in vitro* plantlet cultures were maintained in a growth chamber at a photon flux density (PFD) of 45 μ mol m⁻² s⁻¹, after which they were transferred to *ex vitro* conditions having a PFD of either 150 (low light) or 300 (high light) μ mol m⁻² s⁻¹ and an air CO₂ concentration of either 350 (low CO₂) or 700 (high CO₂) ppm. A number of physiological and biochemical measurements were made on the plantlets at seven-day intervals over a period of 28 days.

Carvalho et al. found rubisco degradation products were present in the leaves of plantlets in both in vitro and ex vitro conditions. However, "under low CO₂ they were maintained for almost all of the 28 days of the acclimatization period, while becoming scarcely detected after 14 days under high CO₂ and after 7 days when high CO₂ was associated with high light." In addition, "patterns of soluble sugars in acclimatizing leaves under high light and high CO₂ also gave an indication of a faster acquisition of autotrophic characteristics." Carvalho et al.'s results thus demonstrate the beneficial impact of high CO₂ concentrations in reducing the oxidative stress induced by the transfer of in vitro-produced plantlets to ex vitro conditions, as "a net benefit from high CO₂ treatments was clearly visible, contributing to an increased stability of Rubisco." Also, "the disappearance of Rubisco large subunit degradation products in persistent leaves subjected to the ex vitro treatments may be considered an indicator of recovery from stress," they write.

Levine et al. (2008) grew well-watered and fertilized wheat plants (Triticum aestivum, cv Yocoro roho) from seed in custom-designed root modules-"consisting of a porous tube embedded in Turface (1-2 mm particle size) substrate containing 5 g Osmocote time release fertilizer per liter"-which were housed in Plexiglas chambers maintained at atmospheric CO₂ concentrations of either 400, 1,500, or 10,000 ppm for periods of 14, 21, and 28 days. The scientists measured a number of plant metabolic properties along with the leaf concentrations of several flavonoids that are capable of scavenging ROS. The 13 researchers report "elevated CO₂ promoted the accumulation of secondary metabolites (flavonoids) progressively to a greater extent as plants became mature." As best as can be determined from the bar graphs of their results, for example, the percentage increase in total wheat leaf flavonoid concentration in going from an atmospheric CO₂ concentration of 400 to 1,500 ppm was 22%, 38%, and 27% at 14, 21, and 28 days after planting, respectively, whereas in going from a CO_2

concentration of 400 to 10,000 ppm, the percentage increase in total flavonoid concentration was 38%, 56% and 86%, respectively, at 14, 21 and 28 days after planting. They report "both elevated CO_2 levels resulted in an overall 25% increase in biomass over the control plants."

The U.S., Japanese, and German scientists write, "the increased accumulation of secondary metabolites in plants grown under elevated CO_2 may have implications regarding plant-herbivore interactions, decomposition rates for inedible biomass, and potential beneficial effects on plant tolerance to water stress (Idso, 1988) and cold stress (Solecka and Kacperska, 2003) due to their potentials for the scavenging of reactive oxygen species (ROS)."

Varga et al. (2012) write, "as well as damaging numerous physiological functions, abiotic stress [such as drought] also leads to higher concentrations of reactive oxygen species, which are present in nature in all plants, but which may damage cell components and disturb metabolic processes when present in larger quantities," citing Omran (1980), Larson (1988), and Dat et al. (2000). They say "many authors have demonstrated that the [atmosphere's] CO₂ concentration has a substantial influence on the stress sensitivity of plants via changes in antioxidant enzyme activity," citing Fernandez-Trujillo et al. (2007), Ali et al. (2008), and Varga and Bencze (2009), so increases in the atmosphere's CO_2 concentration may increase various plant antioxidant enzymes and thereby reduce the negative effects of various abiotic stresses.

Varga et al. grew two varieties of winter wheat within phytotrons maintained at either 380 or 750 ppm CO₂, where the potted plants were watered daily and supplied with nutrient solution twice a week until the start of drought treatments, when drought was induced in three phases—at first node appearance, heading, and grain filling-by completely withholding water for seven days, which dropped the volumetric soil water content in the pots from 20-25% to 3-5%. The four researchers-all of whom were associated with the Agricultural Research Institute of the Hungarian Academy of Sciencesreport they observed "changes in enzyme activity" that "indicated that enhanced CO₂ concentration delayed the development of drought stress up to first node appearance, and stimulated antioxidant enzyme activity when drought occurred during ripening, thus reducing the unfavorable effects of [drought] stress." Varga *et al.* conclude the increases in the antioxidant enzymes they analyzed "may help to neutralize the reactive oxygen species induced by stress during various parts of the vegetation period," which may help society's crops better cope with whatever extremes of moisture insufficiency might be lurking in the future.

Perez-Lopez et al. (2009) noted soil salinity "is one of the major environmental constraints limiting plant productivity and distribution," affecting, as it does, "19.5% of the world's irrigated area" as well as "non-irrigated croplands and rangelands." They grew two barley (Hordeum vulgare L.) cultivars, Alpha and controlled-environment within growth Iranis, chambers at either ambient (350 ppm) or elevated (700 ppm) atmospheric CO_2 concentrations in a 3:1 perlite:vermiculite mixture watered with Hoagland's solution every two days until the first leaf was completely expanded at 14 days, after which a salinity treatment was administered by adding 0, 80, 160, or 240 mM NaCl to the Hoagland's solution every two days for 14 more days. After a total of 28 days, the primary leaf of each barley plant was harvested and assessed for a number of biochemical properties.

In the various ambient-air salinity treatments, the deleterious effects of reactive oxygen species on barley leaves were made apparent through ion leakage and increases in thiobarbituric acid reactive substances (TBARS), which rose as salt concentrations rose, Perez-Lopez *et al.* report. "On the other hand," they continue, "when [the] salinity treatment was imposed under elevated CO₂ conditions, lower solute leakage and TBARS levels were observed, suggesting that the oxidative stress caused by salinity was lower."

Perez-Lopez *et al.* write, "it is concluded that elevated CO_2 protects barley cultivars from oxidative stress," noting "the relief of oxidative stress damage observed in our barley leaves grown under a CO_2 enriched atmosphere has also been observed in alfalfa (Sgherri *et al.*, 1998), pine (Vu *et al.*, 1999) and oak (Schwanz and Polle, 2001b)." Thus it would appear the ongoing rise in the air's CO_2 content may help a wide variety of Earth's plants better cope with the many serious problems caused by high soil salinity.

Farfan-Vignolo and Asard (2012) note "grassland communities constitute an important fraction of the green surface of the Earth, and are worldwide an important source of cattle-food (Carlier *et al.*, 2009; Ciais *et al.*, 2011)." The pair of Belgian researchers investigated several physiological and molecular (antioxidant) responses to water deficit in two major grassland species (*Lolium perenne* L. and *Medicago lupulina* L.) under current ambient (A) and future elevated (E) atmospheric CO₂ concentrations and air temperatures (T), where $ECO_2 = ACO_2 + 375$ ppm, and where $ET = AT + 3^{\circ}C$.

"Not surprisingly," they write, "drought caused significant increases in oxidative damage, i.e., in protein oxidation and lipid peroxidation levels." But they found "in both species the impact of drought on protein oxidation was reduced in future climate conditions [ECO₂ and ET]." And speaking of the stress-reducing effect of ECO₂, they say "this 'CO₂protection effect' is reported for a variety of abiotic stress conditions and species," citing Schwanz and Polle (1998), Sgherri et al. (2000), Geissler et al. (2009), Perez-Lopez et al. (2009), Vurro et al. (2009), and Salazar-Parra et al. (2012). The scientists conclude they "find support for this effect at the level of oxidative cell damage and protein oxidation in water-deficit responses of L. perenne and M. lupulina."

These observations make it clear plants exposed to higher-than-current atmospheric CO_2 concentrations are better equipped to deal with oxidative stress than plants growing at lower CO_2 concentrations. IPCC currently ignores these benefits.

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7.8.1.2 Benefits to Humans

As discussed in the prior section, various environmental stresses generate highly reactive oxygenated compounds that damage plants. Ameliorating these stresses typically involves the production of antioxidant enzymes that scavenge and detoxify the highly reactive oxygenated compounds. When stresses are present, concentrations and/or activities of antioxidants in plants are generally observed to be high so as to counter the effects of the stress. However, plants exposed to higher-than-current atmospheric CO₂ concentrations experience less oxidative stress and thus have a reduced need for antioxidant protection, allowing them to funnel more of their limited resources into the production of other plant tissues or processes essential to their continued growth and development.

In some cases, such resources are invested into the production and enhancement of antioxidative compounds, and these compounds are known to provide health benefits to animals and humans that ingest these plants. The material in this section examines this CO_2 -induced stimulation of antioxidant compounds, revealing another important benefit of atmospheric CO_2 enrichment that remains unreported by IPCC.

It is well-known that reactive oxygen species (ROS) generated during cellular metabolism or peroxidation of lipids and proteins play a causative role in the pathogenesis of cancer and coronary heart disease (CHD), as demonstrated by Slaga *et al.* (1987), Frenkel (1992), Marnett (2000), and Zhao *et al.* (2000). Wilcox *et al.* (2004), for example, note oxidative stress "has been related to cardiovascular disease, cancer, and other chronic diseases that account for a major portion of deaths today."Yu *et al.* (2004) note "antioxidant treatments may terminate ROS attacks and reduce the risks of CHD and cancer,

as well as other ROS-related diseases such as Parkinson's disease (Neff, 1997; Chung *et al.*, 1999; Wong *et al.*, 1999; Espin *et al.*, 2000; Merken and Beecher, 2000)," and "developing functional foods rich in natural antioxidants may improve human nutrition and reduce the risks of ROS-associated health problems."

Willcox *et al.* (2004) investigated the role of exogenous antioxidants in controlling oxidation and reviewed the evidence for their roles in preventing disease. The three nutrition experts state, "diet plays a vital role in the production of the antioxidant defense system by providing essential nutrient antioxidants such as vitamin E, C, and β -carotene, other antioxidant plant phenols including flavonoids, and essential minerals that form important antioxidant enzymes." In addition, they note, "epidemiological data generally indicate a benefit of consuming diets that are higher in antioxidant nutrients, specifically diets high in fruits and vegetables."

While it may be much easier to obtain these antioxidants by simply popping a pill or two (or even three or four), and millions of people do so daily, that approach is probably not as effective as obtaining needed antioxidants via the food one eats.

Willcox *et al.* report, for example, that in many studies of antioxidant health benefits "it is not clear whether the benefit is derived from the specific nutrients under study or another food component having health benefits yet to be discovered," or perhaps "there is a particular combination of antioxidant nutrients that provide protection." Although some epidemiological studies "appear to demonstrate clear associations, direct tests of the relationships with clinical trials have not yielded similar results." They say "the most convincing evidence of antioxidant effect on cancer prevention involves feeding fruits and vegetables rather than individual antioxidants." But what role might atmospheric CO₂ play in the matter?

Wang *et al.* (2003) evaluated the effects of elevated CO_2 on the antioxidant activity and flavonoid content of strawberry fruit they grew outof-doors in six clear-acrylic open-top chambers, two of which they maintained at the ambient atmospheric CO_2 concentration, two of which were maintained at ambient + 300 ppm CO_2 , and two of which they maintained at ambient + 600 ppm CO_2 for a period of 28 months (from early spring of 1998 through June 2000). The fruits of their labor were harvested twice—"at the commercially ripe stage" in both 1999 and 2000—after which they had them analyzed for a number of antioxidant properties and flavonol contents.

Wang *et al.* note "strawberries are good sources of natural antioxidants (Heinonen *et al.*, 1998)." They further report, "in addition to the usual nutrients, such as vitamins and minerals, strawberries are also rich in anthocyanins, flavonoids, and phenolic acids," and "strawberries have shown a remarkably high scavenging activity toward chemically-generated radicals, thus making them effective in inhibiting oxidation of human low-density lipoproteins (Heinonen *et al.*, 1998)." They note previous studies (Wang and Jiao, 2000; Wang and Lin, 2000) have shown "strawberries have high oxygen radical absorbance activity against peroxyl radicals, superoxide radicals, hydrogen peroxide, hydroxyl radicals, and singlet oxygen."

They found strawberries had higher concentrations of ascorbic acid (AsA) and glutathione (GSH) when grown under enriched CO₂ conditions. In going from ambient to +300 ppm and +600 ppm CO₂, for example, AsA concentrations rose by 10 and 13%, respectively, and GSH concentrations increased by 3 and 171%, respectively. They also learned "an enriched CO₂ environment resulted in an increase in phenolic acid, flavonol, and anthocyanin contents of fruit." For nine flavonoids, for example, there was a mean concentration increase of $55 \pm 23\%$ in going from the ambient atmospheric CO₂ concentration to +300 ppm CO₂, and a mean concentration increase of $112 \pm 35\%$ in going from ambient to +600 ppm CO₂. In addition, the "high flavonol content was associated with high antioxidant activity."

Wang *et al.* note "anthocyanins have been reported to help reduce damage caused by free radical activity, such as low-density lipoprotein oxidation, platelet aggregation, and endothelium-dependent vasodilation of arteries (Heinonen *et al.*, 1998; Rice-Evans and Miller, 1996)." In summarizing their findings, they write, "strawberry fruit contain flavonoids with potent antioxidant properties, and under CO₂ enrichment conditions, increased the[ir] AsA, GSH, phenolic acid, flavonol, and anthocyanin concentrations," further noting, "plants grown under CO₂ enrichment conditions also had higher oxygen radical absorbance activity against [many types of oxygen] radicals in the fruit."

Caldwell *et al.* (2005) note "the beneficial effects of isoflavone-rich foods have been the subject of numerous studies," specifically citing Messina (1999) and Birt *et al.* (2001), adding, "foods derived from soybeans are generally considered to provide both specific and general health benefits." They investigated how the isoflavone content of soybean seeds might be affected by the ongoing rise in the air's CO_2 content.

They grew well-watered and fertilized soybean plants from seed to maturity in pots within two controlled-environment chambers, one maintained at an atmospheric CO₂ concentration of 400 ppm and one at 700 ppm. The chambers were initially kept at a constant air temperature of 25°C. At the onset of seed fill, air temperature was reduced to 18°C until seed development was complete, in order to simulate average outdoor temperatures at this stage of plant development. In a second experiment, this protocol was repeated, except that the temperature during seed fill was maintained at 23°C, with and without drought (a third treatment). In a third experiment, seed-fill temperature was maintained at 28°C, with or without drought.

In the first experiment, where air temperature during seed fill was 18° C, the elevated CO₂ treatment increased the total isoflavone content of the soybean seeds by 8%. In the second experiment, where air temperature during seed fill was 23° C, the extra CO₂ increased total seed isoflavone content by 104%. In the third experiment, where air temperature during seed fill was 28° C, the CO₂-induced isoflavone increase was 101%. When drought stress was added as a third environmental variable, the extra CO₂ boosted total seed isoflavone content by 186% when seed-fill air temperature was 23° C, and at a seed-fill temperature of 28° C, it increased isoflavone content by 38%.

Under all the environmental circumstances studied by Caldwell *et al.*, enriching the air with an extra 300 ppm of CO_2 increased the total isoflavone content of soybean seeds. The percent increases measured under the stress situations investigated were always greater than the percent increase measured under optimal growing conditions. Thus the direct effects of atmospheric CO_2 enrichment on the healthpromoting properties of soybean seeds are likely universally beneficial and a boon to humans; Bernacchi *et al.* (2005) characterized the soybean as "the world's most important seed legume."

Ginseng (*Panax ginseng*), the roots of which are widely cultivated in China, South Korea, and Japan and have been used for medicinal purposes since Greek and Roman times, is known for its antiinflammatory, diuretic, and sedative properties and is acknowledged to be an effective healing agent (Gillis, 1997; Ali *et al.*, 2005). Normally, four to six years are required for ginseng roots to accumulate the amounts of the various phenolic compounds needed to produce their health-promoting effects. In an important step in the quest to develop an efficient culture system for the commercial production of ginseng root, Ali *et al.* (2005) investigated the effects of growing ginseng roots in suspension culture in bioreactors maintained in equilibrium with air enriched to CO_2 concentrations of 10,000 ppm, 25,000 ppm and 50,000 ppm for periods of up to 45 days.

Of most immediate concern in such an experiment would be the effects of the ultra-high CO₂ concentrations on root growth. Would they be toxic and lead to biomass reductions or even root death? The answer was a resounding no. After 45 days of growth at 10,000 ppm CO₂, for example, root dry weight was increased by fully 37% relative to the dry weight of roots produced in bioreactors in equilibrium with normal ambient air, and root dry mass was increased by 27% after 45 days at 25,000 ppm CO₂ and by a still smaller 9% after 45 days at 50,000 ppm CO_2 . Although the optimum CO_2 concentration for ginseng root growth clearly resided at some value lower than 10,000 ppm in this study, the concentration at which root growth rate was reduced below that characteristic of ambient air was somewhere significantly above 50,000 ppm, for even at that high CO₂ concentration, root growth was still greater than in ambient air.

Almost everything else measured by Ali et al. was even more dramatically enhanced by the ultrahigh CO₂ concentrations they employed in their experiment. After 45 days of treatment, total root phenolic concentrations were 58% higher at 10,000 ppm CO_2 than at ambient CO_2 , 153% higher at 25,000 ppm CO₂, and 105% higher at 50,000 ppm CO_2 , as best as can be determined from the bar graphs of their results. Total root flavonoid concentrations were enhanced by 228%, 383%, and 232%, respectively, at the same ultra-high CO_2 concentrations. Total protein contents rose by 14%, 22%, and 30%; non-protein thiol contents by 12%, 43%, and 62%; and cysteine contents by 27%, 65%, and 100% under the identical respective sets of conditions. In addition, there were equally large CO₂-induced increases in the activities of a large number of phenol biosynthetic enzymes.

Ali *et al.* note "the consumption of foodstuffs containing antioxidant phytonutrients such as flavonoids, polyphenolics, ascorbate, cysteine and non-protein thiol is advantageous for human health," citing Cervato *et al.* (2000) and Noctor and Foyer (1998). They conclude their technique for the culture of ginseng roots in CO_2 -enriched bioreactors could be used for the large-scale production of an important health-promoting product that could be provided to

the public in much greater quantities than is currently possible.

Stutte *et al.* (2008) studied *Scutellaria* plants, herbaceous perennials that possess numerous medicinal properties, noting they are "rich in physiologically active flavonoids that have a wide spectrum of pharmacological activity." They say leaf extracts of *Scutellaria barbata* have been found to be "limiting to the growth of cell lines associated with lung, liver, prostate, and brain tumors (Yin *et al.*, 2004)," and "extracts of *S. lateriflora* and the isolated flavonoids from the extracts have been shown to have antioxidant, anticancer, and antiviral properties (Awad *et al.*, 2003)." They investigated how the growth of these important plants, and their significant medicinal properties, might be affected by the ongoing rise in the air's CO_2 content.

Stutte et al. measured effects of elevated atmospheric CO₂ (1,200 and 3,000 ppm vs. a control value of 400 ppm) on plant biomass production and plant concentrations of six bioactive flavonoidsapigenin, baicalin, baicalein, chrysin, scutellarein, and wogonin-all of which, they write, "have been reported to have anticancer and antiviral properties," as described in the review papers of Joshee et al. (2002) and Cole et al. (2007). These experiments were conducted in a large step-in controlledenvironment chamber that provided a consistent light quality, intensity, and photoperiod to six small plant growth chambers that had "high-fidelity control of relative humidity, temperature, and CO₂ concentration." Each chamber was designed to monitor nutrient solution uptake by six individual plants that they grew from seed for a period of 49 days.

With respect to plant productivity (fresh and dry weight production), the three U.S. researchers determined increasing the air's CO_2 concentration from 400 to 1,200 ppm resulted in a 36% increase in shoot fresh weight in *S. barbata* and a 54% increase in shoot dry matter, with no further increases between 1,200 and 3,000 ppm CO_2 . In *S. lateriflora*, the corresponding increases in going from 400 to 1,200 ppm CO_2 were 62% and 44%, and in going to 3,000 ppm CO_2 , the total increases were 122% and 70%, respectively.

For total flavonoid concentrations in the plants' vegetative tissues, Stutte *et al.* found, in *S. barbata* "the combined concentration of the six flavonoids measured increased by 48% at 1200 and 81% at 3000 ppm CO₂," and for *S. lateriflora* they report "the total flavonoid content increased by over 2.4 times at 1200 and 4.9 times at 3000 ppm CO₂." In consequence of the compounding effect of increases in both plant

biomass and flavonoid concentration, the total flavonoid content in S. barbata rose by 72% in going from 400 to 1,200 ppm CO₂, and by 128% in going to 3,000 ppm CO₂. In S. lateriflora the corresponding increases were 320% and 1,270%. Stutte et al. conclude their results indicate "the yield and pharmaceutical quality of Scutellaria species can be enhanced with controlled environment production and CO₂ enrichment," and massively so, it appears. In addition, since they say more than 200 substancesof which more than 80% are flavonoids-have been found in a total of 65 Scutellaria species, it would also appear the "increased concentration of flavonoids through CO_2 enrichment," as they conclude, "has the potential to enhance the production and quality of medicinal plants."

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7.8.2 Common Food Plants

• The ongoing rise in the air's CO₂ content is not only raising the productivity of Earth's common food plants but also significantly increasing the quantity and potency of the many healthpromoting substances found in their tissues, which are the ultimate sources of sustenance for essentially all animals and humans.

Studies of the effects of atmospheric CO_2 enrichment on the quality of the plants that comprise our diets have typically lagged far behind studies designed to assess the effects of elevated CO_2 on the quantity of plant production. Some noteworthy exceptions were the early studies of Barbale (1970) and Madsen (1971, 1975), who discovered increasing the air's CO_2 content produced a modest increase in the vitamin C concentration of tomatoes, and Kimball and Mitchell (1981), who demonstrated enriching the air with CO_2 also stimulated the tomato plant's production of vitamin A. A few years later, Tajiri (1985) found a mere one-hour-per-day doubling of the air's CO_2 concentration doubled the vitamin C contents of bean sprouts, and did so when applied over a period of only seven days.

Fast-forwarding a couple of decades, Idso et al. (2002) grew well-watered and fertilized sour orange trees out-of-doors at Phoenix, Arizona, in clearplastic-wall open-top enclosures maintained at atmospheric CO₂ concentrations of either 400 or 700 ppm since November 1987, while evaluating the effects of the extra 300 ppm of CO₂ on the vitamin C concentrations of fully ripened fruit harvested over the eight-year period 1992–1999. In years when the production of fruit was approximately doubled by the extra CO₂, they found the fruit produced in the two CO₂ treatments were of approximately the same size, and the vitamin C concentration of the juice of the oranges grown in the CO₂-enriched air was enhanced by approximately 7% above that of the juice of the ambient-treatment oranges. In years when CO2enriched fruit numbers were more than doubled, however, the CO₂-enriched fruit were slightly smaller than the fruit produced in normal air, and the vitamin C concentration of the juice of the CO₂-enriched fruit rose even higher, to as much as 15% above that of the ambient-treatment fruit. In years when fruit numbers were less than doubled, the CO₂-enriched fruit were slightly larger than the ambient-treatment fruit, and the enhancement of the vitamin C concentration of the juice of the CO₂-enriched fruit was somewhat less than the base value of 7% typical of equal-size fruit.

With respect to the likely long-term equilibrium response of the trees, Idso et al. (2002) report that in five of the last six years of the study, "the 75% increase in atmospheric CO₂ concentration has increased: (1) the number of fruit produced by the trees by $74 \pm 9\%$, (2) the fresh weight of the fruit by 4 \pm 2%, and (3) the vitamin C concentration of the juice of the fruit by 5 \pm 1%." The eight researchers conclude, "there is reason to believe that an atmospheric CO₂ enrichment of the magnitude expected over the current century may induce a large and sustained increase in the number of fruit produced by orange trees, a small increase in the size of the fruit, and a modest increase in the vitamin C concentration of the juice of the fruit, all of which effects bode well for this key agricultural product that plays a vital role in maintaining good health in human populations around the globe."

Further support for the significance of these observations was provided by Idso and Idso (2001), who note "these findings take on great significance when it is realized that scurvy—which is brought on by low intake of vitamin C-may be resurgent in industrial countries, especially among children (Ramar et al., 1993; Gomez-Carrasco et al., 1994), and that subclinical scurvy symptoms are increasing among adults (Dickinson et al., 1994)." In addition, they report, "Hampl et al. (1999) have found that 12 to 20% of 12-18-year-old school children in the United States 'drastically under-consume' foods that supply vitamin C; while Johnston et al. (1998) have determined that 12 to 16% of U.S. college students have marginal plasma concentrations of vitamin C." Hence, "since vitamin C intake correlates strongly with the consumption of citrus juice (Dennison et al., 1998), and since the only high-vitamin-C juice consumed in any quantity by children is orange juice (Hampl et al., 1999), the modest role played by the ongoing rise in the air's CO₂ content in increasing the vitamin C concentration of orange juice could ultimately prove to be of considerable significance for public health in the United States and elsewhere."

Wang *et al.* (2003) grew strawberry plants in six clear-acrylic open-top chambers—two of which were maintained at the ambient atmospheric CO_2 concentration, two of which were maintained at ambient + 300 ppm CO_2 , and two of which were maintained at ambient + 600 ppm CO_2 —for a period of 28 months (from early spring of 1998 through June 2000), harvesting their fruit at the commercially ripe stage in both 1999 and 2000 and analyzing them for antioxidant properties and flavonol contents.

Wang et al. note strawberries are good sources of natural antioxidants and state, "in addition to the usual nutrients, such as vitamins and minerals, strawberries are also rich in anthocyanins, flavonoids, and phenolic acids," and "strawberries have shown a remarkably high scavenging activity toward chemically generated radicals, thus making them effective in inhibiting oxidation of human low-density lipoproteins (Heinonen et al., 1998)." They note previous studies (Wang and Jiao, 2000; Wang and Lin, 2000) "have shown that strawberries have high oxygen radical absorbance activity against peroxyl radicals, superoxide radicals, hydrogen peroxide, hydroxyl radicals, and singlet oxygen."

The researchers determined, first, that strawberries had higher concentrations of ascorbic acid (AsA) and glutathione (GSH) "when grown under enriched CO₂ environments." In going from ambient to +300 ppm and +600 ppm CO₂, for example, AsA concentrations increased by 10 and 13%, respectively, and GSH concentrations increased by 3 and 171%, respectively. They also learned "an enriched CO₂ environment resulted in an increase in

phenolic acid, flavonol, and anthocyanin contents of fruit." For nine flavonoids, for example, there was a mean concentration increase of $55 \pm 23\%$ in going from the ambient atmospheric CO₂ concentration to +300 ppm CO₂, and a mean concentration increase of 112 ± 35% in going from ambient to +600 ppm CO₂. In addition, the "high flavonol content was associated with high antioxidant activity." As for the significance of these findings, Wang *et al.* note "anthocyanins have been reported to help reduce damage caused by free radical activity, such as lowdensity lipoprotein oxidation, platelet aggregation, and endothelium-dependent vasodilation of arteries (Heinonen *et al.*, 1998; Rice-Evans and Miller, 1996)."

Wang *et al.* write, "strawberry fruit contain flavonoids with potent antioxidant properties, and under CO_2 enrichment conditions, increased their AsA, GSH, phenolic acid, flavonol, and anthocyanin concentrations," further noting "plants grown under CO_2 enrichment conditions also had higher oxygen radical absorbance activity against radicals in the fruit."

With respect to a major staple crop, soybeans, Caldwell et al. (2005) write "the beneficial effects of isoflavone-rich foods have been the subject of numerous studies (Birt et al., 2001; Messina, 1999)," and "foods derived from soybeans are generally considered to provide both specific and general health benefits." Caldwell et al. examined how the isoflavone content of soybean seeds might be affected by the ongoing rise in the air's CO_2 content, growing well-watered and fertilized soybean plants from seed to maturity in pots within two controlled-environment chambers, one maintained at an atmospheric CO₂ concentration of 400 ppm and one at 700 ppm. The chambers were initially kept at a constant air temperature of 25°C: at the onset of seed fill, air temperature was reduced to 18°C until seed development was complete, to simulate average outdoor temperatures at this stage of plant development. In a second experiment, this protocol was repeated, except the temperature during seed fill was maintained at 23°C, with and without drought (a third treatment). In a third experiment, seed-fill temperature was maintained at 28°C, with or without drought.

In the first experiment, where air temperature during seed fill was 18° C, the elevated CO₂ treatment increased the total isoflavone content of the soybean seeds by 8%. In the second experiment, where air temperature during seed fill was 23° C, the extra CO₂ increased total seed isoflavone content by 104%. In

the third experiment, where air temperature during seed fill was 28° C, the CO₂-induced isoflavone increase was 101%. When drought-stress was added as a third environmental variable, the extra CO₂ boosted total seed isoflavone content by 186% when seed-fill air temperature was 23° C, and at a seed-fill temperature of 28° C, it increased isoflavone content by 38%.

Under all environmental circumstances studied, therefore, enriching the air with an extra 300 ppm of CO_2 increased the total isoflavone content of soybean seeds. The percent increases measured under the stress situations were always greater than the percent increase measured under optimal growing conditions. Consequently, the direct effects of atmospheric CO_2 enrichment on the health-promoting properties of soybeans, which Bernacchi *et al.* (2005) characterize as "the world's most important seed legume," are likely universally beneficial.

Kim et al. (2005) note important flavonoids "are mainly found in the form of isoflavones in soybean seeds," including "phytoestrogens with various biological potentials such as antioxidative, pharmaceutical, oestrogenic and anticarcinogenic properties, with some acting as antiestrogens and being used as anticancer agents (Peterson and Barnes, 1991; Anderson et al., 1995; Anthony et al., 1996; Arjmandi et al., 1996; Holt, 1997; Chung et al., 2000)." They grew well-watered plants from seed to maturity in pots of sandy loam soil within the closedenvironment plant growth facility of the National Horticultural Research Institute of Korea, where the plants were exposed to natural solar radiation and the natural daily course of ambient air temperature or elevated air temperature (= ambient + 5° C) with either normal soil nitrogen content or added nitrogen equivalent to an extra 40 kg N/ha, and they were maintained at either ambient CO_2 (360 ppm) or elevated CO_2 (650 ppm). At the end of the growing season, the plants were harvested and their total biomass determined. The concentrations of 12 isoflavones found in their seeds-three aglycons, three glucosides, three acetyl conjugates, and three malonyl conjugates-were quantitatively analyzed

Kim *et al.* found the CO_2 -induced increase in total plant biomass at normal ambient temperatures was 96% in the case of normal soil nitrogen and 105% in the case of added nitrogen, and at the warmer temperatures it was 59% in the case of normal soil nitrogen and 68% in the case of added nitrogen. With respect to seed isoflavone concentrations, the CO_2 induced increases of all 12 isoflavones were fairly similar. As a group, at normal ambient temperatures the mean increase was 72% in the case of normal soil nitrogen and 59% in the case of added nitrogen, and at the warmer temperatures it was 72% in the case of normal soil nitrogen and 106% in the case of added nitrogen. Irrespective of soil nitrogen status and air temperature, therefore, increases in the air's CO_2 content produced large increases in soybean biomass, as well as soybean seed concentrations of 12 major isoflavones.

Schonhof et al. (2007) stated the glucosinolates contained in broccoli plants comprise a group of compounds responsible for bioactive many physiological effects, including enhancing the plant's flavor and helping to prevent cancer in people who consume them, citing Mikkelsen et al. (2002). In a set of three experiments conducted in a controlled greenhouse environment, Schonhof et al. grew wellwatered and fertilized broccoli plants in large soilfilled containers at ambient (430-480 ppm) and elevated (685-820 ppm) atmospheric CO_2 concentrations to the stage where fully developed heads could be harvested for glucosinolate analyses. They report the roughly 65% increase in atmospheric CO₂ concentration increased the fresh weight of the broccoli heads by approximately 7% and increased the total glucosinolate concentration of the broccoli inflorescences by 14%, due primarily to identical 37% increases in two particular glucosinolates: glucoiberin and glucoraphanin. The four researchers conclude atmospheric CO₂ enrichment "can enhance the health-promoting quality of broccoli because of induced glucosinolate content changes."

Jin et al. (2009) grew well-watered and fertilized spinach from seed (five to each 3.5-liter pot filled with a loam soil) for approximately three weeks in controlled-environment chambers containing air of either 350 ppm or 800 ppm CO₂. They harvested the them. and measured plants. weighed the concentrations of several of the nutritive substances contained in their leaves. As best as can be determined from the graphs of their results, the extra 450 ppm of CO_2 increased the fresh weight of the spinach shoots by about 67% and their dry weight by approximately 57%. In addition, it boosted the soluble sugar concentrations of their leaves by approximately 29% and soluble protein concentrations by about 52%. The extra CO₂ also increased spinach leaf concentrations of ascorbate, glutathione, and total flavonoids by 21%, 16%, and 3%, respectively.

La *et al.* (2009) noted "epidemiological studies show there is a negative relationship between Brassicaceae vegetable intake and the risk of a number of cancers (Wattenberg, 1993; Kohlmeier and Su, 1997; Price *et al.*, 1998)," adding, "it has been widely recognized that some of the cancerchemoprotective activities in these vegetables are attributable to their contents of glucosinolates (Zhao *et al.*, 1992; Wattenberg, 1993; Tawfiq *et al.*, 1995; Fahey *et al.*, 1997; Rosa *et al.*, 1997; Holst and Williamson, 2004)." They set out to determine what effect the ongoing rise in the air's CO_2 content might have on the production of these important cancerfighting agents in yet another common food plant.

The five scientists placed pairs of seedlings of Chinese kale in 1.8-L pots "fixed in a foam cavity with sponge" within growth chambers maintained at either 350 or 800 ppm CO_2 , where the plant's roots were immersed in culture solutions treated with either 5.0 mmol nitrogen (N) per L (low N), 10 mmol N per L (medium N), or 20 mmol N per L (high N) and allowed to grow for 35 days. The plants then were separated into their primary morphological parts and weighed, and their bolting stems were ground into powder for glucosinolate analyses.

"Regardless of N concentration," the researchers write, the elevated CO₂ treatment "significantly increased plant height [15.64%], stem thickness [11.79%], dry weights of the total aerial parts [11.91%], bolting stems [15.03%], and roots [16.34%]." Also, the elevated CO₂ increased the total glucosinolate concentrations of the bolting stems in the low and medium N treatments by 15.59% and 18.01%, respectively, compared with those at ambient CO₂, although there was no such effect in the high N treatment. Consequently, in terms of the total amount of glucosinolate production within the bolting stems of Chinese kale, these results suggest increases of 33 to 36% may be obtained for plants growing in low to medium N conditions in response to a 450 ppm increase in the air's CO₂ concentration.

Gwvnn-Jones et al. (2012) note "dwarf shrub berries are particularly valued by the human populations at Northern Latitudes as an autumn harvest, but are also consumed by a wide range of animals (Anderson, 1985)." They note the fruit of these shrubs contain high concentrations of flavonoids and anthocyanins (Heinonen et al., 1998; Faria et al., 2005; Heinonen, 2007), which can free-radicals scavenge cancer-causing (Martin-Aragon et al., 1998; Taruscio et al., 2004) and reduce the oxidative stress caused by these compounds in animals (Johnson and Felton, 2001). They state "there is already laboratory evidence suggesting that the consumption of Vaccinium myrtillus berry flavonoids by small mammals can increase the antioxidant capacity of their blood plasma which could promote

their fitness," citing Talavera et al. (2006).

In an open-top chamber study conducted at the Abisko Scientific Research Station in Northern Sweden, Gwynn-Jones et al. assessed the impact of atmospheric CO₂ enrichment (600 vs. 360–386 ppm) on the berry quality of Vaccinium myrtillus and Empetrum hermaphroditum in the final year (2009) of a 17-year experiment. As best as can be determined from the 10 researchers' graphically presented results, it appears the mean concentration of quercetin glycosides in V. myrtillus was increased by approximately 46% by the approximate mean CO₂ concentration increase of 227 ppm. In E. hermaphroditum, syringetin glycoside concentrations were increased by about 36% by the extra CO₂, and five anthocyanins had their concentrations increased as follows: delphinidin-3-hexoside by about 51%, cyanidin-3-hexoside by about 49%, petunidin-3hexoside by about 48%, malvidin-3-pentoside by about 46%, and malvidin-3-hexoside by about 59%. Gwynn-Jones et al. conclude, "consumers of E. hermaphroditum may gain higher antioxidant intake at elevated CO₂," and "some European bird species show preferential feeding towards berries with higher antioxidant contents (Catoni et al., 2008), which could have important implications for the palatability and, therefore, seed dispersal of these species."

It is becoming increasingly evident the ongoing rise in the air's CO₂ content is not only raising the productivity of Earth's common food plants but also significantly increasing the quantity and potency of the many health-promoting substances found in their tissues, which are the ultimate sources of sustenance for essentially all animals and humans. As these foods make their way onto our dinner tables, they improve our health and help us better contend with the multitude of diseases and other maladies that regularly afflict us. It is possible, if not likely, that the lengthening of human lifespan that has occurred over the past half-century or more-as described by Horiuchi (2000) and Tuljapurkar et al. (2000)-may in some significant part be due to the concomitant CO₂-induced increases in the concentrations of the many health-promoting substances found in the various plant-derived foods we eat. Yet these real and many benefits continue to be ignored by IPCC.

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7.8.3 Medicinal Plants

• Atmospheric CO₂ enrichment positively impacts the production of numerous health-promoting substances found in medicinal or "health food" plants, and this phenomenon may have contributed to the increase in human life span that has occurred over the past century or so.

Studies of the effects of atmospheric CO_2 enrichment on the amounts and concentrations of various healthpromoting substances produced by medicinal or "health food" plants have lagged behind studies designed to assess the effects of elevated CO_2 on the quantity of plant production. Nevertheless, enough research has been conducted on this topic to reveal atmospheric CO_2 enrichment positively impacts these important substances.

Stuhlfauth et al. (1987), for example, found a near-tripling of the air's CO₂ content increased the dry weight production of the woolly foxglove plant (which produces the cardiac glycoside digoxin used in the treatment of cardiac insufficiency) by 63% under dry conditions and by 83% when well-watered, and the concentration of digoxin within the plant dry mass was enhanced by 11% under well-watered conditions and by 14% under conditions of water stress. Stuhlfauth and Fock (1990) obtained similar results in a field study, with a near-tripling of the air's CO_2 content leading to a 75% increase in plant dry weight production per unit land area and a 15% increase in digoxin per unit dry weight of plant material, resulting in an actual doubling of total digoxin yield per hectare of cultivated land.

Idso et al. (2000) grew spider lily plants out-ofdoors at Phoenix, Arizona in clear-plastic-wall opentop enclosures that had their atmospheric CO₂ concentrations maintained at either 400 or 700 ppm for two consecutive two-year growth cycles. The 75% increase in the air's CO₂ concentration increased aboveground plant biomass by 48% and belowground (bulb) biomass by 56%. In addition, the extra CO_2 increased the concentrations of five bulb constituents possessing anticancer and antiviral properties. Mean percentage increases in these concentrations were, the researchers write, "6% for a two-constituent (1:1) mixture of 7-deoxynarciclasine and 7-deoxy-transdihydronarciclasine, 8% for pancratistatin, 8% for trans-dihydronarciclasine, and 28% for narciclasine, for a mean active-ingredient percentage concentration increase of 12%." Combined with the 56% increase in biomass, these percentage concentration bulb increases resulted in a mean active-ingredient increase of 75% for the 75% increase in the air's CO₂ concentration. The substances described above have been shown to be effective in fighting a number of devastating human maladies, including leukemia; ovary sarcoma; melanoma; and brain, colon, lung, and renal cancers, as well as Japanese encephalitis and yellow, dengue, Punta Tora, and Rift Valley fevers.

Zobayed and Saxena (2004) studied St. John's wort, a perennial herb native to Europe and West Asia that has been used for treatment of mild to moderate depression, inflammation, and wound healing (Brolis et al., 1998; Stevinson and Ernst, 1999), and which has been reported to be a potential source for anticancer, antimicrobial, and antiviral medicines (Schempp et al., 2002; Pasqua et al., 2003). The two scientists grew shoots of the plant for 42 days under well-watered and fertilized conditions within a greenhouse, where the air's CO_2 concentration averaged 360 ppm, as well as in computer-controlled environment chambers maintained at a mean CO₂ concentration of 1,000 ppm, with all other environmental conditions being comparable between the two treatments.

On the final day of the study, Zobayed and Saxena determined the net photosynthetic rates of the plants in the CO₂-enriched chambers were 124% greater than those of the plants growing in ambient air, and their dry weights were 107% greater. The extra 640 ppm of CO₂ in the high-CO₂ treatment increased plant concentrations of hypericin and pseudohypericin (two of the major health-promoting substances in the plants) by just over 100%. Consequently, the 180% increase in the air's CO₂
content more than doubled the dry mass produced by the well-watered and fertilized St. John's wort plants, and it more than doubled the concentrations of hypericin and pseudohypericen found in their tissues. Thus the CO_2 increase more than quadrupled the total production of these two health-promoting substances.

Mosaleeyanon *et al.* (2005) also studied St. John's wort, growing well-watered and fertilized seedlings for 45 days in controlled-environment chambers at low, medium, and high light intensities (100, 300, and 600 μ mol m⁻² s⁻¹, respectively) at atmospheric CO₂ concentrations of 500, 1,000, and 1,500 ppm. On the 45th day of their experiment, the plants were harvested, and the hypericin, pseudohypericin, and hyperforin (another important health-promoting substance) they contained were extracted from their leaves and quantified.

Under all three light intensities employed in the study, the four researchers found the 1,000-ppm increase in atmospheric CO_2 concentration experienced in going from 500 to 1,500 ppm produced total plant biomass increases of approximately 32%. Over this same CO₂ range, hypericin concentrations rose by 78, 57, and 53%, respectively, under the low, medium, and high light intensities. Pseudohypericin concentrations rose by 70, 57, and 67%, and hyperforin concentrations rose by 102, 23, and 3%. Compared to plants growing outof-doors in air of 380 ppm CO₂ and at light intensities on the order of 1,770 μ mol m⁻² s⁻¹, Mosaleeyanon *et* al. discovered total plant biomass was fully 30 times greater in the high-light, high-CO₂ controlledenvironment treatment, and under the same conditions the concentrations of hypericin and pseudohypericin were 30 and 41 times greater. Thus the researchers demonstrated growing St. John's wort plants in CO₂enriched air in controlled-environment chambers can enormously enhance both plant biomass and hypericin and pseudohypericin contents.

Ziska *et al.* (2005) grew well-watered and fertilized tobacco and jimson weed plants from seed in controlled-environment chambers maintained at atmospheric CO₂ concentrations of either 378 ppm (ambient) or 690 ppm (elevated) and mean air temperatures of either 22.1 or 27.1°C for 50 and 47 days after planting for tobacco and jimson weed, respectively. They sampled the plants at weekly intervals beginning at 28 days after planting for tobacco and 16 days for jimson weed, to determine the effects of these treatments on three plant alkaloids possessing important pharmacological properties: nicotine, in the case of tobacco, and atropine and scopolamine, in the case of jimson weed. At the time of final harvest they found the elevated CO_2 had increased the aboveground biomass production of tobacco by approximately 89% at 22.1°C and 53% at 27.1°C, and had increased that of jimson weed by approximately 23% and 14% at the same respective temperatures. The extra CO_2 also was found to have reduced the concentration of nicotine in tobacco and increased the concentration of scopolamine in jimson weed, but it had no significant effect on the concentration of atropine in jimson weed.

The two significant changes (reduced nicotine in tobacco and increased scopolamine in jimson weed) likely would be characterized as beneficial by most people; as the six scientists report, nicotine is acknowledged to have significant negative impacts on human health, and scopolamine is used as a sedative and as "an antispasmodic in certain disorders characterized by restlessness and agitation, (e.g., tremens, psychosis, delirium mania and Parkinsonism)." Nevertheless, Ziska et al. state "it can be argued that synthetic production of these secondary compounds alleviates any concern regarding environmental impacts on their production from botanical sources," but they note "developing countries (i.e., ~75% of the world population) continue to rely on ethno-botanical remedies as their primary medicine (e.g. use of alkaloids from jimson weed as treatment for asthma among native Americans and in India)." In addition, "for both developed and developing countries, there are a number of economically important pharmaceuticals derived solely from plants whose economic value is considerable (Raskin et al., 2002)."

Another plant with an impressive history of medicinal use is ginseng. Well-known for its antiinflammatory, diuretic, and sedative properties, and long acknowledged to be an effective healing agent (Gillis, 1997), ginseng is widely cultivated in China, South Korea, and Japan, where it has been used for medicinal purposes since Greek and Roman times. Normally, ginseng roots take four to six years to accumulate the amounts of the various phenolic compounds needed to produce their health-promoting effects.

Ali *et al.* (2005) investigated the consequences of growing ginseng plants in suspension culture in bioreactors maintained in equilibrium with air enriched to CO_2 concentrations of 10,000 ppm, 25,000 ppm, and 50,000 ppm for periods of up to 45 days. Of most immediate concern in such an experiment are the effects of the ultra-high CO_2 concentrations on root growth and whether they would be toxic and lead to biomass reductions or even

root death. The answer, according to Ali *et al.*'s experiment was a resounding *no*. After 45 days of growth at 10,000 ppm CO₂, root dry weight was increased by about 37% relative to the dry weight of roots produced in bioreactors in equilibrium with ambient air, and it was increased by a lesser 27% after 45 days at 25,000 ppm CO₂ and by a still smaller 9% after 45 days at 50,000 ppm CO₂. Consequently, although the optimum CO₂ concentration for ginseng root growth likely resides somewhere below 10,000 ppm, the concentration at which root growth is reduced below that characteristic of ambient air resides somewhere above 50,000 ppm, for even at that extremely high CO₂ concentration, root growth was still greater than it was in ambient air.

Almost everything else measured by Ali *et al.* was even more dramatically enhanced by the ultrahigh CO₂ concentrations. After 45 days of treatment, total root phenolic concentrations were 58% higher at 10,000 ppm CO₂ than at ambient CO₂, 153% higher at 25,000 ppm CO₂, and 105% higher at 50,000 ppm CO₂, as best as can be determined from the bar graphs of their results. Total root flavonoid concentrations were enhanced by 228%, 383%, and 232%, respectively; total protein contents rose by 14%, 22%, and 30%; non-protein thiol contents by 12%, 43%, and 62%; and cysteine contents by 27%, 65%, and 100%. There were equally large CO₂-induced increases in the activities of a large number of phenol biosynthetic enzymes.

Ali et al. state "the consumption of foodstuffs containing antioxidant phytonutrients such as flavonoids, polyphenolics, ascorbate, cysteine and non-protein thiol is advantageous for human health," citing Cervato et al. (2000) and Noctor and Foyer (1998). They conclude their technique for the culture of ginseng roots in CO₂-enriched bioreactors could be used for the large-scale production of an important health-promoting product that could be provided to the public in much greater quantities than is currently possible. It should be further noted that as the air's CO₂ content continues to climb, it likely will bring forth a substantial natural increase in the concentrations of health-promoting substances in ginseng and other medicinal plants, leading to better human health the world over. It is likely this phenomenon already has played some role in the lengthening of human life span that has occurred since the dawn of the Industrial Revolution, as described by Horiuchi (2000) and Tuljapurkar et al. (2000), when the air's CO₂ concentration rose from roughly 280 ppm to its current value of close to 400 ppm.

Zou (2005) studied the brown seaweed Hizikia

fusiforme, which serves as both a health-promoting food and a delicacy in China, Japan, and Korea. The researcher collected specimens from intertidal rocks along the coast of Nanao Island, Shantou (China) and maintained them in glass aquariums in filtered natural seawater enriched with 60 µM NaNO3 and 6.0 µM NaH₂PO₄, where the plants were continuously aerated with either ambient air of 360 ppm CO₂ or CO₂enriched air of 700 ppm CO₂. Zou measured the seaweed's relative growth and nitrogen assimilation rates as well as its nitrate reductase activity. Zou reports the slightly less than a doubling of the air's CO₂ concentration increased the seaweed's mean relative growth rate by about 50%, its mean rate of nitrate uptake during the study's 12-hour light periods by around 200%, and its nitrate reductase activity by approximately 20% over a wide range of substrate nitrate concentrations.

Zou notes "the extract of H. fusiforme has an immune-modulating activity on humans and this ability might be used for clinical application to treat several diseases such as tumors (Suetsuna, 1998; Shan et al., 1999)." He also states the alga is "becoming one of the most important species for seaweed mariculture in China, owing to its high commercial value and increasing market demand." In addition, Zou reports "the intensive cultivation of H. fusiforme would remove nutrients more efficiently with the future elevation of CO_2 levels in seawater, which could be a possible solution to the problem of ongoing coastal eutrophication," which in turn suggests rising atmospheric CO₂ concentrations may additionally assist in the amelioration of this important environmental problem.

Hoshida *et al.* (2005) grew the marine alga unicellular *Nannochloropsis* sp.alga in batch culture under normal (370 ppm) and elevated (3,000 and 20,000 ppm) air CO₂ concentrations in an attempt to learn how elevated CO₂ impacted the alga's ability to produce eicosapentaenoic acid (EPA), a major polyunsaturated omega-3 fatty acid that may play an important role in human health related to the prevention of certain cardiovascular diseases (e.g. atherosclerosis, thrombogenesis) and the inhibition of tumor growth and inflammation, as described by Dyerberg *et al.* (1978), Hirai *et al.* (1989), Kinsella *et al.* (1990), and Sanders (1993).

The five researchers note "Nitsan *et al.* (1999) showed that supplementing the diet of hens with *Nannochloropsis* sp. led to an increased content of n-3 fatty acids in the egg yolk, indicating an additional role in enhancing the nutritional value of eggs," and they report "feeding *Nannochloropsis* sp. to rats

caused a significant increase in the content of n-3 polyunsaturated fatty acids (Sukenik *et al.*, 1994)," suggesting the alga may play an "important role as the source for n-3 polyunsaturated fatty acids in human nutrition."

The Japanese scientists found "maximum EPA production was obtained when 20,000 ppm CO₂ was supplied 12 hours prior to the end of the exponential growth," and "total EPA production during 4-day cultivation was about twice that obtained with ambient air." They also report other researchers have obtained similar results, noting EPA is found mainly in thylakoid membranes (Sukenik et al., 1989; Hodgson et al., 1991), and prior experiments have shown "the amount of stroma thylakoid membrane increased in several plants under elevated CO₂ concentrations (Griffin et al., 2001)." In addition, "in Synechococcus lividus, reduction and synthesis of thylakoid membrane occurred by CO₂ deprivation and elevation, respectively (Miller and Holt, 1977)," and "in Chlorella vulgaris, altering the ambient CO₂ concentration varied fatty acid composition (Tsuzuki et al., 1990)." Finally, Hoshida et al. report, "the effect of CO₂ on fatty acid composition and/or fatty acid content had been reported in algae and higher plants (Tsuzuki et al., 1990; Sergeenko et al., 2000; He et al., 1996; Radunz et al., 2000)," and "increased production caused by elevated EPA CO_2 concentration was reported in P. tricornutum (Yongmanitchai and Ward, 1991)." Consequently, as the atmospheric CO₂ concentration continues to rise, concentrations of omega-3 fatty acids will be widely enhanced in both aquatic and terrestrial plants.

Ziska et al. (2008) note, "among medicinal plants, the therapeutic uses of opiate alkaloids from poppy (Papaver spp.) have long been recognized," and they considered it important "to evaluate the growth and production of opiates for a broad range of recent and atmospheric carbon dioxide projected concentrations," which they did for the wild poppy (P. setigerum). The authors grew well-watered and fertilized plants from seed within growth chambers maintained at atmospheric CO₂ concentrations of 300, 400, 500, and 600 ppm for a period of 90 to 100 days, quantifying plant growth and the production of the alkaloids morphine, codeine, papaverine, and noscapine, which were derived from latex obtained from capsules produced by the plants.

Relative to the plants grown at 300 ppm CO_2 , those grown at 400, 500, and 600 ppm produced approximately 200, 275, and 390% more aboveground biomass, respectively, as best as can be determined from the researchers' bar graphs. In addition, "reproductively, increasing CO_2 from 300 to 600 ppm increased the number of capsules, capsule weight and latex production by 3.6, 3.0 and 3.7 times, respectively, on a per plant basis," so, ultimately, "all alkaloids increased significantly on a per plant basis." They conclude, "as atmospheric CO_2 continues to increase, significant effects on the production of secondary plant compounds of pharmacological interest (i.e. opiates) could be expected." These effects, they write, "are commonly accepted as having both negative (e.g. heroin) and positive (e.g. codeine) interactions with respect to public health."

Vurro et al. (2009) note thyme (a well-known culinary and medicinal herb) has "a considerable economic value in the nutraceutical and pharmaceutical industry (Vardar-Uenlue et al., 2003; Konyalioglu et al., 2006)," and "thyme essential oil possesses per se considerable antioxidant capacity (Economou et al., 1991), and may therefore contribute towards the control of antioxidant status in the leaves." They grew well-watered one-year-old thyme plants for three additional months (10 June-10 September) in pots (filled with 40% sand, 25% clay, and 35% silt) out-of-doors within a mini-free-air CO₂enrichment (FACE) system at Ravenna, Italy. The air's CO₂ concentration was maintained at approximately 500 ppm (during daylight hours only), and control plants were continuously exposed to air of approximately 370 ppm CO₂. They measured a number of plant characteristics at the end of each of the three months of the study.

The four researchers state "none of the plants grown under high levels of CO₂ for 90 days presented either significant differences in fresh weight and dry weight compared with controls, or macroscopic alteration of morphogenesis (number and length of nodes/internodes, branching, leaf area and chlorosis, etc.), at any of the sampling times." However, "in plants grown under elevated CO₂, a relative increase in oil yield of 32, 34 and 32% was, respectively, recorded in the first, second and third sampling-time (July, August and September)," and they observed a "general depression of the oxidative stress under elevated CO₂" that led to a "down-regulation of leaf reactive oxygen species-scavenging enzymes under elevated CO2." In layman's terms, the Italian scientists say their results pointed to "a 'low cost' life strategy for growth under elevated CO₂, not requiring synthesis/activation of energy-intensive and expensive metabolic processes." This change in behavior should allow the plants to invest more energy in the production of essential plant oils that have, as Vurro et al. describe it, "considerable economic value in the

nutraceutical and pharmaceutical industry."

Goncalves et al. (2009) write, "the impact of elevated carbon dioxide concentration on the quality of berries, must, and red wine (with special reference to volatile composition, phenolic content, and antioxidant activity) made from Touriga Franca, a native grape variety of Vitis vinifera L. for Port and Douro wine manufacturing grown in the Demarcated [northern Portugal], Region of Douro was investigated during 2005 and 2006." The six Portuguese researchers grew grapevines in open-top chambers maintained at either 365 or 550 ppm CO₂, finding, "in general, the increase of CO₂ did not affect berry characteristics" and "did not significantly change the total antioxidant capacity of the red wines." They write, "thirty-five volatile compounds belonging to seven chemical groups were identified," and, "generally, the same volatile compounds were present in all of the wines." Although some of these compounds were "slightly affected," they note "the red wine quality remained almost unaffected." Thus, Goncalves et al. say their study shows "the predicted rise in CO₂ might strongly stimulate grapevine photosynthesis and yield without causing negative impacts on the quality of grapes and red wine."

Bindi et al. (2001) conducted a two-year (1996, 1997) FACE study of 20-year-old grapevines (Vitis vinifera L., cv Sangiovese) near Rapolano, Siena (Italy). They enriched the air around the plants to 550 and 700 ppm (compared to ambient CO₂ levels in those two years that averaged 363 ppm, per Mauna Loa data), measuring numerous plant parameters in the process, including-after the fermentation process was completed—"the principal chemical compounds that determine the basic red wine quality." They report "elevated atmospheric CO₂ levels had a significant effect on biomass components (total and fruit dry weight) with increases that ranged from 40 to 45% in the 550 ppm treatment and from 45 to 50% in the 700 ppm treatment." In addition, "acid and sugar contents were also stimulated by rising CO₂ levels up to a maximum increase in the middle of the ripening season (8-14%)," but as the grapes reached the maturity stage, the CO₂ effect on these parameters gradually disappeared. In terms of various healthpromoting substances contained in the wine itself, in response to the $\sim 50\%$ increase in atmospheric CO₂ concentration in going from ~363 to ~550 ppm CO₂, as can be calculated from the bar graphs of their results, the concentrations of total polyphenols, total flavonoids, total anthocyanins, and non-anthocyanin flavonoids in the wine rose by approximately 19%, 33%, 31%, and 38%, respectively. Bindi et al. conclude, "the expected rise in CO_2 concentrations may strongly stimulate grapevine production without causing negative repercussions on quality of grapes and wine," and in fact their data suggest the ongoing rise in the air's CO_2 content might slightly enhance the health-protective properties of the wine.

Oliveira et al. (2010) write, "there is a growing interest in the use of inulin as a health food ingredient, as an alternative for low-calorie sweeteners, and as a dietary fiber and fat substitute (Ritsema and Smeekens, 2003)." In addition, they say "it is suggested" a daily intake of low amounts of inulin or its derivatives promotes the growth of beneficial bacteria in the intestinal tract, as well as anti-tumor effects, citing Roberfroid (2005). Hence, they studied Vernonia herbacea, a plant from the Brazilian Cerrado that accumulates inulin-type fructans in underground organs called rhizophores. The five Brazilian researchers grew well-watered and fertilized V. herbacea plants from rhizophore fragments for two months and then transferred them in groups of three to 3-L pots containing forest soil. The plants were maintained in open-top chambers in a glasshouse for 120 days at atmospheric CO₂ concentrations of either 380 or 760 ppm, and the scientists measured the plants' net photosynthetic water rates. use efficiencies, and fructan concentrations after 15, 30, 60, 90, and 120 days of treatment, as well as aboveand below-ground biomass at the end of the experiment.

Oliveira *et al.* write, the "plants under elevated CO_2 presented increases in height (40%), photosynthesis (63%) and biomass of aerial (32%) and underground (47%) organs when compared with control plants." In addition, "water use efficiency was significantly higher in treated plants, presenting a 177% increase at day 60." They found fructan concentration remained unchanged, but because of the significant CO_2 -induced increase in underground organ biomass, "a 24% increase in total fructan yield occurred."

Ghasemzadeh *et al.* (2010) write, "free radicals and single oxygen are recognized as major factors causing various chronic diseases such as cancer, diabetes, *etc.*," and as a result, they note, "the health maintenance function of antioxidant components in various foods has received much attention," citing Byers and Guerrero (1995) and Namiki (1990). They further observe, "phenolic acids and flavonoids are antioxidants with health benefits such as antiinflammatory and anti-tumor effects (Heijnen *et al.*, 2001; Chun *et al.*, 2003; Harborne and Williams, 2000; Chen, 2004)," specifically noting "Sung-jin *et* *al.* (2008) showed that some flavonoid components in green tea are effective in inhibiting cancer or induce mechanisms that may kill cancer cells and inhibit tumor invasion."

The Malaysian researchers grew two varieties of Malaysian young ginger (Zingiber officinale)-Halia Bentong and Halia Bara-from rhizomes planted in a drip-irrigated 1:1 mixture of burnt rice husk and coco peat in polyethylene bags placed within controlledenvironment chambers maintained at atmospheric CO₂ concentrations of either 400 or 800 ppm for a period of 16 weeks. They then harvested the plants and analyzed their leaves and rhizomes for a wide variety of phenolics and flavonoids, along with their free radical scavenging power, which is a measure of their ability to prevent dangerous reactive oxygen species from attacking various parts of the body and causing a large number of potentially life-threatening maladies. Malaysian young ginger is one of the medicinal/food plants used by Polynesians for more than 2,000 years in treating cancer, diabetes, high blood pressure, and many other illnesses

Ghasemzadeh *et al.* found, on average, "flavonoid compounds increased 44.9% in leaves and 86.3% in rhizomes of Halia Bentong and 50.1% in leaves and 79% in rhizomes of Halia Bara when exposed to elevated carbon dioxide conditions." Phenolic compounds increased even more: by 79.4% in leaves and 107.6% in rhizomes of Halia Bentong and 112.2% in leaves and 109.2% in rhizomes of Halia Bara. In addition, the increase in the CO₂ concentration from 400 to 800 ppm increased the free radical scavenging power by 30.0% in Halia Bentong and 21.4% in Halia Bara. Also, "the rhizomes exhibited more enhanced free radical scavenging power, with 44.9% in Halia Bentong and 46.2% in Halia Bara."

The three scientists say their results indicate "the yield and pharmaceutical quality of Malaysian young ginger varieties can be enhanced by controlled environment production and CO₂ enrichment."

Ghasemzadeh and Jaafar (2011) also focused on ginger (*Zingiber officinale* Roscoe), noting it is "an important horticultural crop in tropical Southeast Asia" and is the Asian continent's "most widely used herb." It "contains several interesting bioactive constituents and possesses health promoting properties (Rozanida *et al.*, 2005)." Ghasemzadeh and Jaafar lament "no information is available on the effect of CO_2 concentration on the polyphenolic content and scavenging capacity against active oxygen species of Malaysian young ginger varieties."

The two Malaysian scientists grew two varieties

of ginger (Halia Bentong and Halia Bara) from rhizomes placed in polyethylene bags filled with a 1:1 mixture of burnt rice husk and coco peat for a period of 16 weeks in controlled-environment chambers maintained at two atmospheric CO_2 concentrations (400 and 800 ppm). They measured a number of important plant properties during and after the growing period.

In response to the increase in the air's CO_2 content, Ghasemzadeh and Jaafar state, their research showed the rate of photosynthesis was increased by 65% in Halia Bentong and by 46% in Halia Bara, which led to total biomass increases of 48% in Halia Bentong and 76% in Halia Bara. Total flavonoids in the new rhizomes of Halia Bentong and Halia Bara rose by 82% and 118%, respectively, and total phenolics in the same two varieties rose by 154% and 183%, respectively.

The two researchers say their study revealed "ginger has good free radical scavenging ability and therefore can be used as a radical inhibitor or scavenger, acting possibly as a primary antioxidant." Also, increasing the CO_2 content of the atmosphere "can enhance the antioxidant activity of ginger extract, especially in its rhizomes," which can be of great value because it thereby "increases the concentrations of several therapeutic compounds."

Ibrahim and Jaafar (2011) report "the antioxidant properties in food have been a focus of interest in recent years due to the health maintenance functions of these components that can help reduce the risk of chronic diseases such as cancer, hypertension and diabetes." This phenomenon, they note, "is attributed to the high scavenging activity of antioxidants towards free radicals that are usually associated with these diseases (Namiki, 1990; Byers and Guerrero, 1995)." They used a randomized complete block design 3 by 3 experiment to study and distinguish the relationships among production of secondary total phenolics, total flavonoids, metabolites. gluthatione, oxidized gluthatione, soluble carbohydrate, and antioxidant activities of the Malaysian medicinal herb Labisia pumila Blume under three levels of CO₂ enrichment (400, 800, and 1,200 ppm) for 15 weeks.

The two Universiti Putra Malaysia researchers write, "secondary metabolites, glutathione, oxidized gluthathione and antioxidant activities in a descending manner came from the leaf enriched with 1200 ppm $CO_2 >$ leaf 800 ppm $CO_2 >$ leaf 400 ppm $CO_2 >$ stem 1200 ppm $CO_2 >$ stem 800 ppm $CO_2 >$ stem 400 ppm $CO_2 >$ root 1200 ppm $CO_2 >$ root 800 ppm $CO_2 >$ > root 400 ppm CO_2 ," and "correlation analyses revealed strong significant positive coefficients of antioxidant activities with total phenolics, flavonoids, gluthatione and oxidized gluthatione," indicating "an increase in antioxidative activity of *L. pumila* under elevated CO_2 might be up-regulated by the increase in production of total phenolics, total flavonoids, glutathione, oxidized gluthatione and soluble sugar." Ibrahim and Jaafar conclude their study results imply "the medicinal potential of herbal plants such as *L. pumila* can be enhanced under elevated CO_2 , which simultaneously improved the antioxidative activity that was indicated by the high oxygen radical absorbance activity against peroxyl radicals, superoxide radicals, hydrogen peroxide and hydroxyl radicals."

Also studying Labisia pumila Blume, Jaafar et al. (2012) wrote, "plant antioxidants have been a focus of attention in recent years due to the health preservation functions of these components that can help reduce the threat of chronic diseases such as cancer, diabetes and hypertension." These benefits, they note, are "attributed to the high scavenging activity of antioxidants towards free radicals that are usually associated with these diseases (Byers and Guerrero, 1995)." Among this group of plant compounds are phenolic acids and flavonoids, both of which exhibit, "high anti-inflammatory and antithey state. carcinogenic activities (Heijnen et al., 2001; Chun et al., 2003)." In addition, phenolics and flavonoids can function as reducing agents, free radical scavengers, and quenchers of singlet oxygen formation (Chan et al., 2008). Many of the components of polyphenols have been proven to have significant roles in curing cancer and other human ailments (Harborne and Williams, 2000).

Jaafar *et al.* conducted a split plot 3 x 3 experiment designed to examine the impact of 15 weeks of exposure to three concentrations of CO₂ (400, 800, and 1,200 ppm) on the phenolic and flavonoid compound profiles—as well as the antioxidant activities—of three varieties (*alata*, *pumila*, and *lanceolata*) of *Labisia pumila* Benth. or kacip fatimah, as it is commonly known throughout Southeast Asia. They describe the latter as "a subherbaceous plant with creeping stems from the family Myrsinaceae that is found widespread in Indochina and throughout the Malaysian forest"; it has historically been used to help maintain a healthy female reproductive system.

The three Malaysian researchers report that when exposed to elevated CO_2 (1200 ppm), "gallic acid increased tremendously, especially in var. *alata* and *pumila* (101–111%), whilst a large quercetin increase was noted in var. *lanceolata* (260%), followed closely by *alata* (201%)." They also found "caffeic acid was enhanced tremendously in var. *alata* (338–1100%) and *pumila* (298–433%)," and "rutin continued to increase by 262% after CO₂ enrichment." In addition, they note naringenin was enhanced by 1,100% in var. *pumila*. Finally, they report "the increase in production of plant secondary metabolites in *L*. *pumila* was followed by enhancement of the antioxidant activity under exposure of elevated CO₂."

Moghaddam *et al.* (2011) explain *Centella asiatica* or Gotu Kola is a small herbaceous annual plant that has been used as a medicinal herb or nutraceutical in Ayurvedic, African, and traditional Chinese medicine for more than 2,000 years, valued for its mildly antibacterial, antiviral, and antiinflammatory properties. It also has been used as a rejuvenating diuretic herb that is purported to clear toxins, reduce inflammations and fevers, improve healing and immunity, improve memory, and provide a balancing effect on the nervous system.

The six scientists grew well-watered and fertilized *C. asiatica* plants for four to five weeks in individual polybags filled with a 1:1:1 mix of sand, coco dust, and compost within controlled environment chambers, where CO_2 concentrations of 400 and 800 ppm were maintained, the researchers write, "for two hours every day between 8:30 to 10:30 am." At the end of these four- to five-week periods the plants were harvested and their leaves assessed for total biomass and total flavonoid content. The latter substance is considered to be the source of the many health benefits attributed to the species.

Moghaddam *et al.* report the daily two-hour 400 ppm increase in the controlled environment chambers' atmospheric CO_2 concentration led to a 193% increase in *C. asiatica* leaf biomass, a 264% increase in plant water use efficiency, and a 171% increase in leaf total flavonoid content. The six scientists conclude, "collectively, the enhancement in yield and quality provides an economic motivation to produce a consistent pharmaceutical-grade product for commercial purposes," via what they describe as "controlled environment plant production." It also stands to reason the ongoing rise in the atmosphere's CO_2 concentration should be gradually increasing the medicinal potency of *C. asiatica* plants either growing wild or cultivated out-of-doors.

Ibrahim and Jaafar (2012) studied the oil palm *Elaeis guineensis* (Jacq.)—the highest-yielding vegetable oil producer in the world—which has gained wide recognition because of the health-promoting properties of some of its flavonoids and phenolics, which the two scientists describe as

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"natural antioxidants that may reduce oxidative damage to the human body," citing Mandel and Youdim (2004). For 15 weeks, the pair of researchers grew initially-five-month-old seedlings of three progenies of oil palm (deli AVROS, Deli Yangambi, and Deli URT) within growth chambers maintained at atmospheric CO_2 concentrations of either 400, 800, or 1,200 ppm, measuring a large number of important plant properties and processes.

Ibrahim and Jaafar discovered the production of total flavonoids and phenolics was highest under 1,200 and lowest at 400 ppm CO₂, and "the antioxidant activity, as determined by the ferric reducing/antioxidant potential (FRAP) activity increased with increasing CO₂ levels." In leaves, for example, they found the quantity of "total flavonoids was enhanced by 86% and 132%, respectively, in 800 and 1200 ppm compared to 400 ppm CO₂," and total phenolics "increased by 52% to 91% under elevated CO₂ compared to the ambient CO₂ condition." Ibrahim and Jaafar say their findings "suggest that enrichment with higher than ambient CO₂ level is able to enhance the production of gallic acid and rutin in oil palm seedlings." This finding is important because these bioactive components, as they describe them, "act as free radical scavengers, and hence can reduce the possibilities of major diseases such as cancers of leukemia, breast, bone and lung," citing Kaufman et al. (1999) and Wink (1999).

In light of the research discussed above, it is clear atmospheric CO_2 enrichment positively impacts the production of numerous health-promoting substances found in medicinal or "health food" plants, and this phenomenon may have contributed to the increase in human life span that has occurred over the past century or so (Horiuchi, 2000; Tuljapurkar and Boe, 2000). As the atmosphere's CO_2 content continues to rise, humanity may be helped even more in this regard in the years and decades to come.

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7.8.4 Health-Harming Substances

• There appears to be little reason to expect any significant CO₂-induced increases in human-health-harming substances produced by plants as the atmosphere's CO₂ concentration continues to rise.

Whereas IPCC makes no mention of the CO_2 -induced enhancement of certain health-promoting substances in plants, as described in the subsections above, it is quick to point out the possibility of a CO_2 -induced enhancement in certain health-*harming* substances. The research on that topic is the focus of this subsection.

Wayne et al. (2002) grew common ragweed plants from seed in controlled-environment glasshouses maintained at ambient (350 ppm) and enriched (700 ppm) atmospheric CO_2 concentrations for 84 days. They then sampled the pollen from the central plants of each stand, assessed the pollen's characteristics, and harvested all mature seeds and above-ground shoot material. They report, "standlevel pollen production was 61% higher in elevated versus ambient CO₂ environments" and "CO₂-induced growth stimulation of stand shoot biomass was similar to that of total pollen production." Although the researchers admit it would be "challenging to accurately predict the future threat to public health caused by CO₂-stimulated pollen production"because "it is likely that plant pollen production will also be influenced by factors expected to change in concert with CO₂, including temperature, precipitation, and atmospheric pollutants"-they nevertheless suggest "the incidence of hay fever and related respiratory diseases may increase in the future."

Weber (2002) discussed the study of Wayne *et al.* in a guest editorial published in the same issue of the *Annals of Allergy, Asthma & Immunology.* He begins by noting "one can always wonder whether such manipulations [i.e., those employed in Wayne *et al.*'s study] have any relationship to present reality, or indeed, conditions that one can expect in the near future," and then proceeds methodically to his conclusion: "it would be premature to assume that increased pollen grain numbers necessarily lead to an increased aeroallergen exposure."

Weber notes, "allergenic activity of short ragweed will vary from year to year, even from the same source and supplier (Maasch et al., 1987)," and he cites Lee et al. (1979) as having found "varying potency in plants at the same site from year to year. which [were] attributed to seasonal climatic differences, primarily of rainfall." The latter researchers found a four-fold range in the allergenic potency of ragweed pollen within a single county in Illinois (USA). Consequently, Weber concludes "a constant relationship between pollen mass and allergenic protein content is not a given," and it will remain speculative until scientists determine whether "the increased pollen grains seen with the increased ambient CO₂ levels maintain the same ratio of allergenic proteins."

A further demonstration of the tenuousness of the suggestion of Wayne et al.-that "the incidence of hay fever and related respiratory diseases may increase in the future" because of the near-universal growth-promoting effects of atmospheric CO₂ enrichment-is provided by Rogers et al. (2006). They collected and vernalized ragweed seeds by sowing them in containers kept in a refrigerator maintained at 4°C. They transferred one-third of the seeded containers at 15-day intervals to glasshouse modules maintained at atmospheric CO₂ concentrations of either 380 or 700 ppm, and the seeds were allowed to germinate (also at 15-day intervals, with the middle germination date approximating that of plants currently growing naturally in the vicinity of where the seeds were collected). They kept the seeds under well-watered and fertilized conditions until the seeds senesced. The researchers then harvested the seeds and conducted assessments of plant and allergenic pollen biomass.

As best as can be determined from the graphical representations of Rogers *et al.*'s data, the end-of-season CO₂-induced increase in aboveground plant biomass was about 16% for the date of emergence typical of the present, and the corresponding increase in pollen production was about 32%. For the 15-day earlier date of emergence, which was chosen to represent "anticipated advances of spring several decades into the future" based upon projected rates of future global warming, the end-of-season CO₂-induced change in aboveground plant biomass was only about +3%, and the end-of-season CO₂-induced change in pollen production was actually a negative 3%.

The most meaningful way of viewing the results, then, is to determine the change in pollen production that would occur in going from today's atmospheric CO_2 concentration and date-of-onset of spring (380 ppm, middle date of germination) to the elevated CO_2 concentration and earlier date-of-onset of biological spring (700 ppm, 15-day earlier date of germination); when this is done, the production of allergenic pollen is seen to rise by just 1–2%.

Caporn *et al.* (1999) studied bracken, a weed that poses a potential threat to human health in the United Kingdom and other regions, growing specimens for 19 months in controlled-environment chambers maintained at atmospheric CO₂ concentrations of 370 and 570 ppm and normal and high levels of fertilization. They found the elevated CO₂ consistently increased rates of net photosynthesis in bracken from 30 to 70%, depending on soil fertility and time of year. The elevated CO₂ did not increase total plant dry mass or the dry mass of any plant organs, including rhizomes, roots, and fronds. The only significant effect of the elevated CO₂ on bracken growth was observed in the normal nutrient regime, where elevated CO₂ reduced the area of bracken fronds.

Matros et al. (2006) grew tobacco plants in pots filled with quartz sand placed in controlled-climate chambers maintained at either 350 or 1,000 ppm CO₂ for eight weeks, irrigating them daily with a complete nutrient solution containing either 5 or 8 mM NH₄NO₃. Some of the plants in each treatment were mechanically infected with potato virus Y (PVY) when they were six weeks old. At the end of the study, the researchers report, the plants grown at elevated CO₂ and 5 mM NH₄NO₃ "showed a marked and significant decrease in content of nicotine in leaves as well as in roots," and at 8 mM NH₄NO₃ the same was found to be true of upper leaves but not of lower leaves and roots. In addition, with respect to the PVY part of the study, they found the plants grown at high CO₂ "showed a markedly decreased spread of virus."

Matros *et al.* report "tobacco plants grown under elevated CO_2 show a slight decrease of nicotine contents," and "elevated CO_2 resulted in reduced spread of PVY." Most people likely would consider both of these impacts beneficial; potato virus Y is economically important because it infects many crops and ornamental plants throughout the world, and nicotine is nearly universally acknowledged to have significant negative effects on human health (Topliss *et al.*, 2002).

Mohan *et al.* (2006) investigated the effects of an extra 200 ppm of atmospheric CO_2 on the growth and

development of Toxicodendron radicans, commonly known as poison ivy, as well as its effect on the plant's toxicity, over a period of six years at the Duke Forest FACE facility, where the noxious vine grew naturally in a loblolly pine plantation's understory. The researchers surrounded clumps of it with 4 cm plastic-mesh enclosures to protect them from damage by indigenous white-tailed deer. This long and detailed study revealed atmospheric CO₂ enrichment increased poison ivy photosynthesis by 77% and boosted its water use efficiency by 51%. At the end of the study's sixth year, the aboveground biomass of poison ivy plants in the CO₂-enriched plots was 62% greater than that of poison ivy plants in the ambienttreatment plots. In addition, the high-CO₂-grown plants produced "a more allergenic form of urushiol," the substance that produces the plant's allergic reaction in humans.

Not unsurprisingly, the seven scientists say their findings indicate under future levels of atmospheric CO_2 , poison ivy "may grow larger and become more noxious than it is today." And so it may, but the story is not quite that simple, as the next study indicates.

Londre and Schnitzer (2006) studied woody vines or lianas, focusing on changes over a period of 45 years in 14 temperate deciduous forests of southern Wisconsin (USA). During that time (1959-1960 to 2004–2005), the air's CO₂ concentration rose by 65 ppm, the mean annual air temperature of the region rose by 0.94°C, and its mean winter air temperature rose by 2.40°C, but its mean annual precipitation did not change. The researchers found, contrary to their initial hypothesis, "liana abundance and diameter did not increase in the interiors of Wisconsin (USA) forests over the last 45 years." Toxicodendron radicans, or poison ivy-which they note "grew markedly better under experimentally elevated CO₂ conditions than did competing trees" in the study of Mohan et al. (2006)-decreased in abundance over this time period, and significantly.

The two researchers say their study suggests "lianas are limited in the interiors of deciduous forests of Wisconsin by factors other than increased levels of CO_2 ." It is likely, for example, the growth of interiorforest lianas was limited by the enhanced tree growth provided by the CO_2 increase, which resulted in the trees becoming more competitive with the vines because of CO_2 -induced increases in tree leaf numbers, area, and thickness, all of which would lead to less light being transmitted to the lianas growing beneath the forest canopy. This phenomenon apparently negated the enhanced propensity for growth that was provided the vines by the increase in the atmosphere's CO_2 concentration—the potential growth was not realized because the declining light intensity prevented it.

Londre and Schnitzer provide support for this reasoning in their finding that "compared to the forest interior, lianas were >4 times more abundant within 15 m of the forest edge and >6 times more abundant within 5 m of the forest edge." The two researchers note this "strong gradient in liana abundance from forest edge to interior" "was probably due to light availability." In addition, they say their results "are similar to findings in tropical forests, where liana abundance is significantly higher along fragmented forest edges and within tree fall gaps."

In conclusion, there appears to be little reason to expect any significant CO_2 -induced increases in human-health-harming substances produced by plants as the atmosphere's CO_2 concentration continues to rise.

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