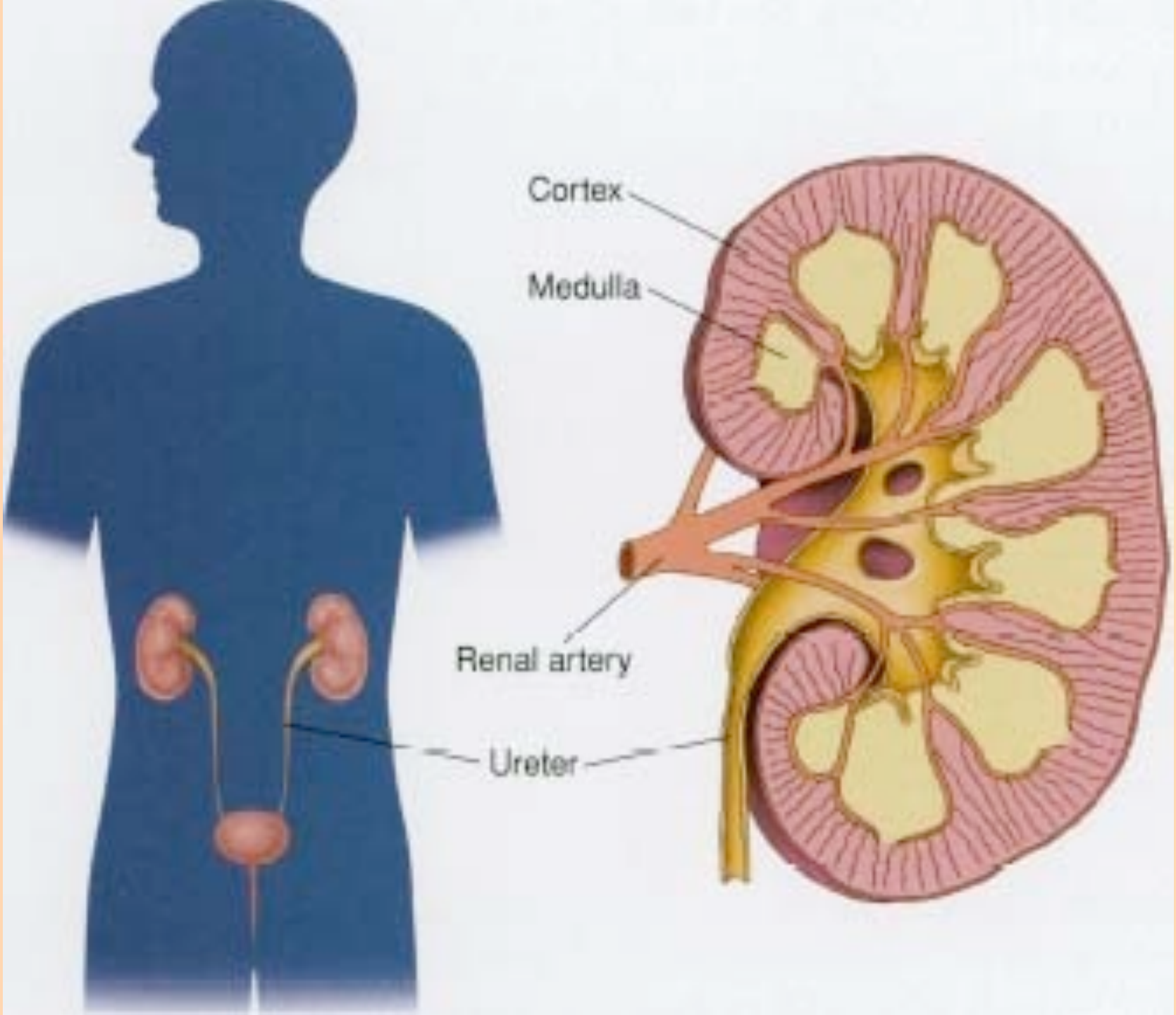
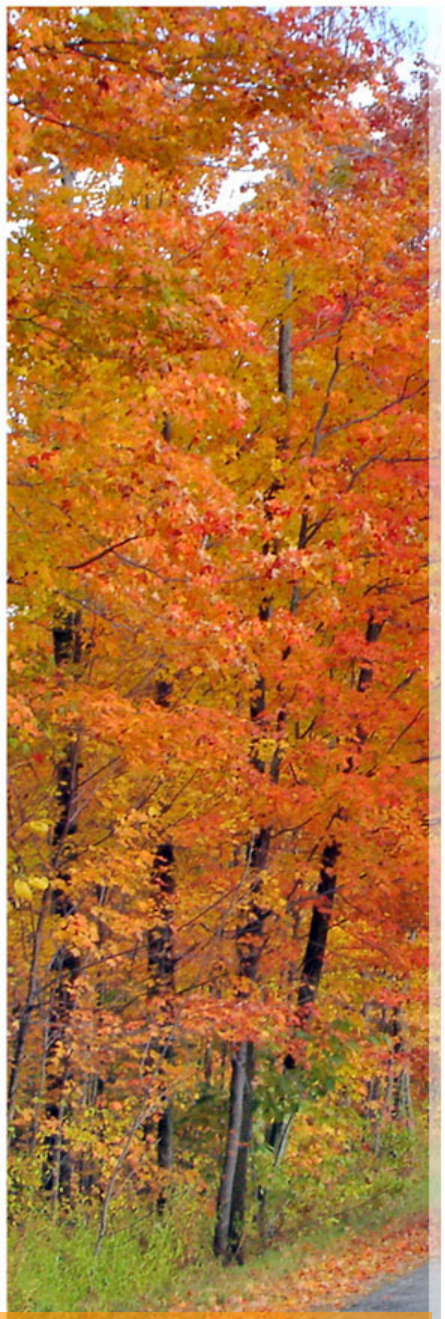
FRUCTOSE DAMAGE

Dr Georges MOUTON
www.gmouton.com

Kleinhoscheid, 06/04/2018


Cortex
Medulla
Renal artery
Ureter



University of Florida
Gainesville

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

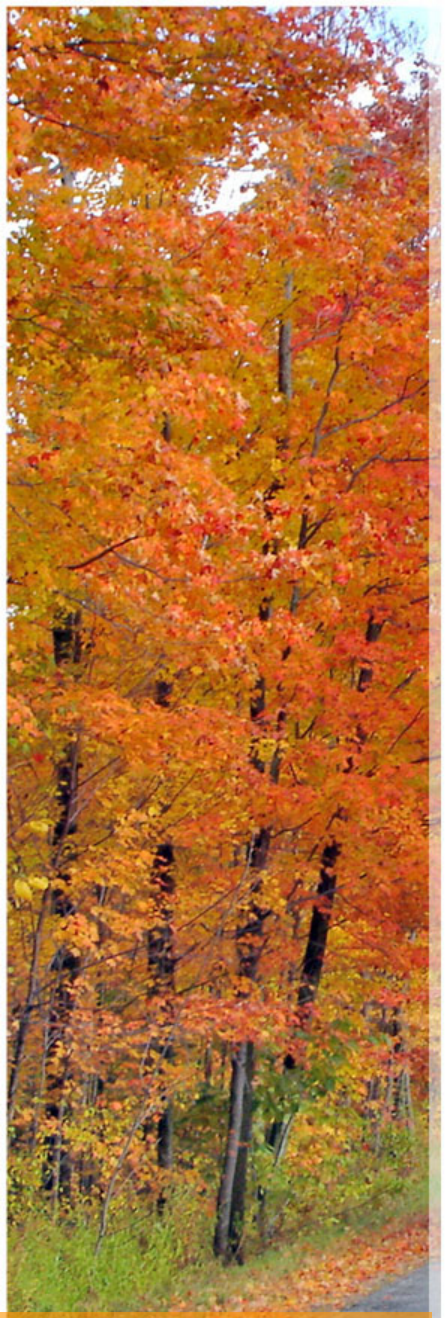
CHRONIC KIDNEY DISEASE

- The present study was conducted to test the hypothesis that consumption of a high-**fructose** diet could accelerate the progression of **chronic kidney disease**. In conclusion, consumption of a high-**fructose** diet greatly accelerates progression of **chronic kidney disease** in the rat remnant kidney model.

Am J Physiol Renal Physiol. 2007 Oct;293(4):F1256-61. Epub 2007 Aug 1.

Fructose, but not dextrose, accelerates the progression of chronic kidney disease.

Gersch MS, Mu W, Cirillo P, Reungjui S, Zhang L, Roncal C, Sautin YY, Johnson RJ, Nakagawa T.



University of Florida
Gainesville

FRUCTOSE DAMAGE

Dr Georges MOUTON
September 2012

CHRONIC KIDNEY DISEASE

- **Fructose** diet, but not glucose diet, significantly increased kidney weight by 6 wk. The primary finding was **tubular hyperplasia and proliferation** involving all segments of the proximal tubules. These studies may provide a mechanism by which **metabolic syndrome** causes **renal disease**.

Am J Physiol Renal Physiol. 2010 Mar;298(3):F712-20. Epub 2010 Jan 13.

Dietary fructose causes tubulointerstitial injury in the normal rat kidney.

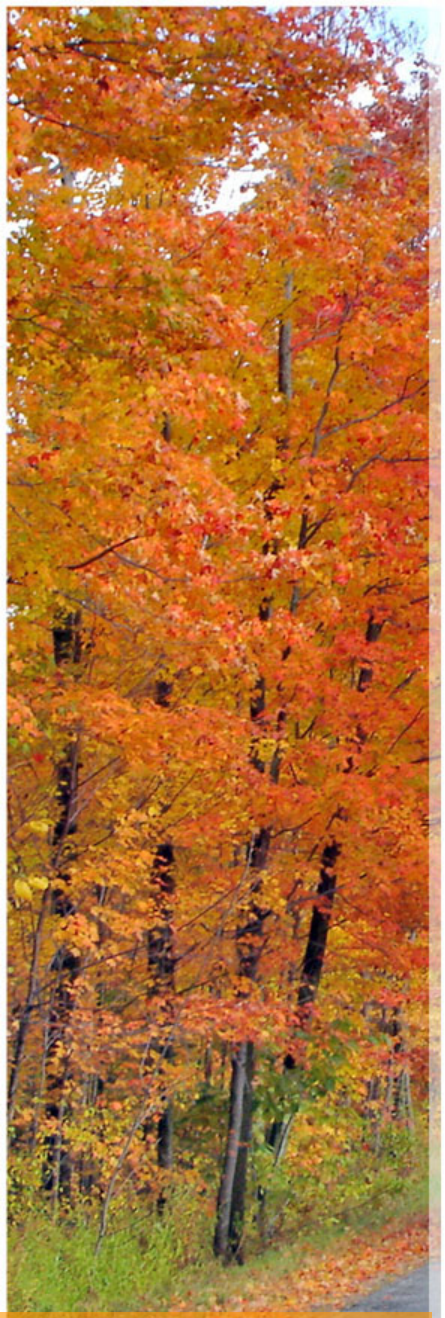
Nakayama T, Kosugi T, Gersch M, Connor T, Sanchez-Lozada LG, Lanaspa MA, Roncal C, Perez-Pozo SE, Johnson RJ, Nakagawa T.

Division of Nephrology, University of Florida, Gainesville, Florida, USA.

UF | UNIVERSITY of FLORIDA

Richard J Johnson, M.D. Professor & former Chief
Division of Nephrology, Hypertension & Renal Transplant

Dr. Richard J Johnson, formerly the J. Robert Cade Professor of Medicine and former Chief of the Division of Nephrology, Hypertension, and Renal Transplantation at the University of Florida, received his undergraduate degree in Anthropology in 1975 from the University of Wisconsin, and his M.D. degree in 1979 from the University of Minnesota in Minneapolis. He completed an internal medicine residency and nephrology and infectious diseases fellowships at the University of Washington Medical Center in Seattle. Dr. Johnson joined the faculty at the University of Washington in 1986, and in 2000 moved to Baylor College of Medicine in Houston, Texas where he was the Chief of Nephrology. In September 2003 he joined the faculty at the University of Florida to take on his current position. Dr. Johnson is nationally and internationally renowned for his work on mechanisms of renal injury and progression, including in glomerulonephritis, diabetes, and hypertension. Recent studies have focused on the pathogenesis of essential hypertension and the role of subtle renal injury. He has published over 300 articles, lectured in over 25 countries, and is currently coeditor with John Feehally of the very successful clinical textbook, Comprehensive Clinical Nephrology. He received the American Society of Nephrology Young Investigator Award in 1994 and is a member of the American Society for Clinical Investigation.



Wright State University - Dayton

FRUCTOSE DAMAGE

Dr Georges MOUTON
September 2012

HIGH BLOOD PRESSURE

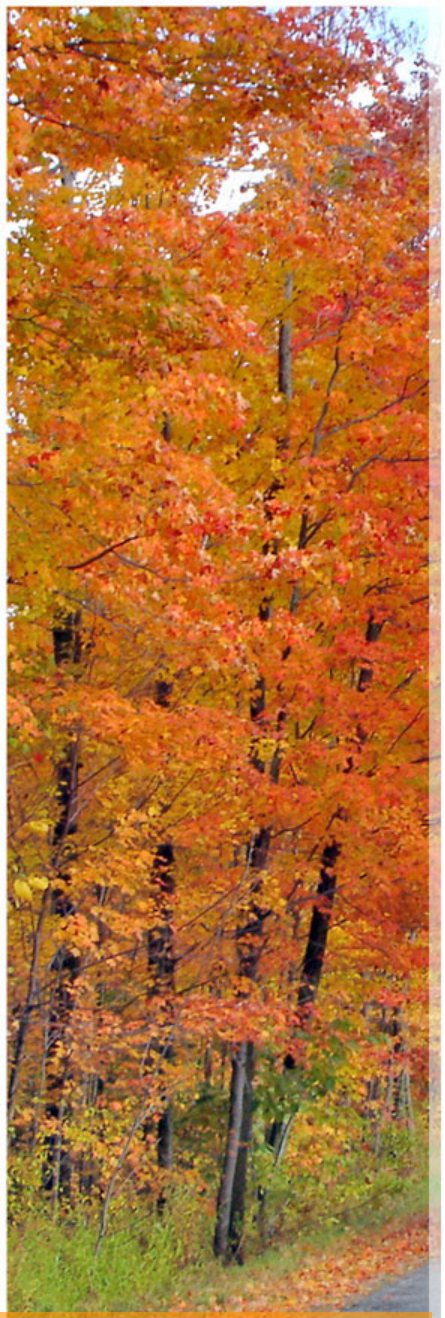
- RESULTS: Fructose diet (8 weeks) produced an increase in mean arterial pressure. The changes occurred only at night, a period of activity for mice. Glucose tolerance was attenuated in the fructose group.
- CONCLUSION: A high fructose diet in mice produced nocturnal hypertension.

Auton Neurosci. 2006 Dec 30;130(1-2):41-50. Epub 2006 Jul 13.

Nocturnal hypertension in mice consuming a high fructose diet.

Farah V, Elased KM, Chen Y, Key MP, Cunha TS, Irigoyen MC, Morris M.

Boonshoft School of Medicine of Wright State University, Department of Pharmacology and Toxicology, Dayton, OH 45401, USA.



University of Colorado Denver

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

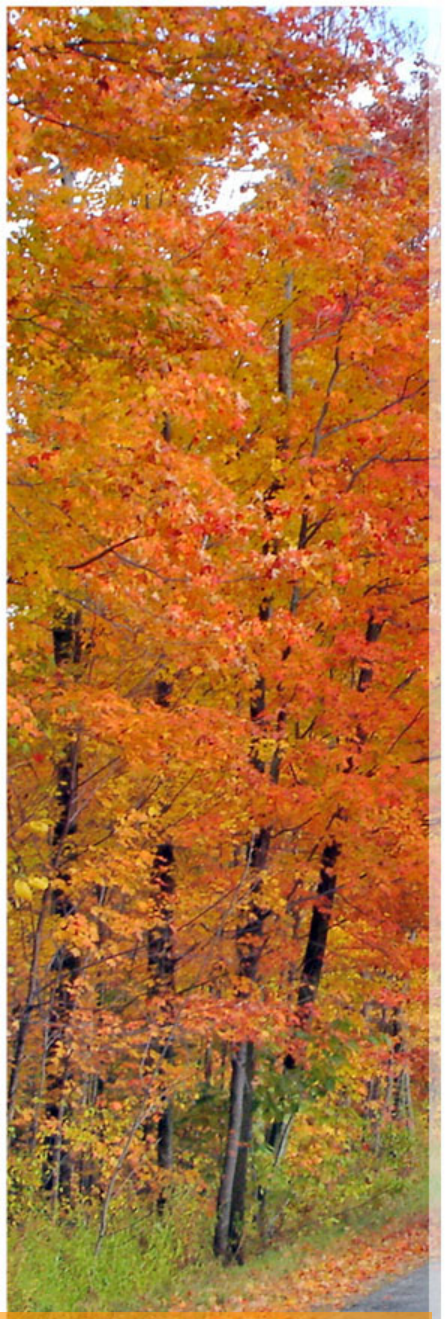
HIGH BLOOD PRESSURE

- The recent increase in **fructose** consumption in industrialized nations mirrors the rise in the prevalence of **hypertension**, but epidemiologic studies have inconsistently linked these observations. (…) These results suggest that high **fructose** intake, in the form of added sugar, independently associates with **higher BP levels** among US adults without a history of hypertension.

J Am Soc Nephrol. 2010 Sep;21(9):1543-9. Epub 2010 Jul 1.

Increased fructose associates with elevated blood pressure.

Jalal DI, Smits G, Johnson RJ, Chonchol M.



University of California San Francisco

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

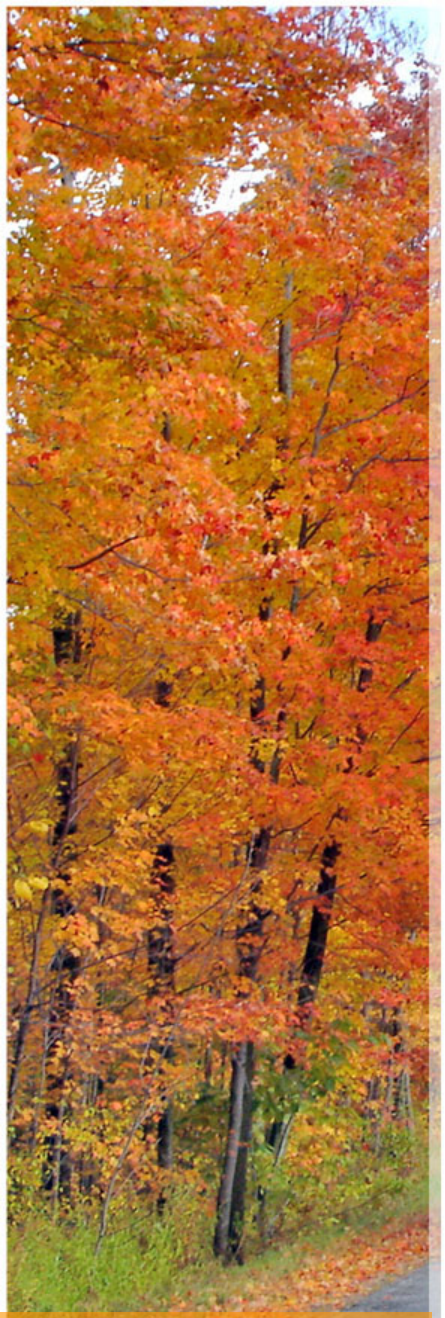
HIGH BLOOD PRESSURE

- OBJECTIVE: To evaluate whether sugar-sweetened beverage consumption, a significant source of dietary fructose, is associated with higher serum uric acid levels and blood pressure in adolescents.
- CONCLUSIONS: These results from a nationally representative sample of US adolescents indicate that higher sugar-sweetened beverage consumption is associated with **higher serum uric acid levels** and **systolic blood pressure**.

J Pediatr. 2009 Jun;154(6):807-13. Epub 2009 Apr 17.

Sugar-sweetened beverages, serum uric acid, and blood pressure in adolescents.

Nguyen S, Choi HK, Lustig RH, Hsu CY.



National Sun Yat-sen University

FRUCTOSE DAMAGE

Dr Georges MOUTON
May 2014

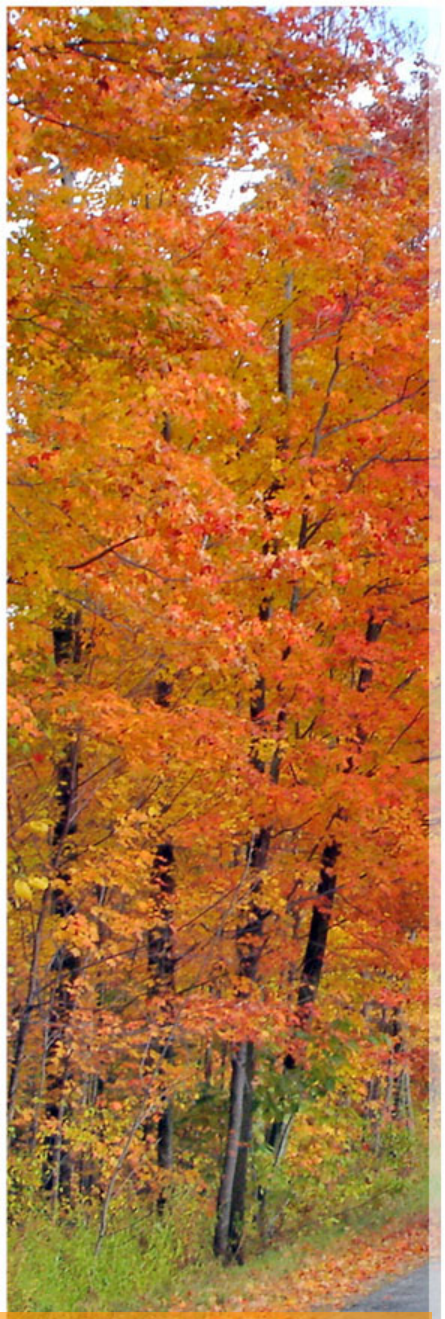
HIGH BLOOD PRESSURE

- Recent clinical studies found that **fructose** intake leads to **insulin resistance** and **hypertension**. **Fructose** consumption promotes protein fructosylation and formation of superoxide. Caffeine displays significant antioxidant ability in protecting membranes against **oxidative damage** and can lower the risk of **insulin resistance**.

Hypertension. 2014 Mar;63(3):535-41. doi: 10.1161/HYPERTENSIONAHA.113.02272. Epub 2013 Dec 23.

Caffeine intake improves fructose-induced hypertension and insulin resistance by enhancing central insulin signaling.

Yeh TC[1], Liu CP, Cheng WH, Chen BR, Lu PJ, Cheng PW, Ho WY, Sun GC, Liou JC, Tseng CJ.



Columbia University
New York

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

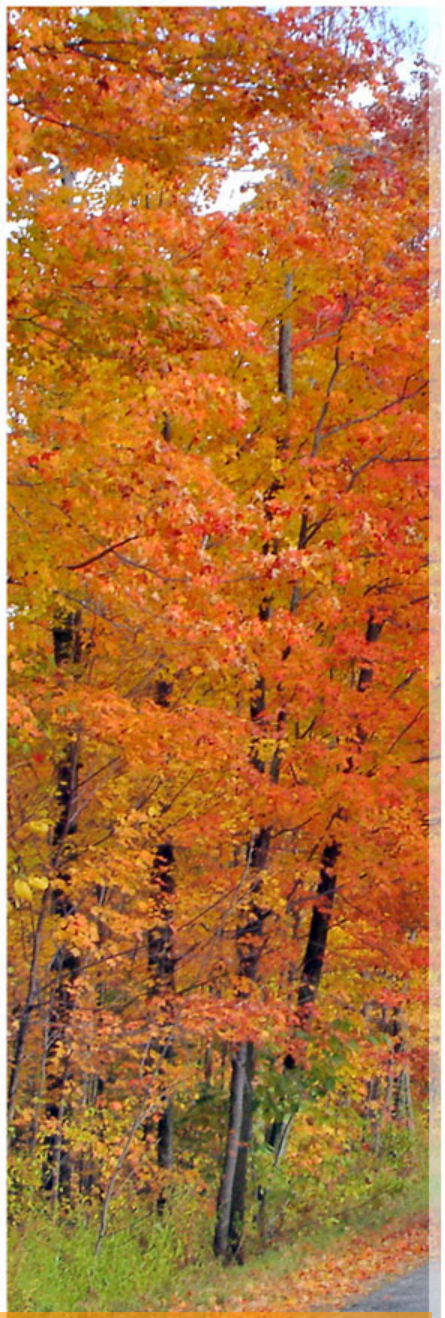
HYPERURICEMIA

- At baseline, 15,745 patients in the Atherosclerosis Risk in Communities Study completed a dietary questionnaire and had measurements of their serum creatinine and uric acid. After 3 and 9 years of follow-up. Compared to participants who drank less, consumption of **over one soda** per day was associated with increased odds of prevalent **hyperuricemia** and **chronic kidney disease**.

Kidney Int. 2010 Apr;77(7):609-16. Epub 2009 Dec 23.

Sugar-sweetened soda consumption, hyperuricemia, and kidney disease.

Bomback AS, Derebail VK, Shoham DA, Anderson CA, Steffen LM, Rosamond WD, Kshirsagar AV.



University of Florida
Gainesville

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

HYPERURICEMIA

- These data provide the first evidence that **uric acid** may be a cause of **metabolic syndrome**, possibly due to its ability to inhibit endothelial function. **Fructose** may have a major role in the epidemic of **metabolic syndrome** and **obesity** due to its ability to **raise uric acid**.

Am J Physiol Renal Physiol. 2006 Mar;290(3):F625-31. Epub 2005 Oct 18.

A causal role for uric acid in fructose-induced metabolic syndrome.

Nakagawa T, Hu H, Zharikov S, Tuttle KR, Short RA, Glushakova O, Ouyang X, Feig DI, Block ER, Herrera-Acosta J, Patel JM, Johnson RJ.

Division of Nephrology, Hypertension, and Transplantation, PO Box 100224, University of Florida, Gainesville, FL 32610, USA. nakagt@medicine.ufl.edu

Hospital Universitario de Burgos

FRUCTOSE DAMAGE

Dr Georges MOUTON
May 2014

GOUT

- From ancient times, **gout** has been related with excessive eating and drinking; however, it has not been until the last decade that a broader knowledge on dietary factors associated with **hyperuricemia** and **gout** has been achieved. Obesity, excessive intake of red meats and alcoholic beverages were already recognized as causal factors from Antiquity. New risk factors, not previously recognized, have been described such as **fructose** and **sweetened beverages**.

Nutr Hosp. 2014 Apr 1;29(4):760-70. doi: 10.3305/nh.2014.29.4.7196.

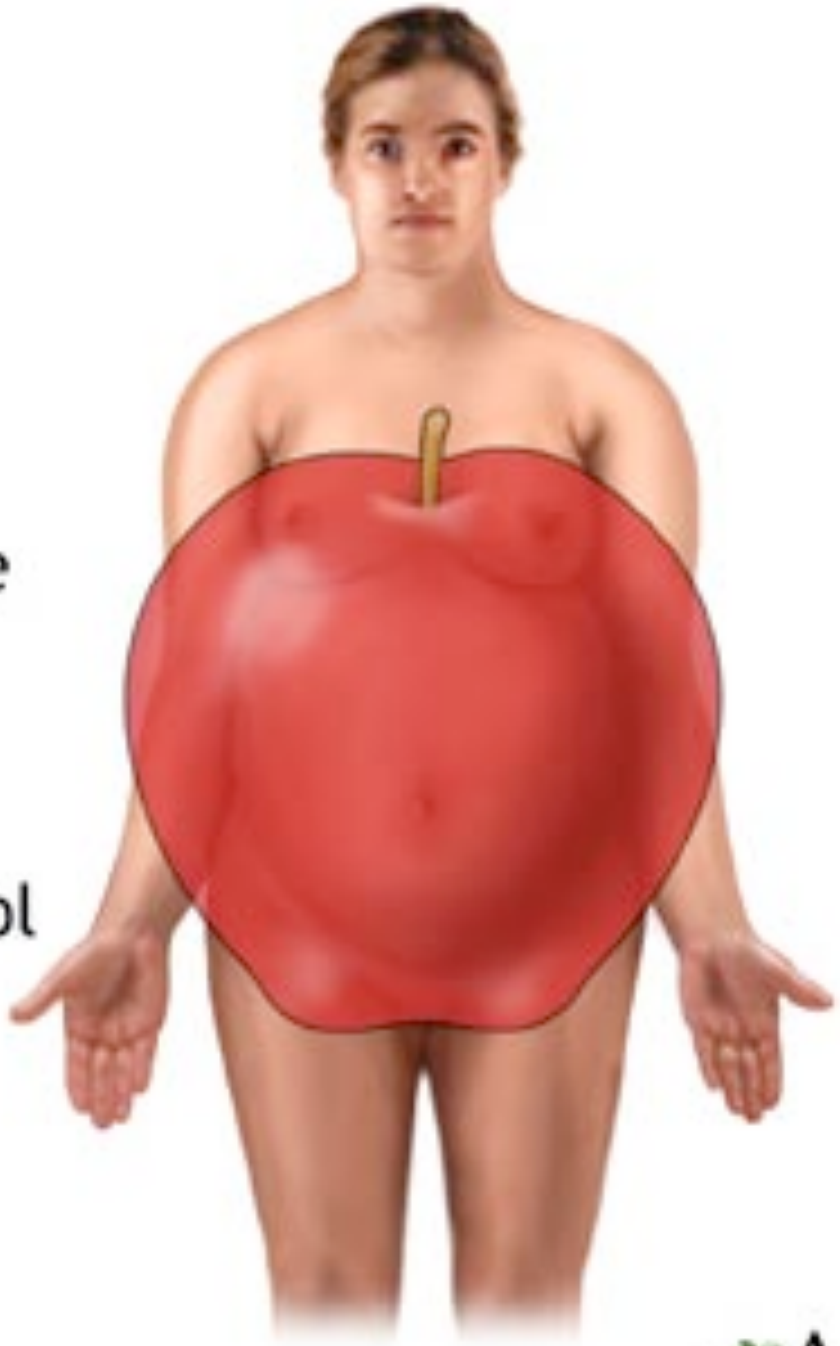
[Hyperuricemia and gout; the role of diet].

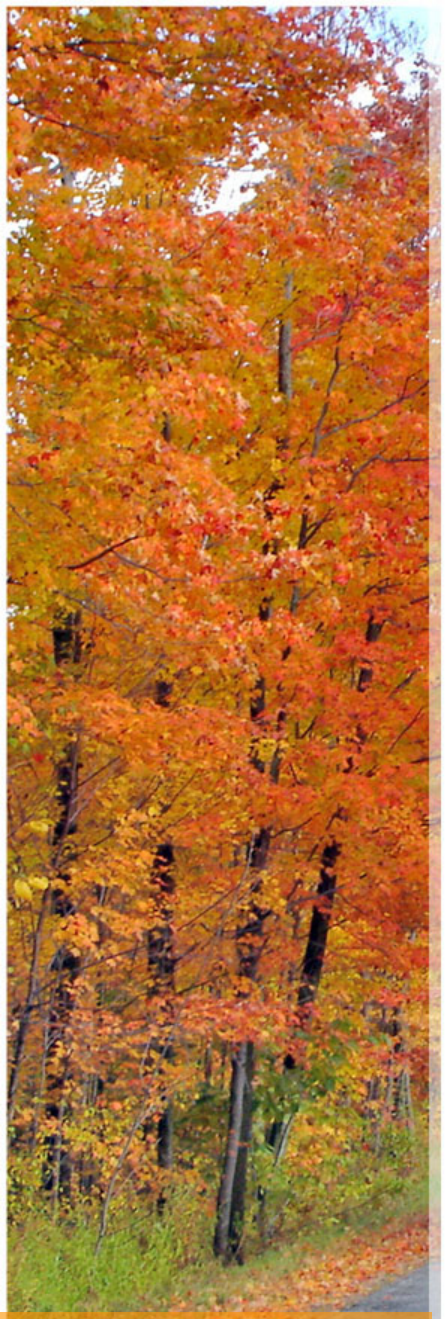
[Article in Spanish]

Álvarez-Lario B[1], Alonso-Valdivielso JL[2].

Metabolic syndrome
(Syndrome X)

- Central obesity
- High blood pressure
- High triglycerides
- Low HDL-cholesterol
- Insulin resistance





Son Llatzer Hospital
Palma de Mallorca

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

METABOLIC SYNDROME

- BACKGROUND: Excessive **fructose** intake causes **metabolic syndrome** in animals. We tested the hypothesis that **fructose** might induce features of **metabolic syndrome** in adult men
- CONCLUSIONS: High doses of **fructose** raise the **BP** and cause the features of **metabolic syndrome**. Excessive intake of **fructose** may have a role in the current epidemics of **obesity** and **diabetes**.

Int J Obes (Lond). 2010 Mar;34(3):454-61. Epub 2009 Dec 22.

Excessive fructose intake induces the features of metabolic syndrome in healthy adult men: role of uric acid in the hypertensive response.

Perez-Pozo SE, Schold J, Nakagawa T, Sánchez-Lozada LG, Johnson RJ, Lillo JL.


Cola
Facts
THE

PRINCETON UNIVERSITY

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

HYPERTRIGLYCERIDEMIA

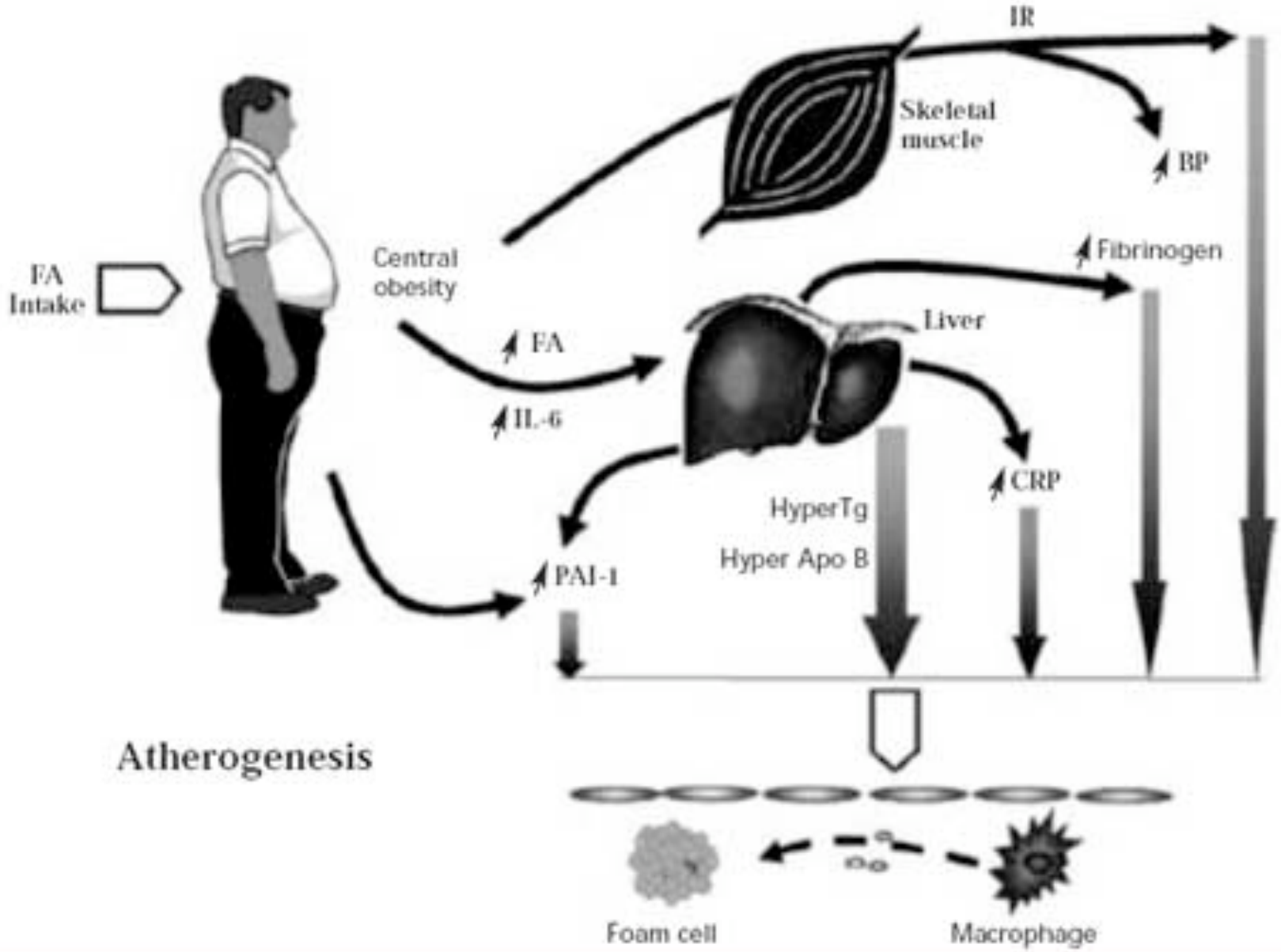
- Both male and female rats with access to high fructose corn syrup (HFCS) gained significantly more **body weight** than control groups. This increase in body weight with HFCS was accompanied by an increase in **adipose fat**, notably in the **abdominal region**, and **elevated** circulating **triglyceride levels**.

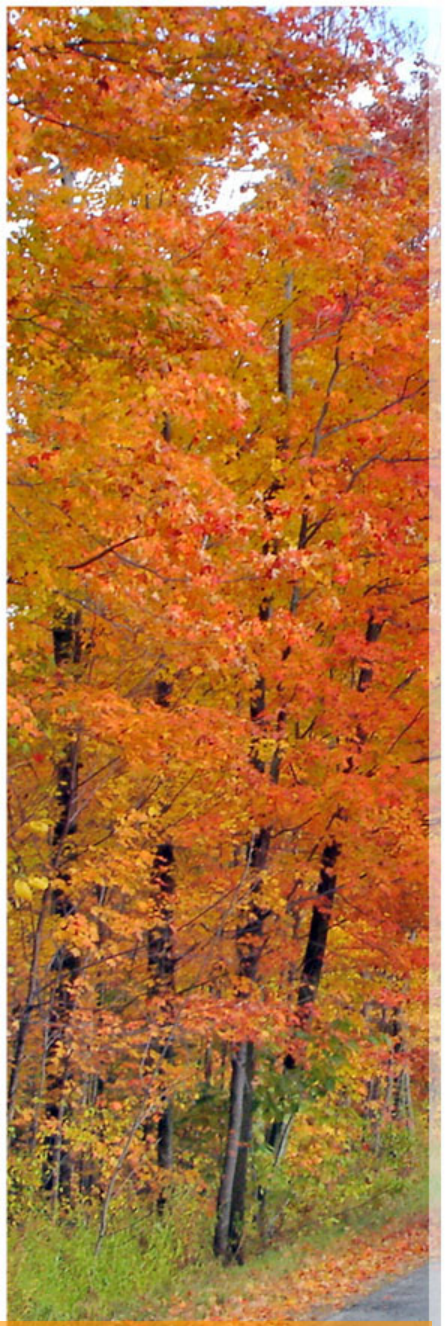
Pharmacol Biochem Behav. 2010 Nov 97(1):101-6. Epub 2010 Feb 26.

High-fructose corn syrup causes characteristics of obesity in rats: Increased body weight, body fat and triglyceride levels.

Bocarsly ME, Powell ES, Avena NM, Hoebel BG.

Linking abdominal obesity to inflammation and atherosclerosis





University of California Davis

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

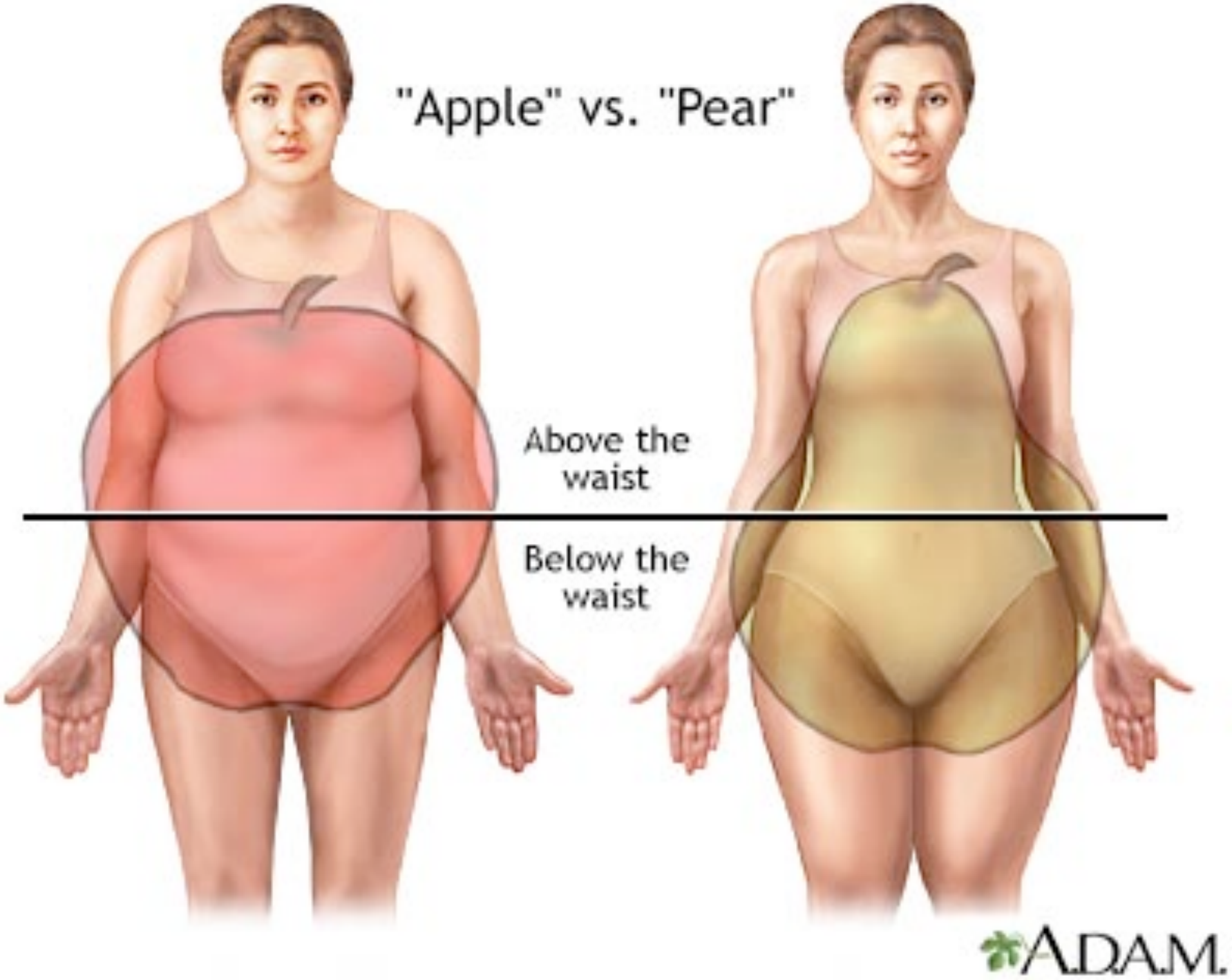
DE NOVO LIPOGENESIS

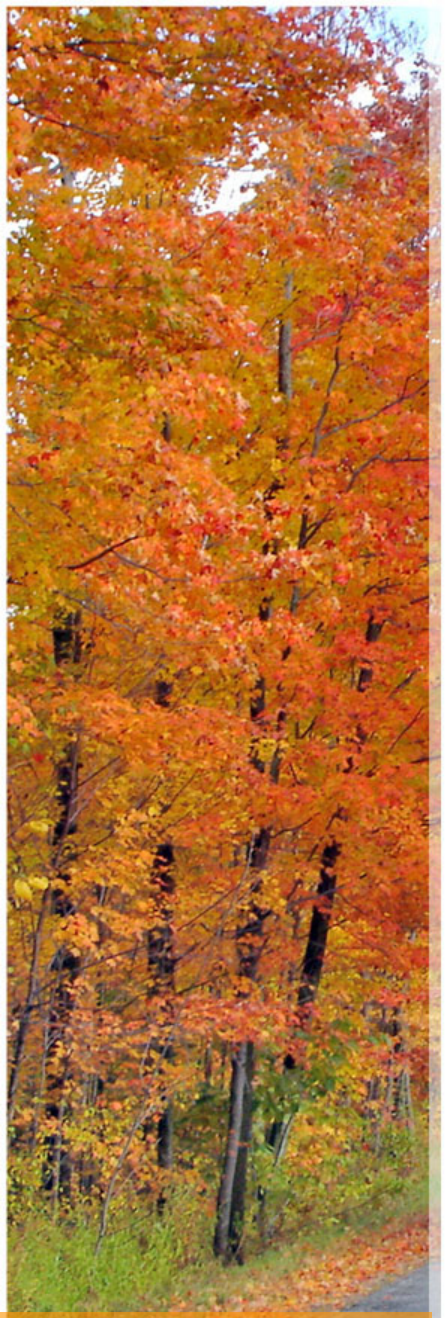
- Studies in animals have documented that, compared with glucose, dietary **fructose** induces **dyslipidemia** and **insulin resistance**. These data suggest that dietary **fructose** specifically increases **hepatic de novo lipogenesis**, promotes **dyslipidemia**, decreases **insulin sensitivity**, and increases **visceral adiposity** in overweight/obese adults.

J Clin Invest. 2009 May;119(5):1322-34. doi: 10.1172/JCI37385. Epub 2009 Apr 20.

Consuming fructose-sweetened, not glucose-sweetened, beverages increases visceral adiposity and lipids and decreases insulin sensitivity in overweight/obese humans.

Stanhope KL, Schwarz JM, Keim NL, Griffen SC, Bremer AA, Graham JL, Hatcher B, Cox CL, Dyachenko A, Zhang W, McGahan JP, Seibert A, Krauss RM, Chiu S, Schaefer EJ, Ai M, Otokozawa S, Nakajima K, Nakano T, Beysen C, Hellerstein MK, Berglund L, Havel PJ.


"Apple" vs. "Pear"
Above the waist
Below the waist
A.D.A.M.



Univ. of Pennsylvania
Philadelphia

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

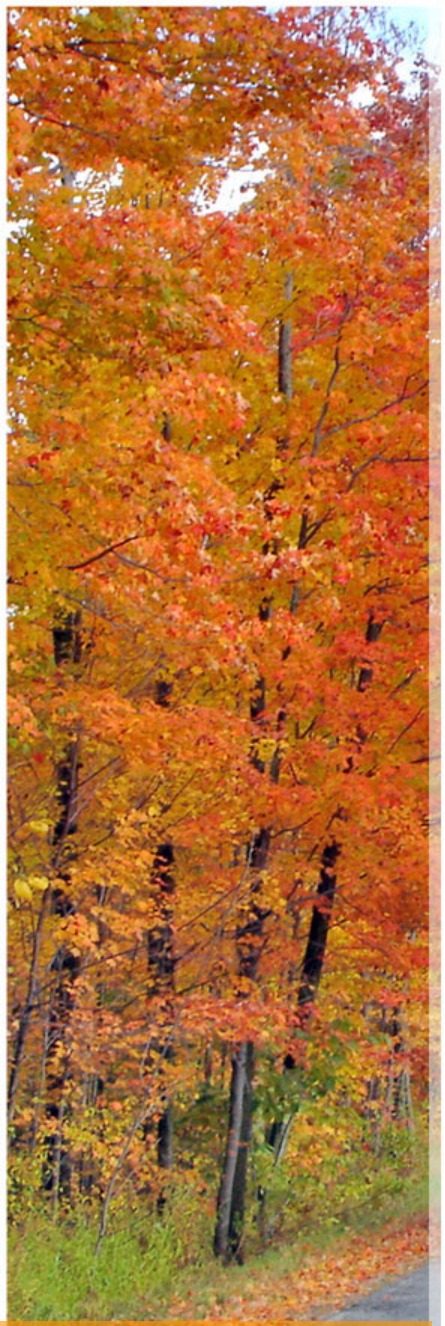
INCREASED ADIPOSITY

- RESULTS: Among children who were initially either at risk for overweight or overweight, increased **fruit juice** intake was associated with **excess adiposity gain**.
- CONCLUSION: This study supports the Institute of Medicine recommendations to reduce **fruit juice** intake as a strategy for **overweight** prevention in high-risk children.

Pediatrics. 2006 Nov;118(5):2066-75.

Fruit juice intake predicts increased adiposity gain in children from low-income families: weight status-by-environment interaction.

Faith MS, Dennison BA, Edmunds LS, Stratton HH.



University of Lausanne
Switzerland

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

LOWER INSULIN SENSITIVITY

- OBJECTIVE: The aim was to assess the effects of **fructose**, a potent stimulator of **hepatic de novo lipogenesis** in healthy offspring of patients with type 2 diabetes.
- CONCLUSIONS: A 7-d high-**fructose** diet increased ectopic lipid deposition in liver and muscle and fasting VLDL-triacylglycerols and **decreased hepatic insulin sensitivity**.

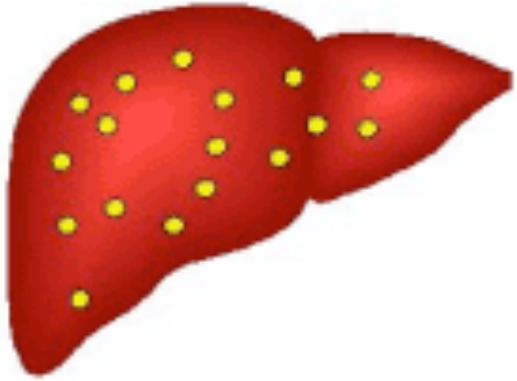
Am J Clin Nutr. 2009 Jun;89(6):1760-5. Epub 2009 Apr 29.

Fructose overconsumption causes dyslipidemia and ectopic lipid deposition in healthy subjects with and without a family history of type 2 diabetes.

Lê KA, Ith M, Kreis R, Faeh D, Bortolotti M, Tran C, Boesch C, Tappy L.

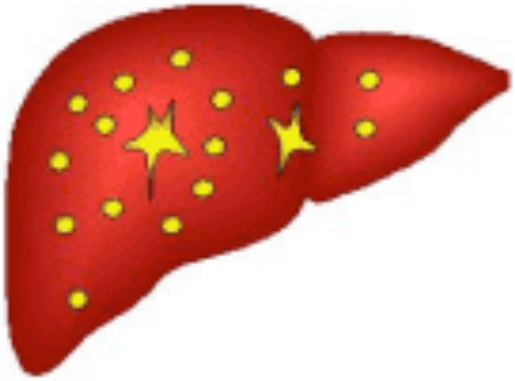
The Spectrum of NAFLD

Fatty Liver



Fat accumulates in the liver

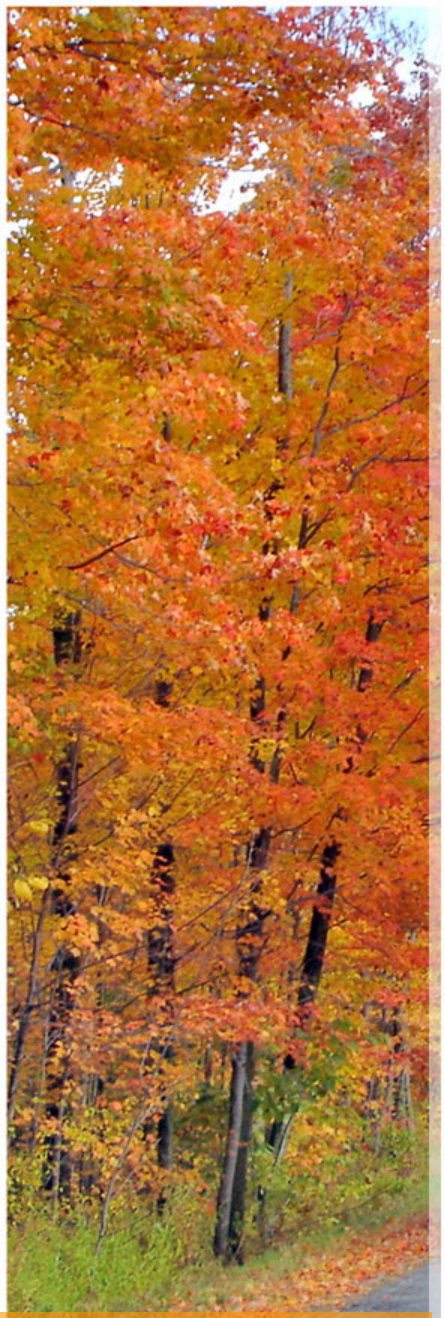
NASH



Fat plus inflammation and scarring

Cirrhosis

Scar tissue replaces liver cells



University of Florida
Gainesville

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

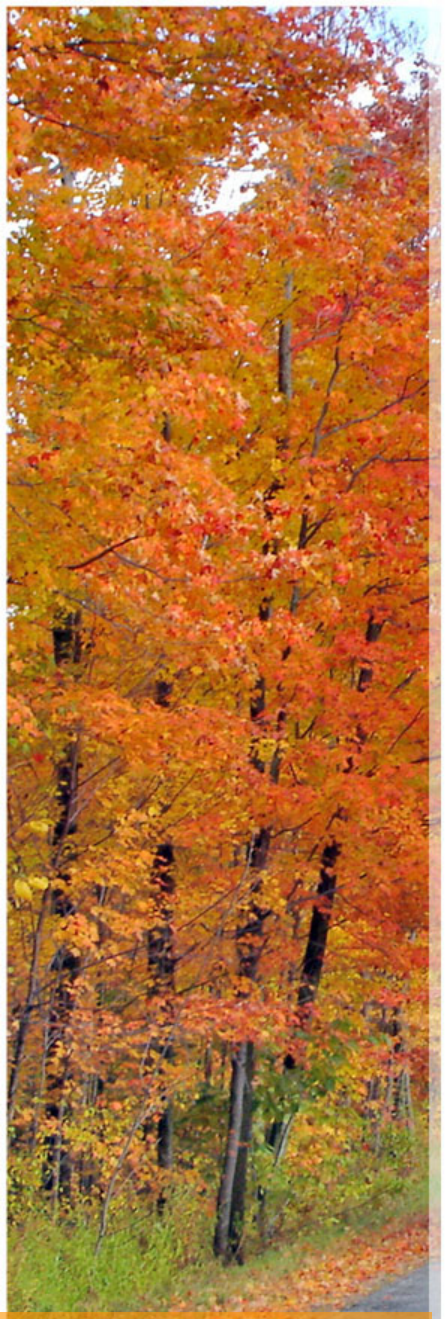
FATTY LIVER DISEASE

- BACKGROUND: While the rise in **non-alcoholic fatty liver disease** (**NAFLD**) parallels the increase in **obesity** and **diabetes**, a significant increase in dietary **fructose** consumption in industrialized countries has occurred.
- RESULTS: Consumption of **fructose** in patients with **NAFLD** was nearly 2- to 3-fold higher than controls.
- CONCLUSIONS: The pathogenic mechanism underlying the development of **non-alcoholic fatty liver disease** (**NAFLD**) may be associated with excessive dietary **fructose** consumption.

J Hepatol. 2008 Jun;48(6):993-9. Epub 2008 Mar 10.

Fructose consumption as a risk factor for non-alcoholic fatty liver disease.

Ouyang X, Cirillo P, Sautin Y, McCall S, Bruchette JL, Diehl AM, Johnson RJ, Abdelmalek MF.



Korea Cancer Center Hospital – Seoul

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

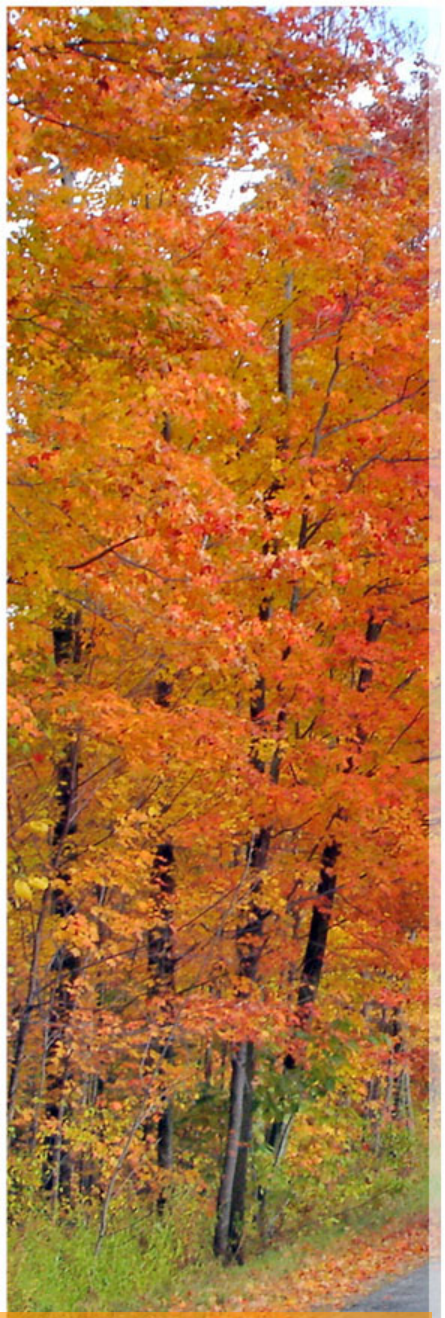
FATTY LIVER DISEASE

- **Non-alcoholic fatty liver disease (NAFLD)** is the most frequent liver disease worldwide, and is commonly associated with the **metabolic syndrome**. We postulate that excessive dietary **fructose** consumption may underlie the development of **NAFLD** and the **metabolic syndrome**. Furthermore, we postulate that NAFLD and alcoholic fatty liver disease share the same pathogenesis.

Nat Rev Gastroenterol Hepatol. 2010 May;7(5):251-64. Epub 2010 Apr 6.

The role of fructose in the pathogenesis of NAFLD and the metabolic syndrome.

Lim JS, Mietus-Snyder M, Valente A, Schwarz JM, Lustig RH.



University of Toronto
Canada

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2010

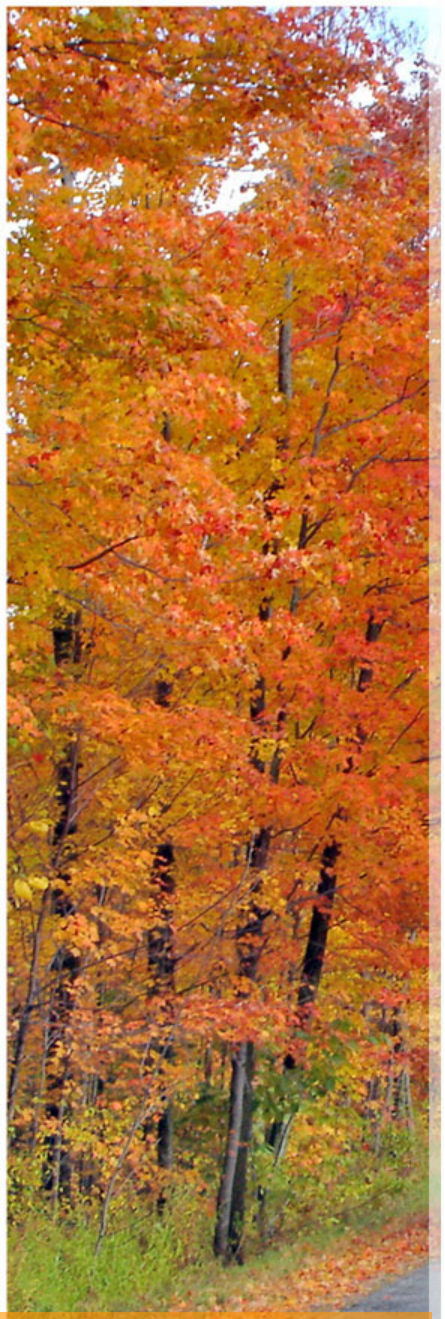
METABOLIC SYNDROME

- RECENT FINDINGS: Recent animal studies have confirmed the link between fructose feeding and **increased plasma uric acid**, a potentially causative factor in **metabolic syndrome**. Human studies have demonstrated fructose's ability to change metabolic hormonal response, possibly contributing to decreased satiety.
- SUMMARY: There is much evidence from both animal models and human studies supporting the notion that fructose is a **highly lipogenic nutrient** that, when consumed in high quantities, contributes to the development of a **prediabetic state**.

Curr Opin Gastroenterol. 2008 Mar;24(2):204-9.

Dietary fructose and the metabolic syndrome.

Miller A, Adeli K.



University of Colorado - Denver

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2013

METABOLIC SYNDROME

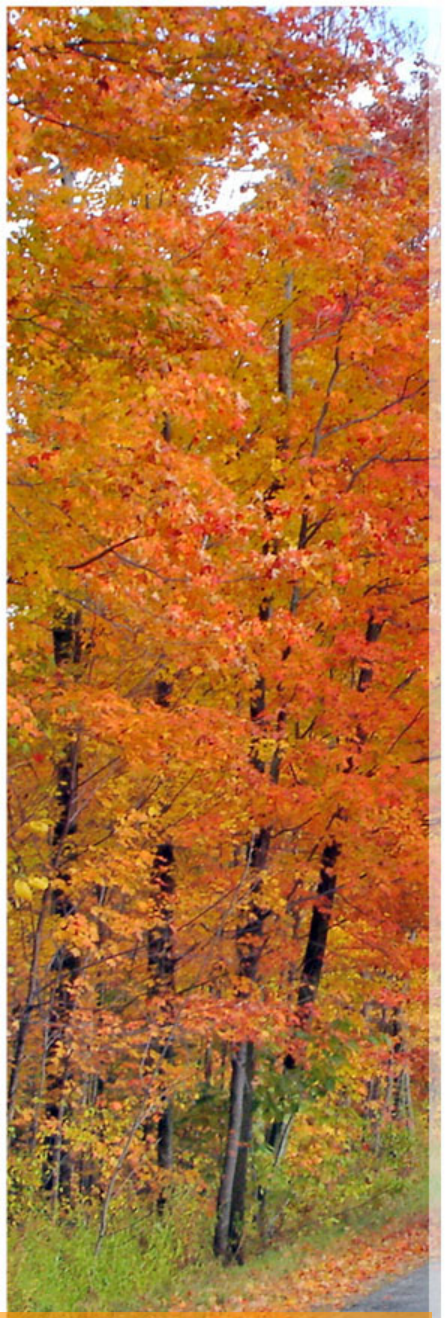
- We conclude that endogenous **fructose** generation and metabolism in the liver represents an important mechanism by which glucose promotes the development of **metabolic syndrome**.

Nat Commun. 2013 Sep 11;4:2434. doi: 10.1038/ncomms3434.

Endogenous fructose production and metabolism in the liver contributes to the development of metabolic syndrome.

Lanaspa MA, Ishimoto T, Li N, Cicerchi C, Orlicky DJ, Ruzicky P, Rivard C, Inaba S, Roncal-Jimenez CA, Bales ES, Diggle CP, Asipu A, Petrash JM, Kosugi T, Maruyama S, Sanchez-Lozada LG, McManaman JL, Bonthron DT, Sautin YY, Johnson RJ.

1] Division of Renal Diseases and Hypertension, University of Colorado, 12700 East 19th Avenue, Room 7015, Denver, Colorado 80045, USA [2].



University of Utah
Salt Lake City

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2013

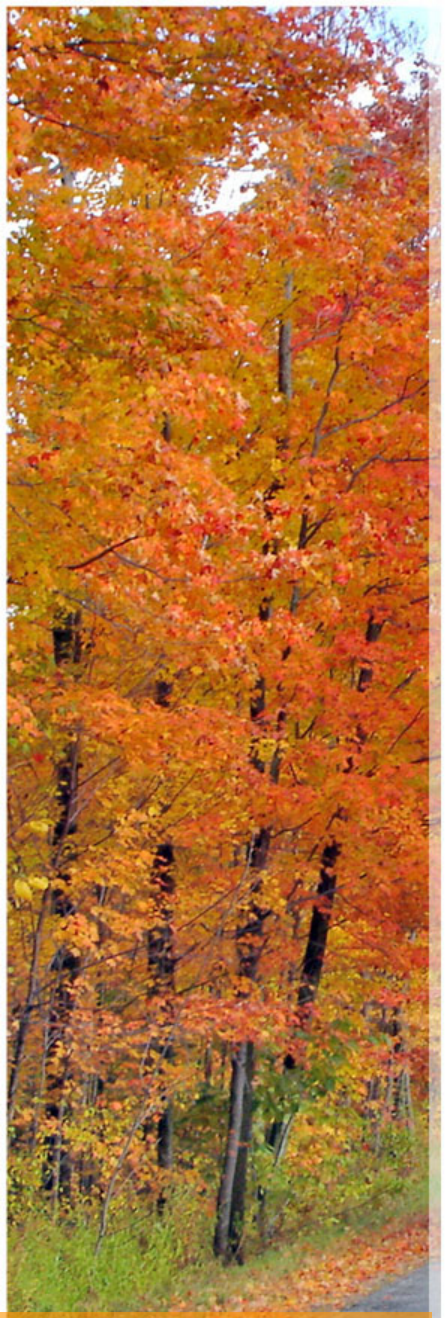
METABOLIC SYNDROME

- We demonstrate that **fructose**/glucose-fed females experience a twofold **increase in mortality** while **fructose**/glucose-fed males control 26% **fewer territories** and produce 25% **less offspring**.

Nat Commun. 2013 Aug 14;4:2245. doi: 10.1038/ncomms3245.

Human-relevant levels of added sugar consumption increase female mortality and lower male fitness in mice.

Ruff JS, Suchy AK, Hugentobler SA, Sosa MM, Schwartz BL, Morrison LC, Gieng SH, Shigenaga MK, Potts WK.
Department of Biology, University of Utah, 257 South 1400 East, Salt Lake City, Utah 84112, USA.



University of Utah
Salt Lake City

FRUCTOSE DAMAGE

Dr Georges MOUTON
October 2013

METABOLIC SYNDROME

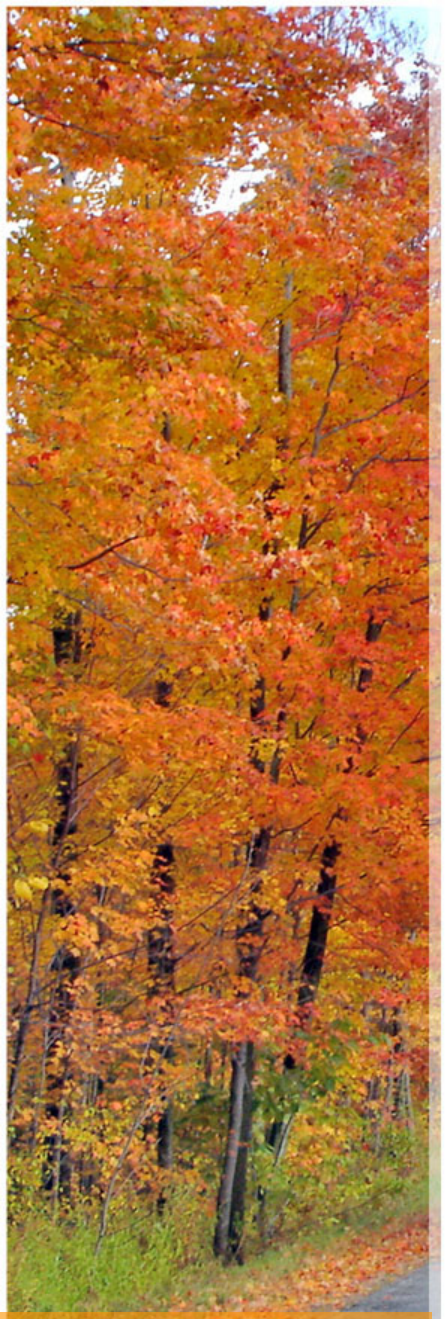
- Clinical defects of fructose/ glucose-fed mice were decreased glucose clearance and increased fasting cholesterol. Our data highlight that physiological adversity can exist when clinical disruptions are minor.

Nat Commun. 2013 Aug 14;4:2245. doi: 10.1038/ncomms3245.

Human-relevant levels of added sugar consumption increase female mortality and lower male fitness in mice.

Ruff JS, Suchy AK, Hugentobler SA, Sosa MM, Schwartz BL, Morrison LC, Gieng SH, Shigenaga MK, Potts WK.
Department of Biology, University of Utah, 257 South 1400 East, Salt Lake City, Utah 84112, USA.


Snapple
Snapple
Mountain Dew
Mountain Dew
Schweppes
Schweppes
Schweppes
Coca-Cola
Sunkist
Sunkist
Sunkist
Diet Coke
Diet Coke
Diet Coke
Diet PEPSI
Diet PEPSI



UCLA
Los Angeles

FRUCTOSE DAMAGE

Dr Georges MOUTON
September 2012

IMPAIRED COGNITION

- We pursued studies to determine the effects of the **metabolic syndrome** on brain, and the possibility of modulating these effects by dietary interventions. We report that high-dietary **fructose** consumption leads to an increase in **insulin resistance** index, and **insulin and triglyceride levels**, which characterize **metabolic syndrome**. Rats fed on an n-3 deficient diet showed memory deficits in a Barnes maze, which were further exacerbated by **fructose** intake.

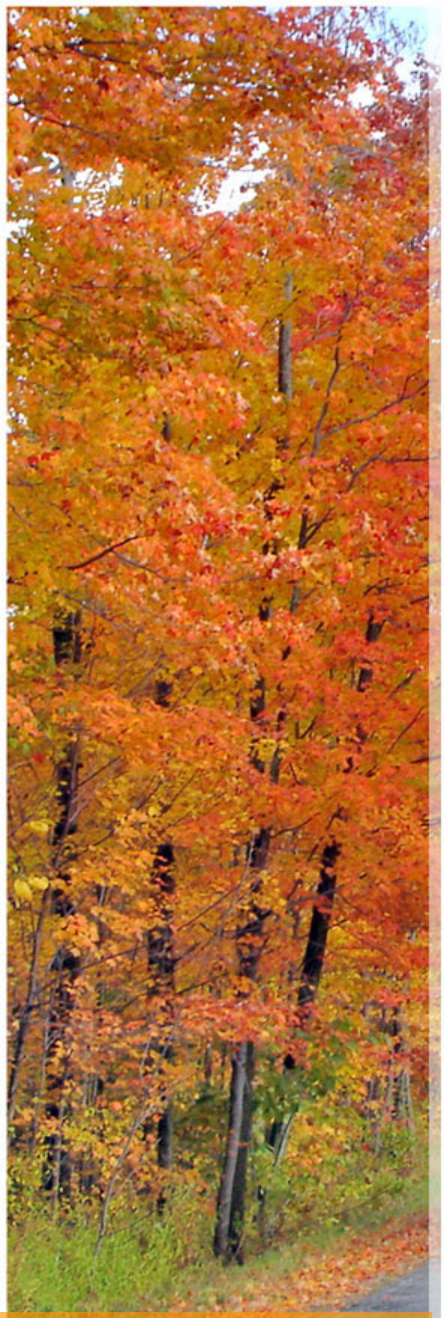
J Physiol. 2012 May 1;590(Pt 10):2485-99. Epub 2012 Apr 2.

'Metabolic syndrome' in the brain: deficiency in omega-3 fatty acid exacerbates dysfunctions in insulin receptor signalling and cognition.

Agrawal R, Gomez-Pinilla F.

Department of Integrative Biology and Physiology, University of California Los Angeles (UCLA), Los Angeles, CA 90095, USA.


HIGH
SYRUP



University of Oregon
Portland

FRUCTOSE DAMAGE

Dr Georges MOUTON
March 2011

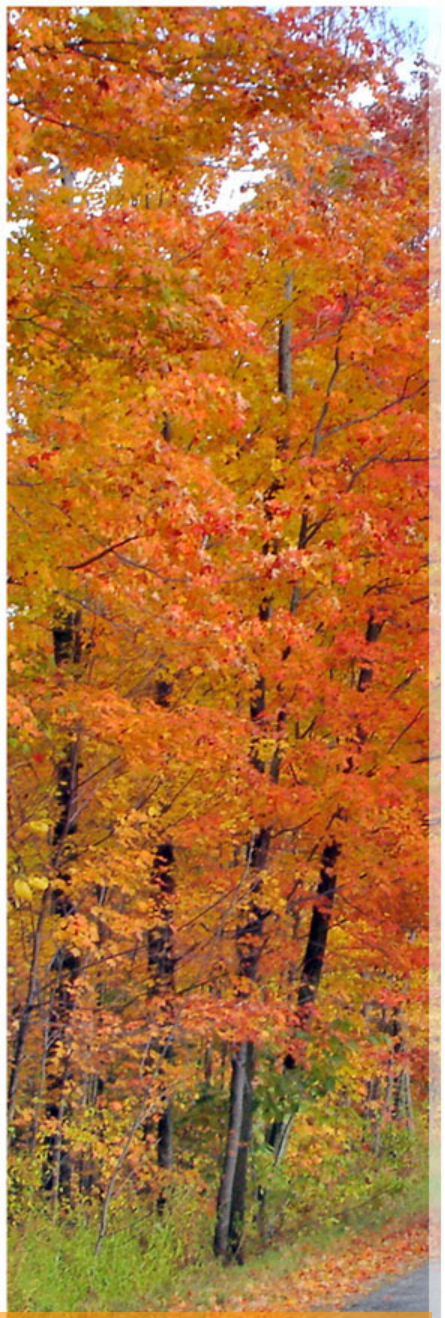
FOOD INTAKE DYSREGULATION

- RESULTS: Blood oxygenation level dependent signal in the cortical control areas increased during glucose infusion (p = 0.002), corresponding with increased plasma glucose and insulin levels. In contrast, **blood oxygenation level dependent signal decreased** in the cortical control areas during fructose infusion (p = 0.006), corresponding with increases of plasma fructose and lactate.

Diabetes Obes Metab. 2011 Mar;13(3):229-34. doi: 10.1111/j.1463-1326.2010.01340.x.

Brain functional magnetic resonance imaging response to glucose and fructose infusions in humans.

Purnell JQ, Klopfenstein BA, Stevens AA, Havel PJ, Adams SH, Dunn TN, Krisky C, Rooney WD.



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FRUCTOSE DAMAGE

Dr Georges MOUTON
March 2011

FOOD INTAKE DYSREGULATION

- CONCLUSION: In normal weight humans, cortical responses as assessed by blood oxygenation level dependent MRI to infused glucose are opposite to those of fructose. Differential brain responses to these sugars and their metabolites may provide insight into the neurologic basis for dysregulation of food intake during high dietary fructose intake.

Diabetes Obes Metab. 2011 Mar;13(3):229-34. doi: 10.1111/j.1463-1326.2010.01340.x.

Brain functional magnetic resonance imaging response to glucose and fructose infusions in humans.

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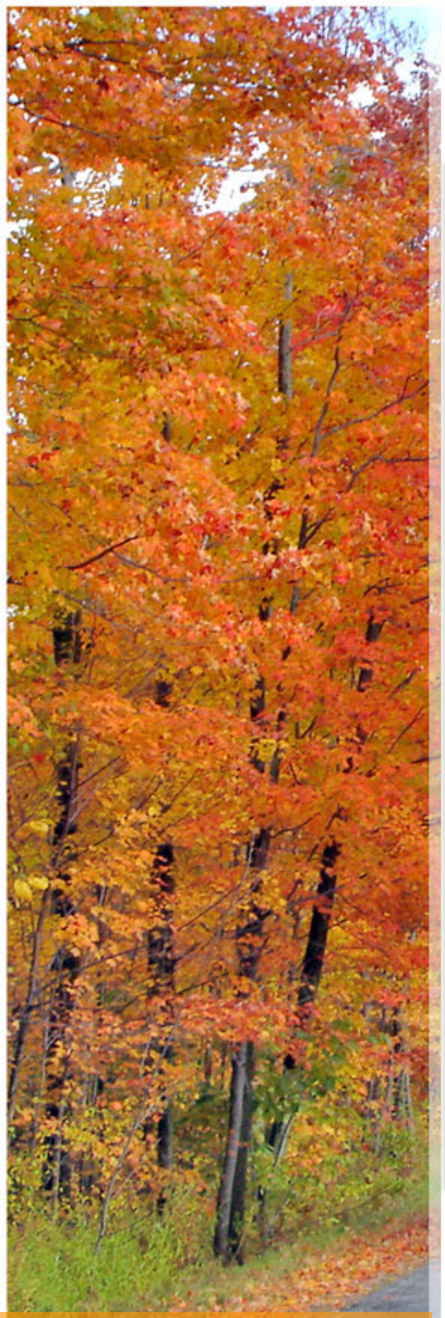


Yale University
School of Medicine

FRUCTOSE DAMAGE

Dr Georges MOUTON
March 2013

FOOD INTAKE DYSREGULATION

Fructose ingestion produces smaller increases in circulating satiety hormones compared with glucose ingestion, and central administration of fructose provokes feeding in rodents, whereas centrally administered glucose promotes satiety.

JAMA. 2013 Jan 2;309(1):63-70. doi: 10.1001/jama.2012.116975.

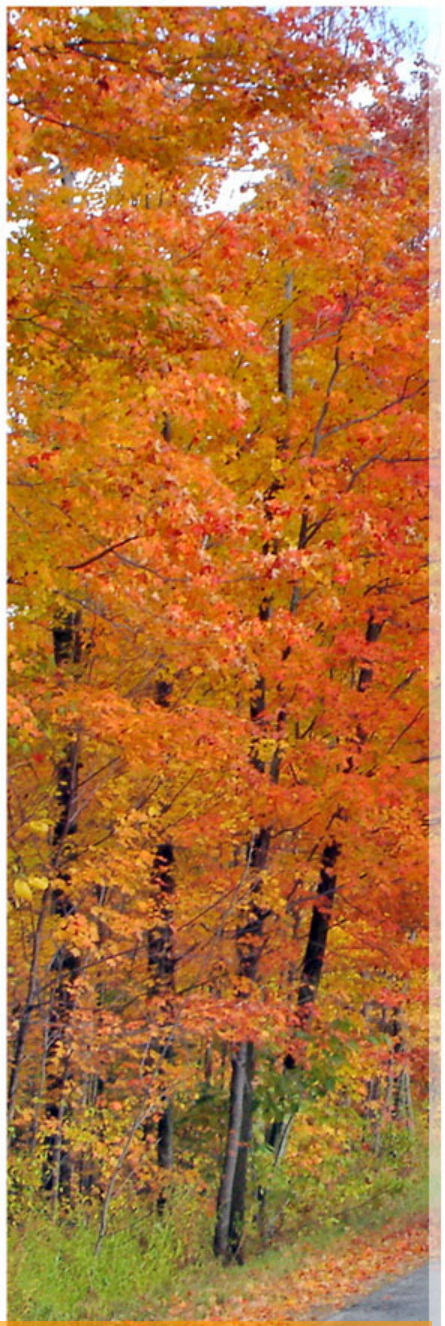
Effects of fructose vs glucose on regional cerebral blood flow in brain regions involved with appetite and reward pathways.

Page KA, Chan O, Arora J, Belfort-Deaguiar R, Dzuira J, Roehmholdt B, Cline GW, Naik S, Sinha R, Constable RT, Sherwin RS.

Section of Endocrinology, Department of Internal Medicine, Yale University School of Medicine, New Haven, CT 06520-8020, USA.

The toxic truth about sugar

Added sweeteners pose dangers to health that justify controlling them like alcohol, argue **Robert H. Lustig, Laura A. Schmidt** and **Claire D. Brindis.**



University of California San Francisco

FRUCTOSE DAMAGE

Dr Georges MOUTON
September 2012

SUMMARY

- Importantly, sugar induces all of the diseases associated with **metabolic syndrome**. This includes: **hypertension** (**fructose** **increases uric acid**, which raises blood pressure); **high triglycerides** and **insulin resistance** through synthesis of **fat in the liver**; **diabetes** and the **ageing process**, caused by damage to lipids, proteins and DNA through non-enzymatic binding of **fructose** to these molecules.

Nature. 2012 Feb 1;482(7383):27-9. doi: 10.1038/482027a.

Public health: The toxic truth about sugar.

Lustig RH, Schmidt LA, Brindis CD.

Department of Pediatrics, University of California, San Francisco, California 94143, USA. rlustig@peds.ucsf.edu

FRUCTOSE DAMAGE

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Kleinhoscheid, 06/04/2018