

Relationship between toxic environmental chemicals, epigenetic factors and Chronic Kidney Disease of unknown etiology in Costa Rica

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- International Medical Geology Association.

Asociación Internacional
de Medicina Geológica.



- Society Environmental Toxicology and Chemistry, SETAC:

Sociedad de Toxicología Ambiental
y Química

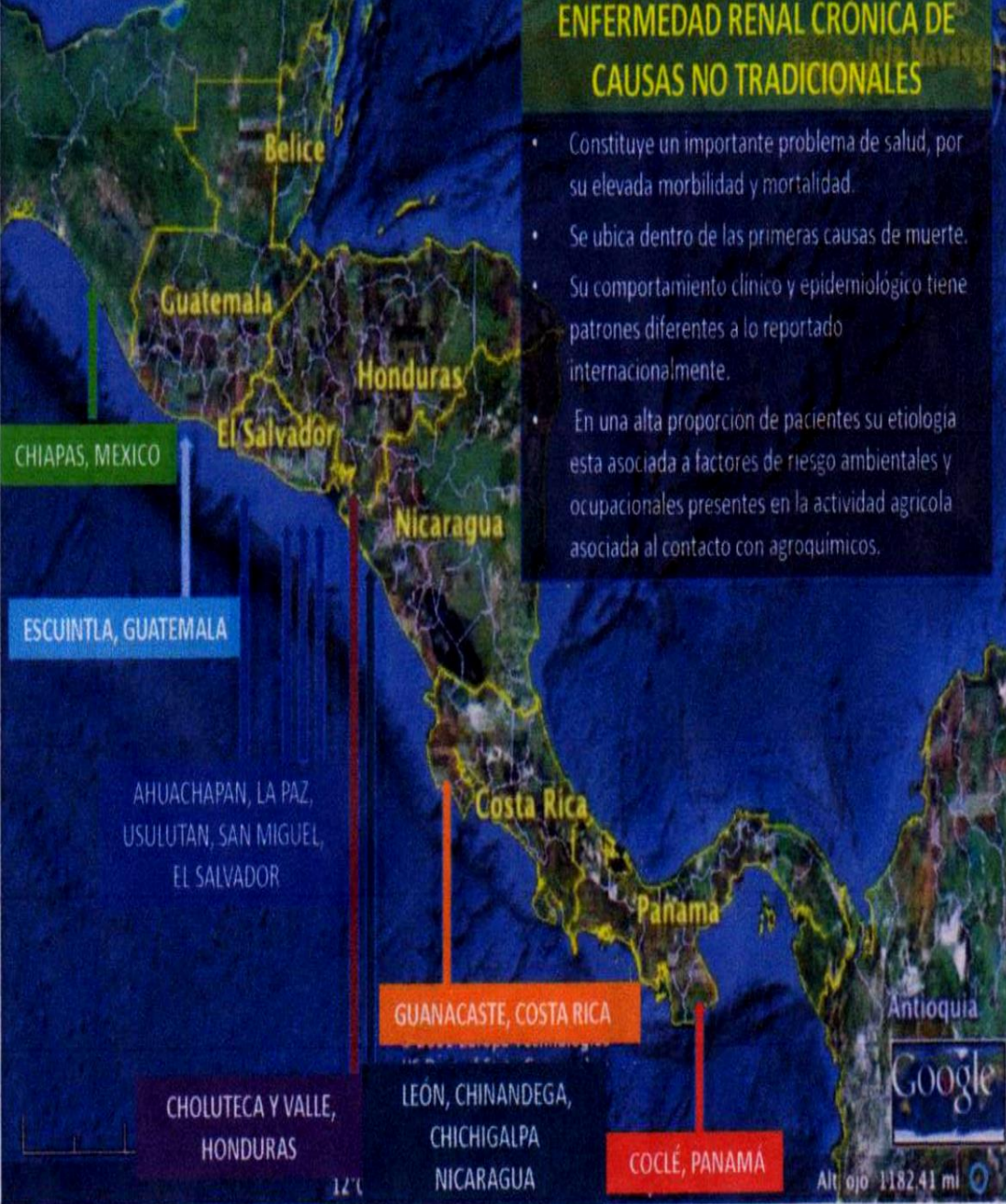


Situation

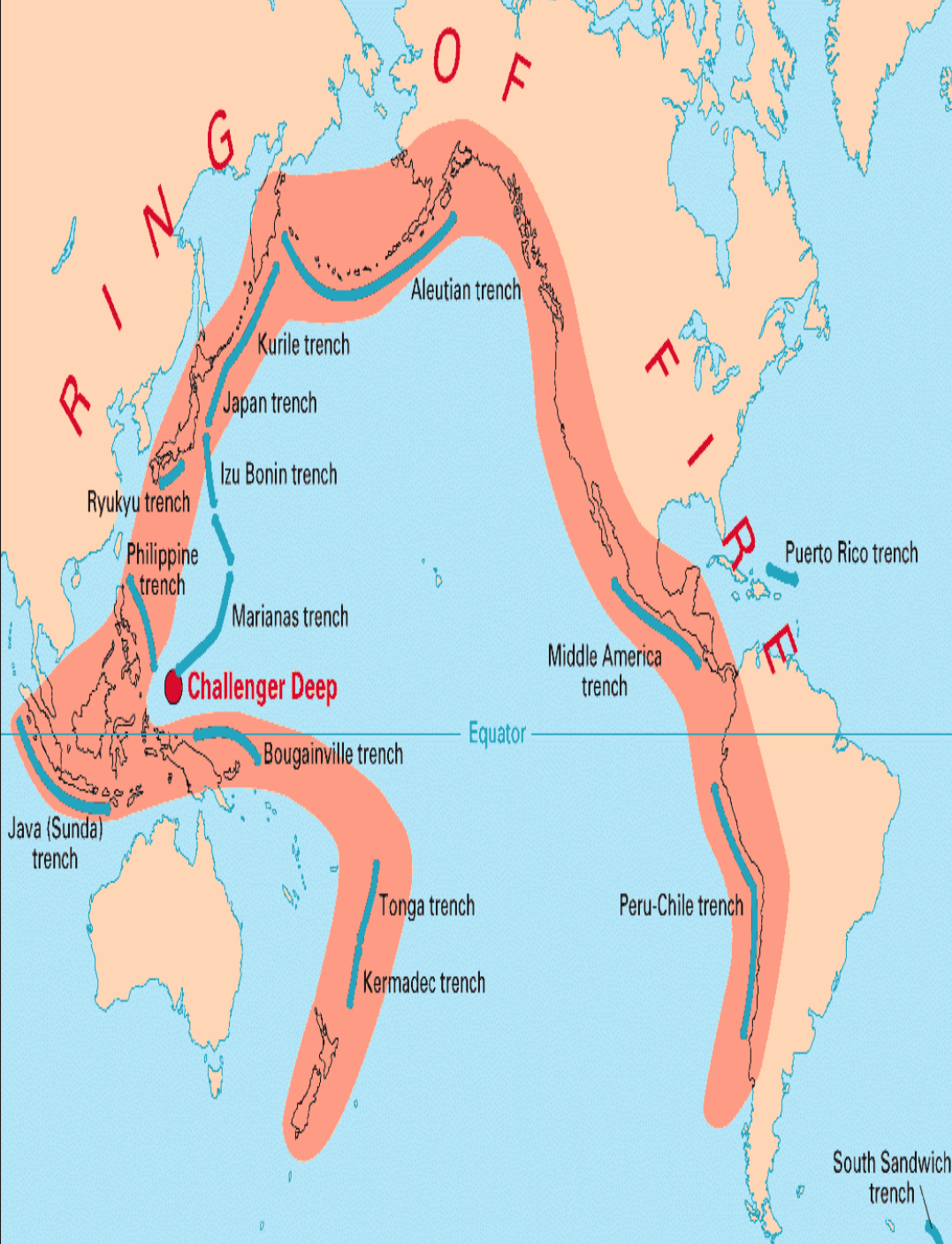
- The epidemic of Chronic Kidney Disease (CKD) affects some areas of Central America, has been considered one of the most important problems of public health in recent years, according to the Panamerican Health Organization.
- Disease affecting thousands of people in rural communities from Nicaragua, El Salvador , Costa Rica and other countries like Sri Lanka and India. More than 16,000 people have died in Central America between 2005 and 2009, according to the World Health Organization.

ENFERMEDAD RENAL CRONICA DE CAUSAS NO TRADICIONALES

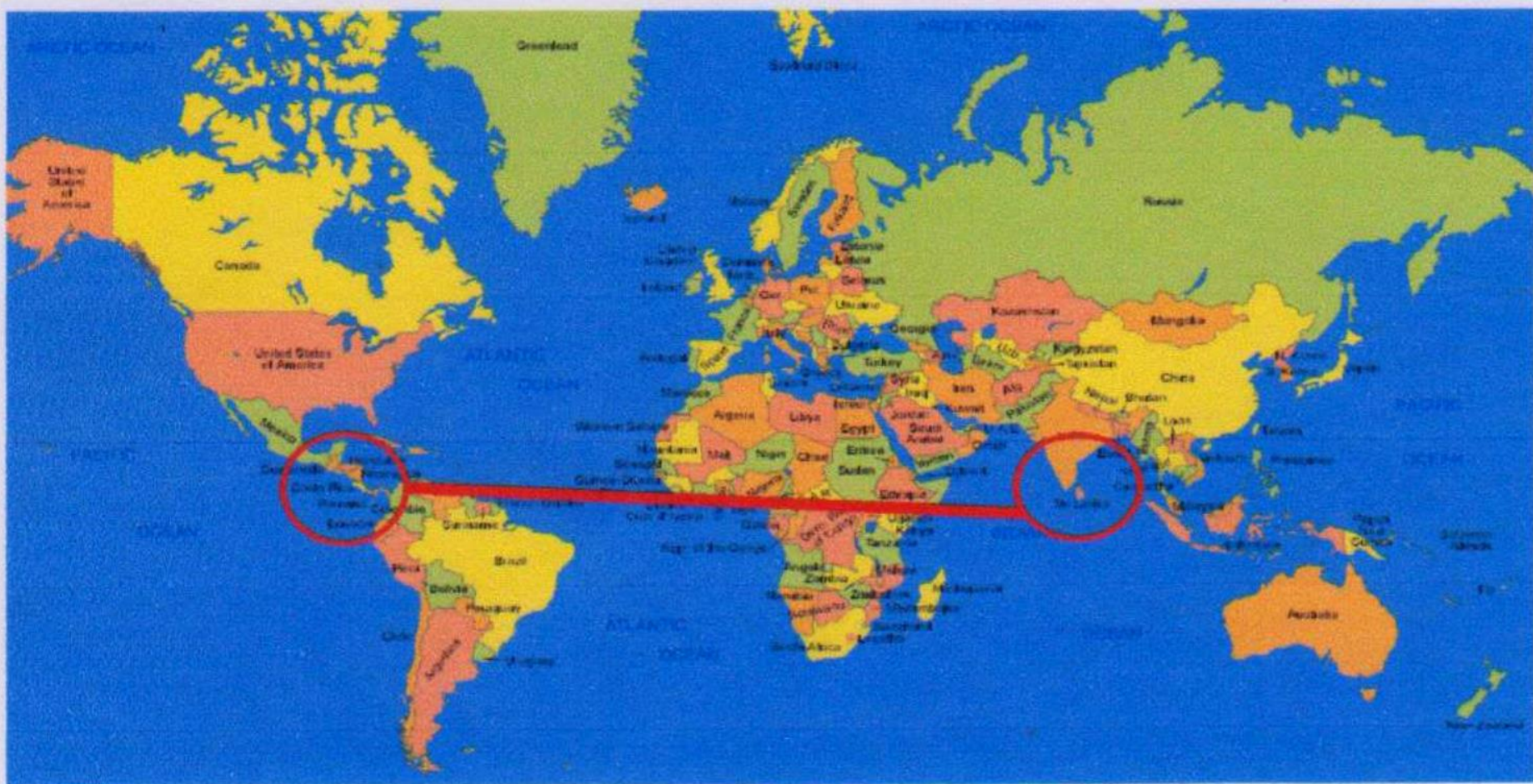
- Constituye un importante problema de salud, por su elevada morbilidad y mortalidad.
- Se ubica dentro de las primeras causas de muerte.
- Su comportamiento clínico y epidemiológico tiene patrones diferentes a lo reportado internacionalmente.
- En una alta proporción de pacientes su etiología esta asociada a factores de riesgo ambientales y ocupacionales presentes en la actividad agrícola asociada al contacto con agroquímicos.



- The problem appears in certain areas of the countries, especially on the Pacific coast from Mexico to Panama. It seems to be related to the volcanic activity at the so-called Ring of Fire



The Ring of fire is an area where a large number of volcanic eruptions and earthquakes occur in the basin of the Pacific Ocean. We can see it in Central America and in a straight line above the line of meridian Ecuador, in this site we find Sri Lanka and India. These regions share certain conditions such as: Sugar cane farming and all its implications, like how it is harvested in spanish zafrá. In this harvesting technique, the farmer burns the plants to facilitate the harvesting. By this practice, soot permeates the skin. Other shared environmental conditions are: similar high temperature and high humidity.



“Sri Lankan Agricultural Nephropathy”

- North Central Province.
- Alta prevalencia de ERC de causa desconocida.
- Predominante en hombres agricultores.
- Nefritis intersticial crónica.
- De etiología multifactorial: arsénico, cadmio, residuos de pesticidas, agua dura + características de los suelos.

Chronic Kidney Disease (CKD)

CKD is an irreversible kidney damage that stops the performance of normal vital functions such as removing toxics and regulating both water and blood chemicals such as sodium, potassium, phosphorus and calcium.

Chronic kidney disease: traditional causes

- Chronic kidney disease (CKD) is a serious global public health problem, the behavior of this illness is epidemic.
- The world-wide reported traditional causes of CKD are diabetes mellitus (DM) (30% to 40%) and hypertension (HTA) (25% to 30%), mainly associated with risk factors like a lifestyle and aging (> 60 years).

CKD of known vrs CKD of unknown causes

| | CKD KNOWN ETIOLOGY | CKD UNKNOWN ETIOLOGY |
|----------------------|---|--|
| WHO WILL BE AFFECTED | Elderly people | Predominant in young people (men), farmworkers. |
| CAUSES | Diabetes Mellitus Hypertension , Renal diseases (primary glomerulopathies) | It Is not due to traditional causes. Toxic causes associated with environmental and occupational safety Hypothesis: toxic, ischemic and dehydration causes. |
| RISK FACTORS | Diabetes Mellitus hypertension Obesity dislipidemias | Farm work, strenuous work, living in endemic areas, exposure to occupational and environmental toxics, social factors (poverty, low education, poor living conditions, poor access to health services). |

CKD of known vrs CKD of unknown causes

| | CKD KNOWN ETIOLOGY | CKD UNKNOWN ETIOLOGY |
|---|-----------------------|---|
| PROTEINS (ALBUMIN) IN URINE | high | low |
| STRUCTURE OF KIDNEY PREDOMINANTLY AFFECTED | Glomerulos | Tubules and interstitium |
| WORLDWIDE DISTRIBUTION | Global | Central America, Southern Mexico, Sri Lanka, India, Vietnam, Nepal, Egypt, countries of the Balkan region. |

¿Quiénes la padecen?

Población general
Mayores de 60 años
Ambos sexos



Jóvenes
Agricultores
Sexo masculino

Factores de riesgo

Diabéticos
Hipertensos
Obesos



Agricultura
Exposición laboral
Metales pesados
Agroquímicos

Sitio del daño Predominante

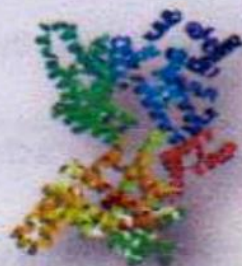
Daño glomerular



Daño tubular e intersticial

Marcadores encontrados

Albumina
Proteínas de alto peso molecular



Proteínas de bajo peso molecular
B-2-microglobulina
NGAL
KIM-1



*One Century of the Discovery
of Arsenicosis in Latin America*



5th INTERNATIONAL CONGRESS ON ARSENIC IN THE ENVIRONMENT

Toxicological Risk Analysis for consumption of
water containing arsenic in Canton Bagaces,
Guanacaste, Costa Rica



- The 50 % of the patients had values of arsenic in hair from about 0,445 mg/Kg up to 0,995 mg/kg , children being the most affected.
- These patients had the following biomarker values and clinical testing of renal function.

Sample mean values

| Age | Arsenic in hair (mg/kg) | Creatinin Up to 1 mg/dL | Cistatin C Up to 0,98 mg/L |
|-------------------------|----------------------------|----------------------------|-------------------------------|
| Children 10-12 years | 0,693 | 0,71 | 1,10 |
| Adults 19-74 years | 0,635 | 0,91 | 1,17 |

Agroquímicos
y plaguicidas

Glifosato (herbicida, quelante
de metales)
2,4-D (herbicida, ácido
2,4-diclorofenoxiacético y dioxina)
Clorpirifós (insecticida, inhibidor
de la colinesterasa)
Cipermetrina (insecticida,
modulador de los canales de sodio)
Paraquat (herbicida, especie
reactiva de oxígeno = produce
radicales libres que reaccionan
con el oxígeno formando radicales
superóxido = necrosis tubular
aguda)

Exposición a metales
y toxinas

Cadmio
Arsénico
Plomo
Sílice (de la quema de caña de
azúcar)
Ácido aristolóquico
Antiinflamatorios no esteroideos
(iatrogénicos)

Causas metabólicas

Hipocalemia
Hiperuricemia

Causas infecciosas

Leptospirosis
Hanta virus

Deshidratación recurrente
y estrés térmico

Rabdomiólisis subclínica
Deshidratación con estimulación
de vasopresina
Deshidratación con activación de
aldosa reductasa y fructocinasa en
el túbulo renal
Uricosuria
Golpe de calor

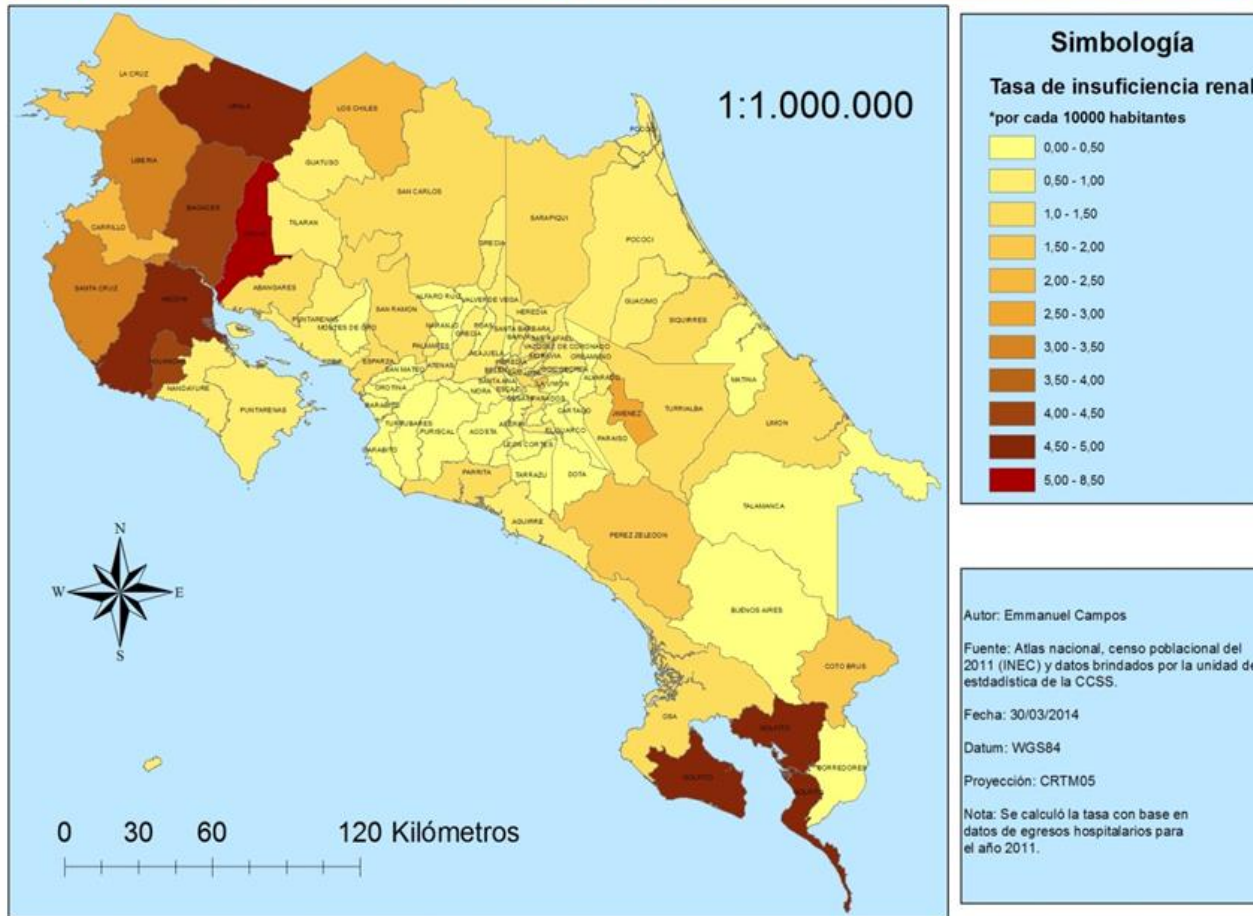
- Causes proposed for the NM that were reviewed during the Second Workshop of CENCAM in 2015.

What is the toxicokinetic of glyphosate?

- The toxicokinetic studies also indicate that human glyphosate exposures estimated from urine biomonitoring fall thousands-of-fold short of external doses capable of producing blood concentrations sufficient to result in the breast milk concentrations described in the MAA report.
- Finally, in contrast to highly lipophilic compounds with bioaccumulation potential in breast milk, the physico-chemical properties of glyphosate indicate that it is highly hydrophilic (ionized) at physiological pH and unlikely to preferentially distribute into breast milk.

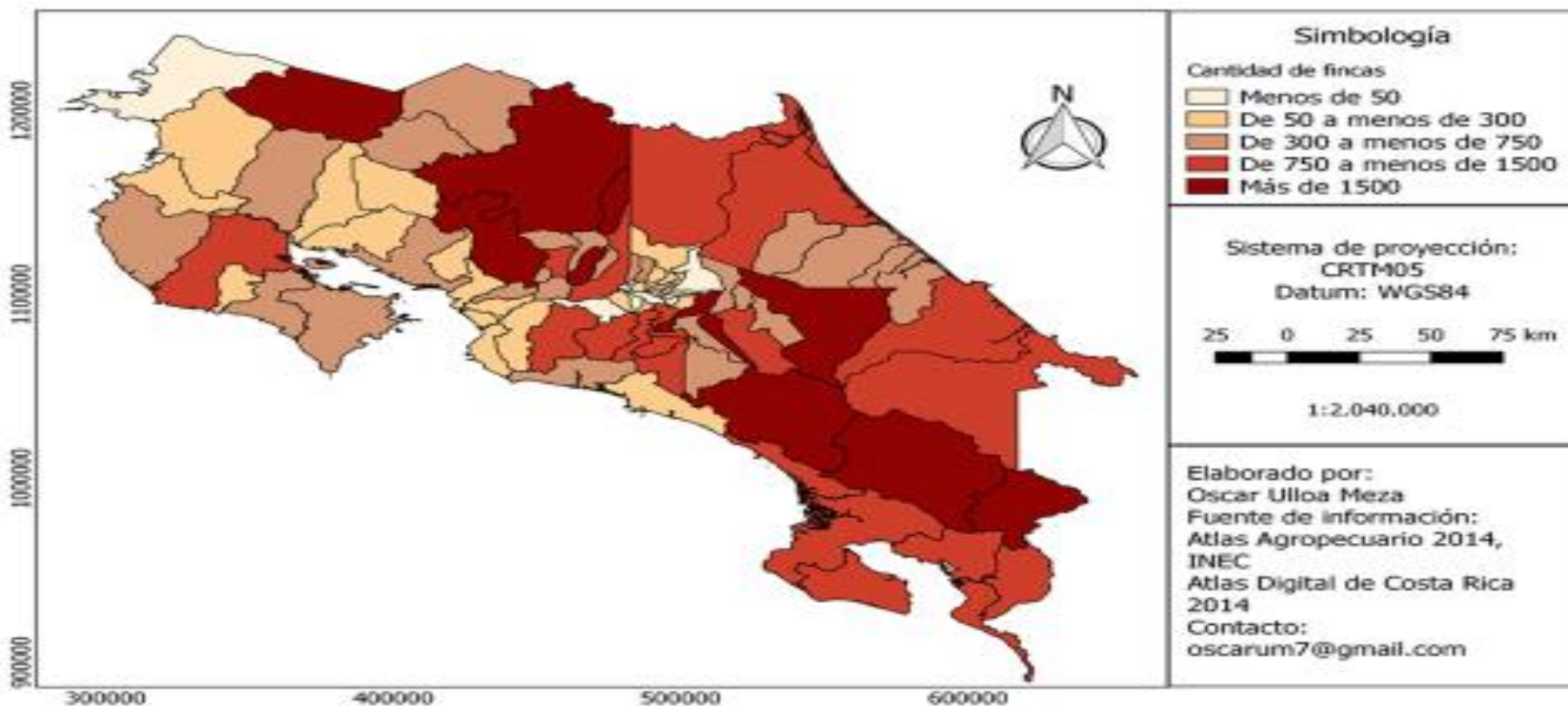
CKD Rate in Costa Rica by cantons in 2011

Mapa de tasa de insuficiencia renal para los cantones de Costa Rica en el 2011.



Statistical relationship between drinking water with arsenic, and the incidence of CKD as determined with a Pearson Correlation Coefficient of **0.791** with **p: 0.002**.

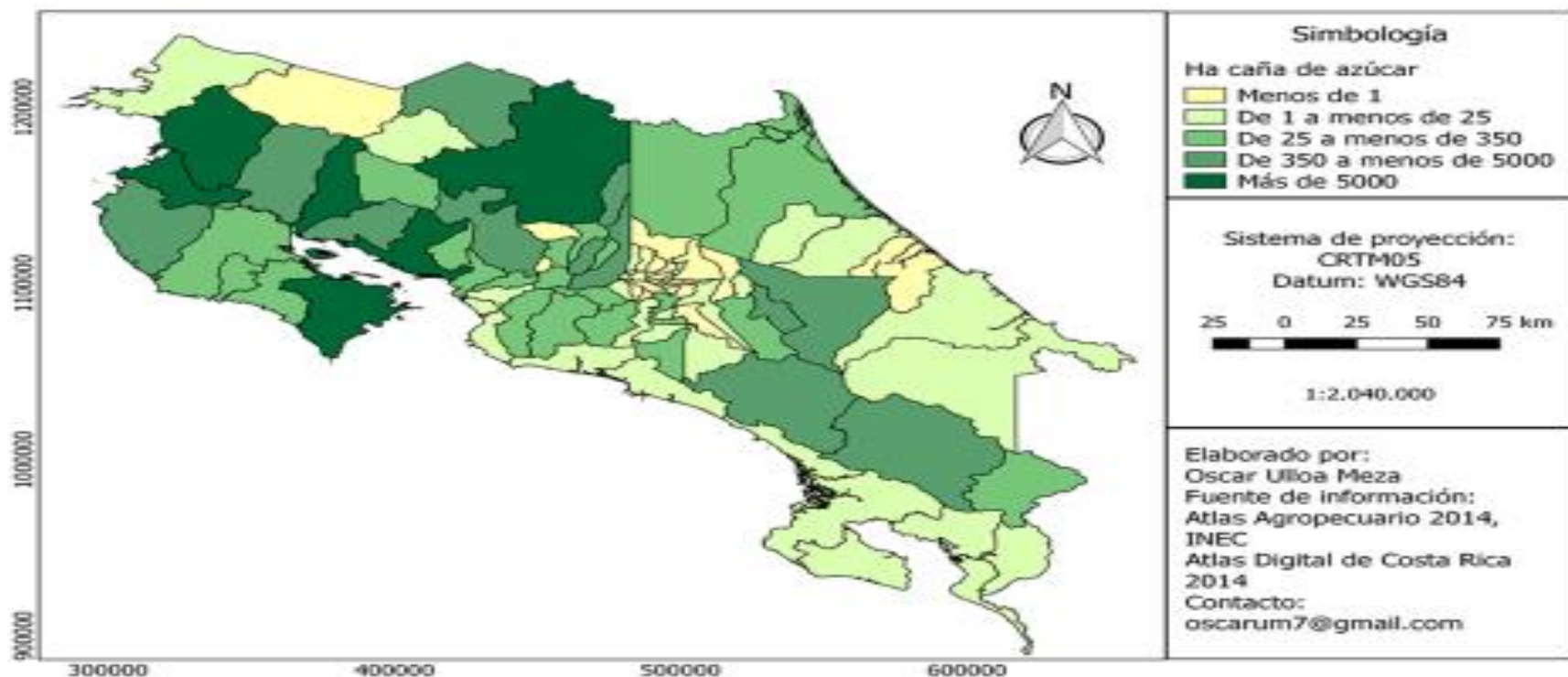
- Farms with main agricultural activity in CR



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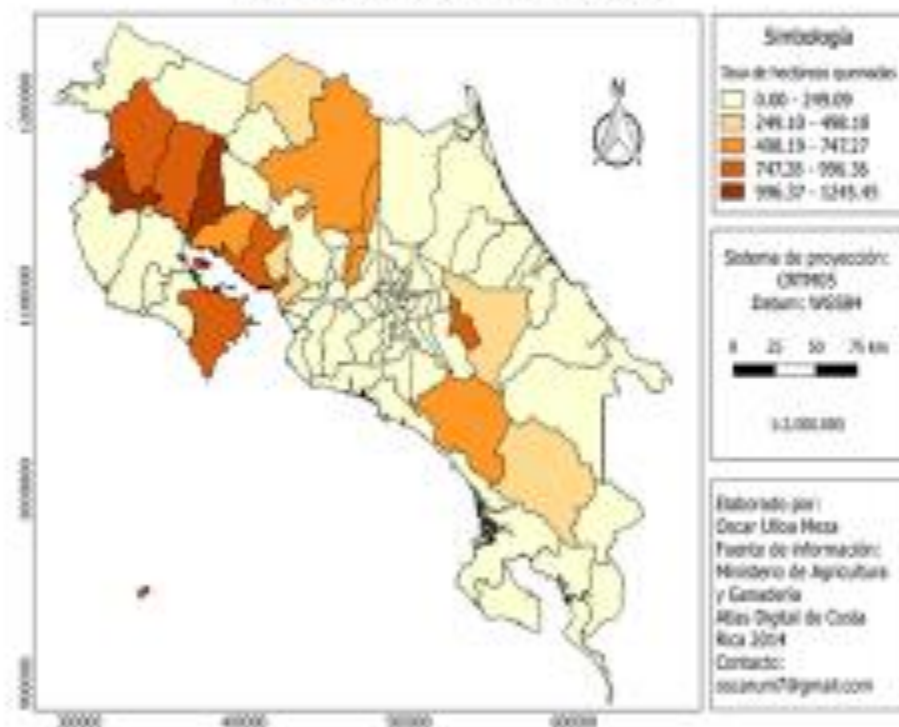
- Sugar cane planted in CR



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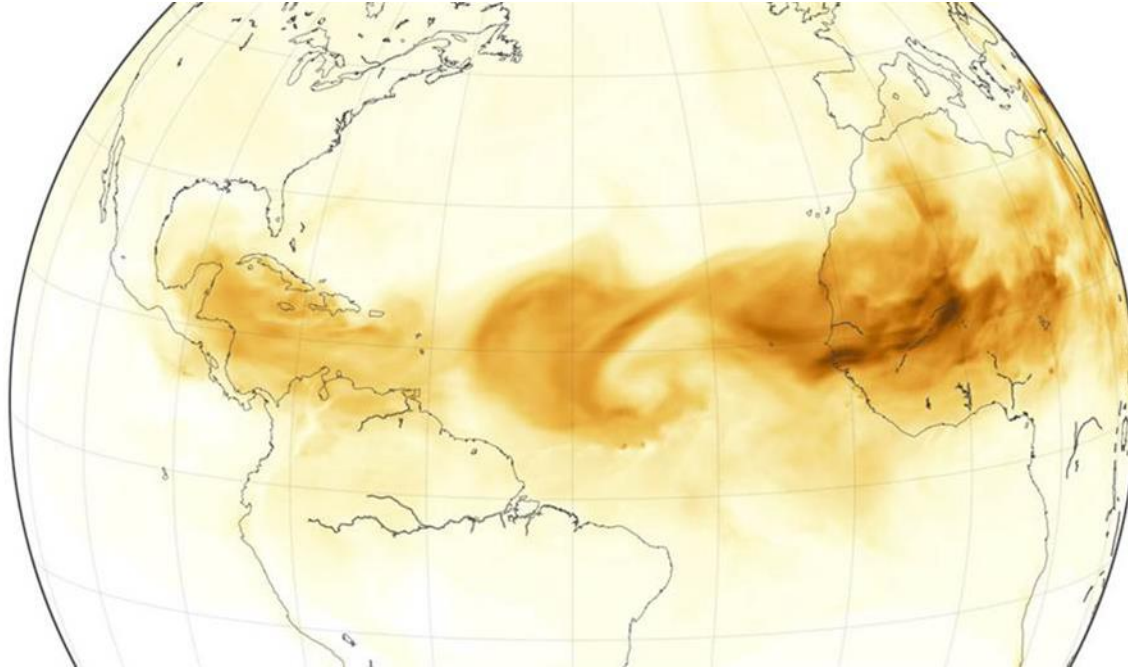
Tasa de hectáreas de caña de azúcar quemadas por cada 10 000 hectáreas de terreno en Costa Rica



Puntos de muestreo de agua determinados como positivos por arsénico en Costa Rica



Nube de polvo del Sahara



Distribución del polvo del Sahara en Mesoamérica por acción del viento. Tomado de Martins (2018).

Ubicación de las montañas cercanas a Cañas, Guanacaste



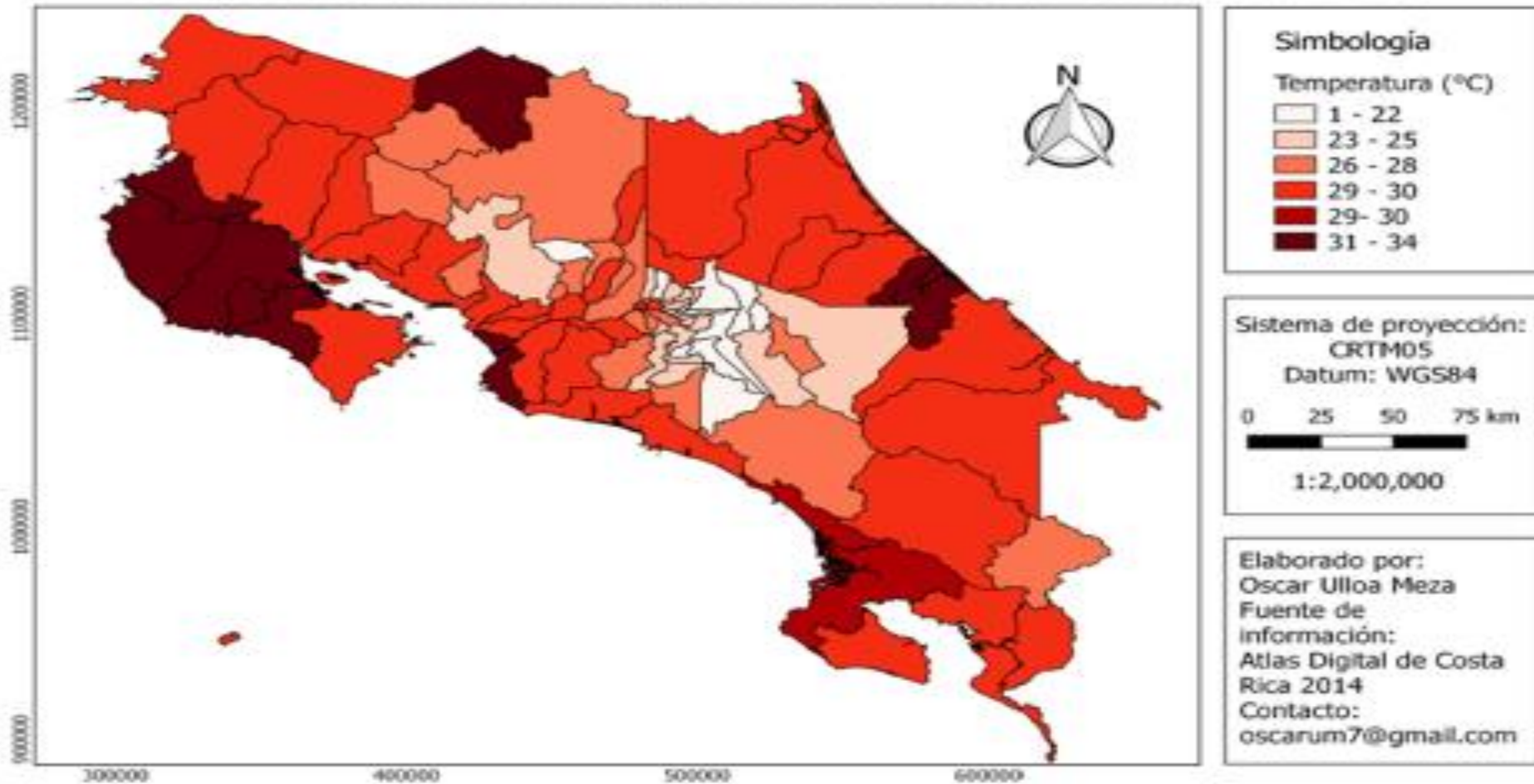
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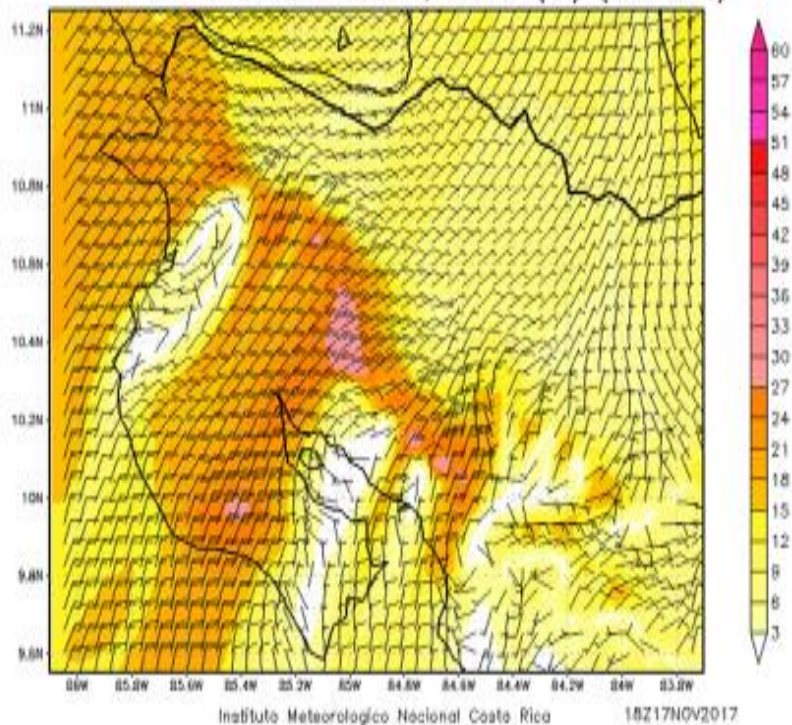
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Temperatura máxima promedio anual en Costa Rica

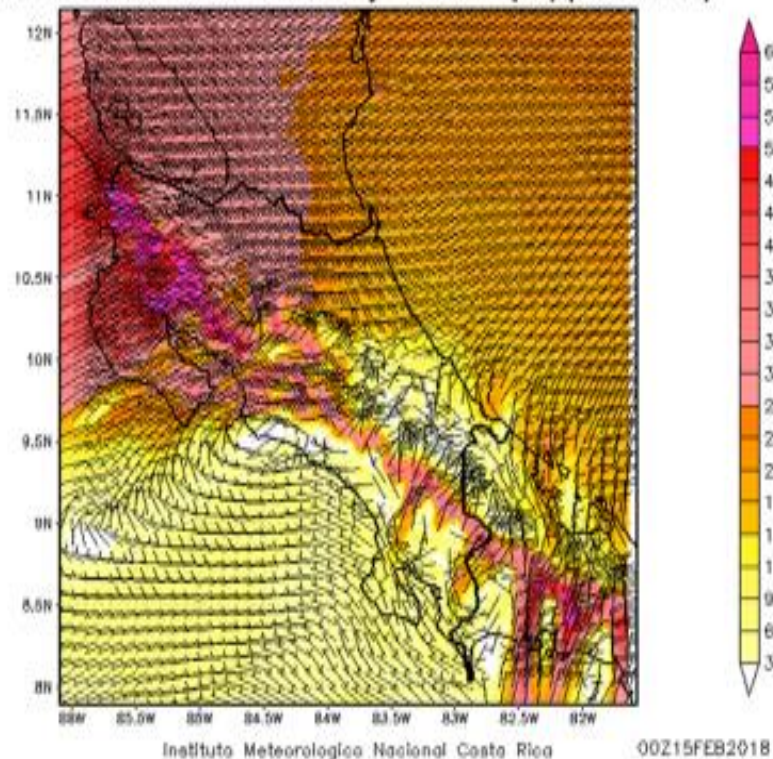


IMN-SARAPIQUI: Guanacaste, Viento (Kt) (925 hPa)



Modelo computacional del viento en Guanacaste para el 17 de noviembre de 2017. Fuente: (IMN, 2017).

IMN-SARAPIQUI: Barbas y Viento (Kt)(925 hPa)



Modelo computacional del viento en Guanacaste para el 15 de febrero de 2018. Fuente: (IMN, 2018).



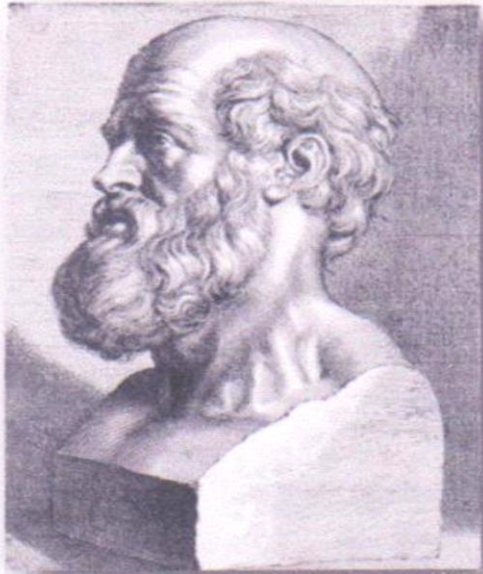
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“The occurrence of disease in human populations is influenced by the quality of air, water and food; the topography of the land and the life habits “

Hipocrates 450 BC