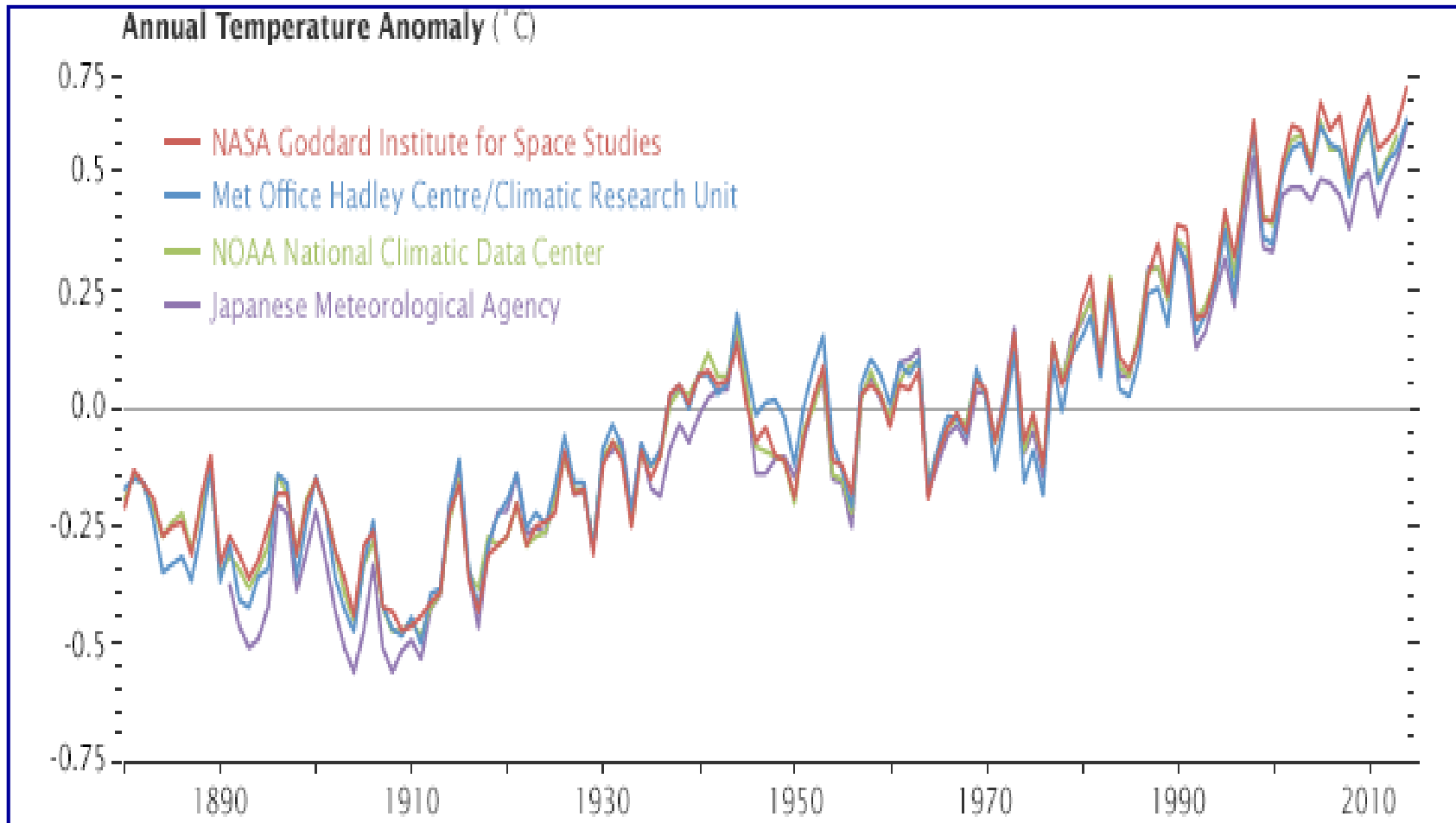


# Heat Stress, Dehydration Climate and Health

**Richard J Johnson MD**  
**University of Colorado**

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.

# World Temperature Change Over Last Century

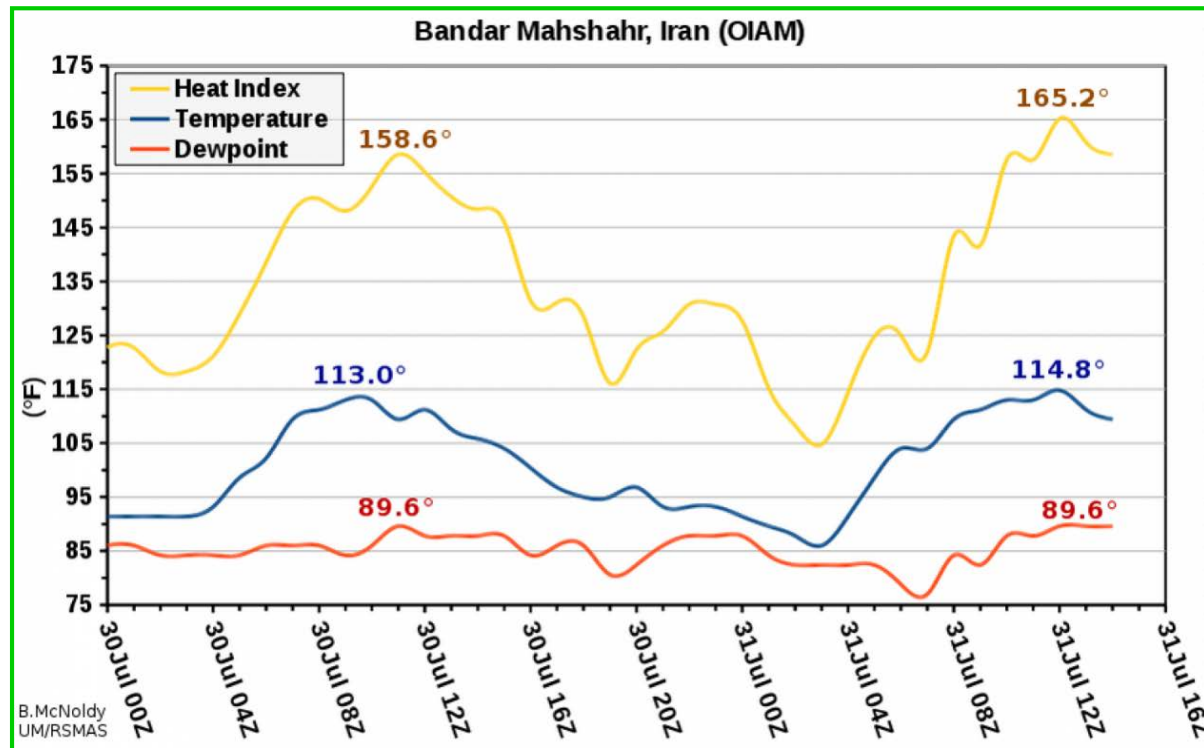


Mean temperatures have increased 0.8 degree C since 1880, with two-thirds of the change since 1975

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

Fischer and Knutti  
Nature Clim Change  
2015;5:560

# Iran city hits suffocating heat index of 165 degrees, near world record



The Washington Post, July 31<sup>st</sup>, 2015 <http://www.washingtonpost.com/blogs/capital-weather-gang/wp/2015/07/30/iran-city-hits-suffocating-heat-index-of-154-degrees-near-world-record/>

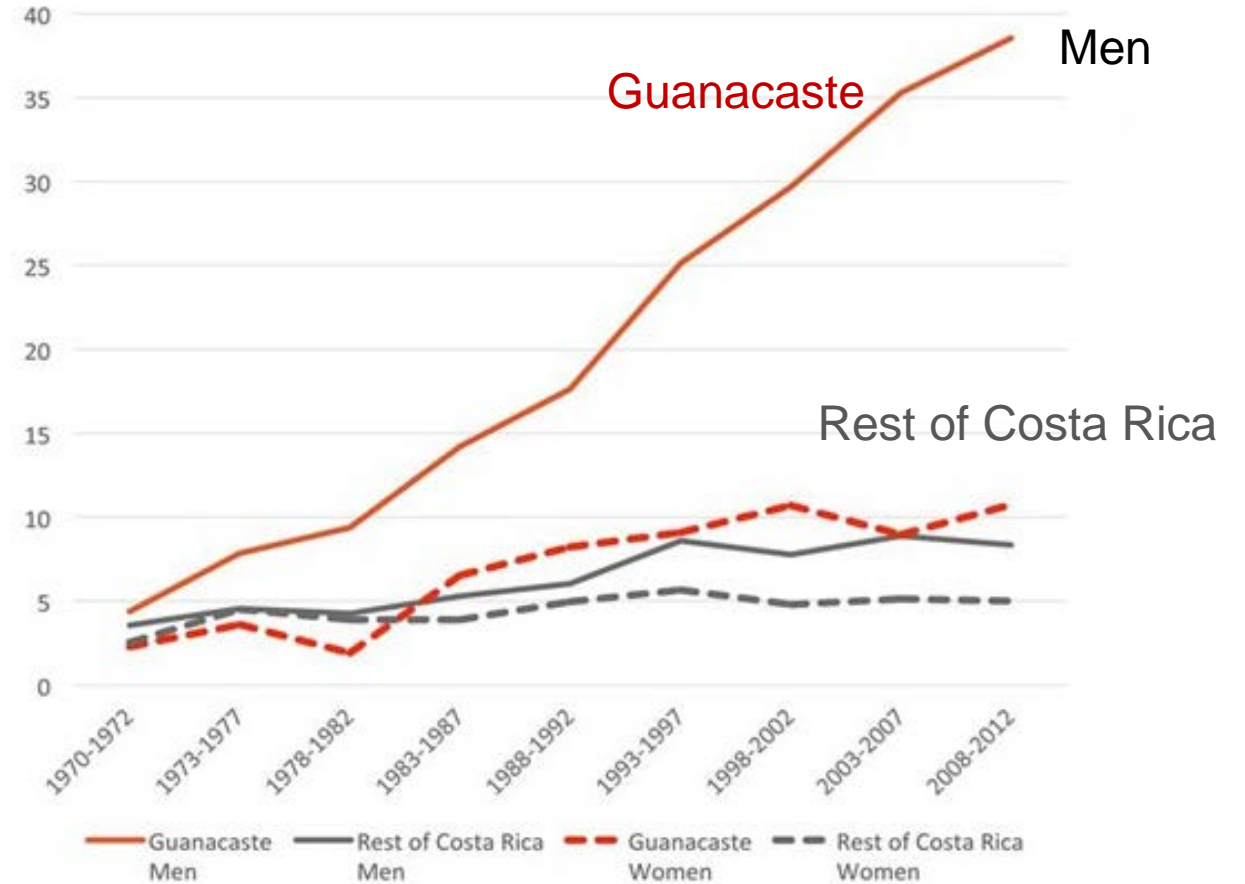
# The Kidney: An Organ hit hard by Dehydration



## 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





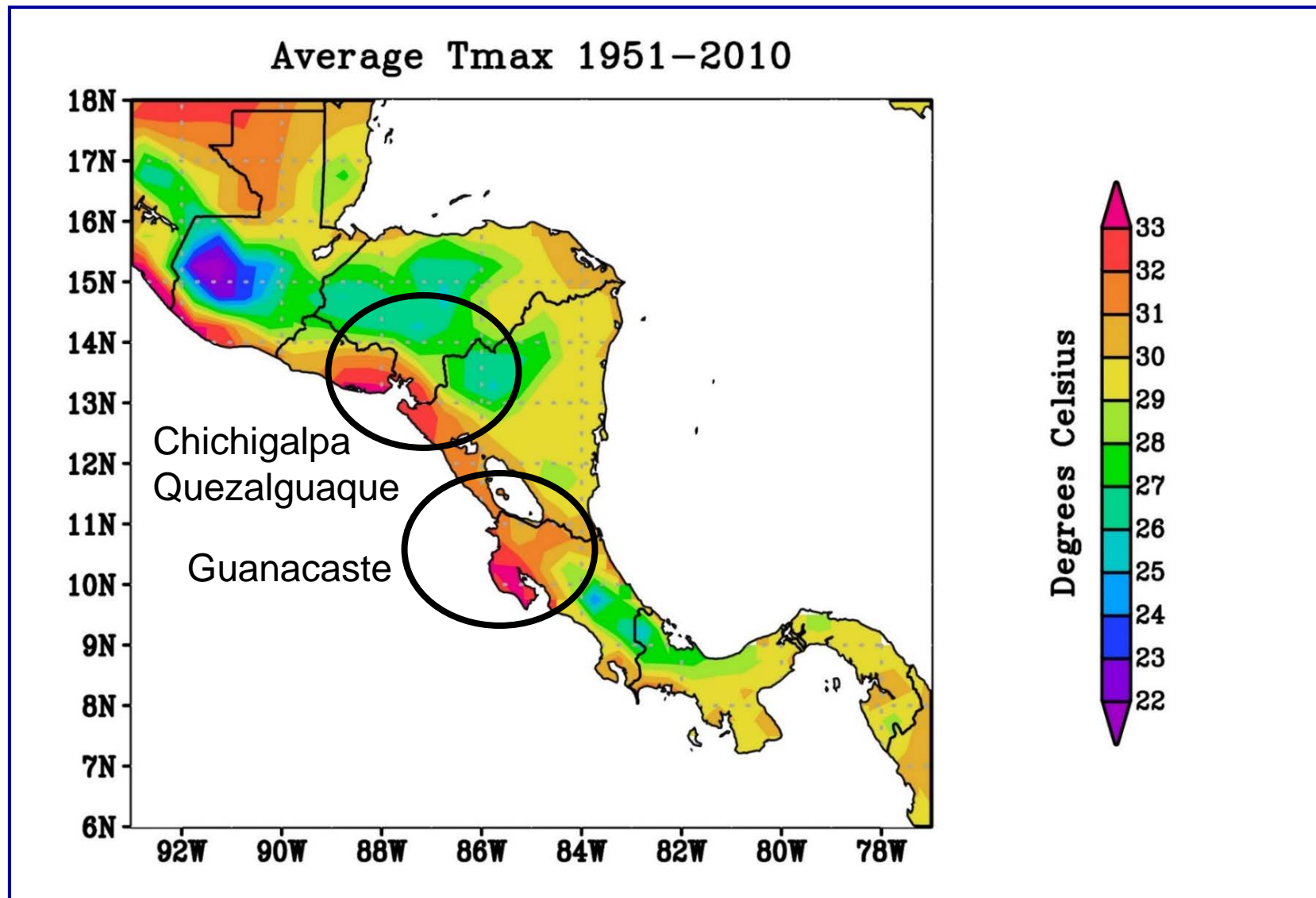
# Mesoamerican Nephropathy



- 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**

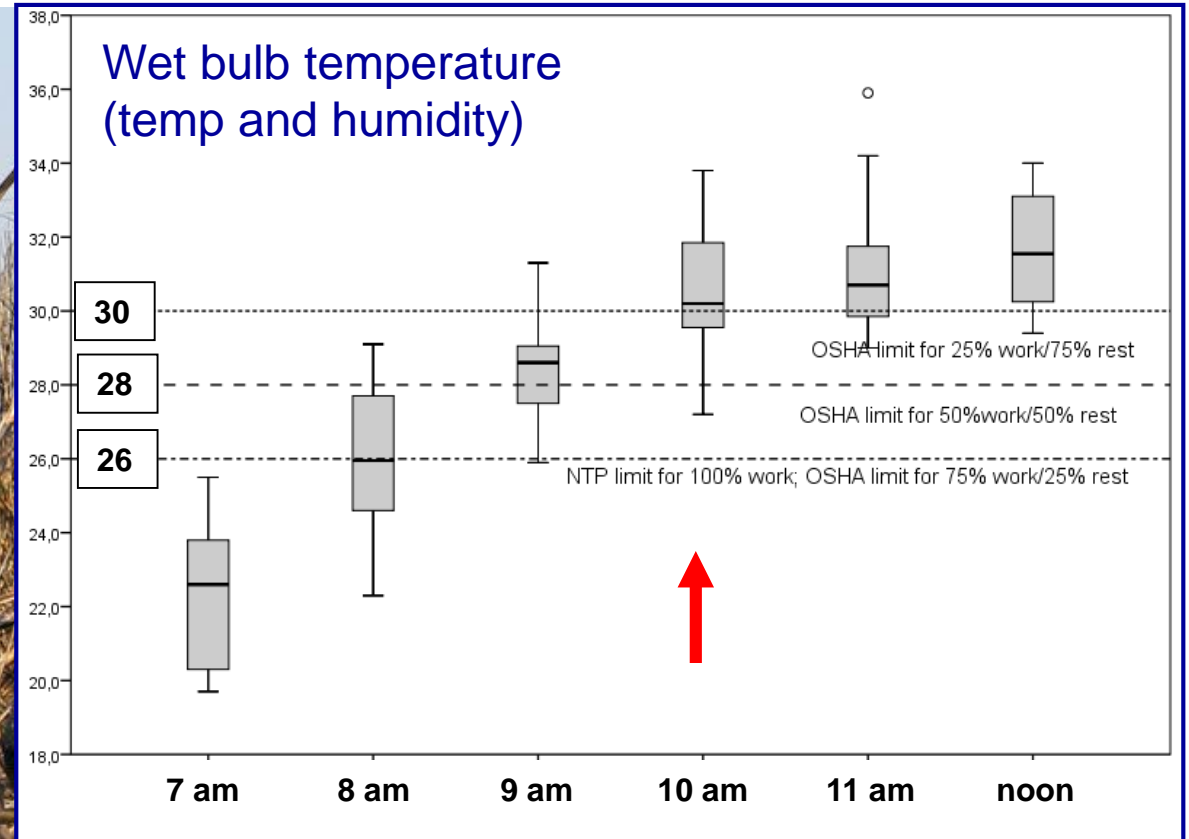
- **Disease occurs in occupations that do not use pesticides (miners, construction workers, fishing industry, port workers)**
- **During the season, those cutting sugarcane are at higher risk for kidney damage than those who are applying the pesticides**



**Central America:  
Site of High Solar  
Radiation  
Correlates with  
Site of CKD  
Epidemic**



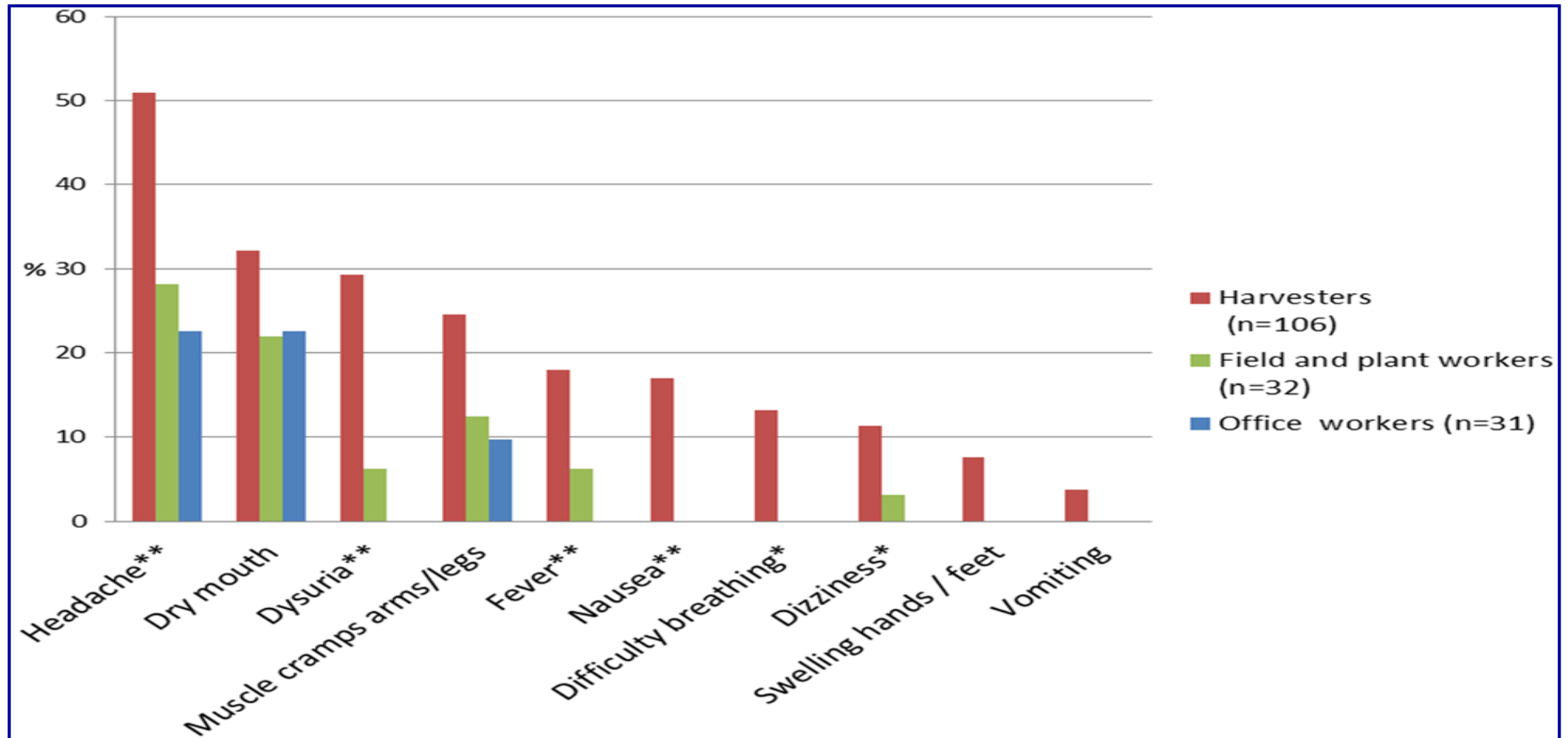
# Sugar Cane Workers are Exposed to Extreme Heat



- Work starts at 5:30 am
- By 9:30 am they are working under heat conditions that exceeds 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

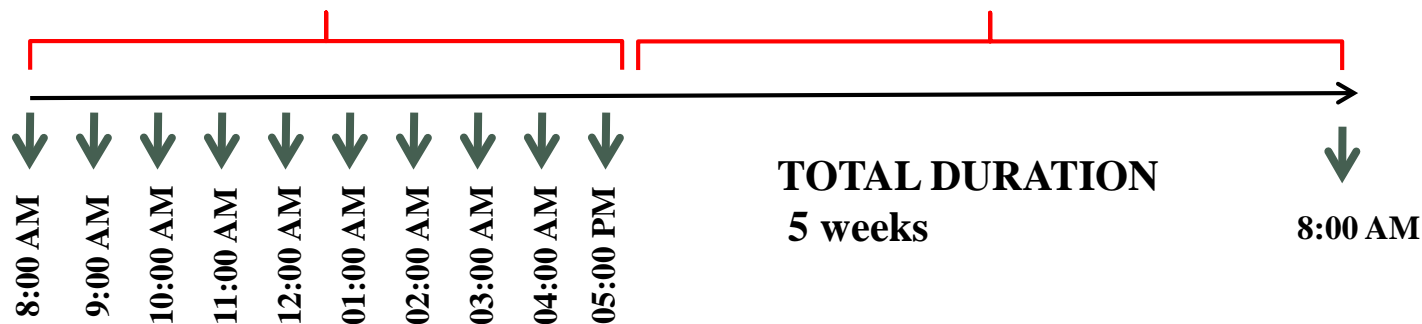
Heat: + water

Heat: water at night

(Heat = Dehydrated)

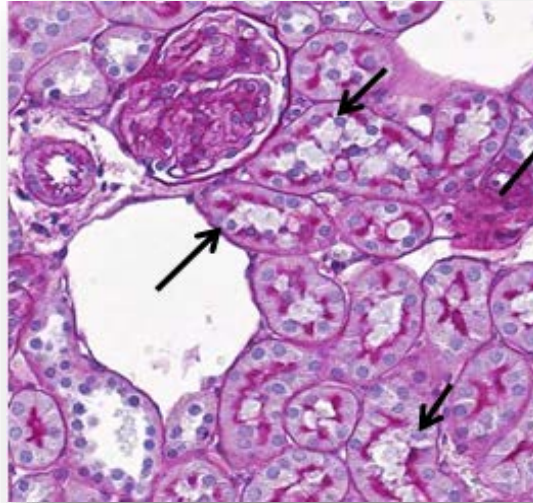
Heating at 39.5 °C  
30 min every hour

No heating

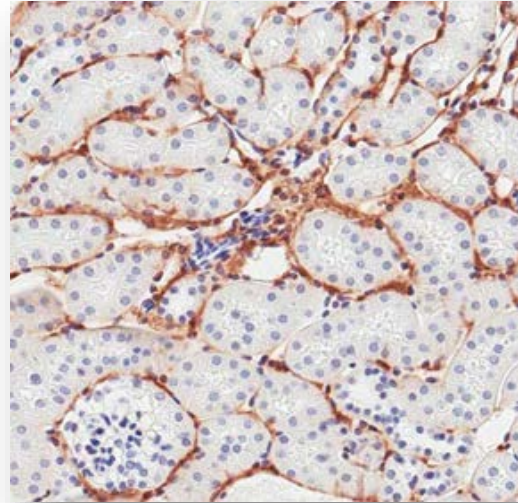




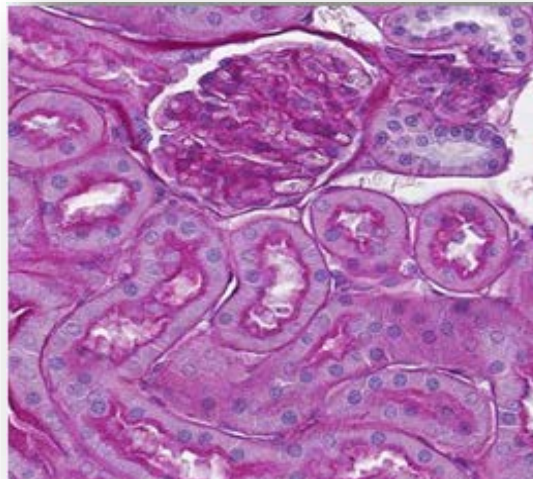
# Recurrent Dehydration Causes Chronic Kidney Disease in Laboratory Mice



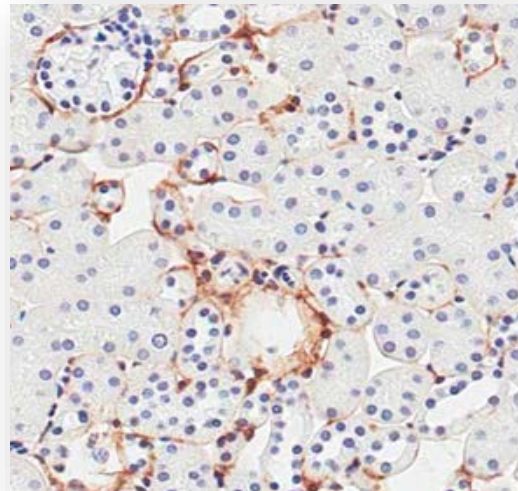
Heat +Dehydrated



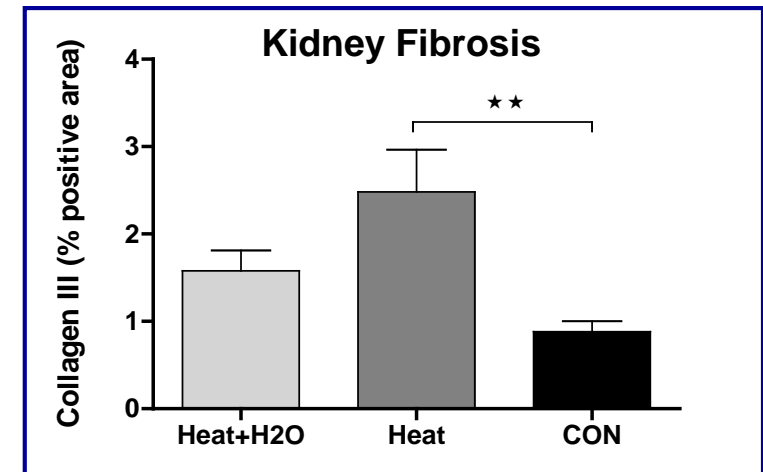
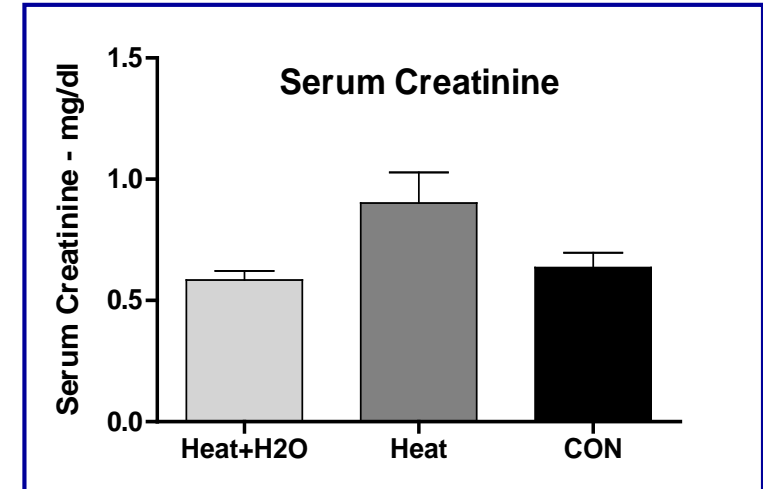
Heat + Dehydrated



Heat + hydration

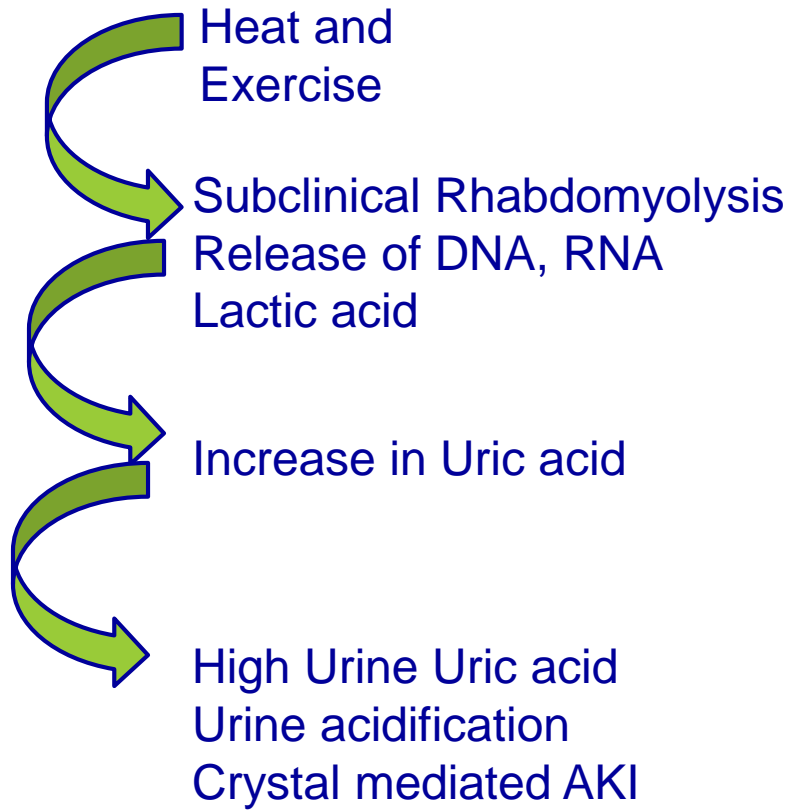


Heat + hydration

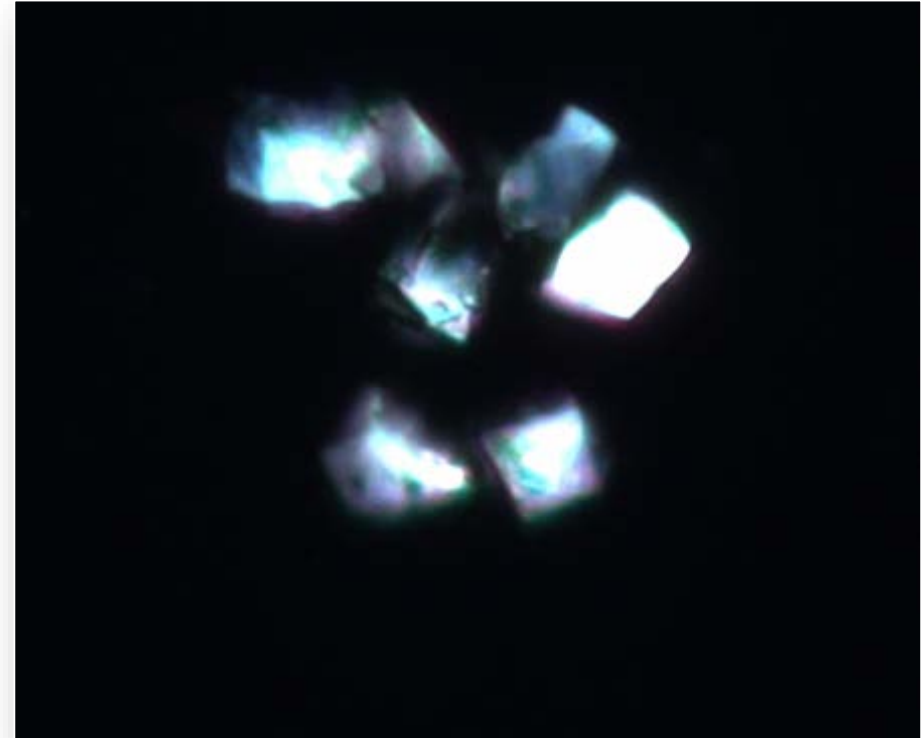




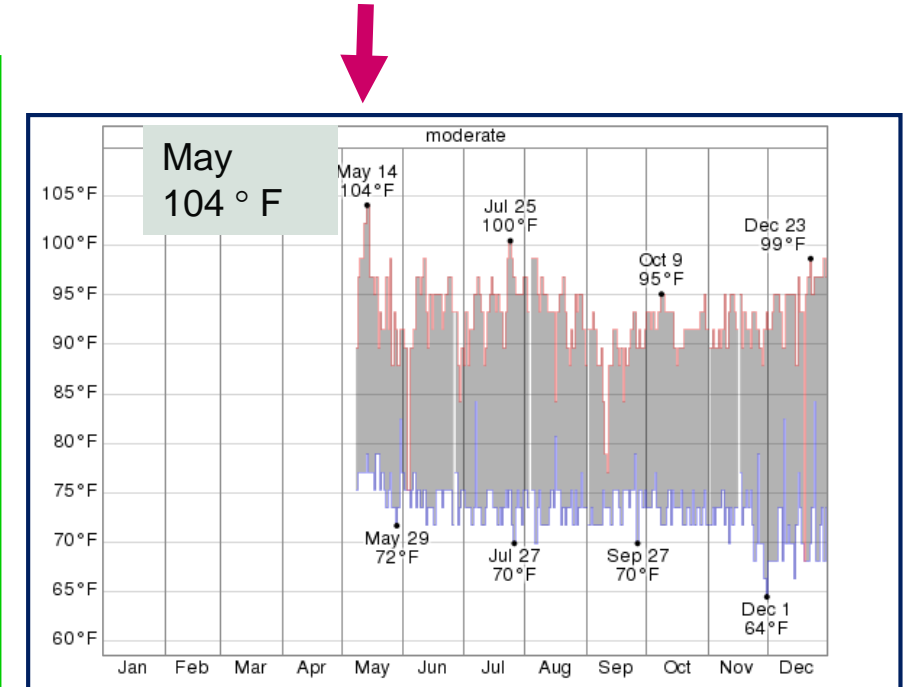
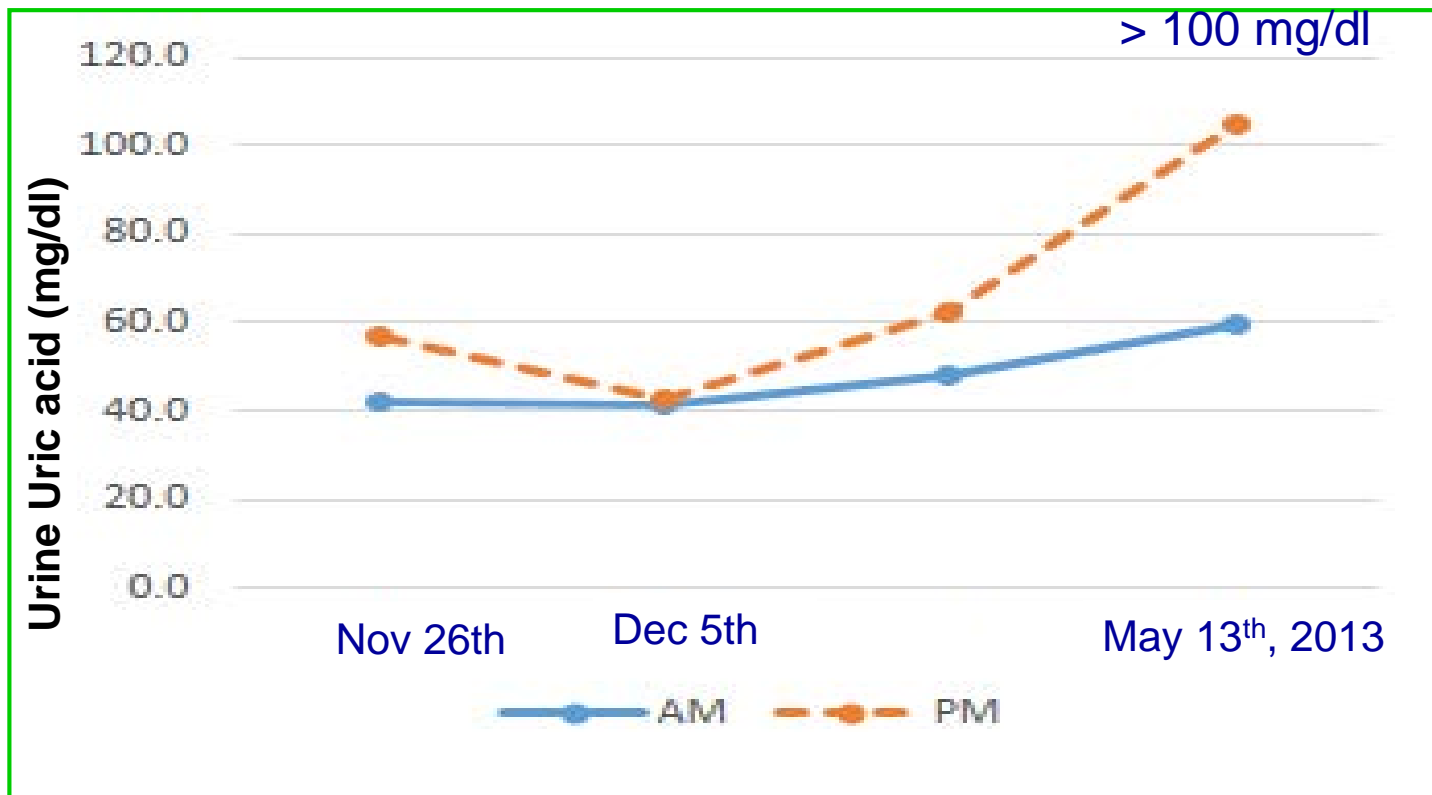
# Mesoamerican Nephropathy: A Uric acid Disorder?



# **Urate crystals are Common in the Urine of Sugarcane workers during the sugarcane harvest**



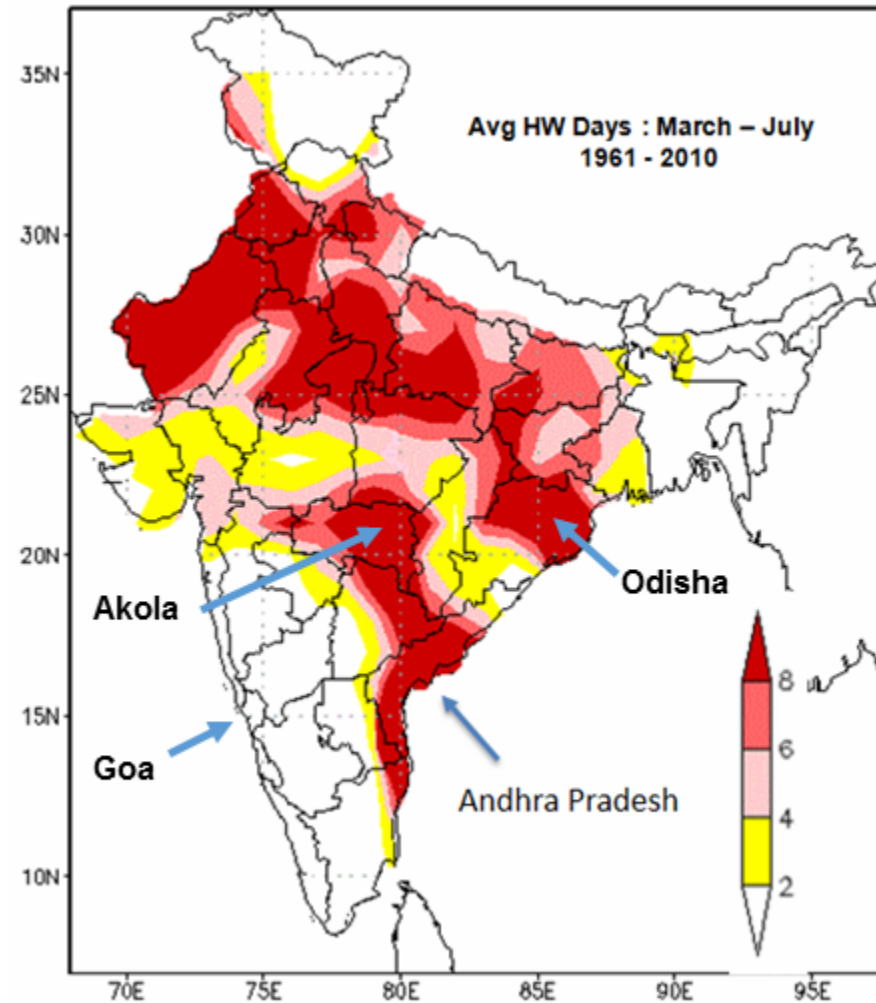
# Sugar cane Workers in Chinandega, Nicaragua Showed Marked Uricosuria in One of Four Urines



# World “CKD HOT SPOTS” Chronic Interstitial Nephritis in Agricultural Workers

<u>Country</u>	<u>Location</u>
▪ India, south	Andhra Pradesh (Uddanam Coast) Goa Chimakurthy mandal Akola districts in Maharashtra
▪ Sri Lanka	North Central Province
▪ Mexico	Tierra Blanca , Vera Cruz
▪ Egypt	El Minya, Upper Egypt
▪ Saudi Arabia	Tabuk Area
▪ Sudan	Rural Areas
▪ Thailand	Northeastern

# 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



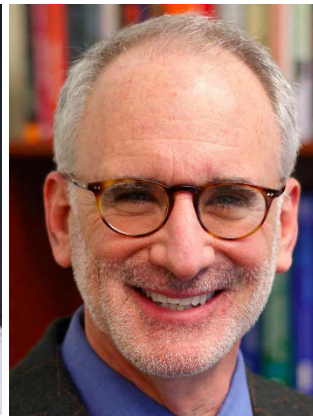
Balaji Rajagapolan



Henry Diaz



Jay Lemery



Lee Newmai



Liliana Tenney



Rosemary Rochford



Jaime Butler-Dawson

# Special Thanks



Carlos Roncal



Gaby Sanchez-Lozada



Miguel Lanaspá



Ramon Garcia



Jason Glaser



Tamara Milagres

## **And to all collaborators, especially**

Aurora Aragon

Lars Barregard

Theo Bodin

Ricardo Correa Rotter

Henry Diaz

Marvin Gonzalez

Emmanuel Jarquin

Diana Jalal

Channa Jayasumana

Jay Lemery

Magdalena Madero

Lee Newman

David Wegman

Catharina Wesseling

Ilana Weiss

Anika Wernerson

Ganghadar Taduri