Dr Johnson has funding with the NIH, DOD, and VA Merit. He is on the scientific board of Amway and XORT therapeutics. He has patents and patent applications related to uric acid and fructose metabolism and is a member of a startup company, Colorado Research Partners LLC that is developing inhibitors of sugar metabolism.
Mean temperatures have increased 0.8 degree C since 1880, with two-thirds of the change since 1975.

Global Warming is responsible for 75% of moderate heat extremes throughout the globe.


http://earthobservatory.nasa.gov/Features/WorldOfChange/decadaltemp.php
Iran city hits suffocating heat index of 165 degrees, near world record

The Kidney: An Organ hit hard by Dehydration

Classic Teaching

- Sweat--- loss of sodium and water
- Kidneys must concentrate the urine
- This occurs with some retention of urea and creatinine but was generally thought to be reversible
- However, a newly recognized type of chronic kidney disease is being observed among workers in hot regions of the world
An Epidemic of Chronic Kidney Disease

[Map of Central America highlighting Guanacaste and Rest of Costa Rica]

[Graph showing rising trends for Guanacaste and Rest of Costa Rica for Men and Women]
Mesoamerican Nephropathy

- Occurs predominantly along the Pacific Coast.
- Primarily men working in sugar cane fields, but can occur with other occupations.
- Presents with asymptomatic elevation in creatinine, low grade proteinuria, and chronic tubulointerstitial nephritis.
- To a lesser extent affects women, possibly children.
- 20,000 Deaths so far!
Pesticides are Likely not the Cause of Mesoamerican Nephropathy

- Disease occurs in occupations that do not use pesticides (miners, construction workers, fishing industry, port workers)
- During the season, those cutting sugarcane are at higher risk for kidney damage than those who are applying the pesticides
Central America: Site of High Solar Radiation Correlates with Site of CKD Epidemic
Sugar Cane Workers are Exposed to Extreme Heat

- Work starts at 5:30 am
- By 9:30 am they are working under heat conditions that exceed the recommendations of the OSHA (Occupational Safety Health Administration)

*Crowe et al Am Indus Med 56:1157; 2013*
Symptoms of Dehydration are Common in Sugarcane Workers

Could Mesoamerican Nephropathy be a Dehydration Disorder?
Can Heat Induced Dehydration cause CKD?

GROUPS
- Controls
- Heat: + water
- Heat: water at night

(Heat = Dehydrated)

Heating at 39.5 °C
30 min every hour

No heating

TOTAL DURATION
5 weeks

Roncal-Jimenez et al Kidney Int. 2013
Recurrent Dehydration Causes Chronic Kidney Disease in Laboratory Mice

Roncal-Jimenez et al. Kidney Int. 2013
Mesoamerican Nephropathy: A Uric acid Disorder?

- Heat and Exercise
- Subclinical Rhabdomyolysis
- Release of DNA, RNA
- Lactic acid
- Increase in Uric acid
- High Urine Uric acid
- Urine acidification
- Crystal mediated AKI
Urate crystals are Common in the Urine of Sugarcane workers during the sugarcane harvest.
Sugar cane Workers in Chinandega, Nicaragua Showed Marked Uricosuria in One of Four Urines

Urine Uric acid (mg/dl)

Nov 26th  Dec 5th  May 13th, 2013

> 100 mg/dl

May 104 °F
World “CKD HOT SPOTS” Chronic Interstitial Nephritis in Agricultural Workers

<table>
<thead>
<tr>
<th>Country</th>
<th>Location</th>
</tr>
</thead>
<tbody>
<tr>
<td>India, south</td>
<td>Andhra Pradesh (Uddanam Coast)</td>
</tr>
<tr>
<td></td>
<td>Goa</td>
</tr>
<tr>
<td></td>
<td>Chimakurthy mandal</td>
</tr>
<tr>
<td></td>
<td>Akola districts in Maharashtra</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>North Central Province</td>
</tr>
<tr>
<td>Mexico</td>
<td>Tierra Blanca, Vera Cruz</td>
</tr>
<tr>
<td>Egypt</td>
<td>El Minya, Upper Egypt</td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>Tabuk Area</td>
</tr>
<tr>
<td>Sudan</td>
<td>Rural Areas</td>
</tr>
<tr>
<td>Thailand</td>
<td>Northeastern</td>
</tr>
</tbody>
</table>
Sites of Heat Waves in India are Associated with Epidemics of Chronic Kidney Disease
Heat Stress Associated CKD: The first epidemic due to Global Warming

- An Epidemic of CKD is occurring in Central America
- The primary risk factor is recurrent dehydration
- Recurrent dehydration and heat stress causes CKD in animals
- The injury may be mediated by elevated uric acid and uricosuria
- These pathways may be involved in other types of AKI and CKD
- Global warming and increased intake of sugary beverages may have a role in why CKD is increasing
Collaborative Involvement of Climatologists

1. First, to perform **climate modeling to address key climate characteristics important for the development of disease**, including temperature (maximum temperature, percent of extremely hot days that surpass a set temperature, mean temperature, humidity, heat indices), water (monsoon, rain patterns, total precipitation) and wind measurements. This may involve both historic climate data and global climate models.

2. Second, **application of the climate models will be performed on a finer scale for various ‘hot spots’** where impact on disease incidence and prevalence has been identified.

3. Third, **climate modeling will be used to predict where epidemics may be occurring** but are still not recognized.

4. Fourth, **to generate clinical-climate relationships** by monitoring changes in temperatures in a targeted area on shorter time scales (hourly, daily basis) coupled with the real time hydration measurements.

5. **Fifth, to predict the onset of heat waves (heat warning systems)** that could alert workers to reduce work hours and increase hydration to prevent kidney damage.
## A Call to Arms

- Need for Climatologists and Heat Wave Warnings
- Worker Health: Need for Preventive Measures
- Physicians/Health Care: Need to Optimize Hydration Solutions
- Better Recognition of Kidney Injury: Biomarkers and Genetics
- Prediction Mapping: Identifying Sites Based on Climate and Work
- Food Security: How to Improve Food Production in Safe Way
The Colorado Climate and Health Consortium
Special Thanks

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