

Climate Change and the Evolution of Humans

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Walter Orr Roberts

A Visionary in his Time



Walter Orr Roberts
(1915-1990)

- Astronomer, physicist, educator, and philanthropist
- First Director of the National Center for Atmospheric Research (NCAR)
- Helped Establish Boulder, Colorado as a Major Center for Scientific Research
- Published “The Climate Mandate” in 1979 with Henry Lansford that set the stage for discussion about changing climate and its impact

Asteroid Belt between Mars and Jupiter



Source: Wikipedia

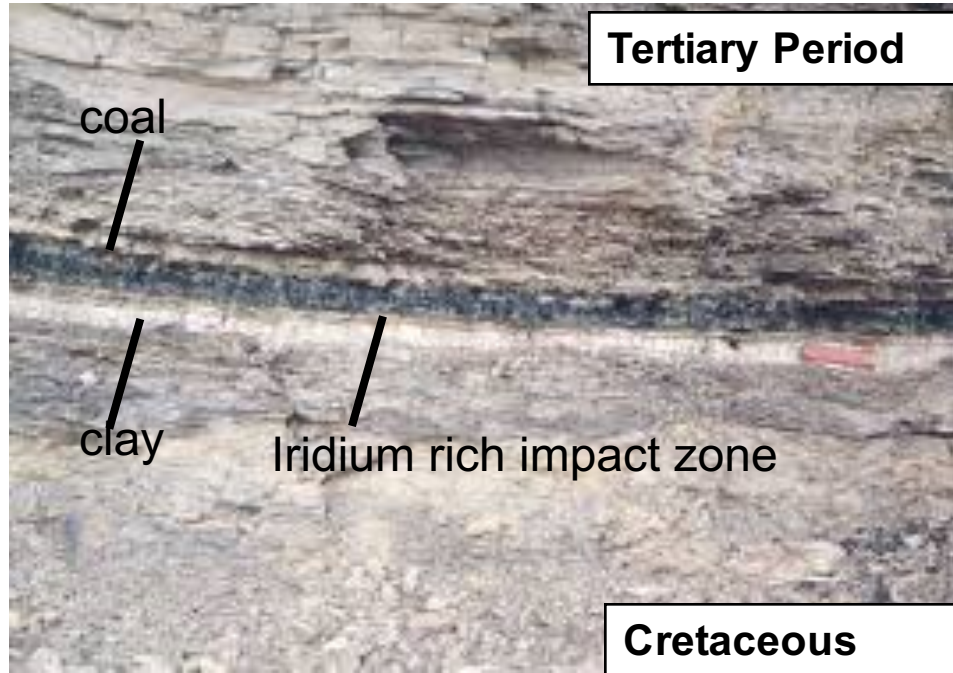
The End of the Dinosaurs: An Asteroid Collision sends a giant meteor towards Earth



Evidence for an Asteroid Impact 65 million years ago



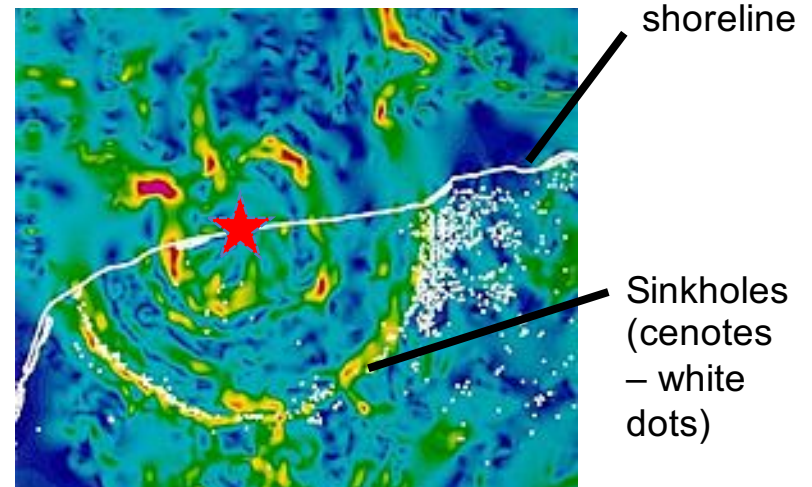
Luis and Walter Alvarez



Walter Alvarez, a geologist, wanted to measure how long the layer separating the Cretaceous and Tertiary Period took to form, and asked his father, the Nobel Laureate, Luis Alvarez. Luis suggested to measure iridium as it collects at a constant rate from atmospheric (meteor) dust that gathers over time. They had a surprise!

Source: Alvarez LW, Alvarez W, Asaro F, Michel HV. Extraterrestrial cause for the cretaceous-tertiary extinction. Science 1980; 208:1095-108.

Chicxulub Impact, 66 million years ago



Source: Hildebrand, AR.; Penfield, GT.; et al Chicxulub Crater; a possible Cretaceous Tertiary boundary impact crater on the Yucatan Peninsula Mexico *Geology* 1991; **19** (9): 867–871

Evidence for an Impact Winter Following the Chicxulub Impact



•**Source:** Robertson DS. Survival in the first hours of the Cenozoic. *Geol Soc Am Bull* 2004; 116: 760; Vellekoop J, et al. Rapid short-term cooling following the Chicxulub impact at the Cretaceous-Paleogene boundary *PNAS*. 2014;111:7537-41

Some small mammals survived the meteor impact



Survival of the Fittest

CHARLES DARWIN

On the Origin of Species

By Means of Natural Selection



“It is not the strongest of the species that survives, nor the most intelligent. It is the one that is the most adaptable to change.”

Three key aspects for survival

- Find or store enough food and water
- Continue to reproduce
- Avoid predators and survive catastrophes

**As environment continues to change,
species may have to evolve to survive**

Origin of Species Published November 24th, 1859

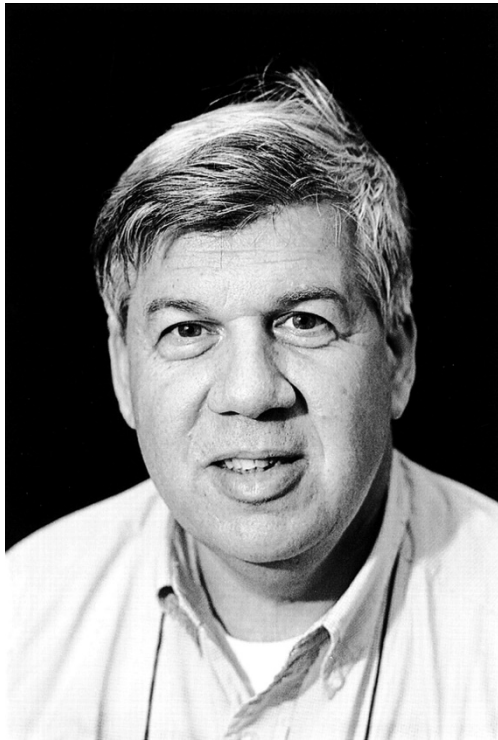
The Versatility (Imperfection) of Life: The Ability to Evolve



- If reproduction was made without error, everyone would be the same
- But reproduction is imperfect, with about one error for each 1 million DNA base pairs that are copied, leading to about 60 new (germline) mutations when a person is born
- Sometimes duplications of segments of DNA also occur by error

• **Source** 1000 Genomes Project Consortium : A map of human genome variation from population-scale sequencing **Nature**. 2010 Oct 28;467(7319):1061-73.

“Punctuated” Equilibrium in which Evolution Accelerates

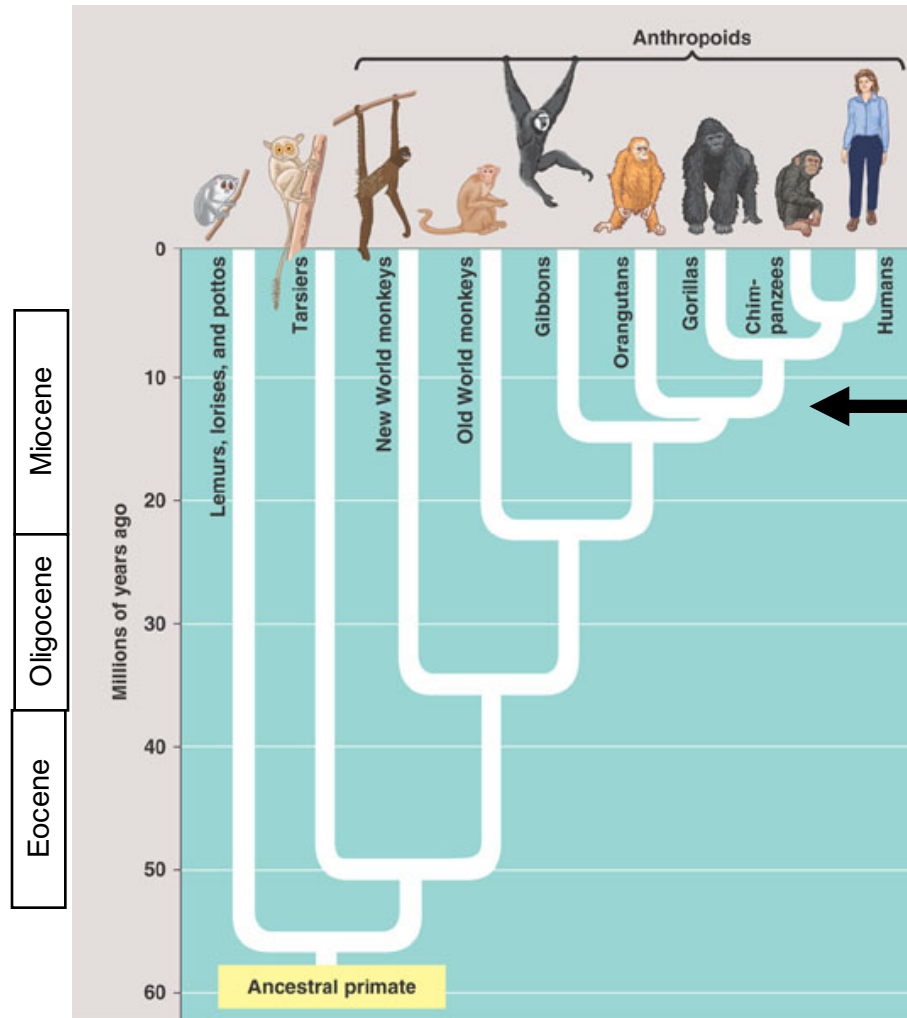


Stephen Jay Gould
(1941-2002)

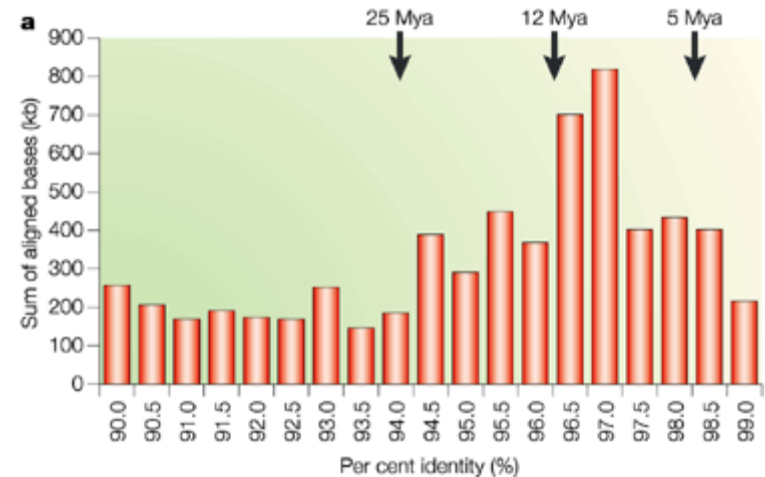


During periods of upheaval where survival is borderline, evolution will speed up as spontaneous mutations that even provide subtle advantage may take over a population

A Period of Rapid Evolution: The Mid Miocene

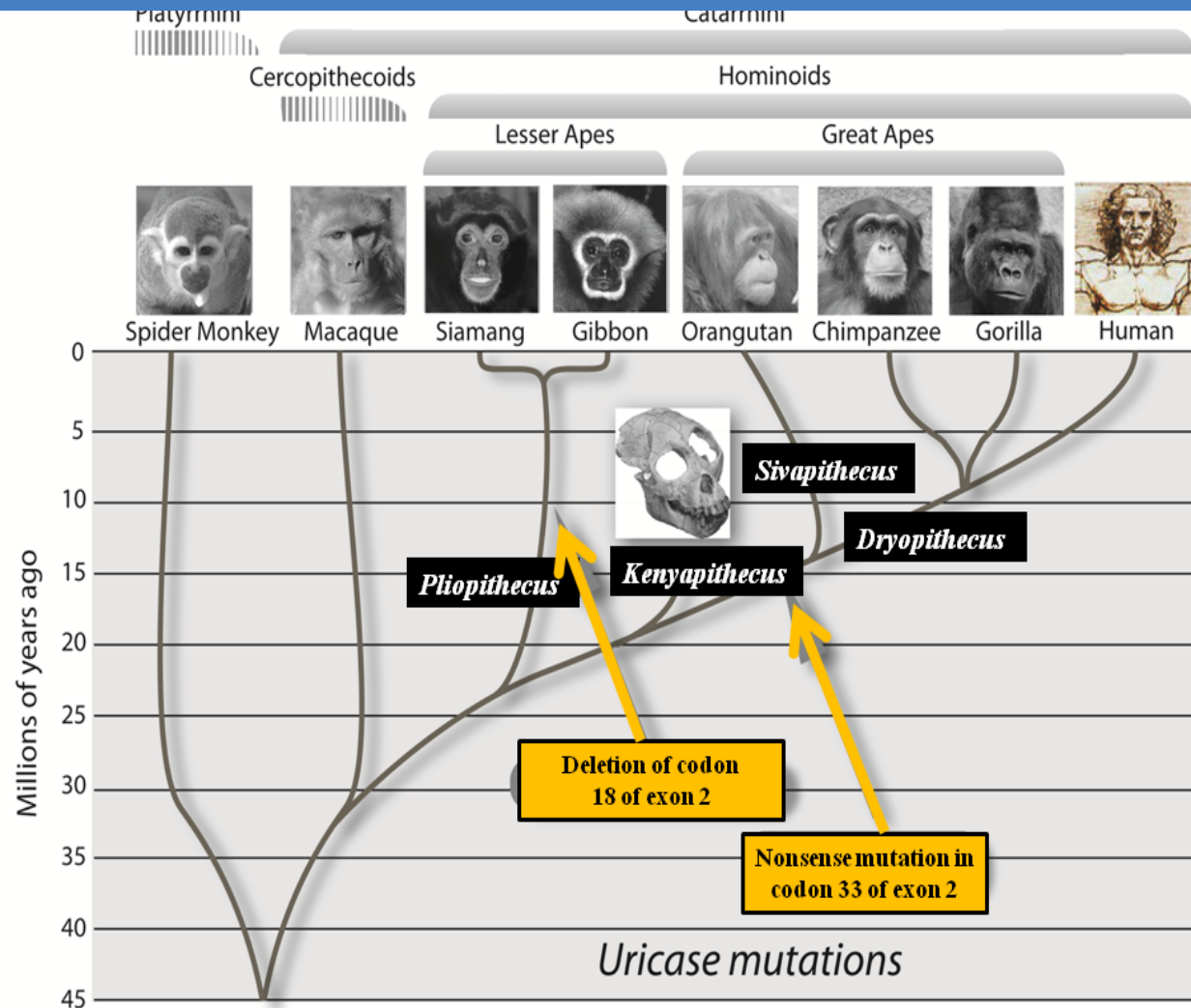


Frequency of Segmental Duplications in Primate Genome



- Source: Samonte RV and Eichler EE. Segmental duplications and the evolution of the primate genome. Nat Rev Genetics 2002; 3:65-72

Dual Uricase Mutations Occurred in the Miocene



A Mutation in Uric acid Metabolism occurred in Humans

Man and
Apes

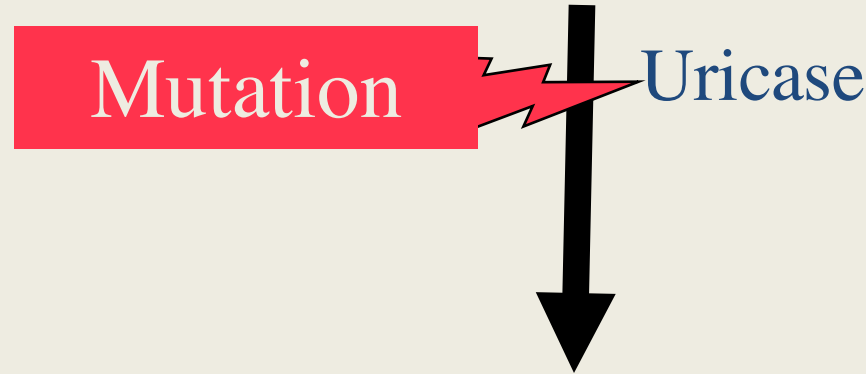
↑ Uric Acid

Mutation

Uricase

Most
mammals

Allantoin



Uric acid in Other Species: Role in Reproduction, Water, Alarm



White color of butterfly wings



Crystals used to magnify light



Female release uric acid to induce male to secrete sperm



Birds conserve water by excreting solid urate (guano) to help rid excess nitrogen

Uric acid causes Gout



A Model of Chronic Hyperuricemia



Normal Rat

Uric Acid (0.5-1.4 mg/dl)

Uricase inhibitor



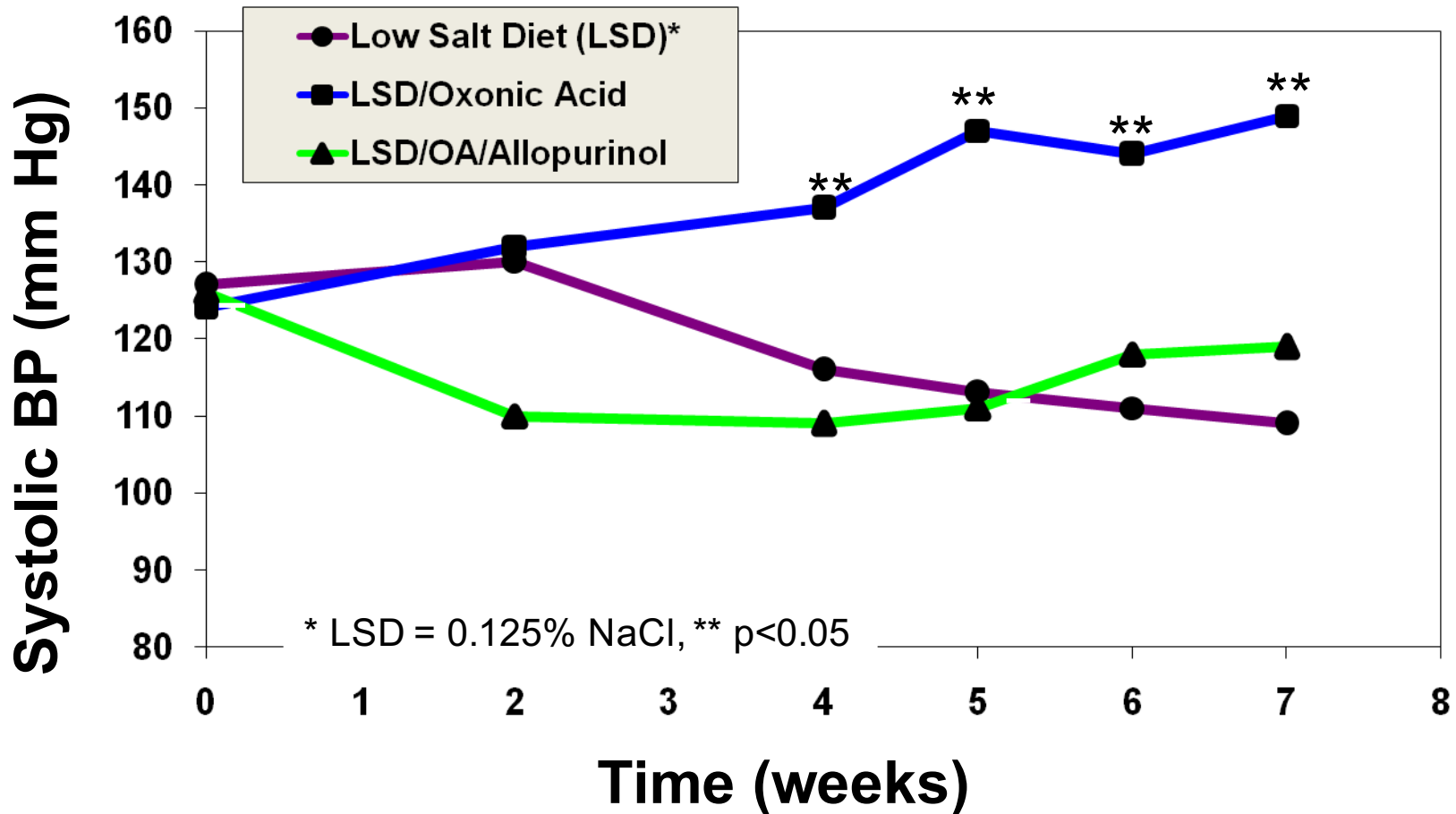
Oxonic acid (OA)



Hyperuricemic Rat

Uric Acid (2.0-3.0 mg/dl)

Inhibition of Uricase Raises Blood Pressure in the Rat

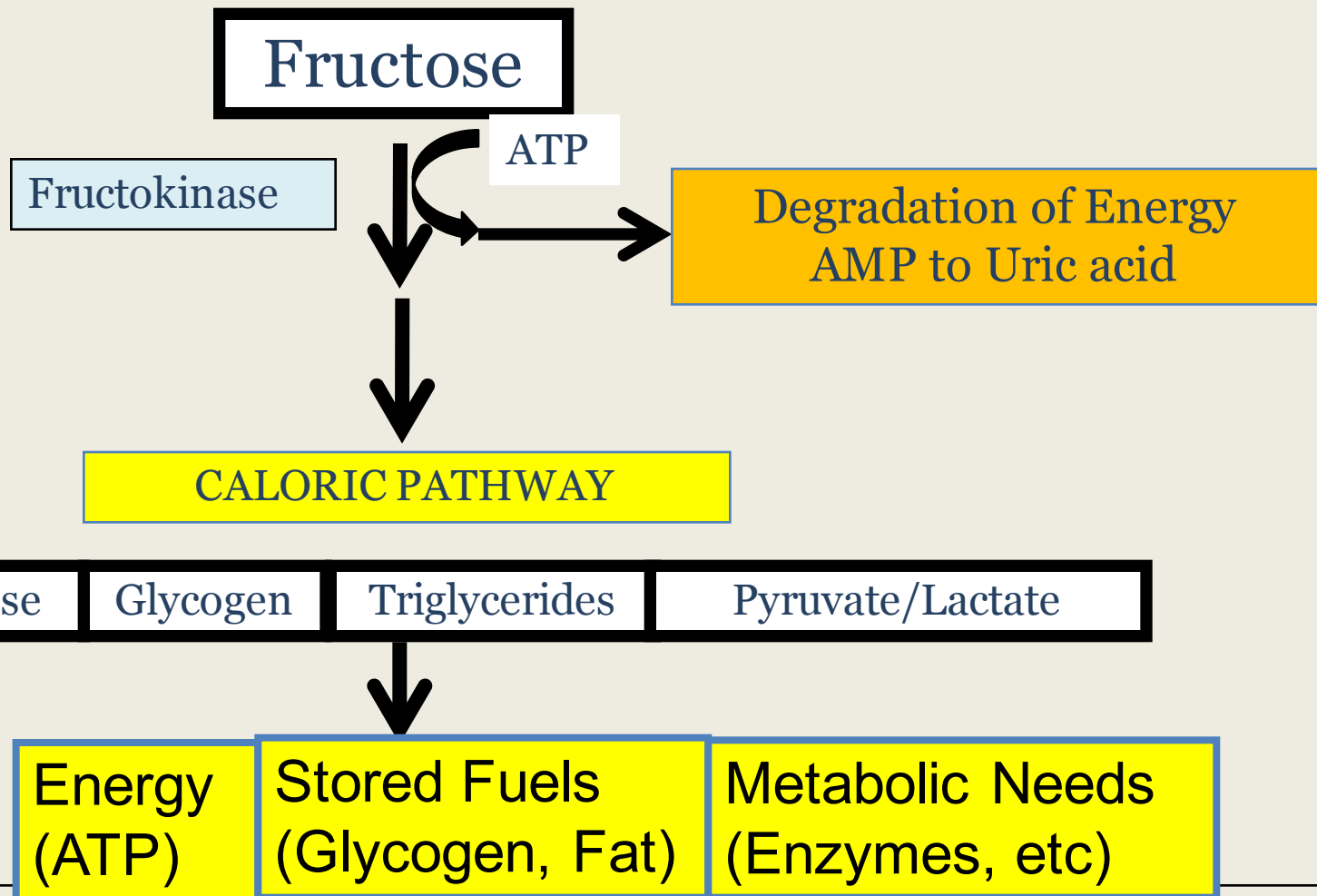


Sugar and Fructose

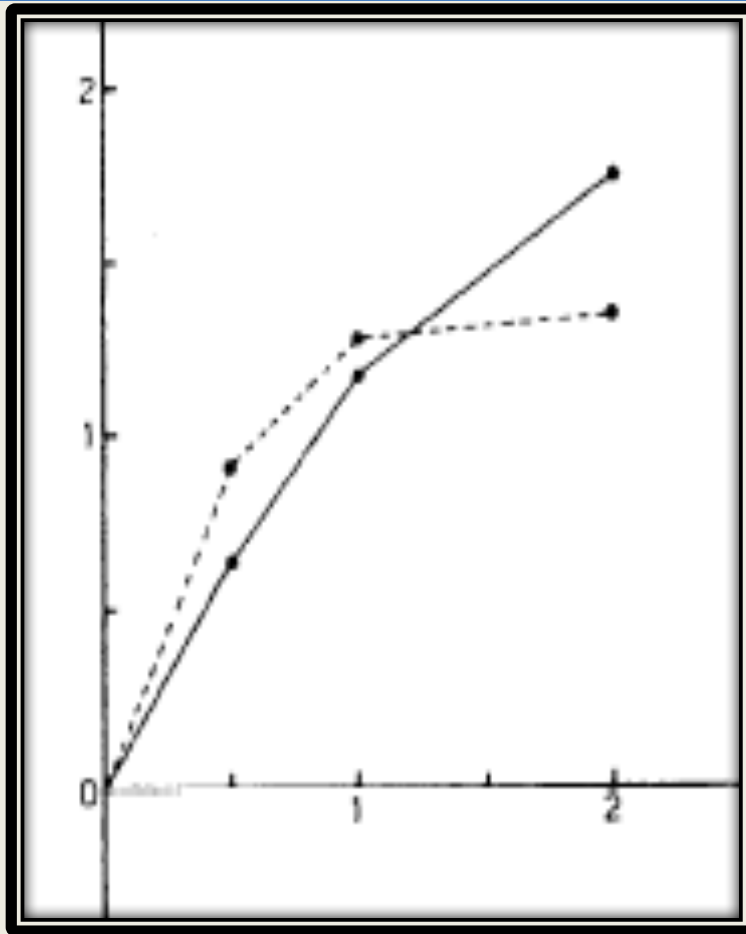


- Sugar (sucrose): fructose/glucose
- High fructose corn syrup (HFCS)- fructose/glucose
- Fructose is in honey and fruit

Fructose the Only Nutrient that Causes Energy Depletion Before Energy is Produced



Fructose Acutely Raises Serum Uric Acid



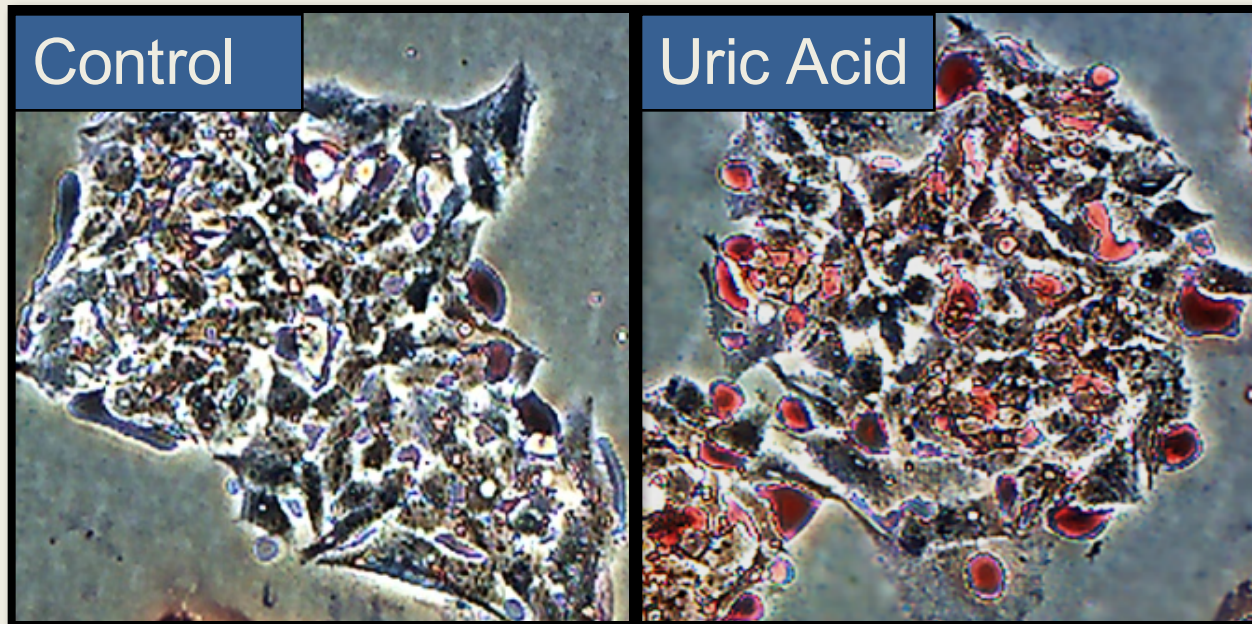
Fructose (1 g/kg body wt) increases serum uric acid within 30 minutes

Gout, a High Uric acid Condition, is Associated with the Metabolic Syndrome

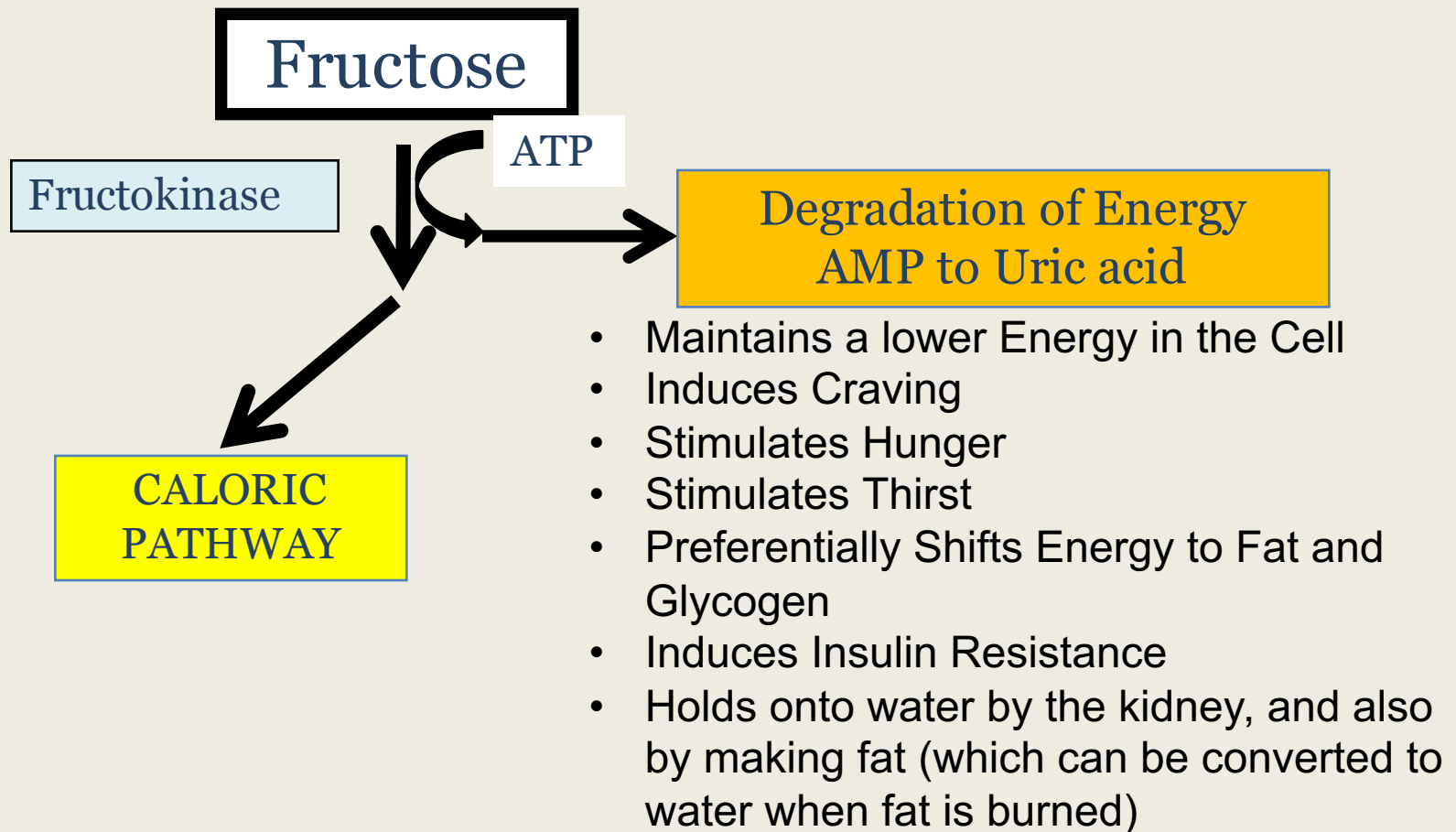


- Obesity 60-80%
- Hypertension 50-60%
- Metabolic Syndrome 70-80%
- Chronic Kidney Disease 50-100%
- Cardiovascular Disease in 90%

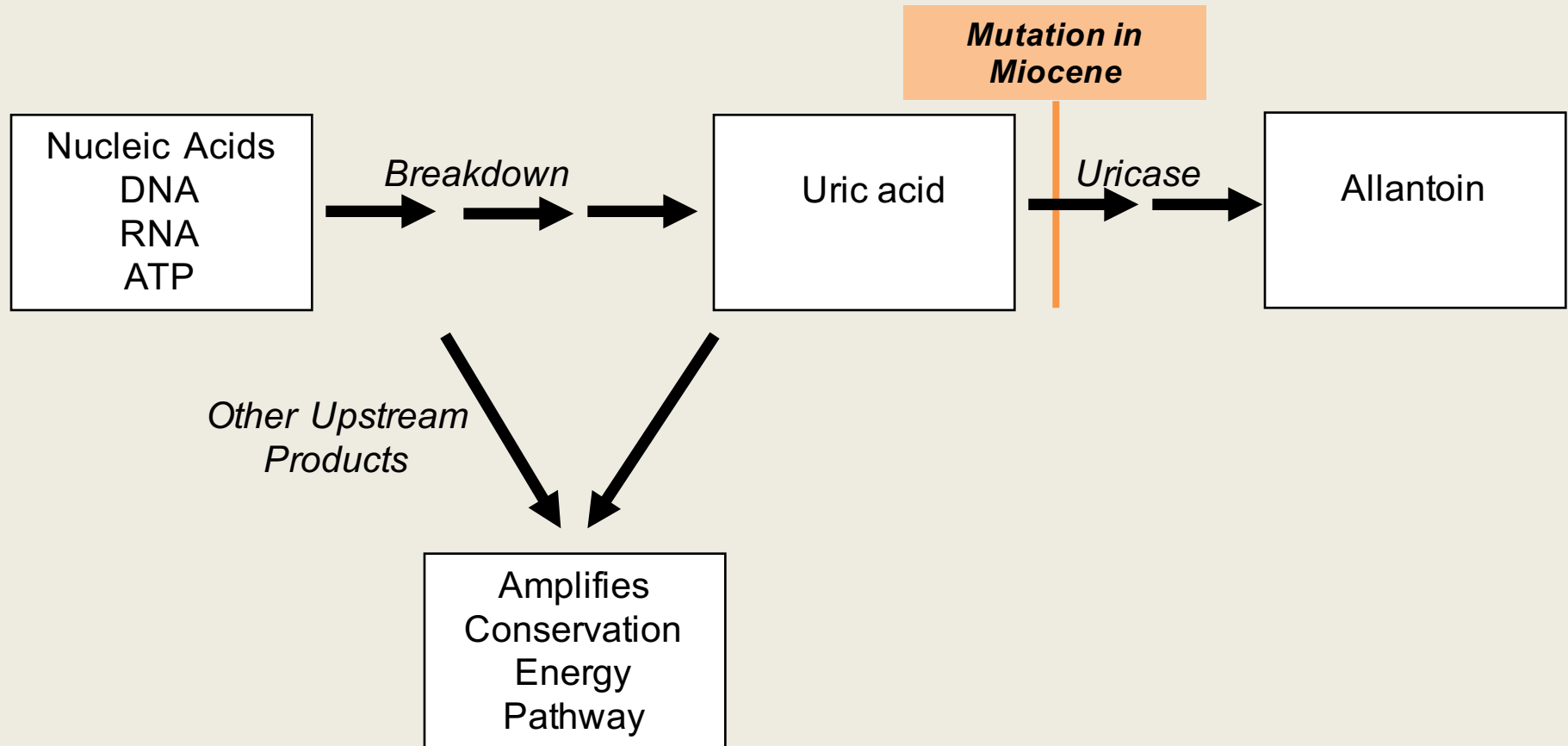
Uric acid Increases Fat in Liver Cells



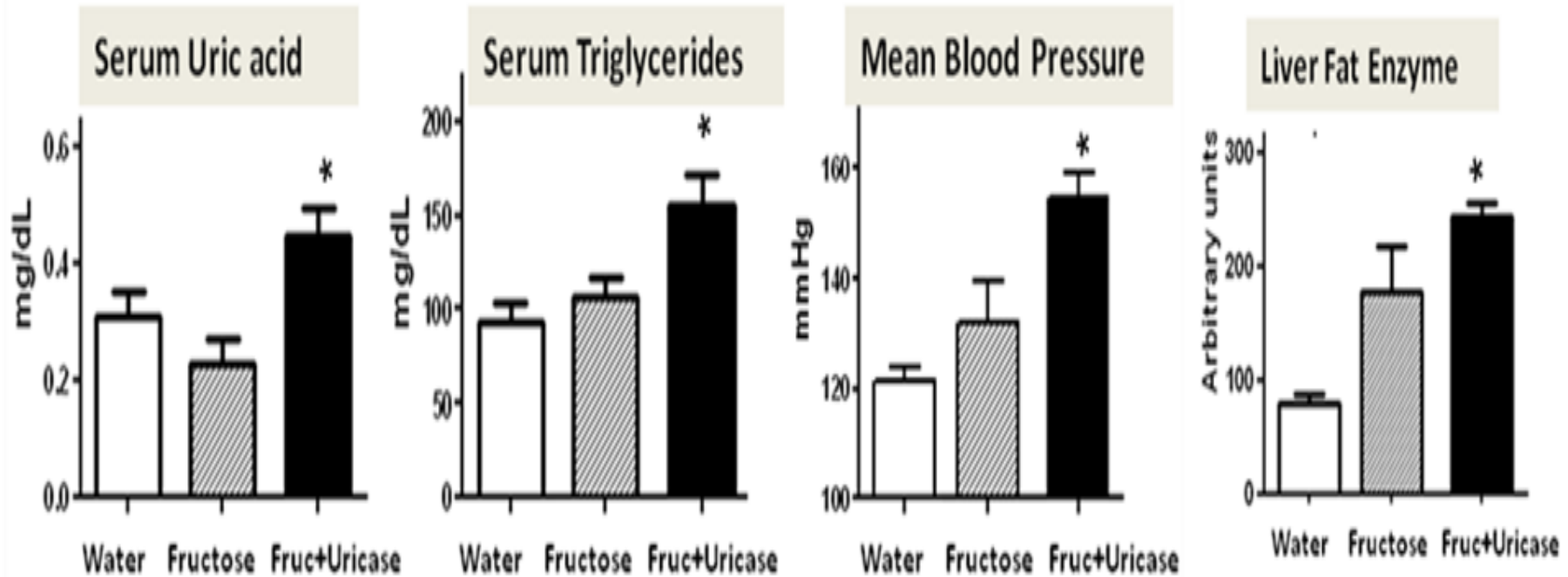
The Energy Degradation Pathway Activates a “Conservation of Energy Signal”



Mutation of Uricase in the Nucleic Acid Degradation Pathway Enhances this Survival Pathway

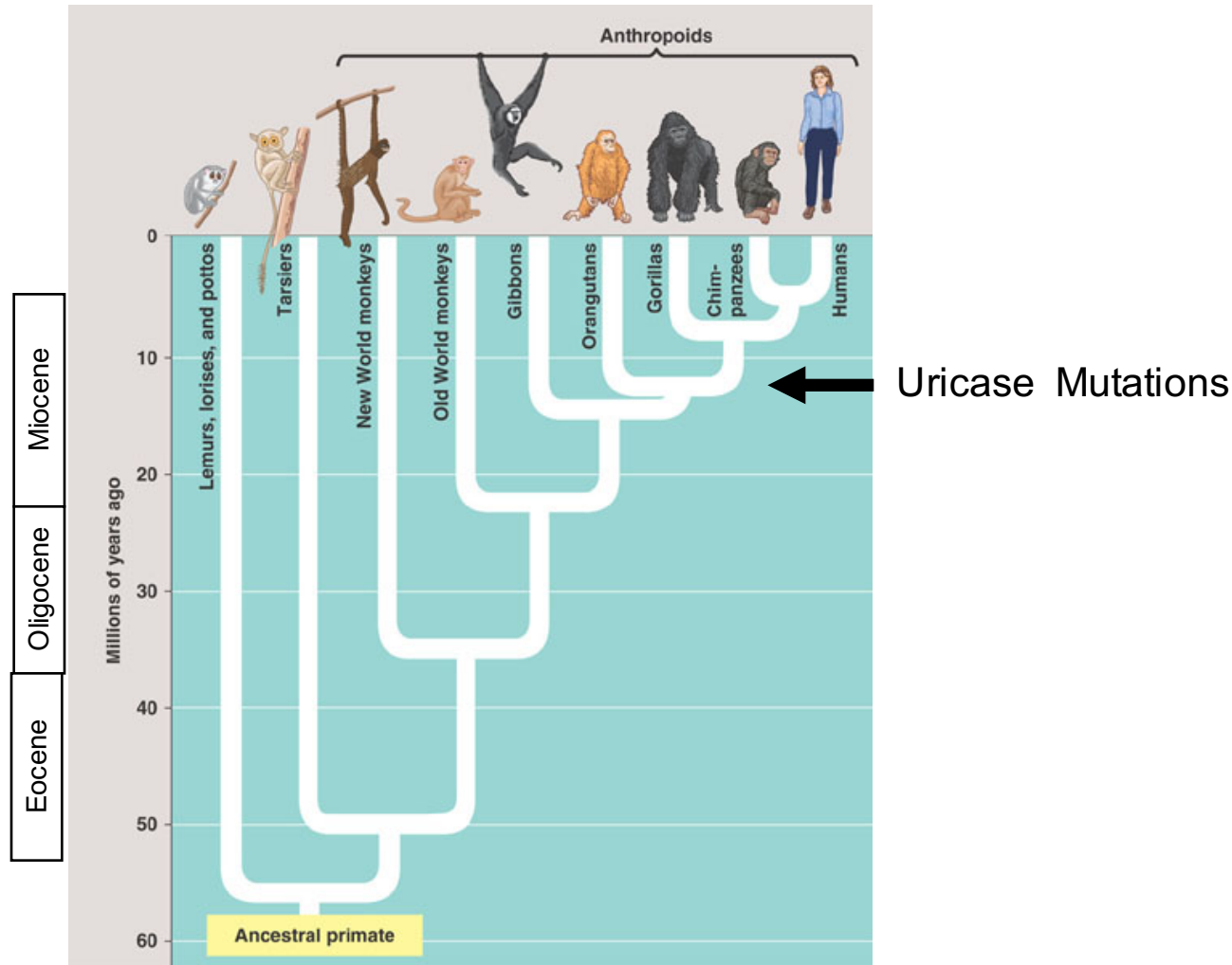


Uricase Inhibition Increases Fructose Effects in the Rat

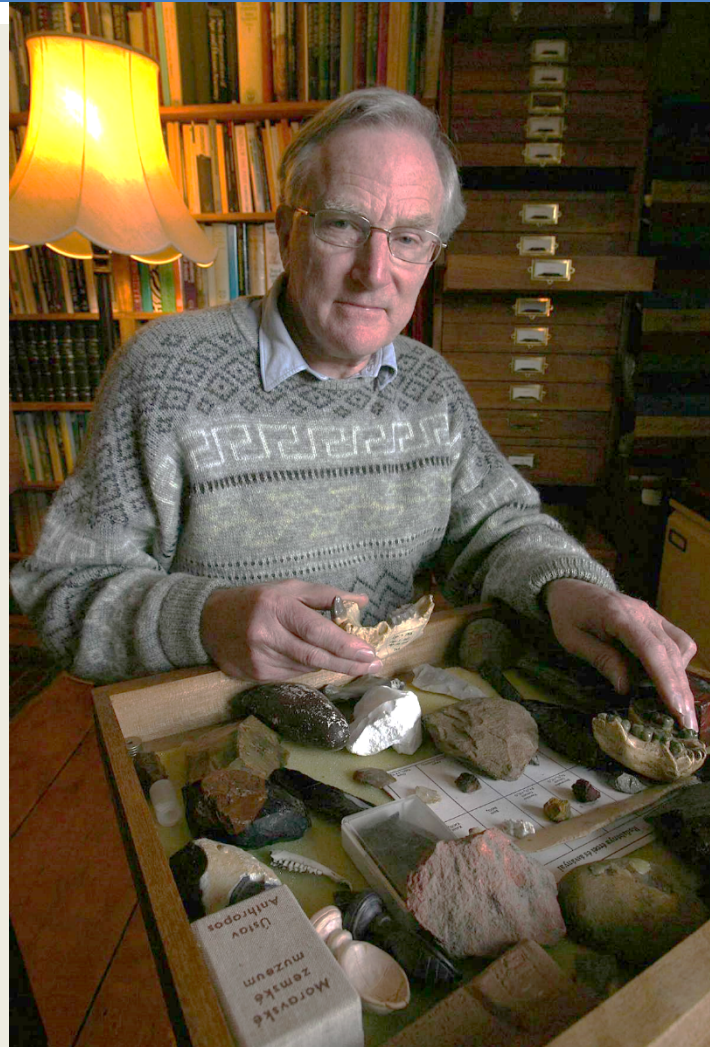


Rats were given soft drinks consisting of 7% Fructose and 3% glucose

What happened in the the Mid Miocene?



Seeking Expert Opinion: Peter Andrews, Museum of Natural History in London



The Emergence of the Ape in the Miocene, 20-24 Million Years Ago



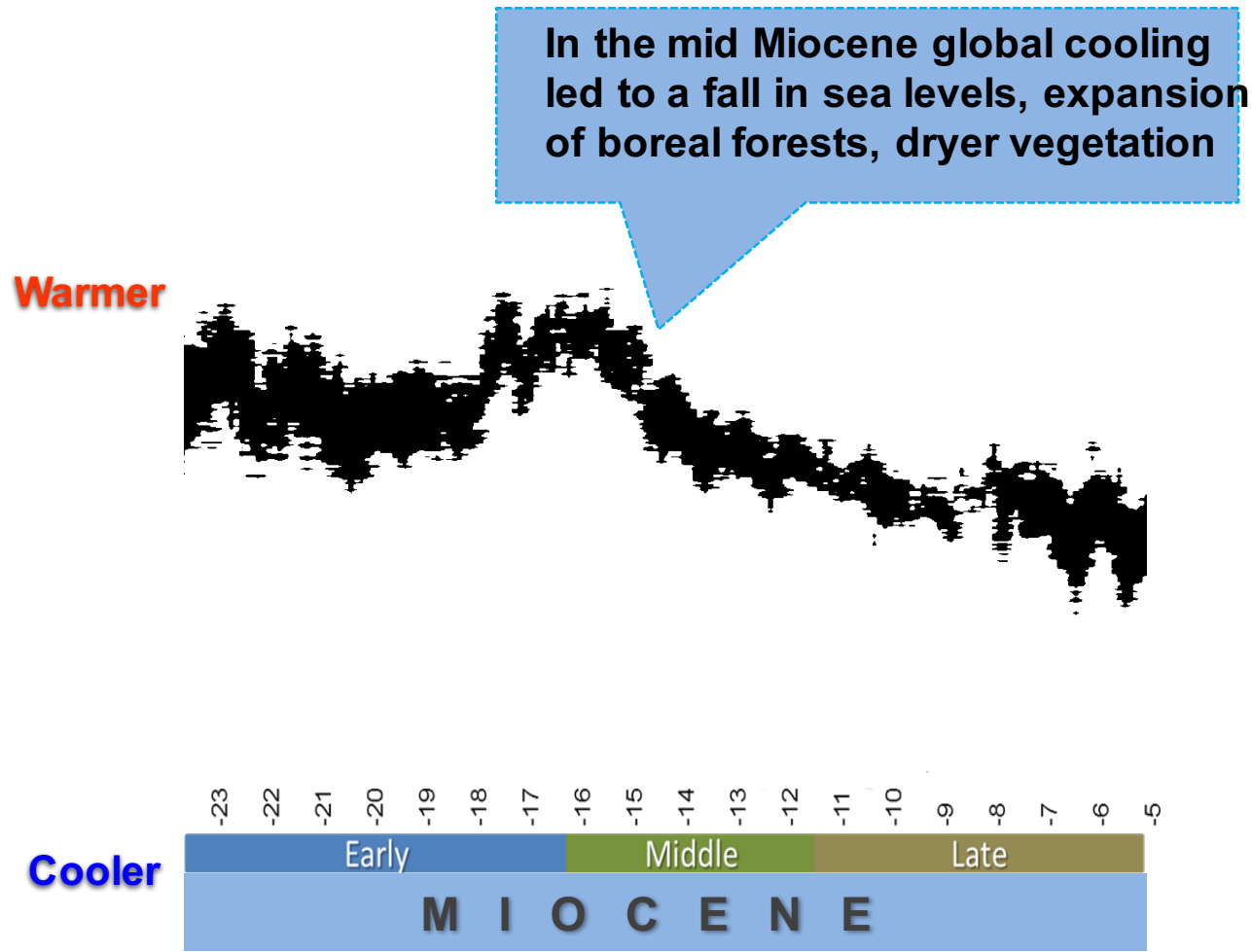
John Sibbick / Natural History Museum John Sibbick / Natural History M

Early Miocene Apes were Fruit Eating: Fructose was their Main Food



**Early Miocene apes
were fruit eating and
lived in lush tropical
rain forests in Africa
(22-17 MYA)**

Global Cooling in the Miocene



Global Cooling Caused a Drop in Sea Level allowing Apes to Enter Europe



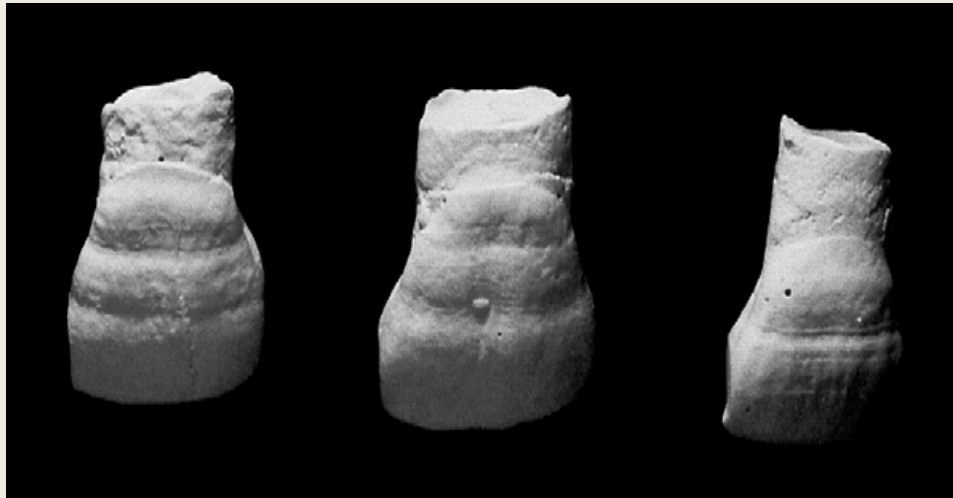
Crossing the
landbridge into
Eurasia across the
Tethys Sea

Loss of the Fig in Europe Impacted Survival in Europe where Seasonality Started to Occur



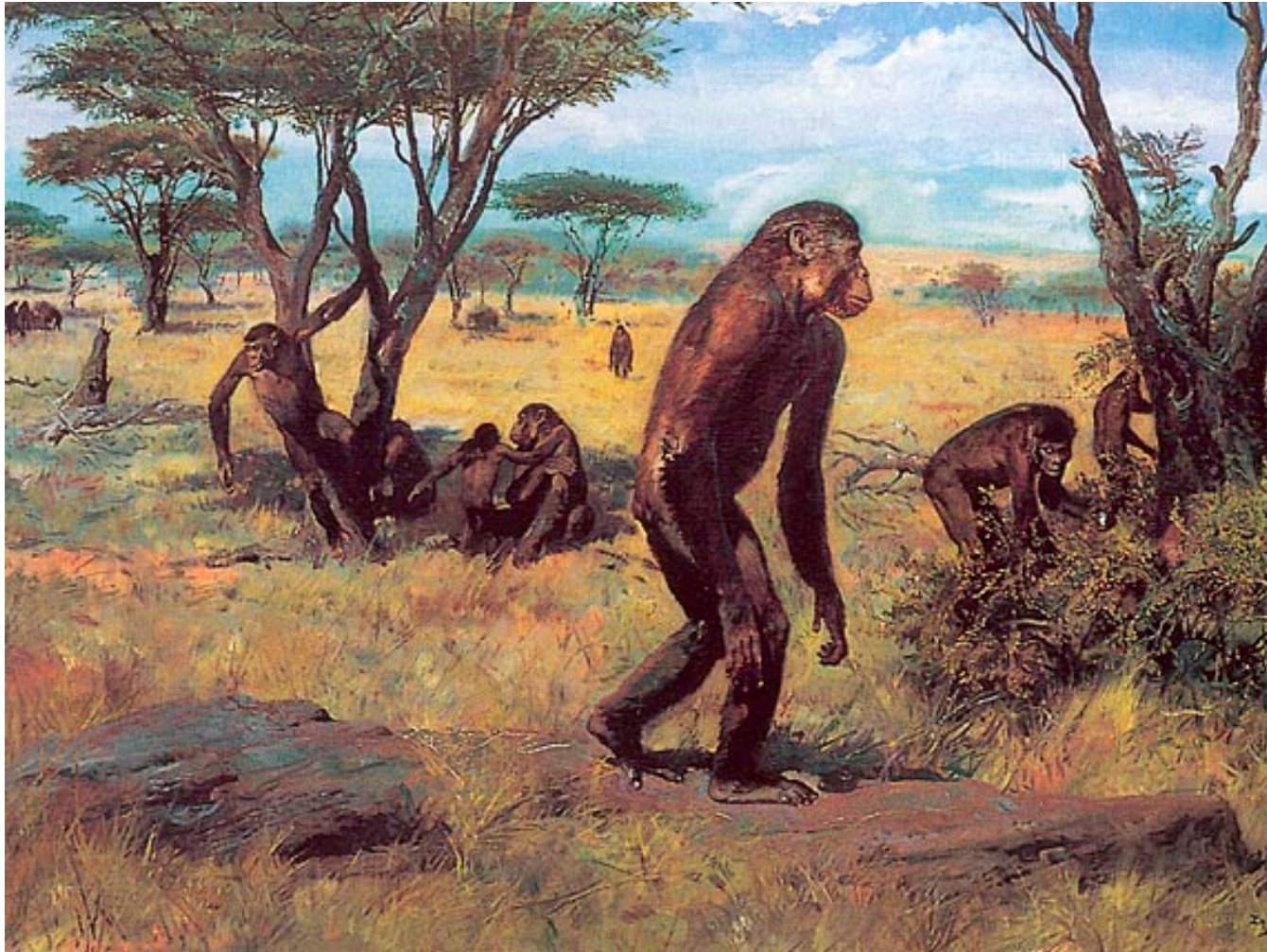
Chimpanzee
in Fig Tree

Eurasian Apes Showed Evidence of Seasonal Starvation Due to Decrease in Fruit Supply

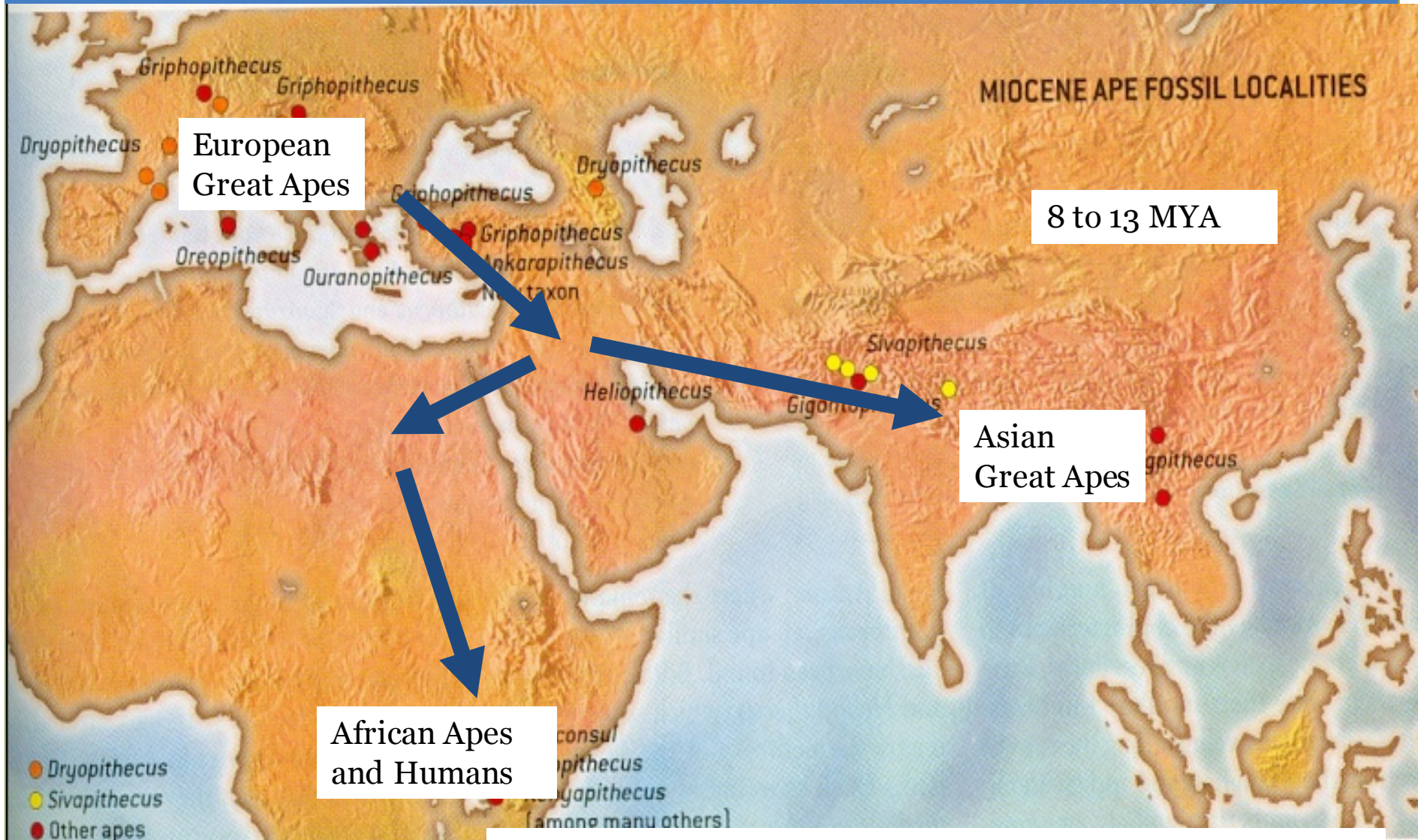


Stress lines on teeth from
Seasonal Starvation in
Kenyapithecus
(Paçalar, Turkey)

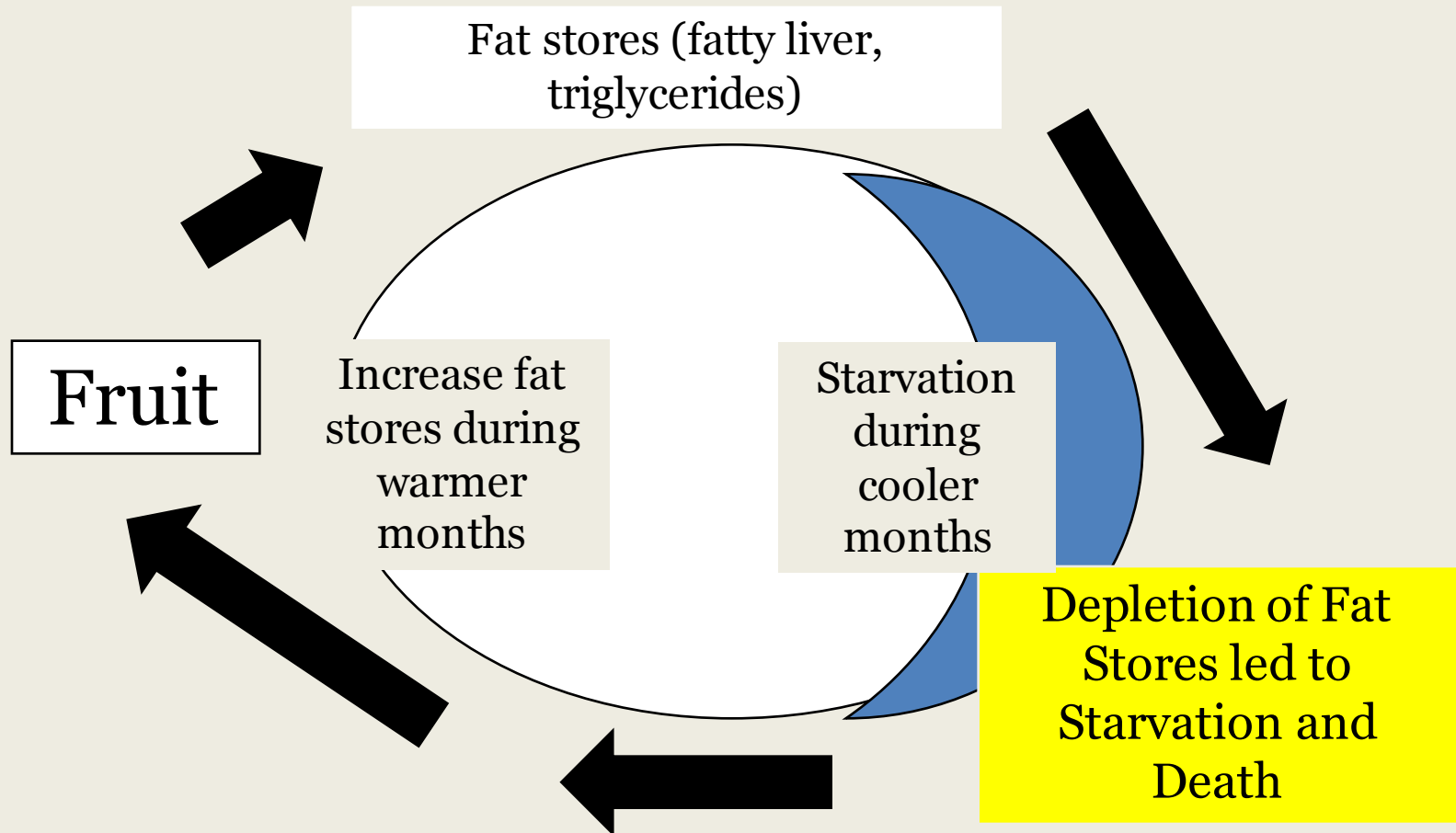
Apes began foraging for new foods, resulting in changing dentition and axial skeleton



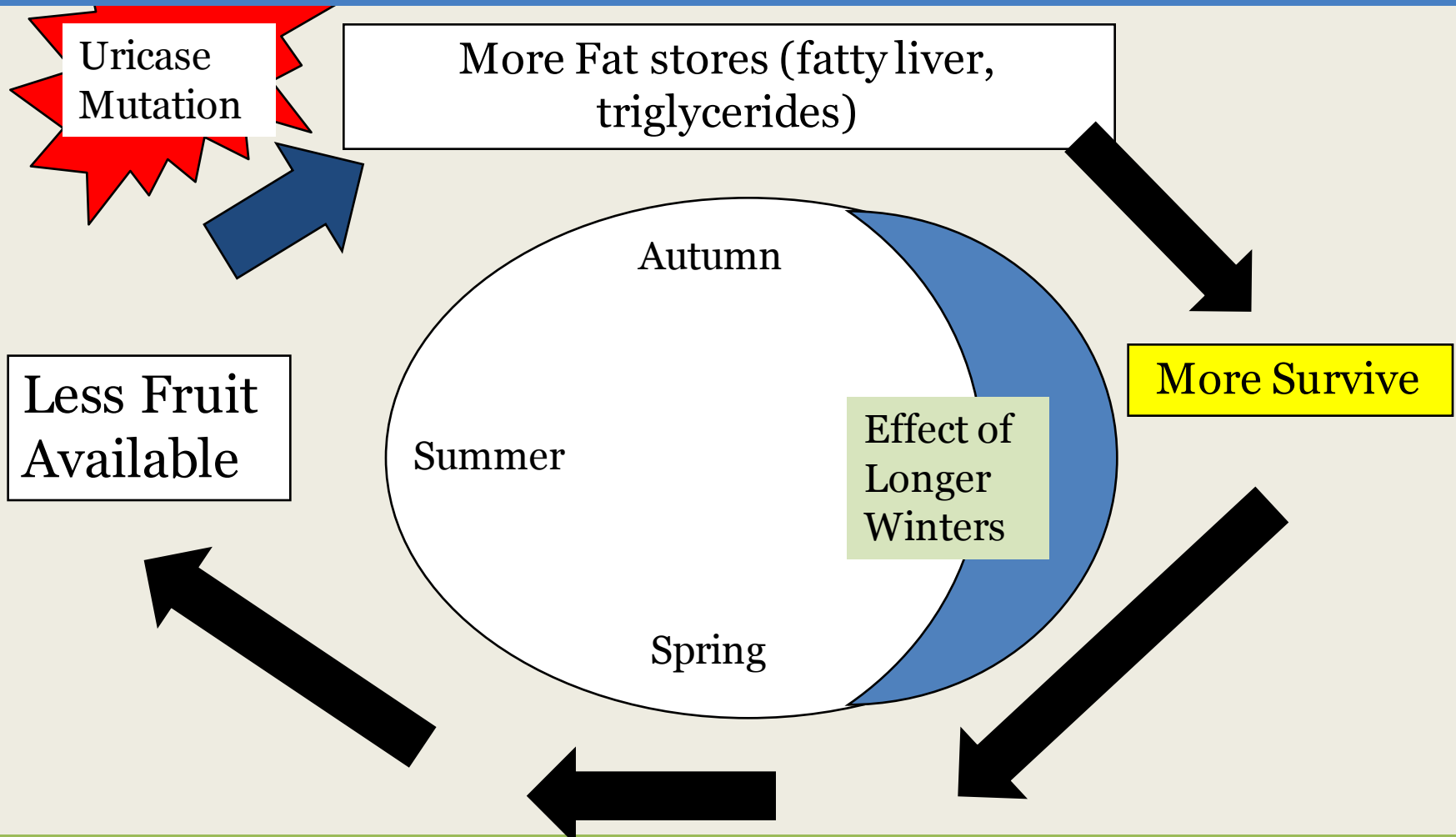
Fossil Records suggest a few European Ancestral Apes Survived and went 'Back to Africa'



Seasonal cooling resulted in a loss of fruits (figs) and led to Starvation

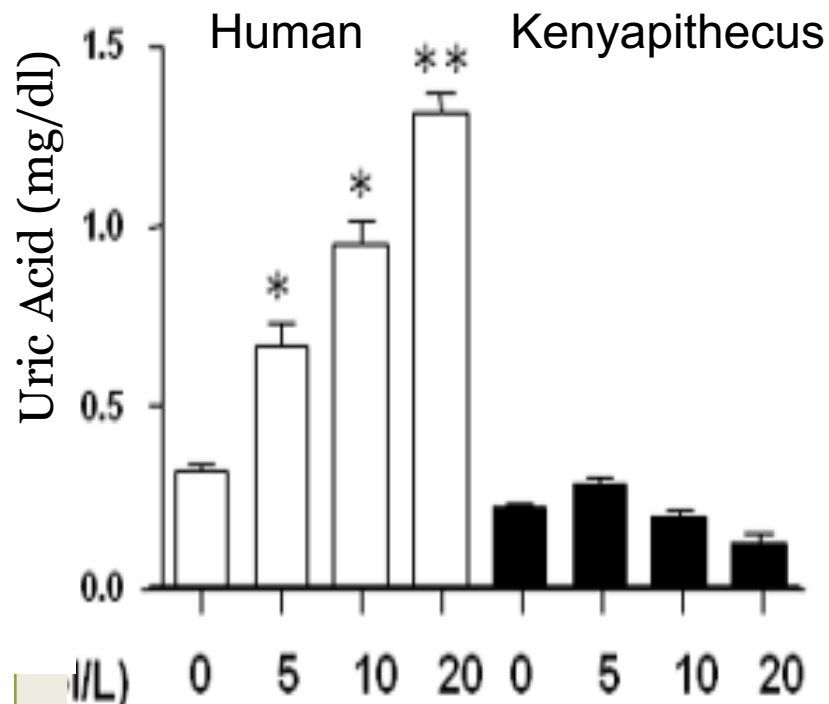


Hypothesis: Could a Loss of Uricase Provided a Survival Benefit?



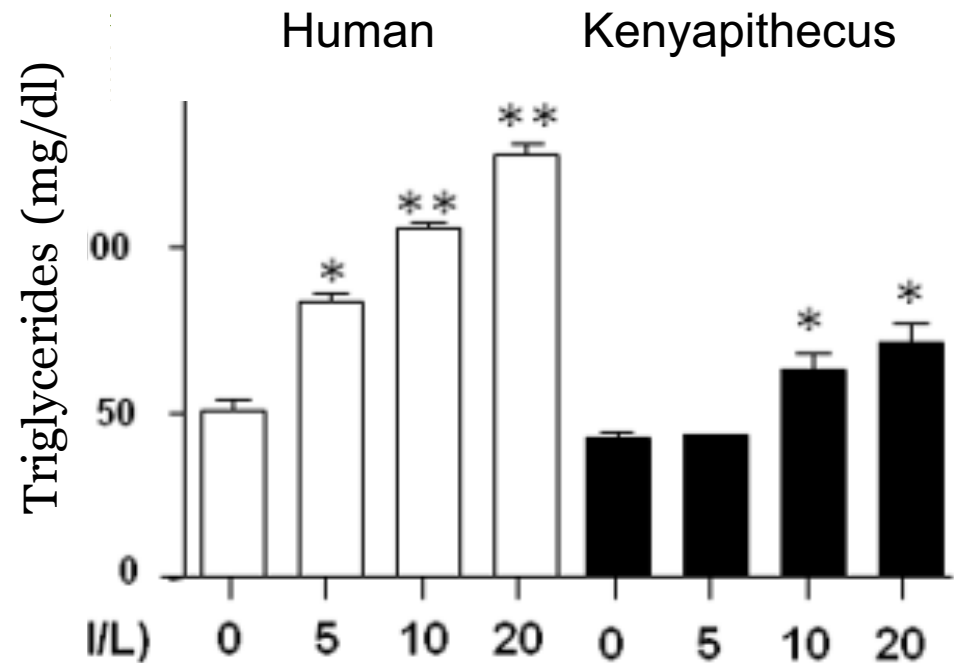
Kenyapithecus Uricase Blunts the Effect of Fructose to Increase Liver Fat

Intracellular Uric acid



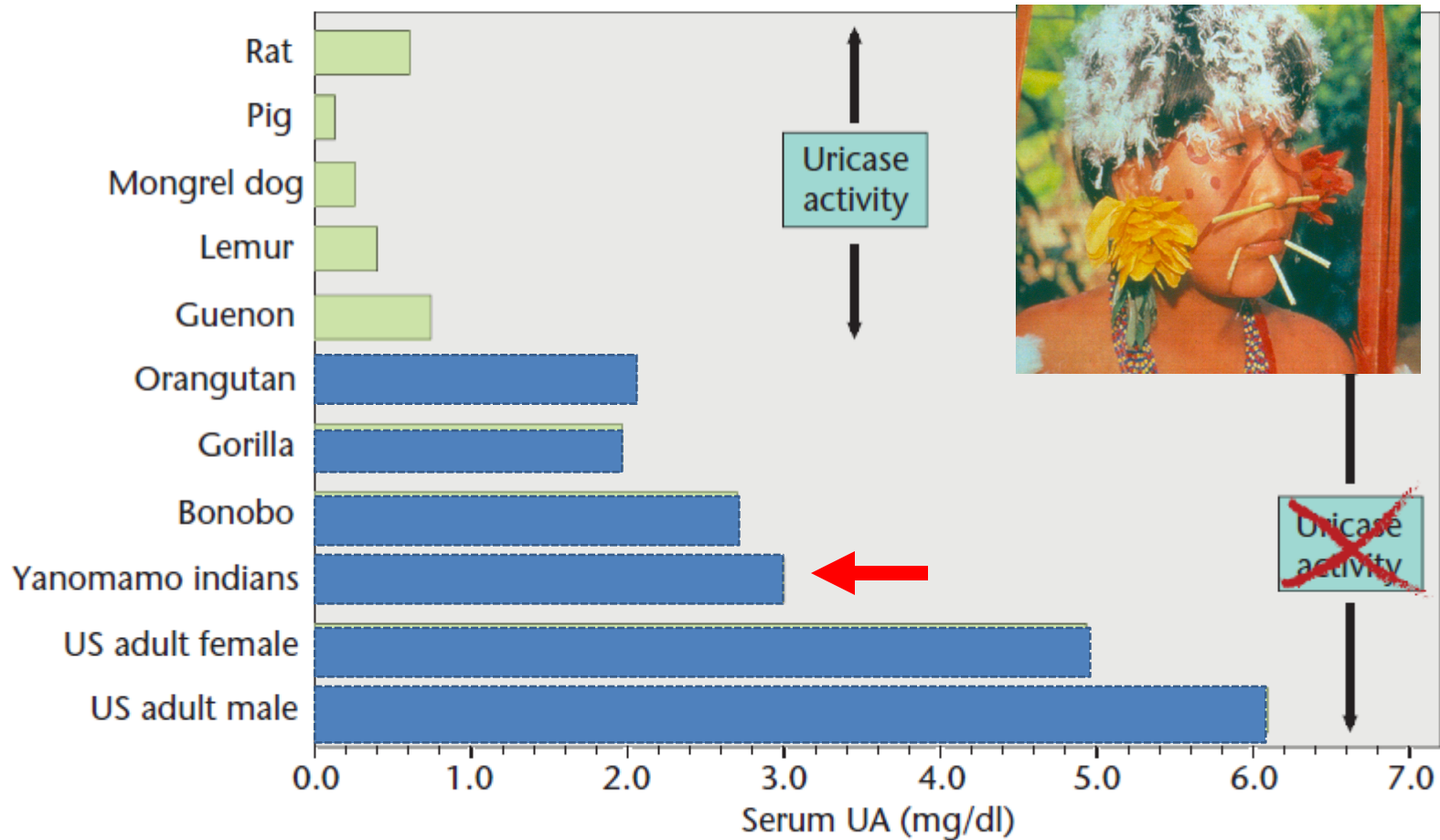
Fructose

Intracellular Triglycerides



Fructose

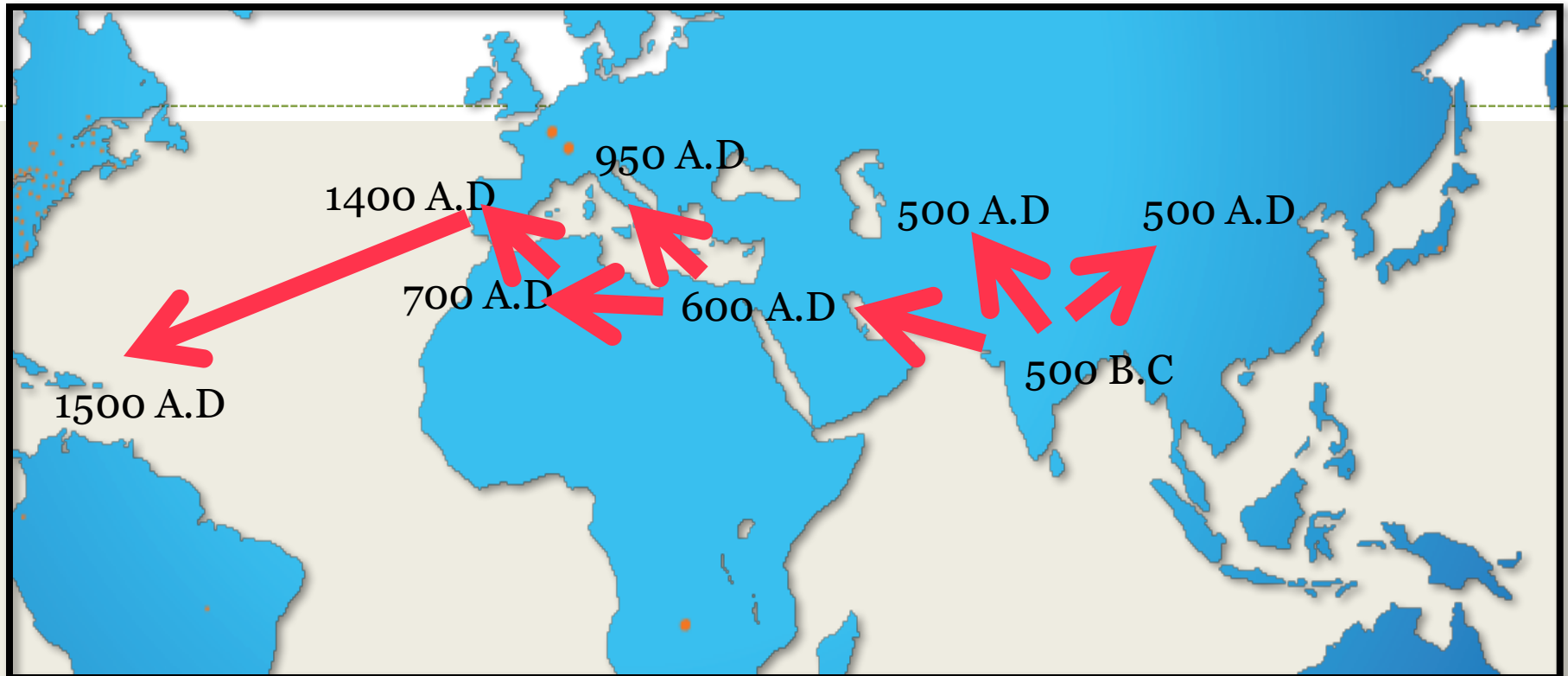
Indigenous Tribes such as Yanomamö Indians have Relatively Low Uric Acid Levels



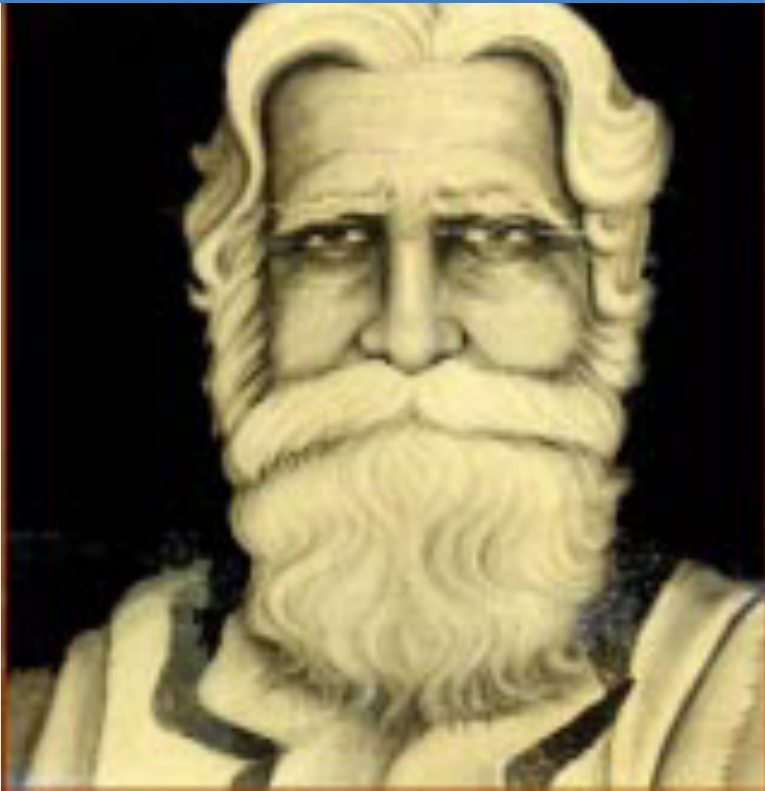
The Discovery of Sugar Cane and the Rise of Sugar



The Spread of Sugarcane



Sushruta Describes Diabetes in the Ganges Valley of India



Sushruta

Diabetes develops in the individual who “is in the habit of taking sweet liquids”

Sugar and Royalty– The Adipose Rex Syndrome



King Charles the Fat, Holy Roman Emperor, 888 A.D.

Sancho the Fat, King of León (NW Spain and Portugal) 966 A.D.

Sactius the Fat, King of Spain 1000 A.D.

William the Conqueror (1066-1087 A.D.)

Louis VIth (Louis the Fat), King of France 1137 A.D.

King John of England (1199-1216 A.D.)

Saint Thomas Aquinas of Italy 1225-1274 A.D.

Pope "Fat" Leo Xth 1521 A.D.

King Henry VIIIth 1532 A.D.

King Edward I of England ordered 1877 pounds of sugar for the royal household in 1287 and 6,258 pounds of sugar in 1288

One pound of sugar equaled 28 pounds of cheese or 34 dozen eggs

Sugar as a Medicine



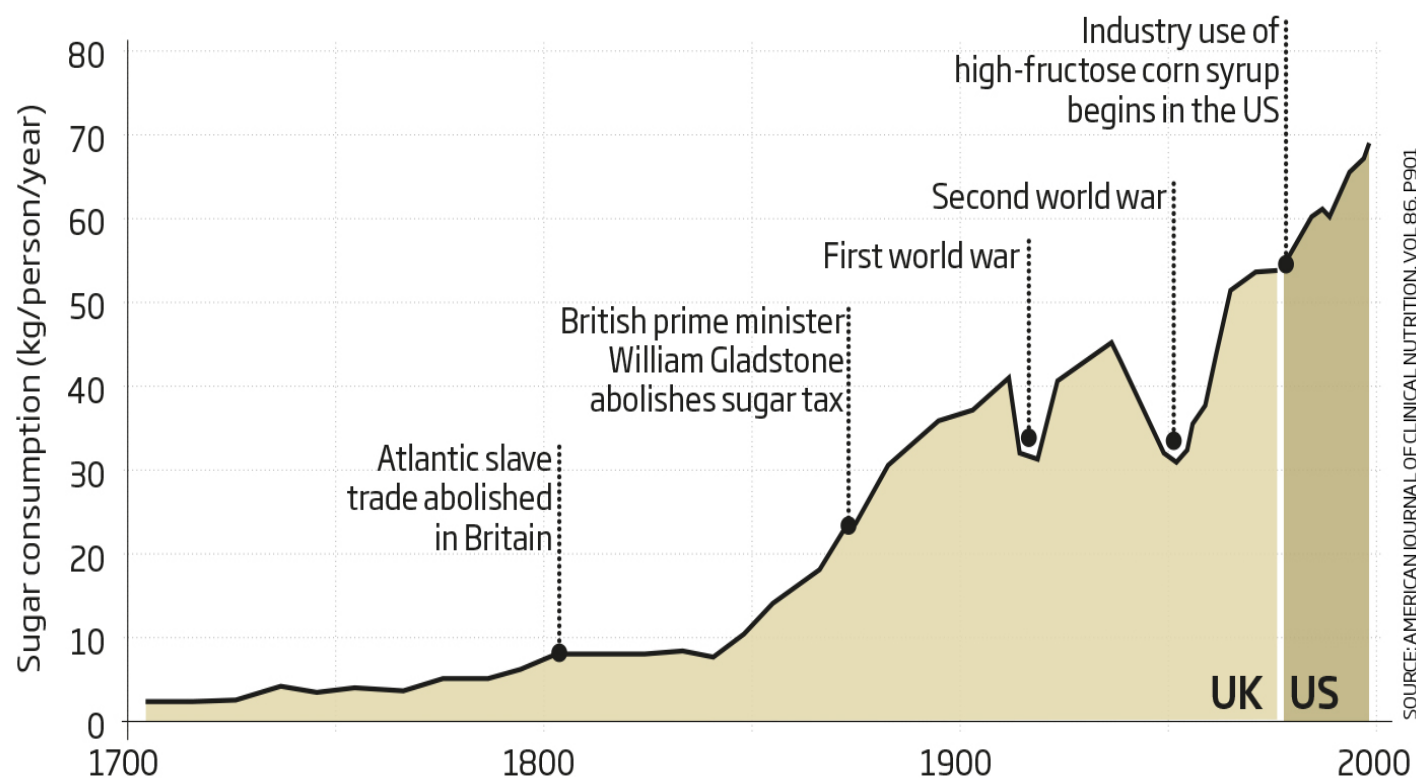
St Thomas Aquinas was an Italian Priest in the 13th Century who liked sugar so much that he argued it was a medicine and could be eaten during the fast

He went on to become very obese

Increased Production in Sugar Plantations makes Sugar Affordable



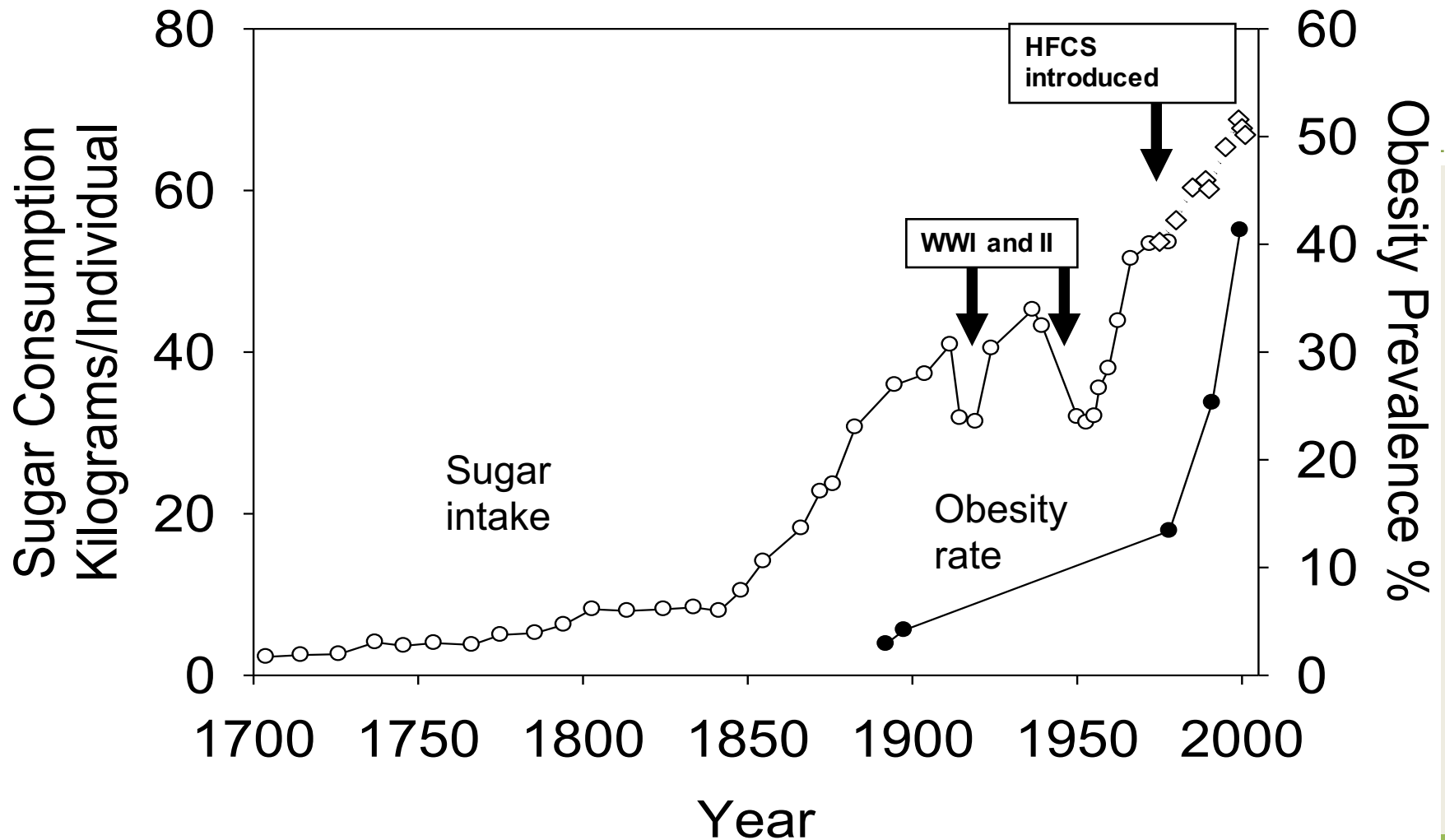
The Rise of Sugar



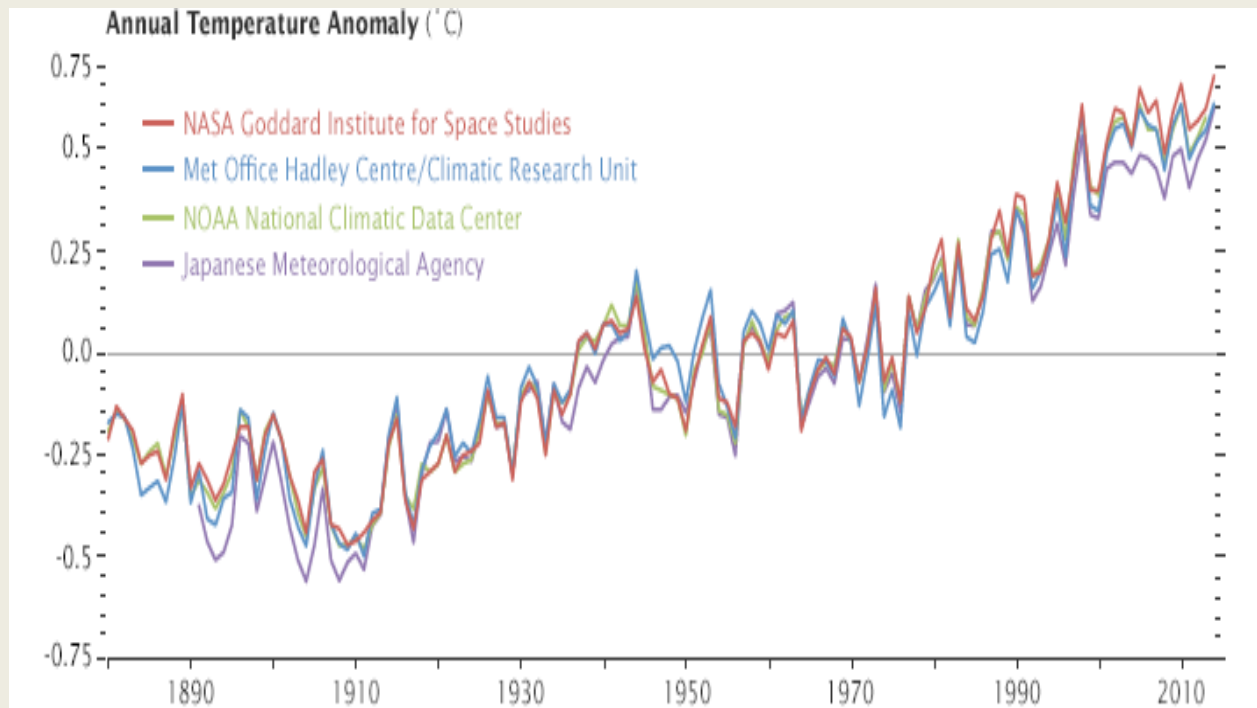
Sugar intake per year

1700	4 lbs
1800	18 lbs
1900	90 lbs
2000	155 lbs

Sugar Intake Correlates with Obesity Rates



Climate Change is Occurring again: World Temperature Over Last Century

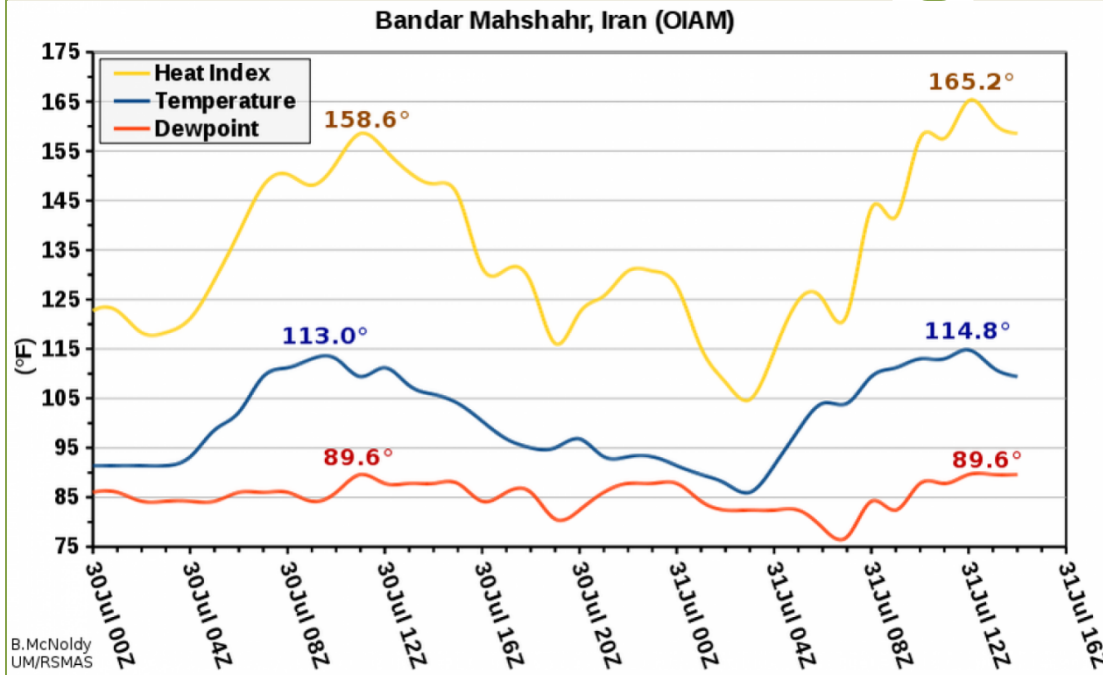


Mean temperatures have increased 0.8 degree C since 1880, with two-thirds of the change since 1975

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

Fischer and Knutti
Nature Clim Change
2015;5:560

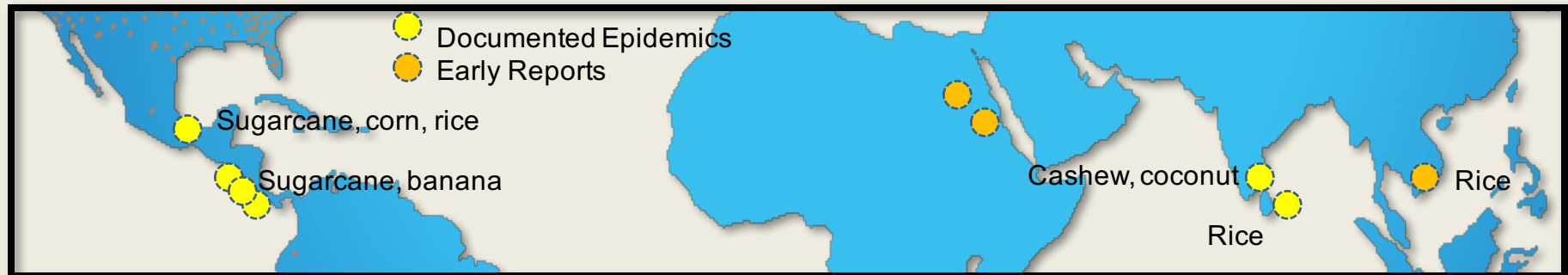
Iran city hits suffocating heat index of 165 degrees, near world record



The Washington Post, July 31st, 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/>

Global Warming is not simply a concern of the future

Epidemics of Kidney Failure are occurring now



Affected Individuals are Young Men working under hot conditions

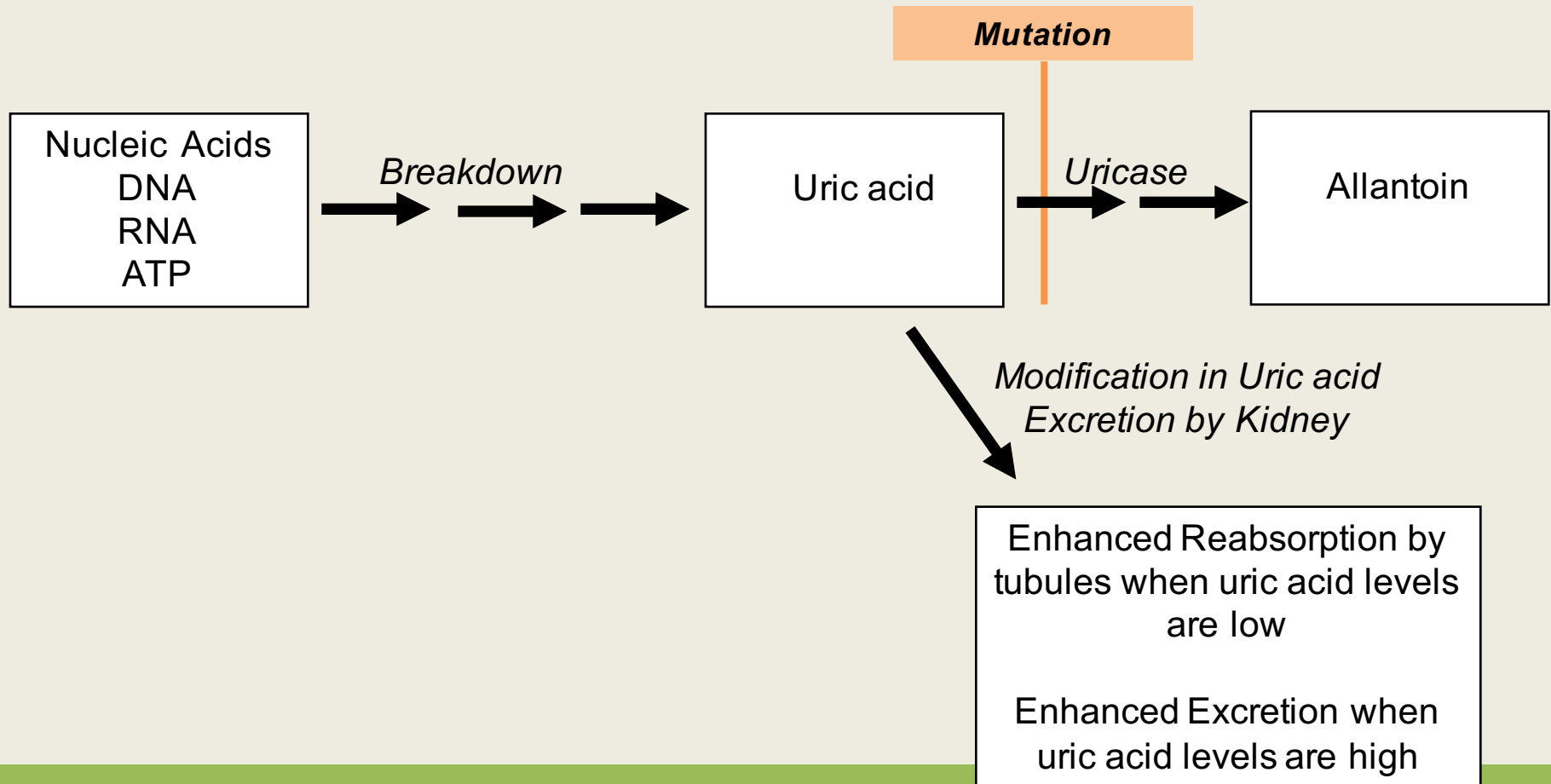


Young People Working Manually Outside in Hot Environments

- Characterized by recurrent dehydration and heat stress
- Often poor, disadvantaged, inadequate medical care

Are we maladapted for this new environmental Challenge?

Mutation of Uricase Resulted in Kidney Becoming primarily responsible for regulating blood levels of uric acid



Heat Stress Nephropathy: A Uric acid Disorder?

Heat and Exercise

Subclinical Muscle injury
Release of DNA from muscle

Metabolism of DNA
Increases Serum Uric Acid

No uricase

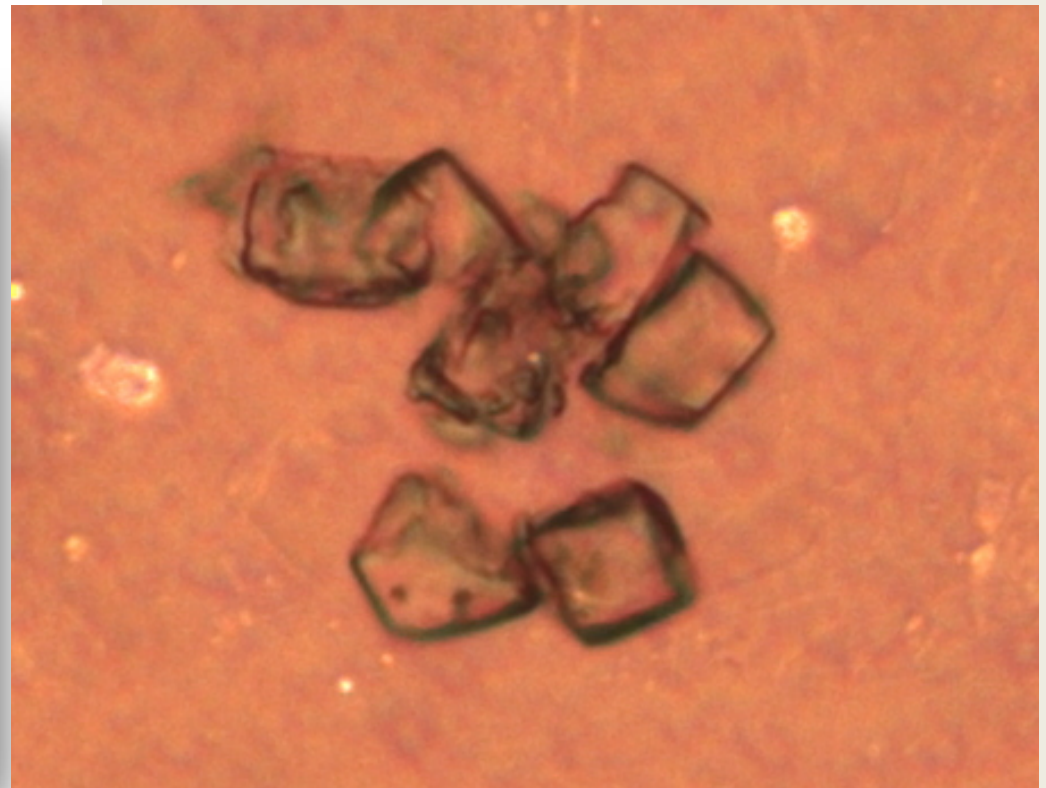
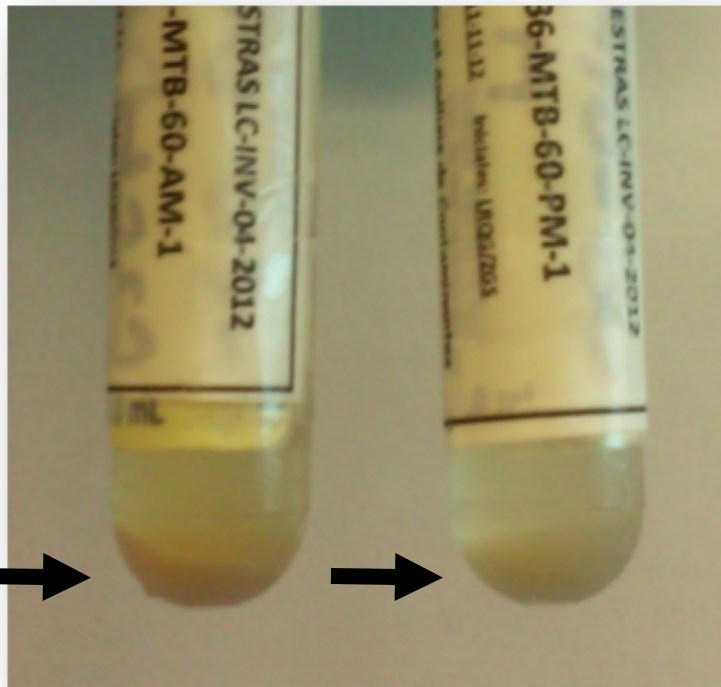
Urine uric acid increases,
forms crystals and causes
kidney damage



Cane Workers Develop Large Urine Sediments with Uric acid Crystals

AM

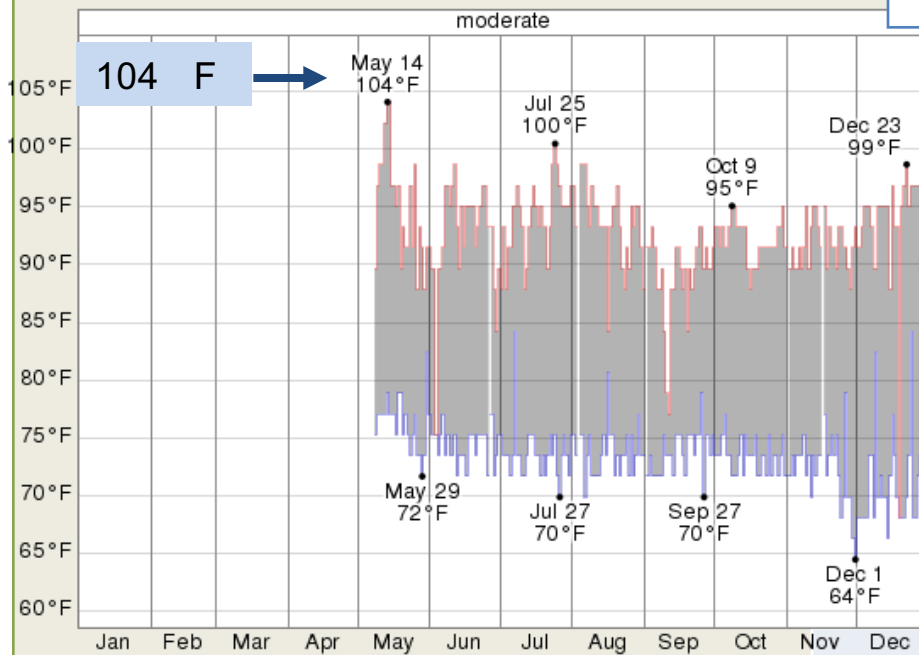
PM



The crystals are of a magnitude that is known to cause kidney damage

Record Temperature in San Miguel, El Salvador, May 14th, 2013 linked with kidney injury in 7 sugarcane cutters

**Results of 7 Sugarcane Workers in
Chichigalpa, May 13th 2013**



May 13	Supernatant	Sediment	Total
1	61.9	20.2	82.2
2	97.7	36.4	134.1
3	153.6	7.9	161.5
4	113.7	19.8	133.5
5	114.0	15.3	129.3
6	97.8	9.0	106.8
7	147.5	55.9	203.5
	112.3	23.5	135.8

Summary

Survival of the Fittest requires three major functions:

- ability to find and store food/water
- avoid predators and survive catastrophes
- continue to reproduce

Evolution Accelerates During Periods of Environmental Stress as mutation with subtle advantage may take over when current mechanisms are failing

A Conservation of Energy pathway has been identified that activates pathways to reduce energy metabolism and allow the conservation of fat and water

During a period of global cooling and near extinction, our ancestors acquired a mutation in uricase that accelerates this conservation pathway providing survival advantage

This same mutation is now

- increasing our sensitivity to sugar/fructose and increasing our risk for obesity and diabetes
- increasing our risk for kidney injury in the setting of heat stress

Special Thanks



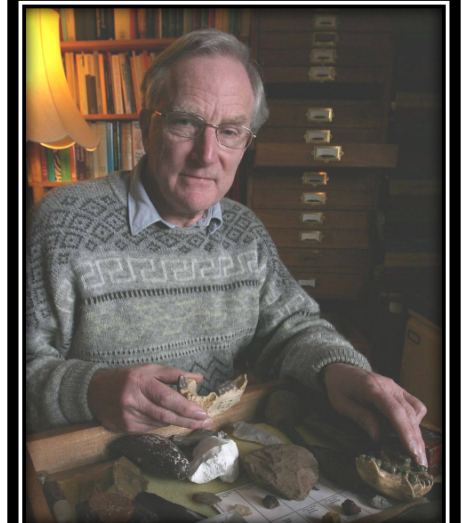
Miguel
Lanaspa PhD



Carlos Roncal
MS (equiv)



Gaby Sanchez-
Lozada, PhD



Peter Andrews
PhD

And to all of my collaborators, past and present

Special Thanks to All My Collaborators, Past and Present



Marilda
Mazzali



Duk-Hee
Kang



Taka
Nakagawa



Dan
Feig



Gaby Sánchez-
Lozada



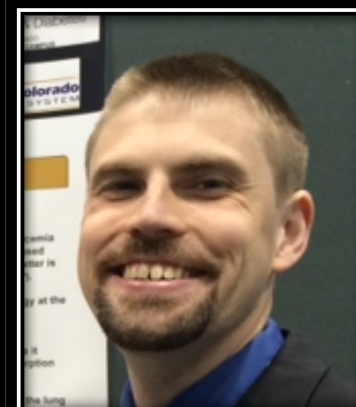
Miguel
Lanaspá



Takuji
Ishimoto



Yuri
Sautin



Thomas
Jensen



Mehmet
Kanbay

The Thrifty Gene Hypothesis of James Neel



James Neel with the Yanomamo Indians

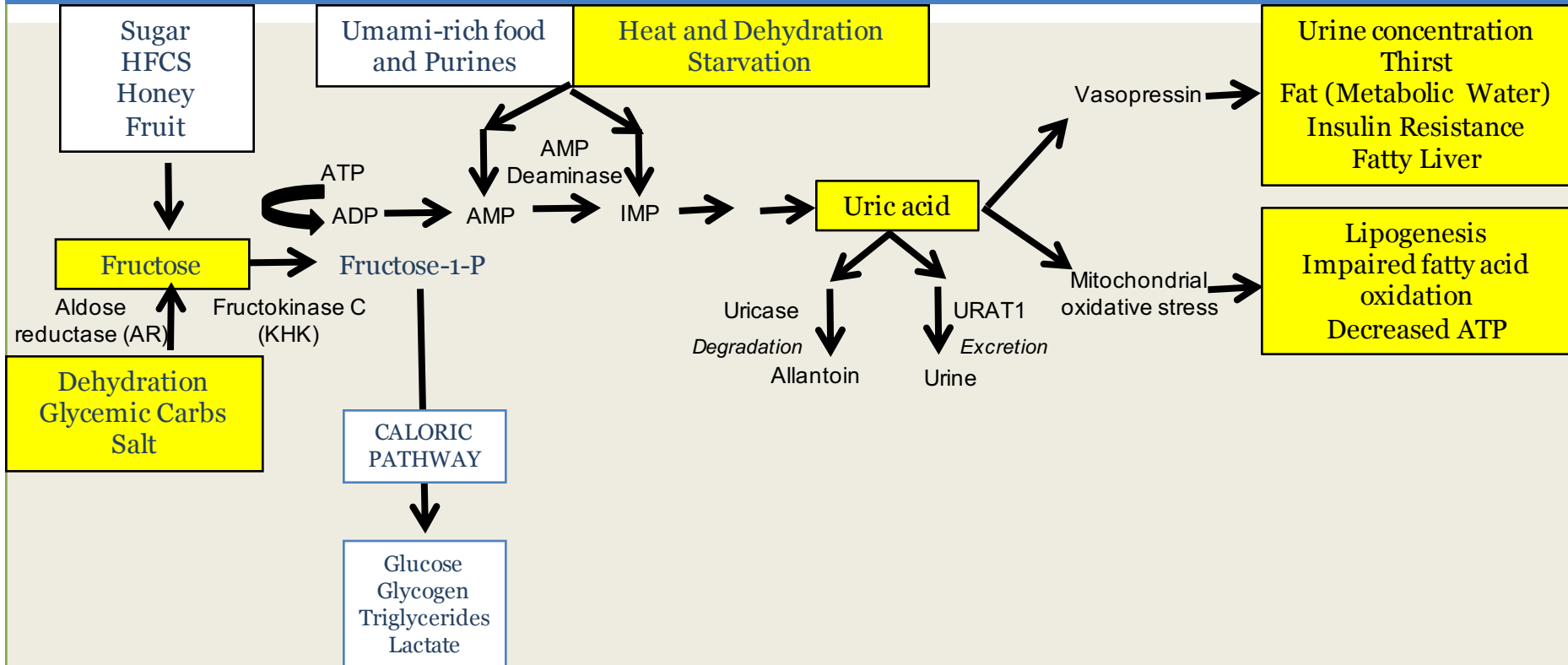
“the diabetic genotype....is a thrifty genotype in the sense of being exceptionally efficient in the intake or utilization of food”

What about Fruits????

- Relatively Lower Content of Fructose
- Have other good components (vitamin C, antioxidants, flavonols, fiber, potassium, etc)



The Energy “Conservation” Pathway



Projected Temperatures in the USA

