Climate change and kidney disease—threats and opportunities

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Over the past few centuries, human activity has fundamentally changed our planet. Indeed, the current epoch has been described as the *anthropocene*, whereby humans constitute the most potent driver of change to the Earth's systems.[1] Human beings now live on every continent and have had a direct impact on at least 83% of the Earth's surface.[2] Human activities have profoundly altered the functioning of the planet's ecosystems and are triggering the mass extinction of both terrestrial and marine life. Increasingly, leading health journals are referring to the concept of "planetary boundaries" within which humanity can safely operate, highlighting that the crossing of these boundaries risks abrupt and irreversible consequences for global human communities and ecological systems.[1] One planetary boundary that is being rapidly approached is the atmospheric concentration of carbon dioxide that determines our climate, with substantial implications for human health.

In 2009 and again in 2015, Joint Commissions from the *Lancet* and University College of London outlined the major threats to global health from climate change.[3,4] These included changing patterns of disease, water and food insecurity, air pollution, extreme climatic events, and population displacement. Taken together, these impacts are now viewed as the greatest public health challenge of the 21st century.[3,4] At the same time, the most recent *Lancet* commission report highlighted that addressing climate change may well be the greatest opportunity we have had to improve global health.[4]

The medical community will be at the forefront of responding to the health impacts of climate change. It also will have a vital role to play in preparedness planning, education, and advocacy. This paper describes the changing patterns of disease that are likely to confront renal physicians due to climate change over coming decades. It also discusses the health co-benefits achievable from actions that mitigate our impact on the climate, with particular focus on the unique opportunity this presents for stemming the rising tide of lifestyle-related chronic kidney disease among global populations.

Heat-related renal diseases

Acute kidney injury. The increased frequency and intensity of heat waves across continents since 1950 have been clearly documented.[5] Climate models predict that heat waves will become still more frequent, severe, and persistent in a future warmer climate, particularly in the high latitudes of North America and Europe.[5]

This has potential implications for rates of acute kidney injury (AKI), with multiple studies demonstrating increased hospital admissions from AKI during heat waves.[6] During the severe European heat wave of 2003, kidney failure was a prominent cause of excess mortality.[6] Susceptible individuals include those well known to nephrologists: the elderly, those with chronic kidney disease (CKD), and/or taking medications such as diuretics, β-blockers, and angiotensin-converting enzyme inhibitors.

Chronic kidney disease. Of possibly greater significance, there has been recent recognition of epidemics of CKD involving individuals exposed to recurrent extreme heat.[7] These have been confirmed in regions of Central America, Sri Lanka, and India and suspected in particular "hot spots" in the Middle East, Africa, and North America. Those affected are primarily young male laborers from rural communities required to perform strenuous work under very hot conditions (e.g., sugar cane harvesters). They typically present with asymptomatic increases in creatinine and minimal proteinuria, which commonly progresses to end-stage kidney disease.[7] Limited biopsy data have shown chronic tubulointerstitial disease and secondary glomerulosclerosis, often with an ischemic component.[7] The death toll is high, estimated at >20,000 in Central America alone.

The definitive underlying cause of CKD in these cases remains unproven, and it is possible that an unidentified toxic or infectious agent might be involved. However, epidemiologic and experimental studies raise concern that this entity represents a form of heat-induced nephropathy.[7] In terms of mechanism, heat stress, overexertion, and water shortage can lead to any combination of rhabdomyolysis, hyperosmolarity, hyperthermia, and extracellular volume depletion.[7] It has been postulated that these processes might result in AKI via activation of the vasopressin, aldose reductase and fructokinase pathways, hypokalemia-induced renal vasoconstriction, uricosuria and urate crystal formation, and/or a reduction in renal blood flow.[7] In turn, it is well documented that repeated AKI can lead to CKD.

Nephrolithiasis. Increased ambient temperature and sunlight indices have also been recognized as major risk factors for kidney stone formation.[8] This is assumed to be due to heat-associated sweating, a compensatory reduction in urine volume, and subsequent urinary supersaturation with stone-forming salts. A possible contribution might also come from increased urinary calcium excretion due to higher vitamin D levels in individuals in sun-exposed regions, although data supporting this are limited.

Quantifying the relationship between temperature and stone formation, 1 study documented a 36% to 39% excess risk of nephrolithiasis across 5 metropolitan areas in the United States, with a mean daily temperature of 30 °C relative to 10 °C.[8] A second study from Seoul, South Korea, reported a relative risk of nephrolithiasis of 2.54 (95% confidence interval 1.67–3.87) with a mean daily temperature of 29 °C compared with 13 °C.[9]

By the end of this century, the global average temperature is expected to increase by 1 to 4.5 °C due to anthropogenic greenhouse gas (GHG) emissions (Figure 1).[5] Increasing nephrolithiasis prevalence rates are expected with this. Using a climate model of intermediate severity warming, Brikowski *et al.*[10] have predicted that the US is likely to see an extra 1.6–2.2 million-lifetime cases of nephrolithiasis by 2050 due to climate change, at an additional cost to the health care system of $0.9–1.3 billion annually. They have further suggested that the proportion of the US population living in high-risk zones for nephrolithiasis will increase from 40% in 2000 to 70% by 2095.

Renal disease from vector-borne diseases

At warmer temperatures, mosquitoes (responsible for most vector-borne diseases) feed more frequently and produce more offspring.[4,11] Parasites and viruses also complete incubation faster in the female mosquito, increasing the proportion of infective vectors. Because of this, climate is an important determinant of both the incidence and geographic distribution of vector-borne diseases.

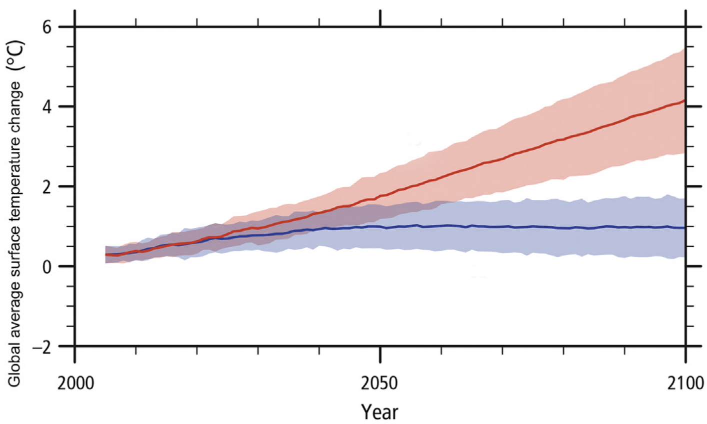

Figure 1 | Projected global average surface temperature change from 2006 to 2100. Changes are relative to the period 1986 to 2005. The red line indicates the temperature change that is likely to occur if emissions continue at their current levels. The blue line indicates the likely change in temperature with major, nearly immediate reductions in greenhouse gas emissions. Uncertainty in predictions is represented by the shaded areas. Adapted from IPCC, 2014: *Climate Change 2014: Synthesis Report. Contribution of Working Groups I, II and III to the Fifth Assessment Report of the Intergovernmental Panel on Climate Change*, Figure SPM.6. IPCC, Geneva, Switzerland.