Brigham and Women's Hospital
Founding Member, Mass General Brigham

Mesoamerican Nephropathy:
A Chronic Kidney Disease Epidemic in Central America

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DISCLOSURES

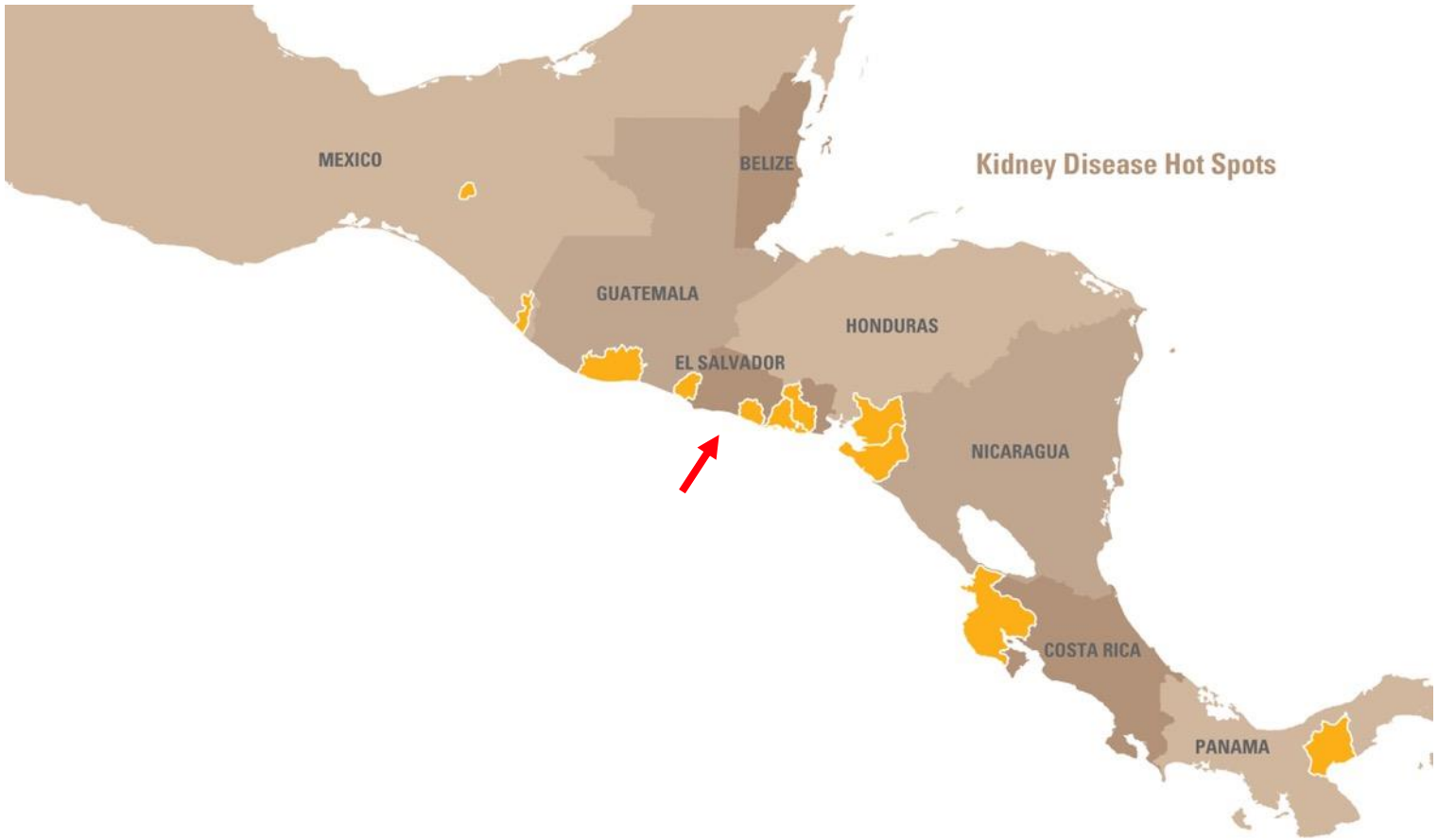
No relevant disclosures

OBJECTIVES

- Understand the epidemiology, clinical characteristics, and suspected causes of Mesoamerican Nephropathy.

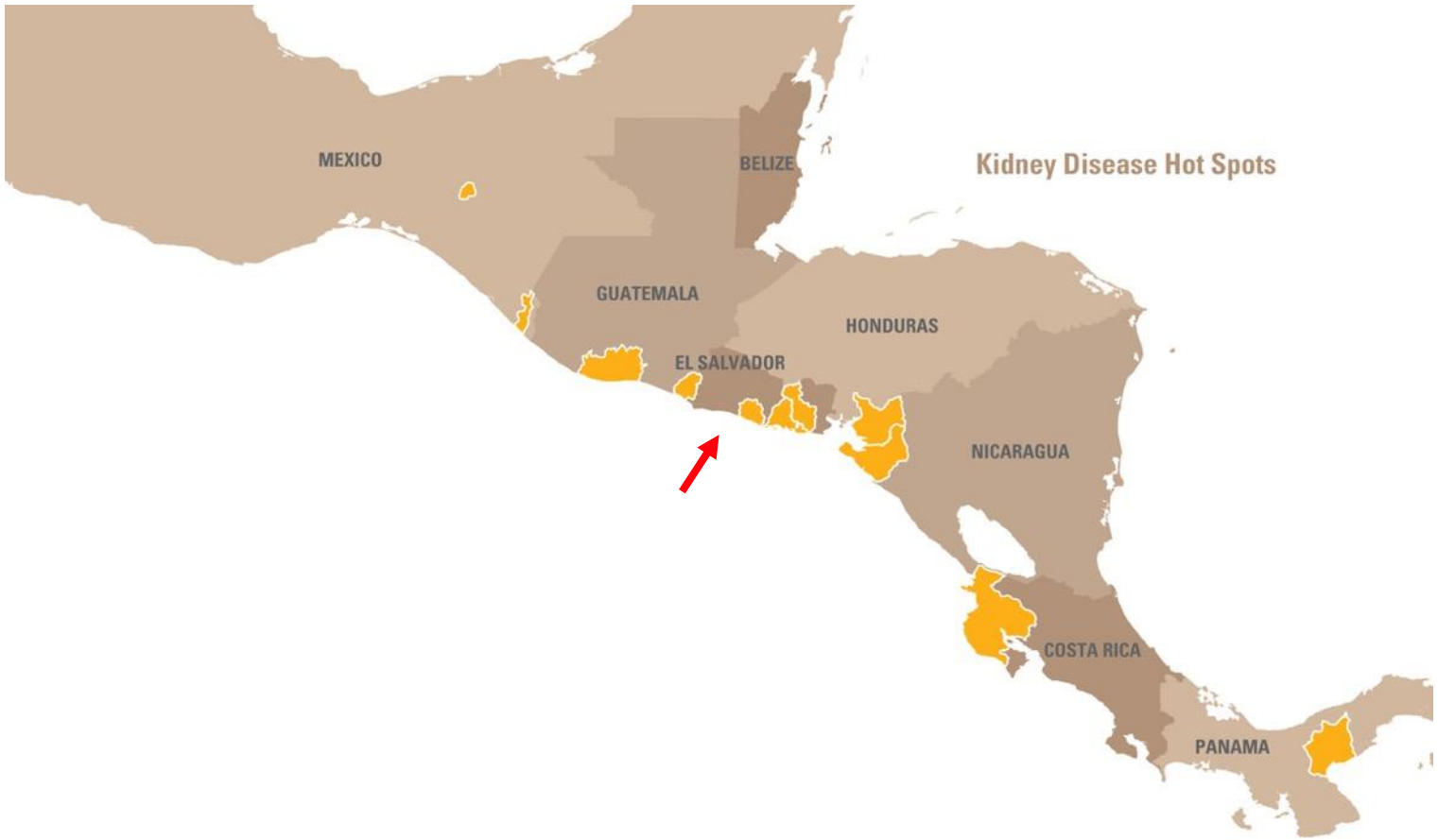
- Appreciate the emerging role of heat in chronic kidney disease.

Mesoamerican Nephropathy (MeN)



Science 2014

Mesoamerican Nephropathy (MeN)



Nefropatía terminal en pacientes de un hospital de referencia en El Salvador

Ramón García Trabanino,[1] Raúl Aguilar,[2] Carlos Reyes Silva,[1] Manuel Ortiz Mercado[1] y Ricardo Leiva Merino[3]

Rev Panam Salud Publica/Pan Am J Public Health 12(3), 2002

Diabetes: ~ 15%
HTN: ~ 7%
No diagnosis: ~ 67%

Science 2014

Beat the heat. Cane cutters in El Paisnal, El Salvador, start work at the break of dawn to take advantage of the cooler morning hours.

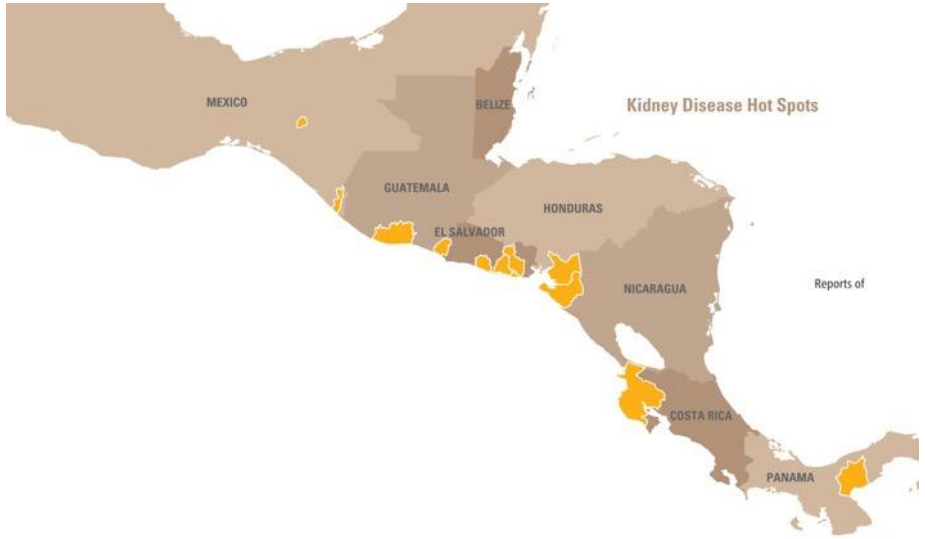
Mesoamerica's Mystery Killer

Scientists have come up with a gallery of rogues to explain an epidemic of kidney disease in Central America. But the culprit has stayed one step ahead

Science 2014

Mesoamerican Nephropathy (MeN) Demographics

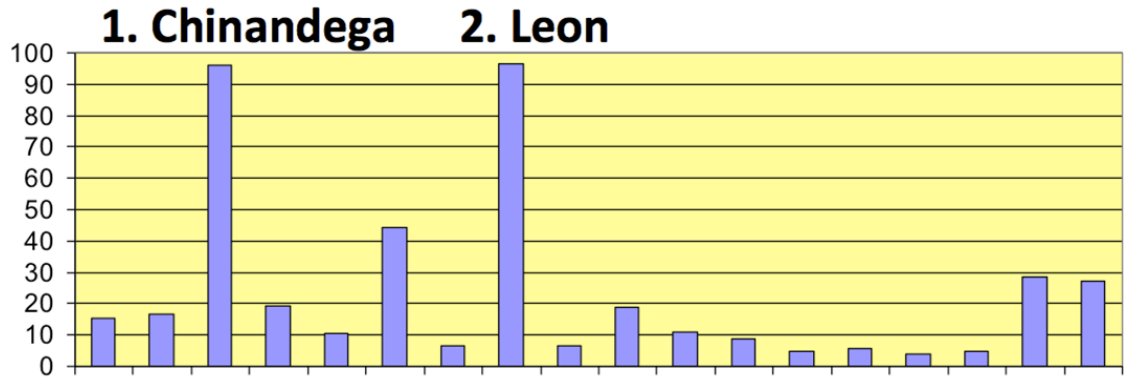
- Coastal, low altitude
- Pacific vs. Caribbean
- Agricultural workers
- Other manual laborers
- Males >> Females
- 40% men in some communities



Common risk factor across countries and communities is strenuous labor in hot, humid climates

What is a hotspot?

Mortality rate/100,000 from kidney disease in the Americas



O'Donnell NDT 2010

Clinical characteristics of MeN

Consistent

Young age

No traditional risk factors

Minimal proteinuria

Small echogenic kidneys

Bx: tubulointerstitial dz >> glomerular dz

Frequent

Hyperuricemia

Family history

Sometimes

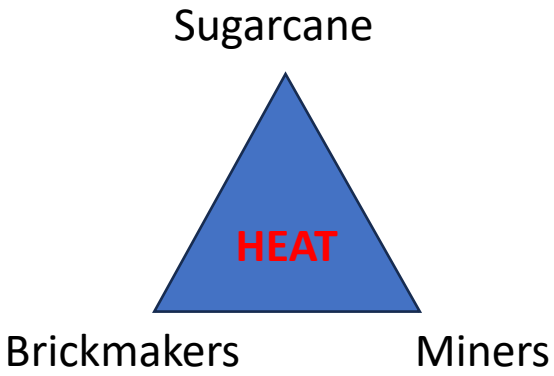
Hyponatremia

Hypokalemia

HypoMg

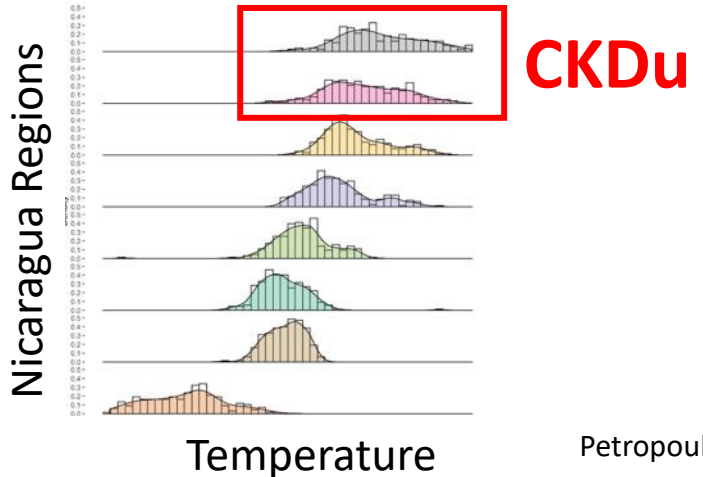
Leukocyturia

Epidemiological evidence that heat causes MeN



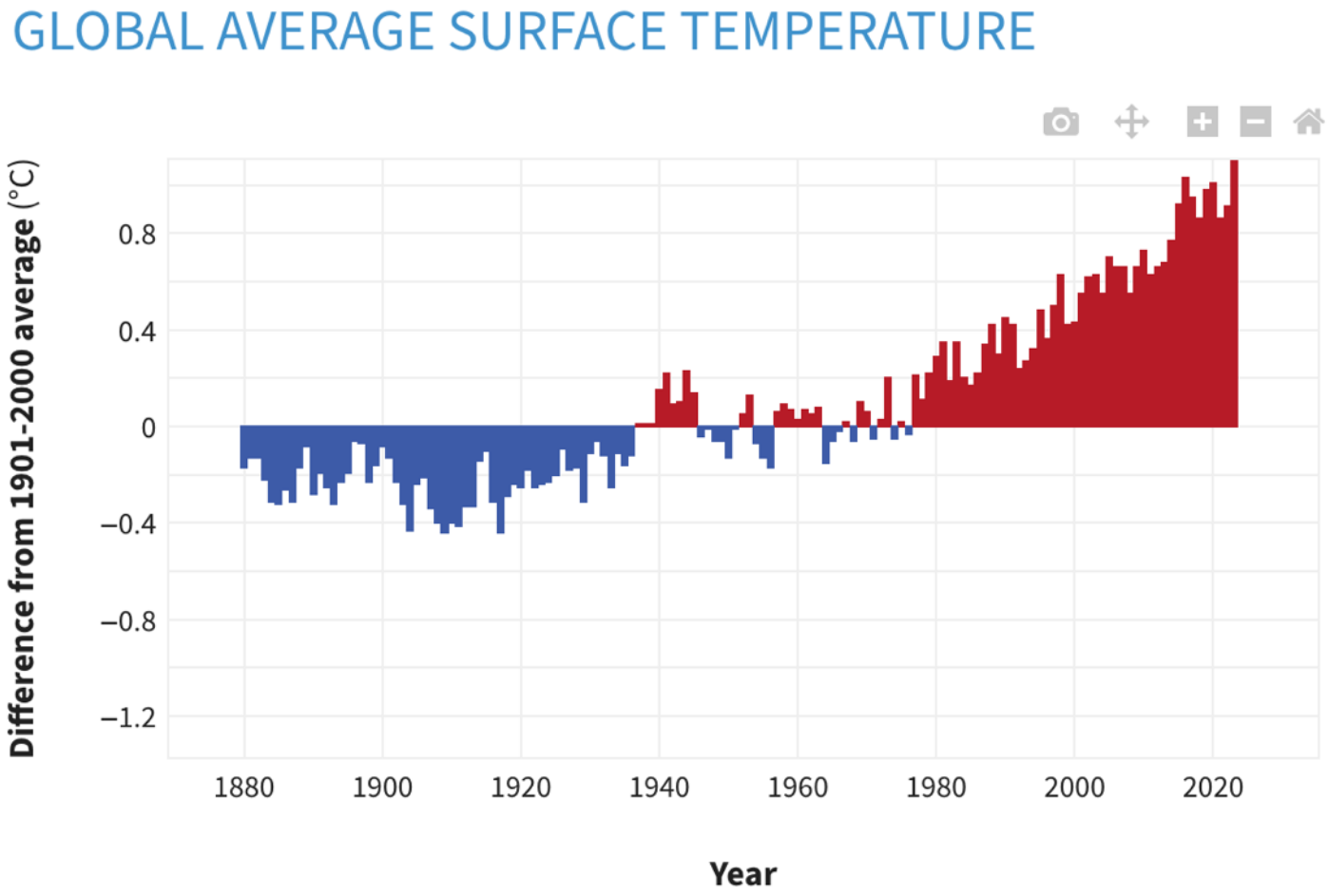
- Heat and heat stress are the common risk factor across high risk occupations.
- Risk of MeN highly correlated with heat stress of specific job tasks.
- Risk of MeN increases with rising temperature within regions.

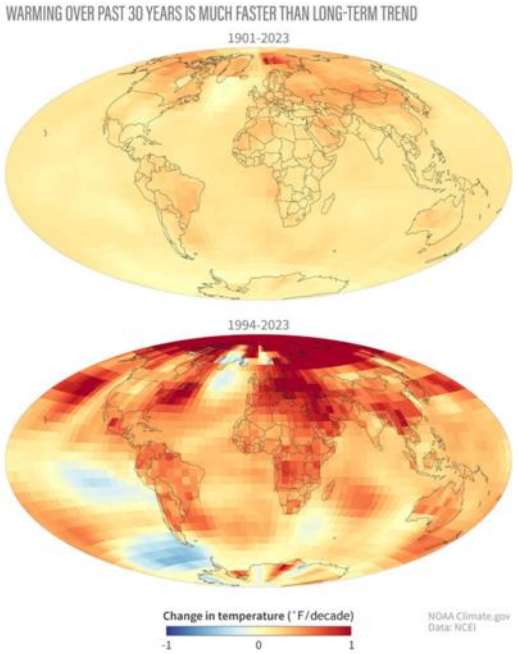
Cane Cutters >
Irrigators >
Fumigators>
Other workers



Petropoulos 2021

Rising temperatures worldwide





Climate.gov

Leading suspects . . .

Toxins

Agrichemicals
Aristolochia

Medications

NSAIDs
Gentamicin

Heat

Heavy Metals

Lead
Nickel
Cadmium
Arsenic

Infectious

Leptospirosis, Hantavirus
(Malaria, Dengue, Zika, etc.)

Heat-induced CKD in South African Miners

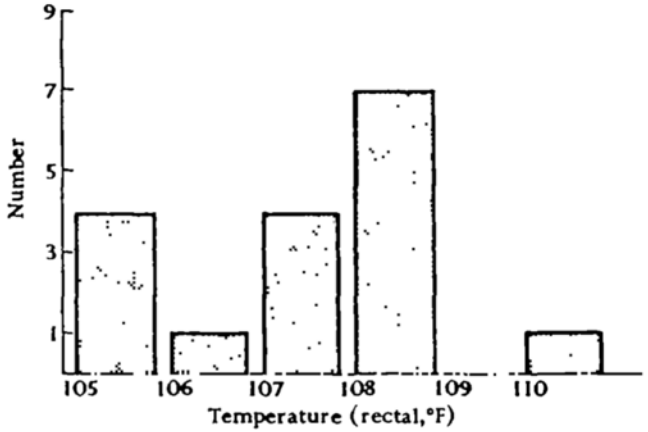


FIG. 3. The initial temperatures in 17 cases of heatstroke.

CHRONIC INTERSTITIAL NEPHRITIS AFTER HEATSTROKE

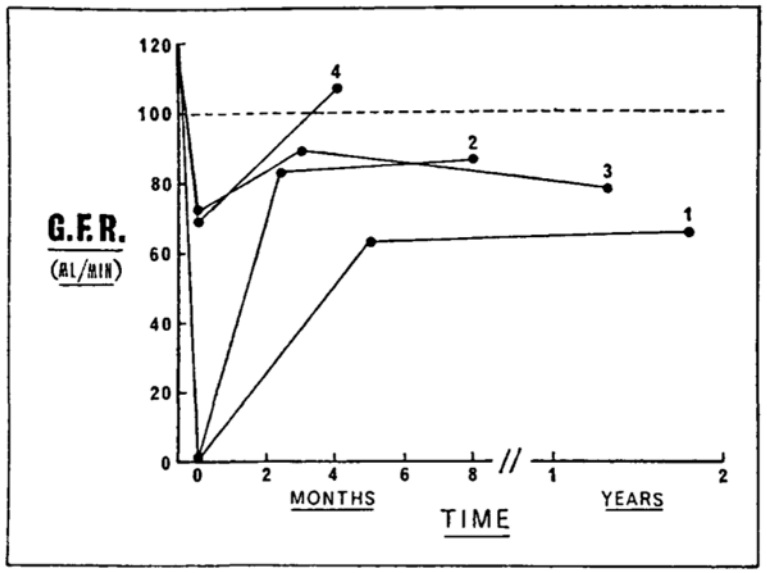


FIG. 1. Serial estimations of the glomerular filtration rates in the four patients.

CHRONIC INTERSTITIAL NEPHRITIS AS A CONSEQUENCE OF HEATSTROKE[1]

BY M. C. KEW, C. ABRAHAMS, AND H. C. SEFTEL

(From Department of Medicine, Johannesburg Hospital and University of the Witwatersrand, and South African Institute for Medical Research, Johannesburg)

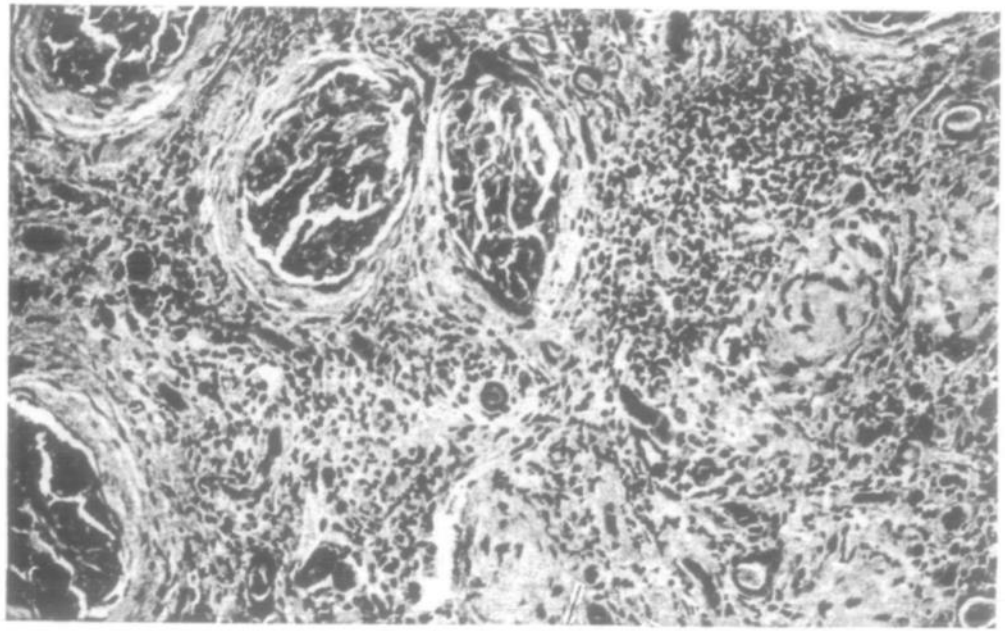
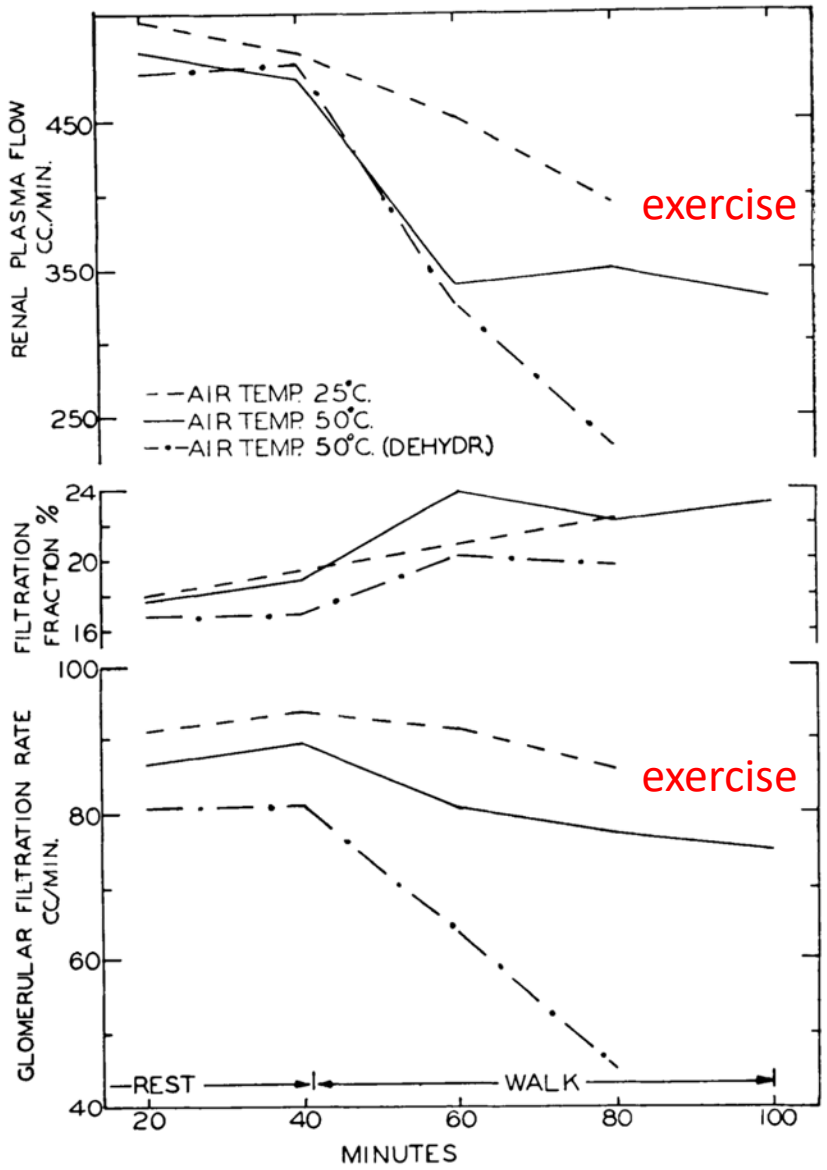


FIG. 5. Photomicrograph of third renal biopsy in *Case 1* showing a marked periglomerular fibrosis, interstitial fibrosis, round-cell infiltrate into the interstitial tissue and tubular atrophy. (Haematoxylin and eosin ×200.)

Kew et al. 1969, 1970

Renal Plasma Flow

GFR



exercise

exercise in heat

exercise

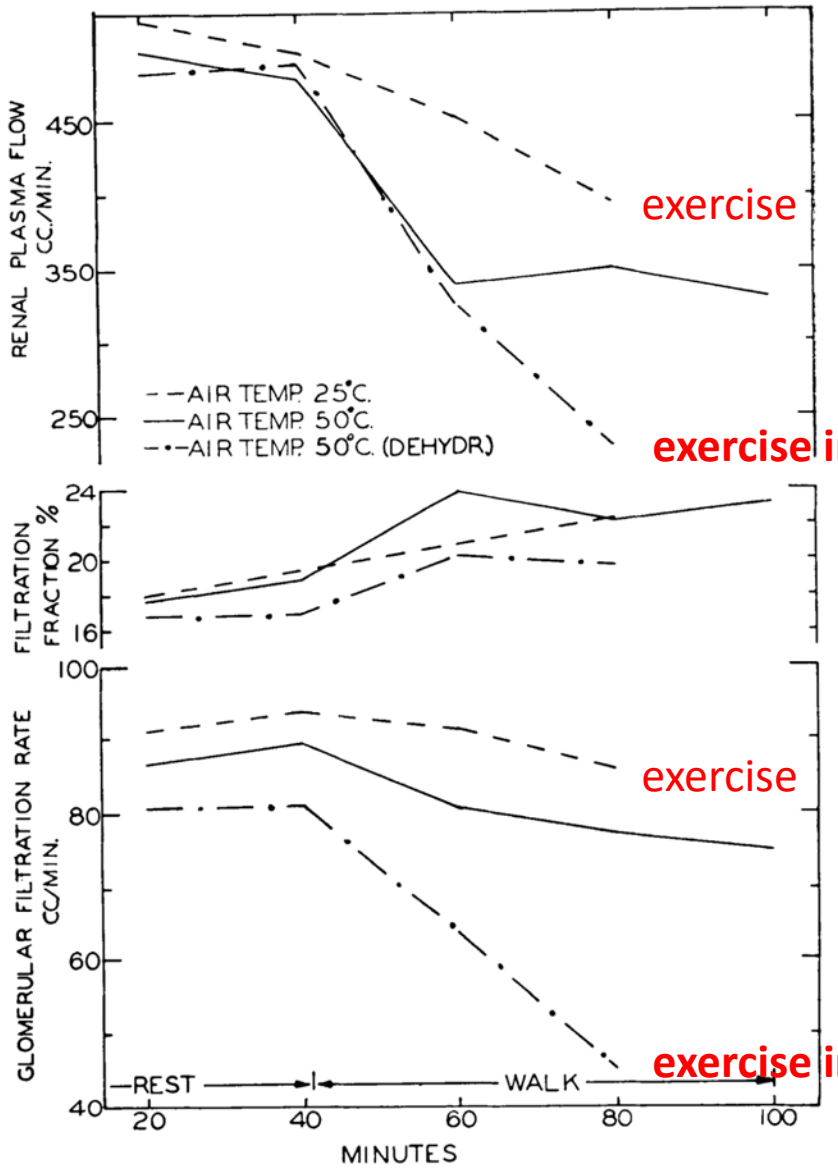
exercise in heat

Fig. 1. Effect of work, heat stress and dehydration on glomerular filtration rate, renal plasma flow and filtration fraction. The data are average values of *subjects* S. R., D. M., R. C. and J. S., who completed all clearance periods in all experiments.

Smith 1951

Renal Plasma Flow

GFR



exercise

exercise in heat

exercise in heat with dehydration

exercise

exercise in heat

exercise in heat with dehydration

Fig. 1. Effect of work, heat stress and dehydration on glomerular filtration rate, renal plasma flow and filtration fraction. The data are average values of *subjects* S. R., D. M., R. C. and J. S., who completed all clearance periods in all experiments.

Smith 1951

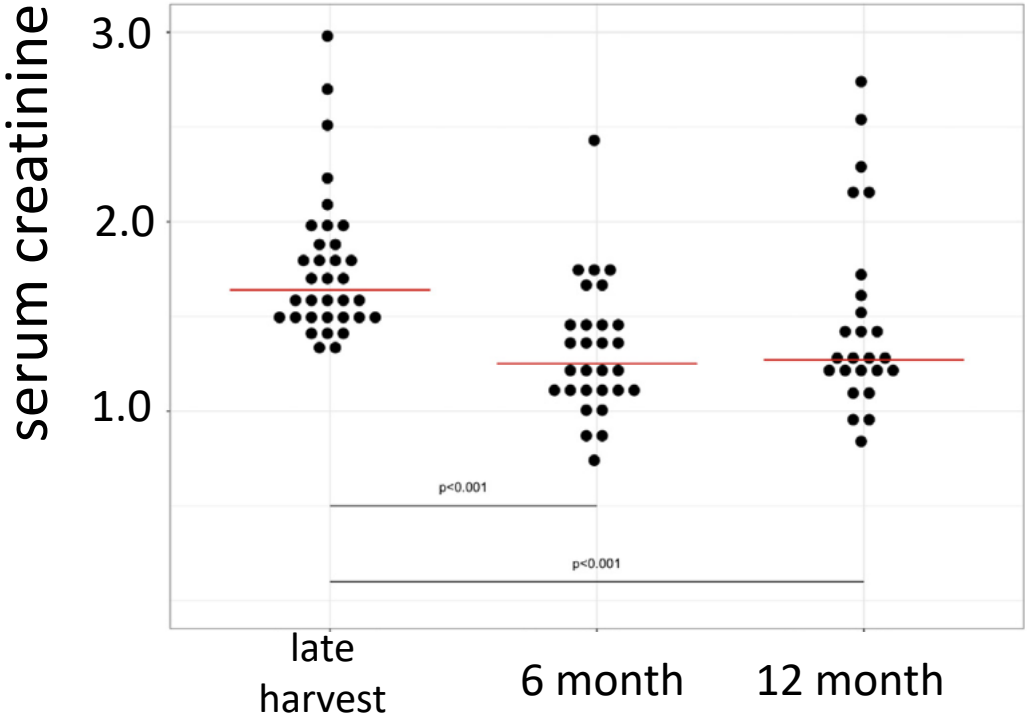
Cyclic AKI episodes

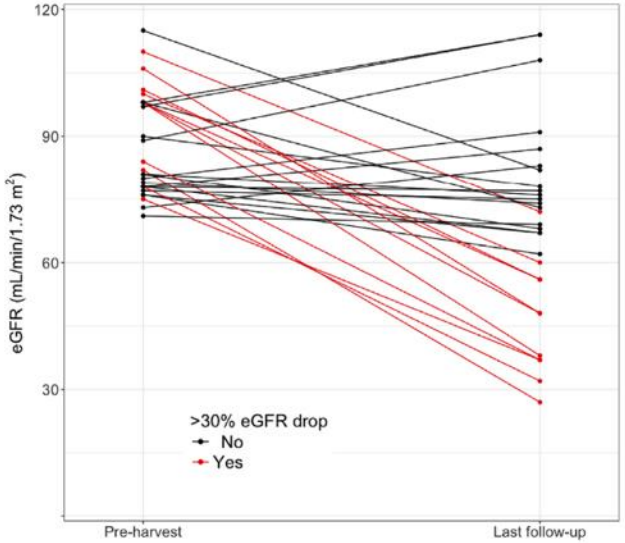
Original Investigation

AJKD

Acute Kidney Injury in Sugarcane Workers at Risk for Mesoamerican Nephropathy

Joseph Kupferman, Oriana Ramírez-Rubio,* Juan José Amador, Damaris López-Pilarte, Elissa H. Wilker, Rebecca L. Laws, Caryn Sennett, Ninoska Violeta Robles, Jorge Luis Lau, Alejandro José Salinas, James S. Kaufman, Daniel E. Weiner, Madeleine K. Scammell, Michael D. McClean, Daniel R. Brooks, and David J. Friedman*





Pre-Harvest ~18 months

>10% of workers had acute or sub-acute kidney injury

Biopsies from Sugarcane workers with AKI

www.kidney-international.org clinical investigation

Early detection of acute tubulointerstitial nephritis in the genesis of Mesoamerican nephropathy

Rebecca S.B. Fischer[1,9], Chandan Vangala[2,9], Luan Truong[2,3], Sreedhar Mandayam[2], Denis Chavarria[4], Orlando M. Granera Llanes[5], Marcos U. Fonseca Laguna[5], Alvaro Guerra Baez[5], Felix Garcia[6], Ramón García-Trabanino[7,8] and Kristy O. Murray[1]

www.kidney-international.org clinical investigation

Clinical markers to predict progression from acute to chronic kidney disease in Mesoamerican nephropathy

Rebecca S.B. Fischer[1], Chandan Vangala[2], Sreedhar Mandayam[2], Denis Chavarria[3], Ramón García-Trabanino[4,5], Felix Garcia[6], Linda L. Garcia[1] and Kristy O. Murray[1]

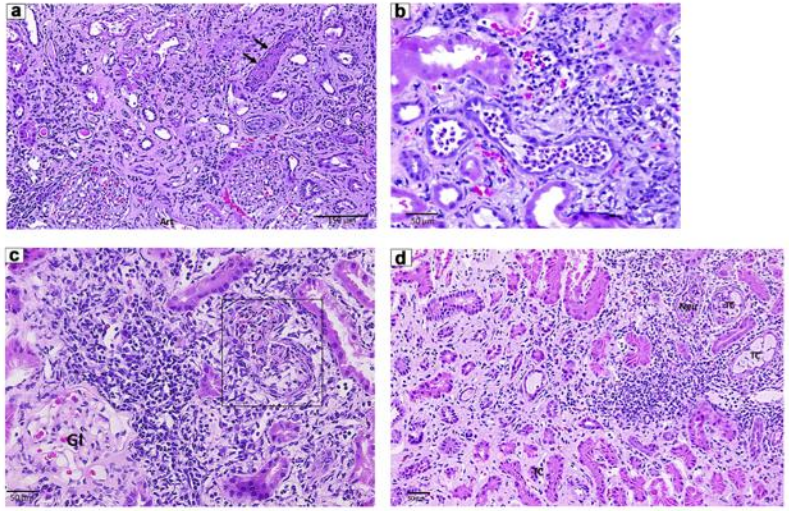
Workers present with:

Elevated Temperatures

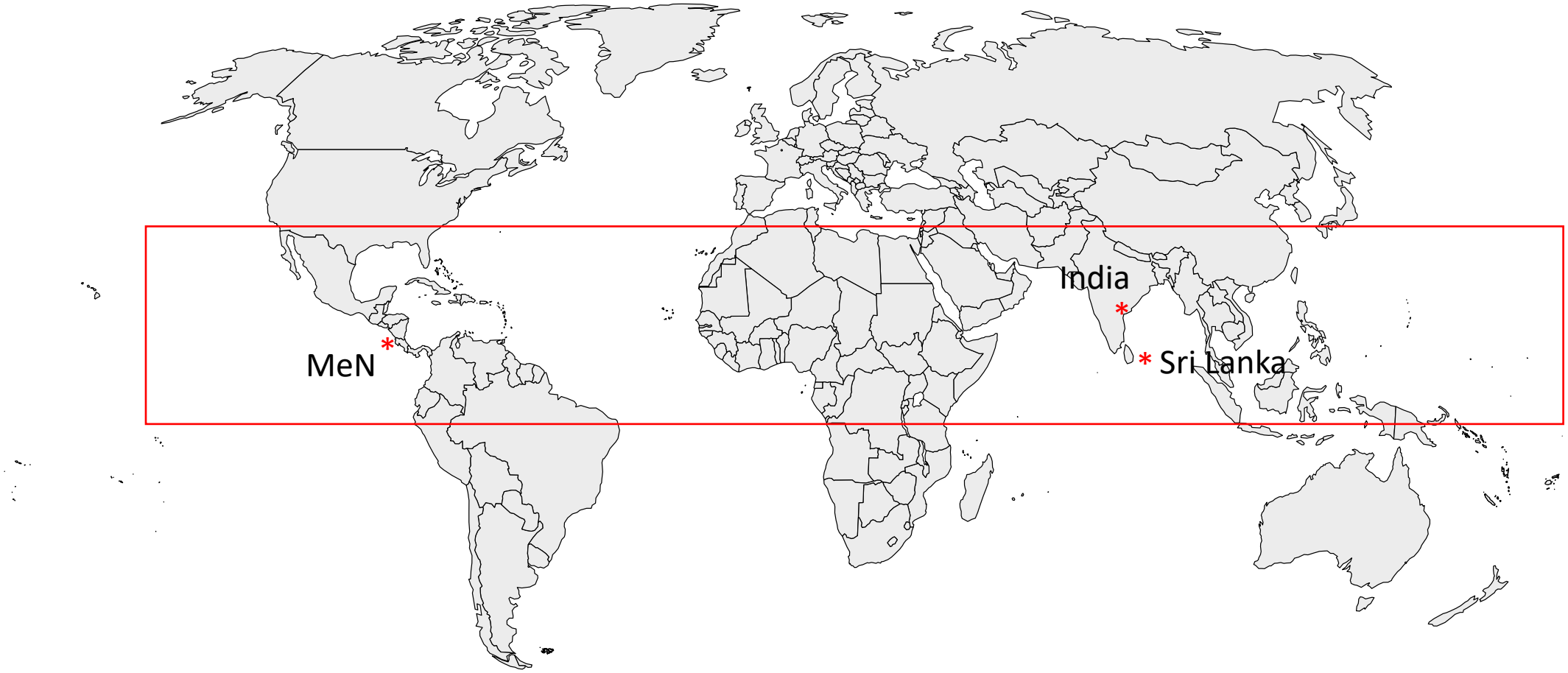
Elevated Creatinine

Symptoms of volume loss

Sterile Urine

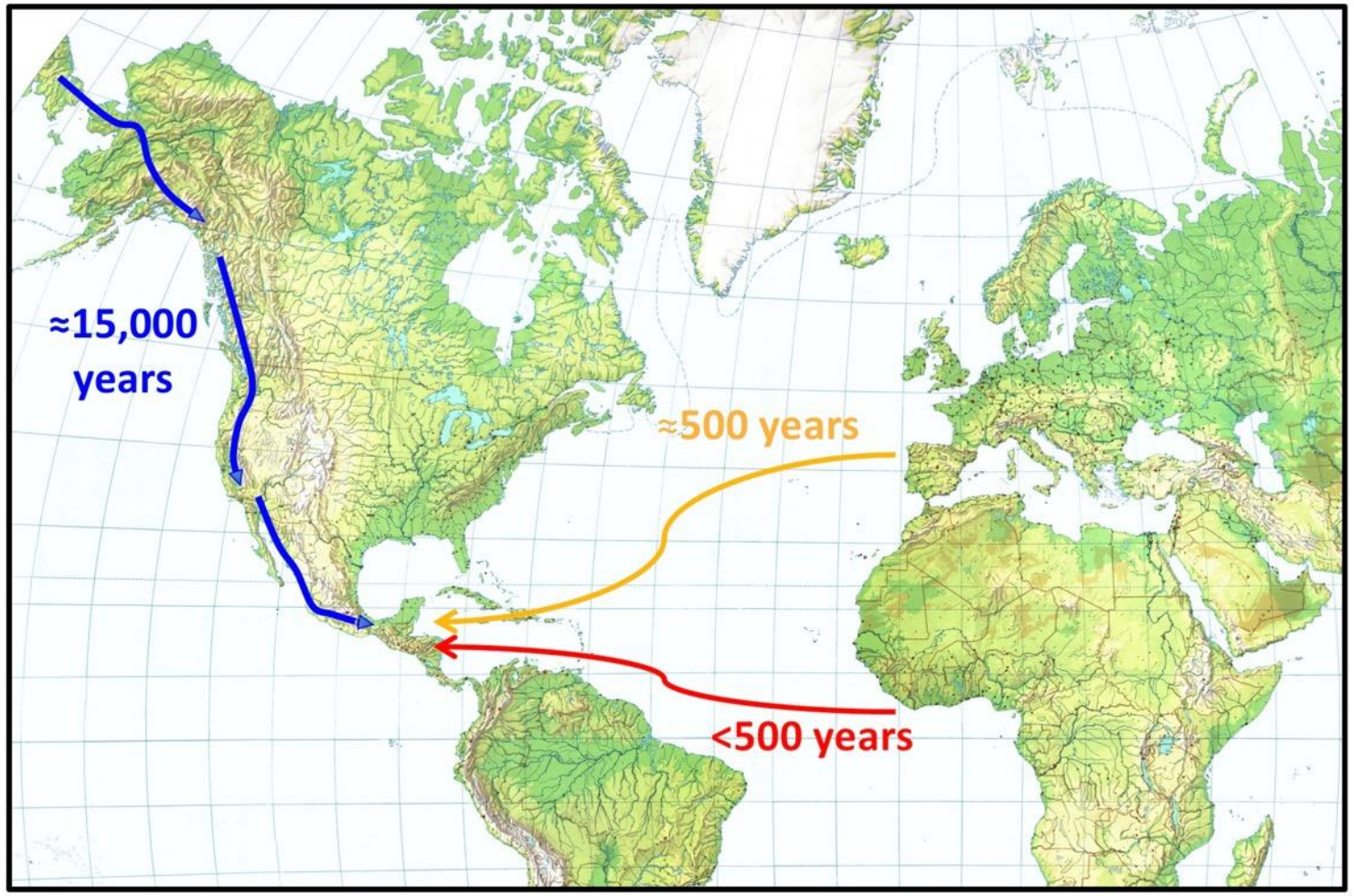


Why the restricted range of CKDu?



What is unique about this environment?

What is unique about the inhabitants?

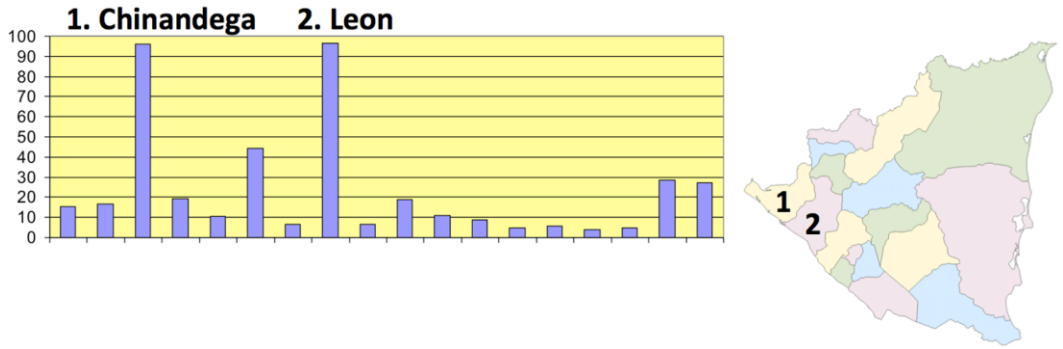


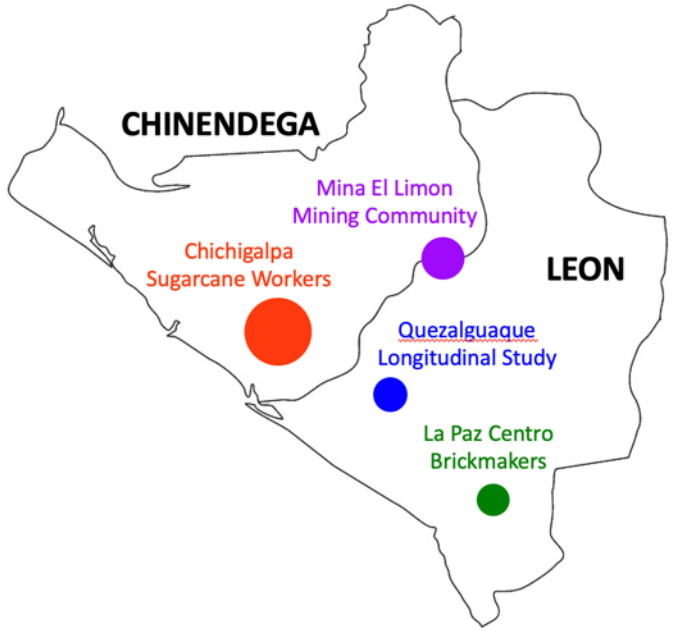
Genetic Studies of Mesoamerican Nephropathy

Rationale:

1. People working under similar conditions and exposed to similar risk factors in many other tropical climates do not develop kidney disease at high rates

2. Hard to explain why some workers get kidney disease while others working side by side do not get kidney disease



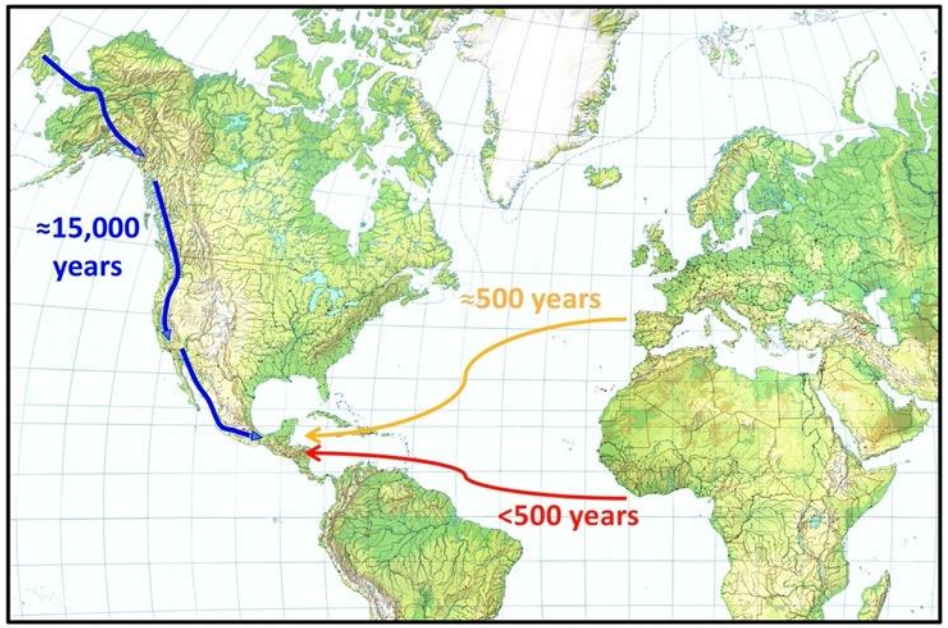


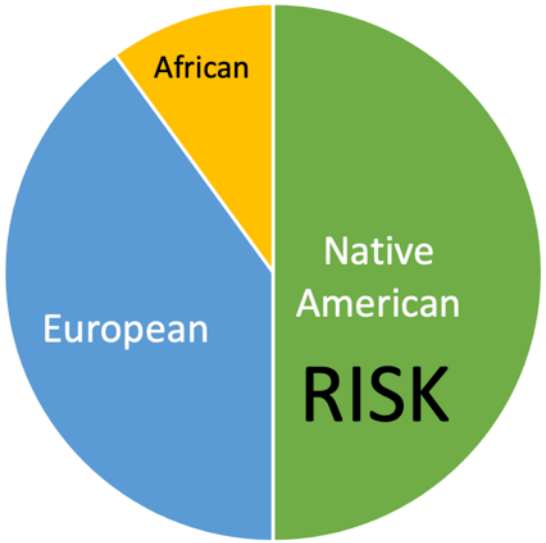
Genetic Susceptibility to Mesoamerican Nephropathy?

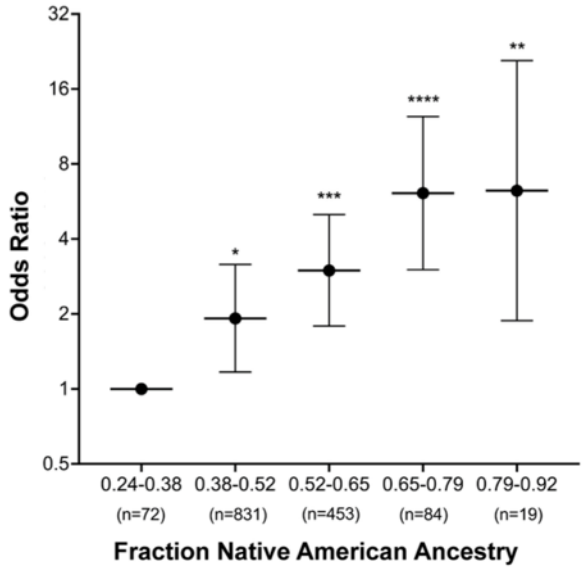
PNAS RESEARCH ARTICLE | GENETICS

Genetic risk factors for Mesoamerican nephropathy

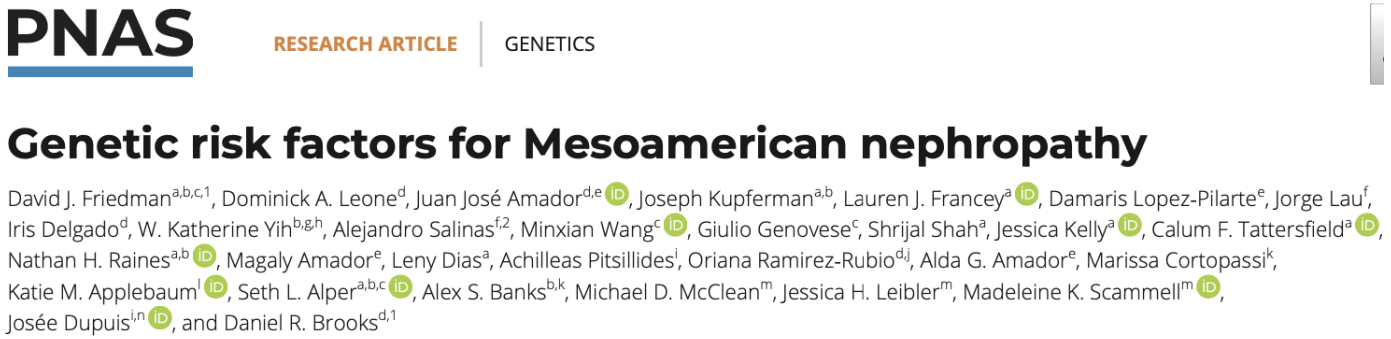
David J. Friedman[a,b,c,1], Dominick A. Leone[d], Juan José Amador[d,e], Joseph Kupferman[a,b], Lauren J. Francey[a], Damaris Lopez-Pilarte[e], Jorge Lau[f], Iris Delgado[d], W. Katherine Yih[b,g,h], Alejandro Salinas[f,2], Minxian Wang[c], Giulio Genovese[c], Shrijal Shah[a], Jessica Kelly[a], Calum F. Tattersfield[a], Nathan H. Raines[a,b], Magaly Amador[e], Leny Dias[a], Achilleas Pitsillides[i], Oriana Ramirez-Rubio[d,j], Alda G. Amador[e], Marissa Cortopassi[k], Katie M. Applebaum[l], Seth L. Alper[a,b,c], Alex S. Banks[b,k], Michael D. McClean[m], Jessica H. Leibler[m], Madeleine K. Scammell[m], Josée Dupuis[i,n], and Daniel R. Brooks[d,1]







PNAS 2025

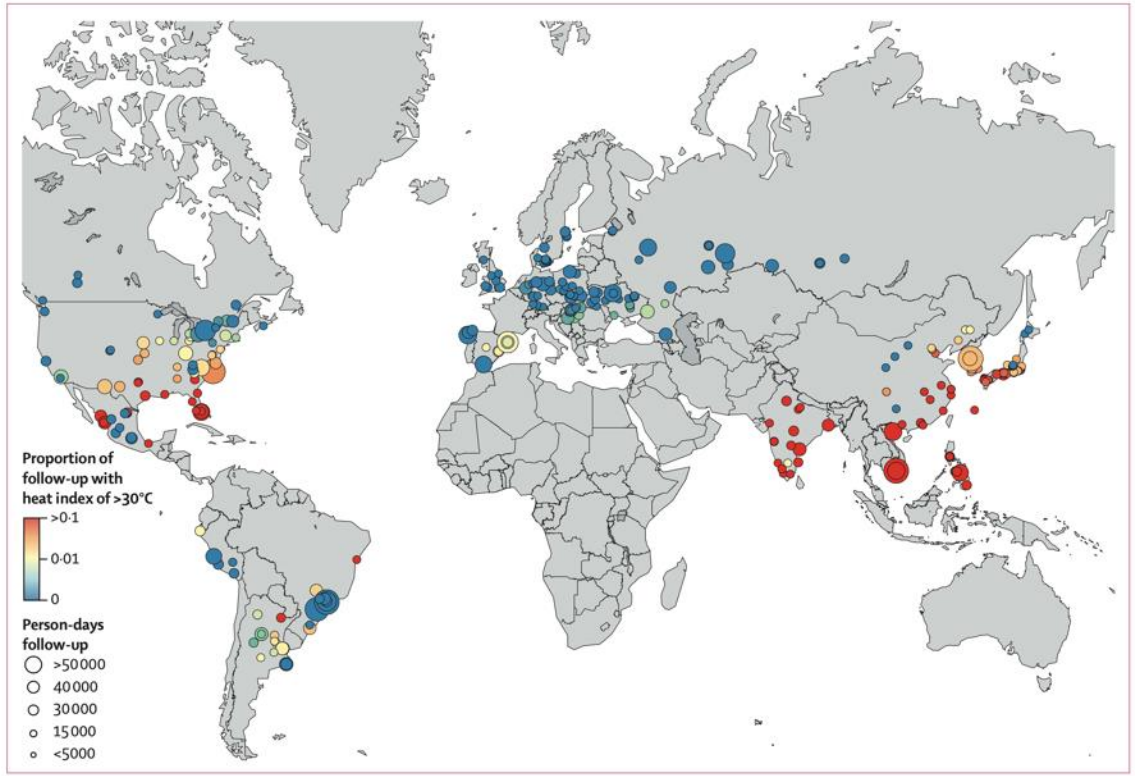


- Genetic Variants in OPCML associated with Mesoamerican nephropathy
- OPCML is a brain gene originally described in vasopressin-secreting cells of the hypothalamus
- Protective variants associated with enhanced urine concentrating capacity among sugarcane workers
- Mouse knock-out models suggest OPCML regulates salt and water handling, temperature regulation

Ambient heat exposure and kidney function in patients with chronic kidney disease: a post-hoc analysis of the DAPA-CKD trial

Zhiyan Zhang, Hiddo J L Heerspink, Glenn M Chertow, Ricardo Correa-Rotter, Antonio Gasparrini, Niels Jongs, Anna Maria Langkilde, John J V McMurray, Malcolm N Mistry, Peter Rossing, Robert D Toto, Priya Vart, Dorothea Nitsch, David C Wheeler*, Ben Caplin**

Lancet Planet Health 2024



Ambient heat exposure and kidney function in patients with chronic kidney disease: a post-hoc analysis of the DAPA-CKD trial

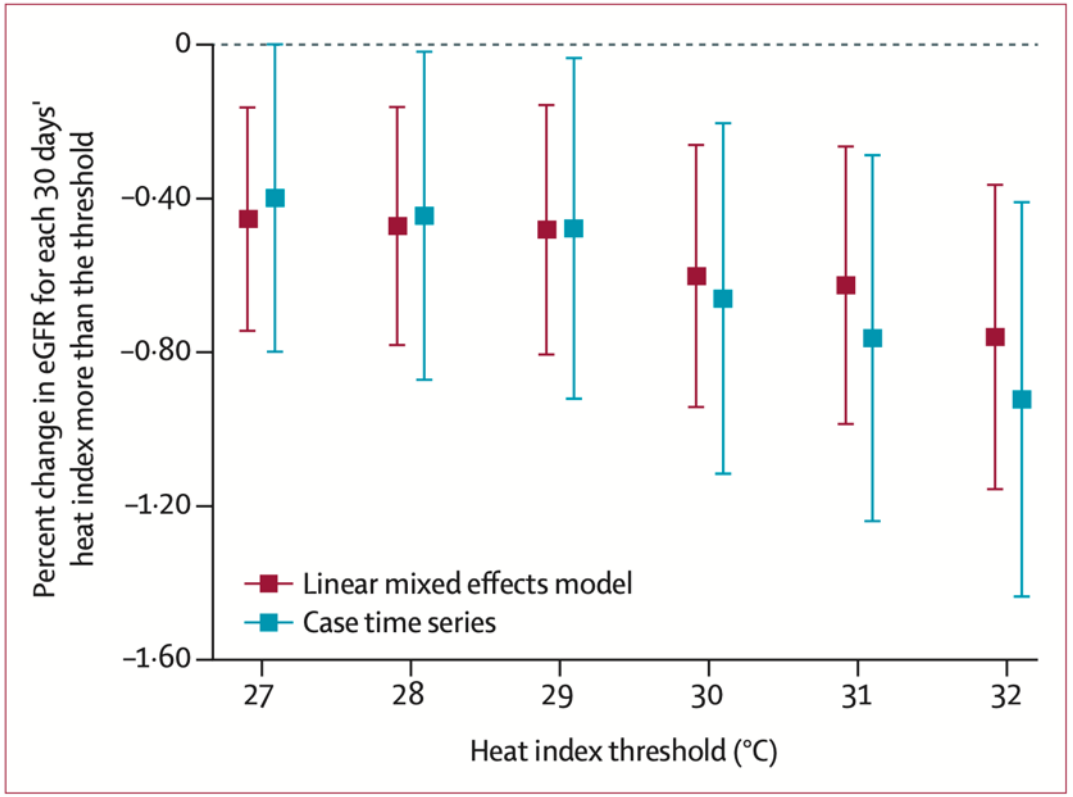


Figure 2: **Association between heat index and change in eGFR at different heat index thresholds**

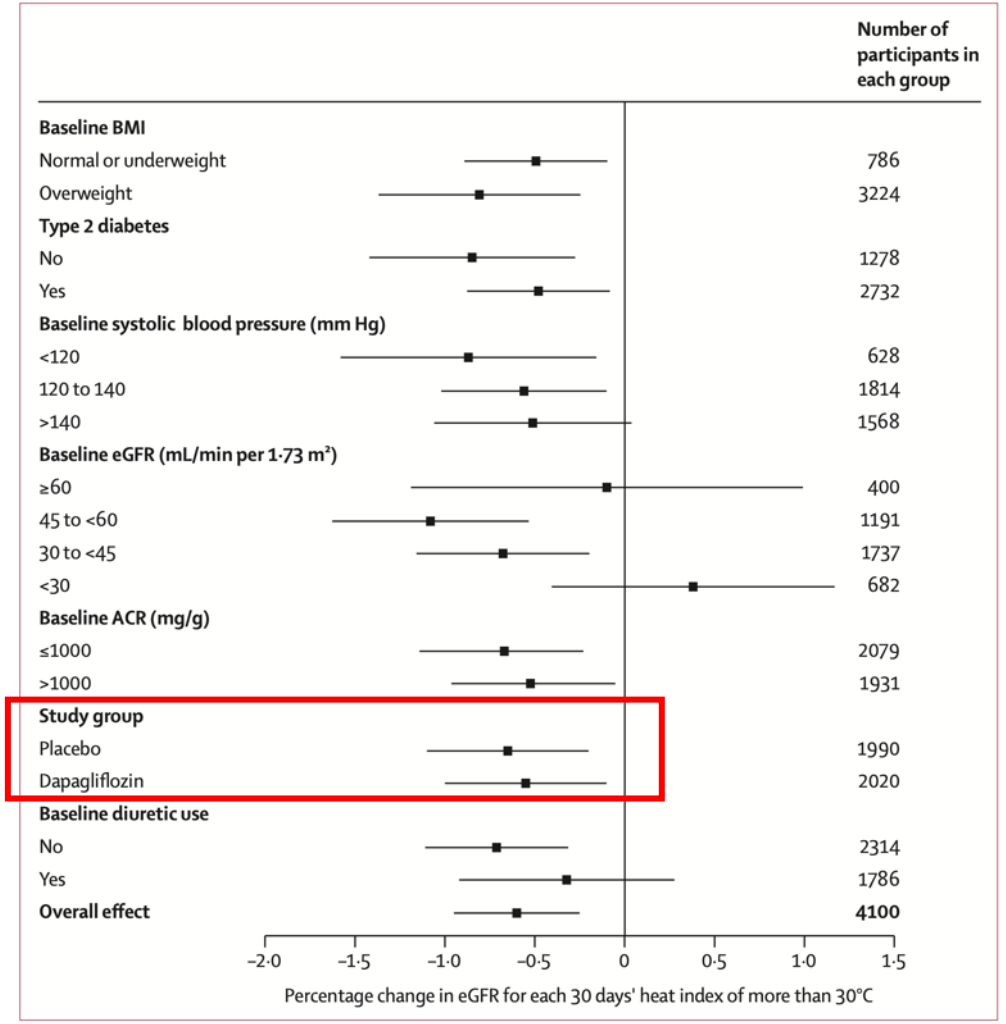
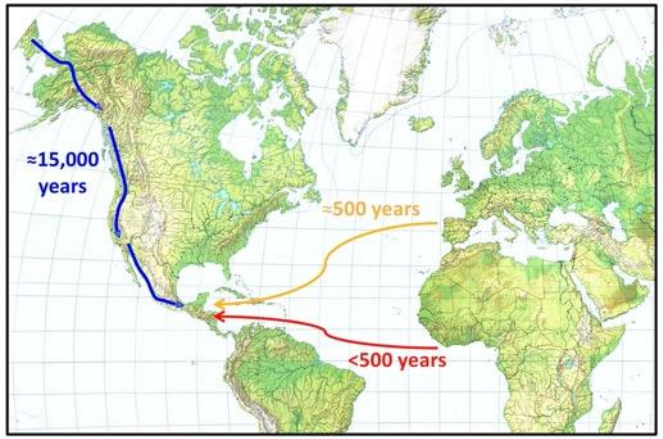


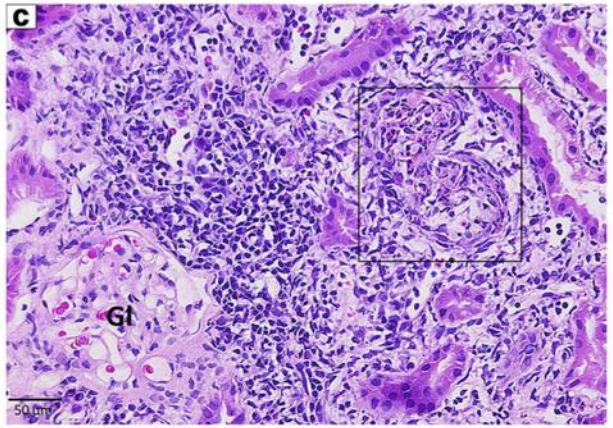
Figure 3: **Associations between heat index and change in eGFR in subgroups**

3.7 ml/min/year faster eGFR decline in hottest sites vs. median temperature sites

TAKE HOME MESSAGES

- MeN occurs in “hotspots” where one common element is strenuous labor in hot, humid climates
- Repetitive AKI episodes may lead to accumulated kidney injury
- Biopsies tend to show tubulointerstitial nephritis with varying degrees of inflammatory infiltrate
- There are differences in susceptibility between populations and between individuals within a population
- Other environmental factors are probably important in specific hotspots





Questions

Which feature of Mesoamerican Nephropathy is correct:

a. Occurs about equally in males and females
b. Associated with high grade proteinuria
c. Hard to distinguish from diabetic nephropathy
d. Often associated with high uric acid levels

Mesoamerican Nephropathy is one presentation of CKDu. Other major hotspots of CKDu include:

a. Sri Lanka and India
b. Australia and New Zealand
c. The Balkan states
d. South America

References

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NEJM 2019

Genetic Risk Factors for Mesoamerican Nephropathy
Friedman D et al
PNAS 2025

Heat-induced Kidney Disease: Understanding the Impact
Elinder CG
J Internal Med 2025