MINI REVIEW

Global warming: the implications for urologic disease

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Global warming is receiving more attention in both the lay and scientific press. However, many individuals still view global warming as an abstract, distant concern that has little, if any, impact on their daily lives. As urologists, it is important to realize that global warming may influence some of the diseases that we treat. Much of the scientific basis for the link between climate and urologic disease is still in its nascent stages. However, a review of the emerging literature suggests that climatic changes may well alter the frequency of some urologic conditions.

Key Words: global warming, urologic disease

Introduction

Ninety-seven percent of climate scientists agree that climate-warming trends over the past century are very likely due to human activities.[1] Emissions, primarily carbon dioxide, erode the ozone layer, increase the amount of ultraviolet radiation reaching the earth's surface and contribute significantly to global warming. The concentrations of carbon dioxide are about 30% higher than they were 150 years ago at the dawn of the industrial revolution.[2] The earth's average surface temperature has risen about 1.4 degrees Fahrenheit since the late 19th century which has been largely driven by increased carbon dioxide and other human-made emissions into the atmosphere.[3] Most of the warming has taken place in the past 35 years with the 5 warmest years on record taking place since 2010.

Objective data such as shrinking of the polar ice sheets, a global rise of sea levels of about eight inches in the last century and acidification of the oceans have all been documented.[1] The compelling question for us is what impact will these environmental changes have on the diseases that urologists treat? Let us review four potential urologic consequences of global warming.

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Global warming and urolithiasis

The etiology of urolithiasis is multifactorial and includes genetic predisposition, dietary and environmental factors. However, Brikowski et al[4] have reported a climate-related increase in the prevalence of urolithiasis in the United States (U.S.). They used two models, a non-linear and linear model to examine the potential impact of climate change on the prevalence of urolithiasis in the U.S. The non-linear model was based primarily on data derived from the Second Cancer Prevention Survey of 1982 in which a history of stone disease was elicited from greater than one million subjects.[5] An alternative linear model described the temperature dependence of stone prevalence based on data from high mean annual temperature locales[6] and data from a Veterans Administration dataset from the Urologic Diseases in America project.[7]

Their analysis is that an unanticipated result of global warming is the likely northward expansion of the "stone belt." They estimate that the portion of the U.S. population living in high-risk zones for urolithiasis will grow from 40% in 2000 to 56% by 2050 to 70% by 2095.[4] They further estimate that there will be a climate-related increase of 1.6 to 2.2 million lifetime cases of nephrolithiasis by 2050 with an associated cost increase of 0.9-1.3 billion dollars annually (year - 2000 dollars) which represents a 25% increase over current expenditures.[4] Similar predictions have been suggested by Romero et al.[8]

Global warming and infertility

It has been accepted urologic dogma that heat is harmful to male reproduction. Reducing intra-scrotal temperature is the underpinning for the surgical repair of varicoceles.[9,10] There is also abundant animal data that suggests that high temperatures negatively affect reproduction in nonhuman male mammals.[11] Lam and Miron first reported that atypically warm months lead to a decline in births 9 to 10 months later in humans.[12] Provocative work recently reported by Barreca et al[13] further suggests that transient increases in ambient temperature may impact reproduction rates. They reviewed the effects of temperature shocks on birth rates in the U.S. between 1931 and 2010. They found that days with a mean temperature about 80 degrees Fahrenheit caused a large decline in births 8 to 10 months later. They estimated that each additional greater than 80 degree Fahrenheit day caused birth rates to fall by approximately 0.6% 8 months later, 0.40% 9 months later and 0.21 % 10 months later. All these effects were significant at the 5% level. There was a rebound effect, 11-13 months later, which only compensated for about 50% of the decreased births. They considered changes in frequency of intercourse and their model appeared to be free of other biases. This work, although provocative, is preliminary, and future studies will need to be done to verify the significance of global warming and its potential impact on male fertility.

Global warming and type 2 diabetes mellitus

The diagnosis and treatment of erectile dysfunction comprises an important portion of urologic practice. Type 2 diabetes mellitus (DM) is a major cause of erectile dysfunction. Therefore, any environmental changes that contribute to an increased incidence of type 2 DM are potentially impactful on urologic practice.

Blauw et al recently speculated that type 2 diabetes incidence and glucose intolerance increase with higher outdoor temperatures.[14] Using meta-regression they determined an association between annual temperature and diabetes incidence between 1996 to 2009 for each U.S. state separately. They found similar results on a global scale. In a prior study, Hanssen et al[15] reported that acclimatization of patients with type 2 diabetes to moderate cold for only 10 days improved insulin sensitivity as determined by a greater glucose infusion rate. It has been hypothesized that an increase flux of fatty acids toward brown adipose tissue results in a compensatory increased flux of glucose to other metabolically active tissues which improves systemic insulin sensitivity.[16]

Recently, Lee at al[17] found a positive association between outdoor temperature and glycosated hemoglobin (HgbA1c) which suggests that systemic glucose homeostasis may be influenced by environmental temperature. Blauw and associates hypothesize that cold temperature exposure activates brown adipose tissue which are the fat stores that the body uses to generate heat.[14] Potentially an increased flux of fatty acids into brown fat could result in a compensatory increased flux of glucose to other metabolically active tissues which would therefore improve insulin sensitivity at lower temperatures. However, some experts caution against an over interpretation of this work, claiming it is a case of correlation and not causation.[18]

Global warming/UV radiation/vitamin D/prostate cancer

Ozone depletion does not cause global warming, per se, but both of these environmental problems have a common cause-human activities that generate pollutants that alter the atmosphere.[19] The ozone layer is thinned by increasing concentrations of chlorofluorocarbons. These chemicals can remain in the atmosphere for decades.[19] NASA scientists have reported that ultraviolet radiation has increased over the past 30 years, but has stabilized since the mid-1990s.[20] Although not conclusively proven at this time, both ozone depletion and global warming could indirectly impact prostate cancer by permitting increased ultraviolet radiation exposure which could increase vitamin D production in the skin.

It has been reported that vitamin D deficiency affects almost 50% of the world's population.[21] This is due to a variety of factors, but decreased sunlight exposure is a contributing factor. It is well established that UV radiation modulates vitamin D production which in turn can influence prostate cancer.

Vitamin D is synthesized in the body starting in the skin under the stimulation of ultraviolet light when a cholesterol precursor molecule (7-dehydrocholesterol) is converted into a vitamin D hormone precursor, cholecalciferol (vitamin D3). Vitamin D3 is then hydroxylated in the liver to 25(OH)D3 and then converted in the kidney to 1,25 dihydroxycholecalciferol or calcitriol.[22]

The possible relationship between vitamin D levels and prostate cancer is still evolving and under study by multiple investigators. Vitamin D has potentially several beneficial effects which could modulate cancers in general including the induction of the p53 homolog, inhibition of angiogenesis, inhibition of motility and invasion and induction of differentiation.[22] Vitamin D has

also been reported to influence monocyte/macrophage differentiation, T cell function and cytokine production.

Some recent studies report exciting data regarding the link between vitamin D and prostate cancer. Murphy et al[23] reported a link between lower vitamin D levels and higher Gleason score (greater than or equal to 4+4) and stage in European men on prostate biopsy. In African-American men, they found increased risk of prostate cancer on biopsy correlated with lower serum vitamin D levels.[23]

However, the relationship between serum vitamin D levels and prostate cancer is not straightforward. Tuohimaa et al[24] have reported a U shaped risk of prostate cancer with both low and high vitamin D levels in Nordic men. The identification of low vitamin D levels and increased prostate cancer risk was not surprising, but the association of increased risk and high vitamin D levels was unexpected. The authors speculated that high vitamin D concentration may affect vitamin D metabolism within the prostate, leading to increased 24 hydroxylation.[25] This would result in reduced concentration of the biologically active 1alpha 25(OH)2-vitamin D3 in the prostate which causes weak proliferative action. The exact relationship vitamin D levels and prostate cancer risk and severity remains an ongoing focus of investigation. However, there is significant evidence to suggest that higher UV radiation exposure can potentially correct low vitamin D levels into the normal range and therefore decrease prostate cancer risk. There is epidemiologic data that supports this hypothesis. Schwartz and Hanchette have reported that Caucasian mortality rates from prostate cancer are significantly inversely correlated with ultraviolet radiation.[26]

Conclusion

Global warming has potentially a widespread impact on multiple aspects of society. Urologists need to be aware that the ultimate environmental and medical consequences of global warming are still evolving and are not totally predictable. Urologists would be wise to become engaged in the ongoing dialogue on both the causes and solutions of global warming as they may have significant urologic sequelae. □

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