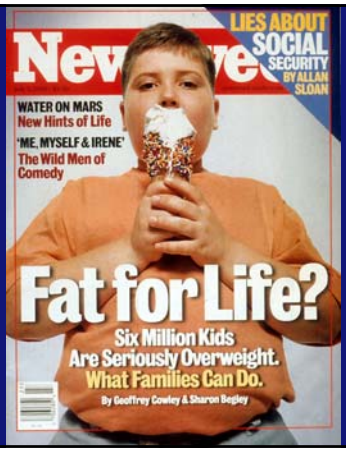
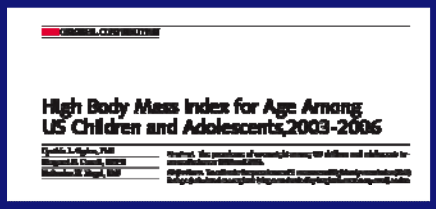
Sugar — the bitter truth

Robert H. Lustig, M.D.
Division of Endocrinology
Department of Pediatrics
University of California, San Francisco

UCSF Pediatric Advances, May 29, 2009



The CDC says that the childhood obesity epidemic is slowing down—

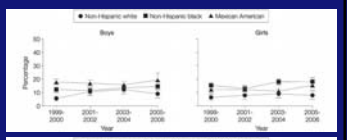


Ogden et al. JAMA 299:2401-2405, 2008

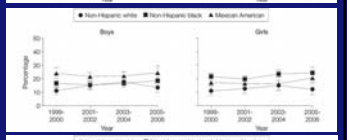
But is it?

Secular trends in childhood obesity prevalence in U.S. 1999-2006

Severely Obese:
BMI for Age > 97th %ile



Obese:
BMI for Age > 95th %ile



Overweight:
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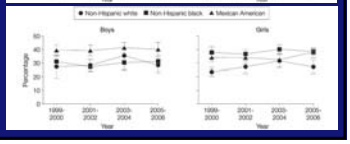

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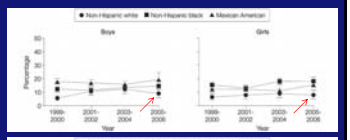

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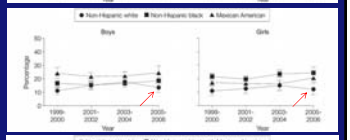

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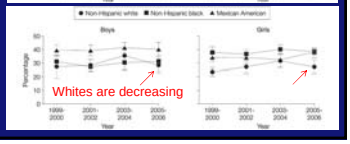

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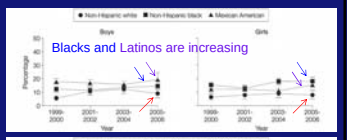

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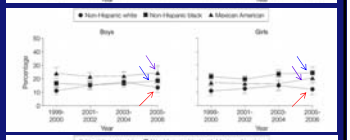

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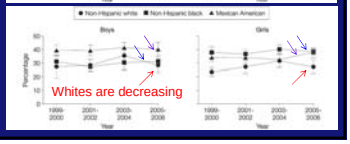
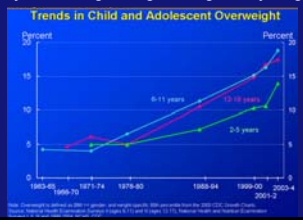


Ogden et al. JAMA 299:2401-2405, 2008

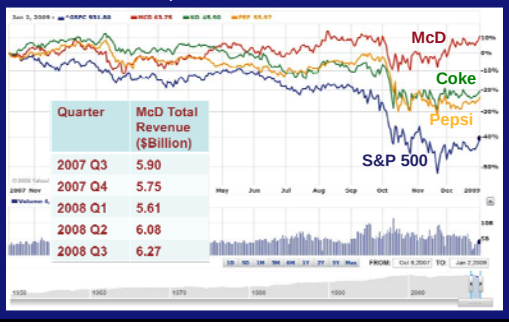
So is the epidemic of childhood obesity really slowing down?

- The prevalence of obesity amongst Whites is decreasing, but amongst Blacks and Latinos (and Asians) is increasing
- Minorities compose an increasing percentage of American children annually
- This JAMA paper analyzed mean data from all ages 2-19; but in the 2-5 year old age range, things are just getting worse



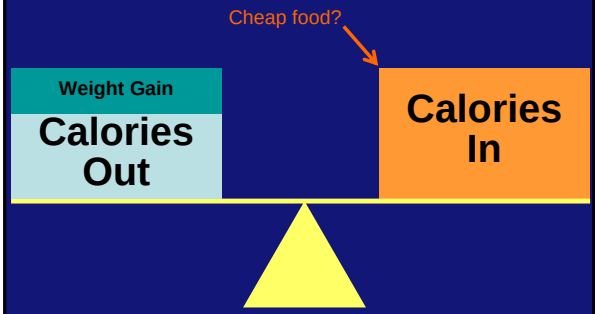
So is the epidemic of childhood obesity really slowing down?

- Despite the economic downturn of 2008, McDonald's revenues and stock price continues to rise; and Coke and Pepsi still fared better than the S&P 500

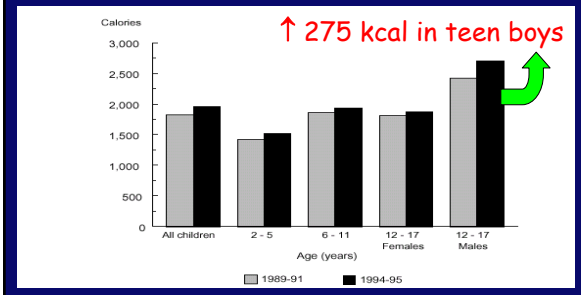


Quarter	McD Total Revenue ($Billion)
2007 Q3	5.90
2007 Q4	5.75
2008 Q1	5.61
2008 Q2	6.08
2008 Q3	6.27

The First Law of Thermodynamics

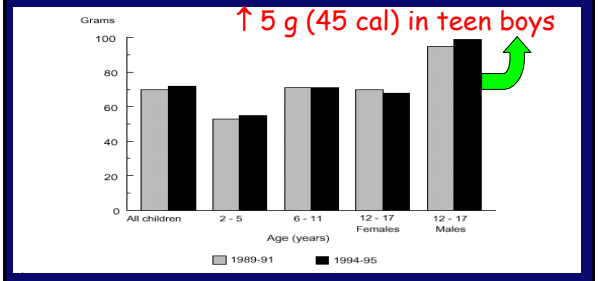


Total Caloric Intake



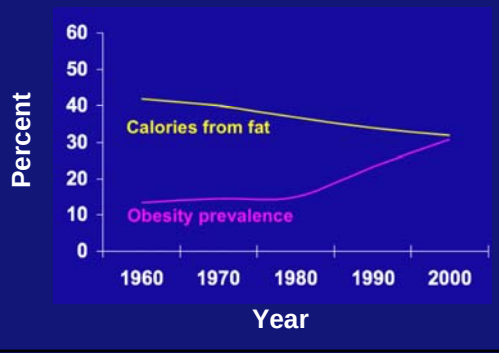
Children 2-17 yrs, CSFII (USDA) 1989-91 vs. 1994-95
http://www.usda.gov/cnpp/FENR%20V11N3/fenrv11n3p44.PDF

Fat Intake: Grams

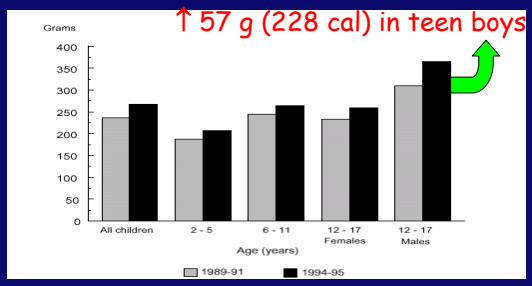


Children 2-17 yrs, CSFII (USDA) 1989-91 vs. 1994-95

Prevalence of Obesity Compared to Percent Calories from Fat Among US Adults

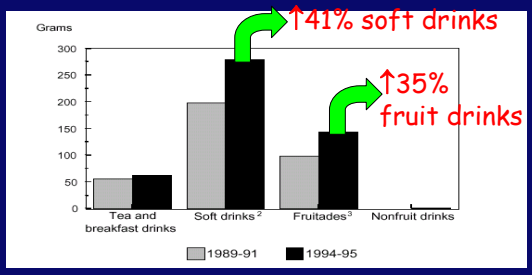


Carbohydrate Intake: Grams



Children 2-17 yrs, CSFII (USDA) 1989-91 vs. 1994-95

Beverage Intake



Children 2-17 yrs, CSFII (USDA) 1989-91 vs. 1994-95

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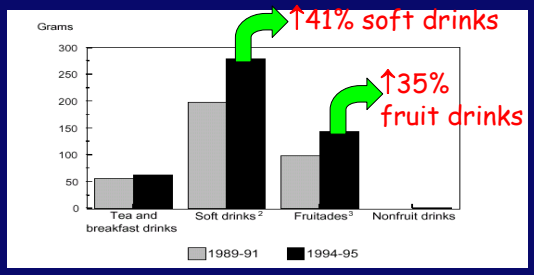


Children 2-17 yrs, CSFII (USDA) 1989-91 vs. 1994-95

One can of soda/day = 150 cal x 365 d/yr ÷ 3500 cal/lb = 15.6 lbs/yr

Meta-Analysis of Soft Drinks and Obesity

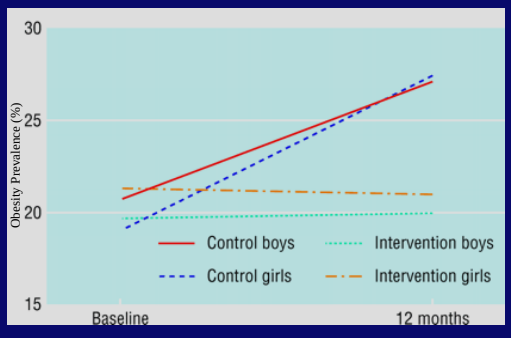
88 cross-sectional and longitudinal studies regressing soft drink consumption with —

• energy intake	r = 0.16 (*P* < 0.001)
• body weight	r = 0.08 (*P* < 0.001)
• milk and calcium intake	r = -0.12 (*P* < 0.001)
• adequate nutrition	r = -0.10 (*P* < 0.001)

Those studies funded by the beverage industry demonstrated smaller effects than independent studies

Vartanian et al. Am J Public Health epub March 2007; 10.2105/AJPH.2005.083782

Curtailing soft drinks limits childhood obesity



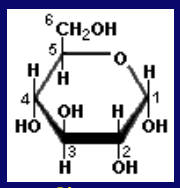
James et al. BMJ 328:1237, 2004

High Fructose Corn Syrup

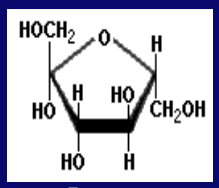
Current US annual consumption of HFCS

• 63 pounds per person

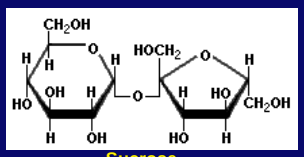
High Fructose Corn Syrup is 42-55% Fructose; Sucrose is 50% Fructose



Glucose



Fructose



Sucrose

USA Today, Dec 9, 2008 P. 7D

Health

New data not so sour on corn syrup

High-fructose sweetener is found no worse than sugar

Center for Science in the Public Interest

Corn Refiners Association

Press Release, February 6, 2008

Unlikely Duo Opposes San Francisco Soft Drink Tax Plan
Corn Refiners and CSPI Agree High-Fructose Corn Syrup No Worse Than Sugar

WASHINGTON—The nonprofit Center for Science in the Public Interest has long supported small taxes on soft drinks to help pay for bike paths, nutrition education, and other obesity-prevention programs. But CSPI opposes a measure proposed by San Francisco Mayor Gavin Newsom because it would tax only drinks made with high-fructose corn syrup and not drinks made with other forms of sugar. Less surprisingly, the Corn Refiners Association also opposes the measure, but the two groups cosigned an unusual joint letter to Mayor Newsom urging him to reconsider his plan.

"We respectfully urge that the proposal be revised as soon as possible to reflect the scientific evidence that demonstrates no material differences in the health effects of high-fructose corn syrup and sugar," wrote CSPI executive director Michael F. Jacobson and Corn Refiners Association president Audrae Erickson. **"The real issue is that excessive consumption of any sugars may lead to health problems."**

The letter goes on to explain that high-fructose corn syrup and sucrose, or table sugar, are similar in composition and that several studies have shown that the two types of sugars are similarly metabolized by the body.

Secular trend in fructose consumption

Natural consumption of fruits and vegetables
- 15 gm/day

Prior to WWII (estimated):
- 16-24 gm/day

1977-1978 (USDA Nationwide Food Consumption Survey):
- 37 gm/day (8% of total caloric intake)

1994 (NHANES III):
- 54.7 gm/day (10.2% of total caloric intake)

Adolescents:
- 72.8 gm/day (12.1% of total caloric intake)
- 25% consumed at least 15% of calories from fructose

Bray, Am J Clin Nutr 86:895, 2007; Vos et al. Medscape Med J 10:160, 2008

The perfect storm from three political winds

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1. Richard Nixon and USDA Secretary Earl Butz (1973)
   - food should never be an issue in a presidential election

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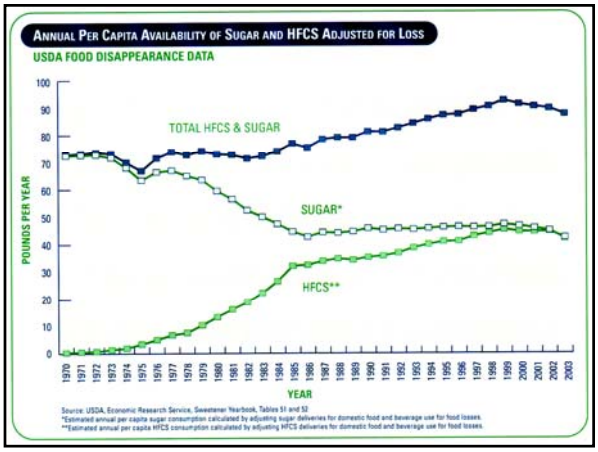
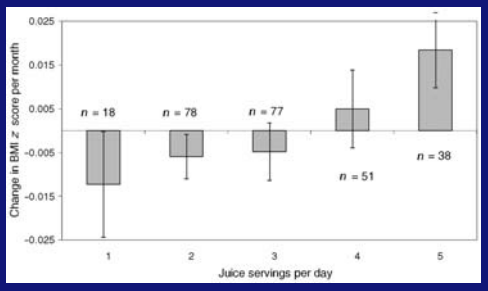
2. The advent of High Fructose Corn Syrup
   - invented in 1966 in Japan
   - introduced to the American market in 1975

Influence of corn sweeteners on the price of sugar

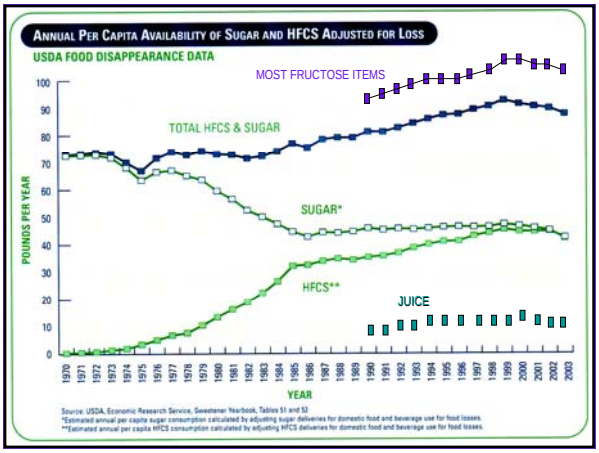
U.S. Department of Agriculture



Juice is sucrose:
Change in BMI z-score in lower socioeconomic status children versus number of fruit juice servings per day



Faith MS et al. Pediatrics 118:2066, 2006



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2. The advent of High Fructose Corn Syrup
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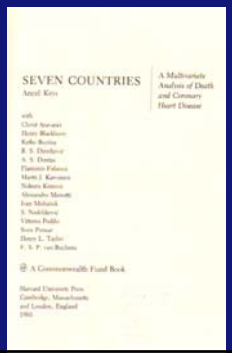
3. The USDA, AMA, and AHA call for dietary fat reduction
   - Early 1970's: discovery of LDL
   - Mid 1970's: Dietary fat raises LDL (A → B)
   - Late 1970's: LDL correlated with CVD (B → C)
   - 1982: If A → B, and B → C, then A → C, therefore no A, no C

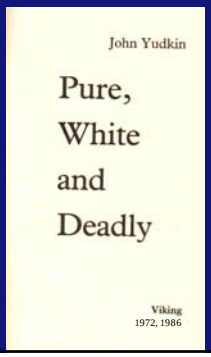
The macronutrient wars 1970-1980


SEVEN COUNTRIES

A Multivariate Analysis of Death and Coronary Heart Disease

A Commonwealth Fund Book

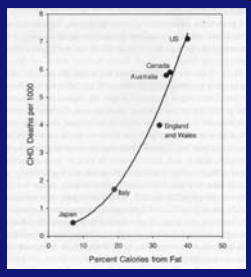
Harvard University Press
Cambridge, Massachusetts
and London, England
1980


John Yudkin

Pure, White and Deadly

Viking
1972, 1986

Seven Countries
Correlation of CHD with dietary fat



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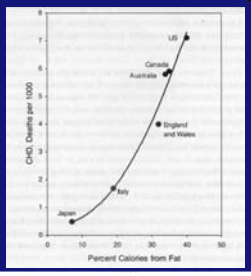


Page 262: Diet

The fact that the incidence rate of coronary heart disease was significantly correlated with the average percentage of calories from sucrose in the diets is explained by the intercorrelation of sucrose with saturated fat. Partial correlation analysis shows that with saturated fat constant there was no significant correlation between dietary sucrose and the incidence of coronary heart

Comparisons of coronary death rates with estimates of national diets in in-

The low-fat craze

The content of low-fat home-cooked food can be controlled

But low-fat processed food means substitution with carbohydrate

Which carbohydrate?

Either
- High fructose corn syrup (55% fructose)
- Sucrose (50% fructose)

e.g. Nabisco Snackwells® Oreos
(—2g fat, +13g CHO (+4g sugars))

Adulteration of our food supply

Addition of fructose
- palatability (esp. with decreased fat)
- browning agent

Removal of fiber
- shelf life
- freezing

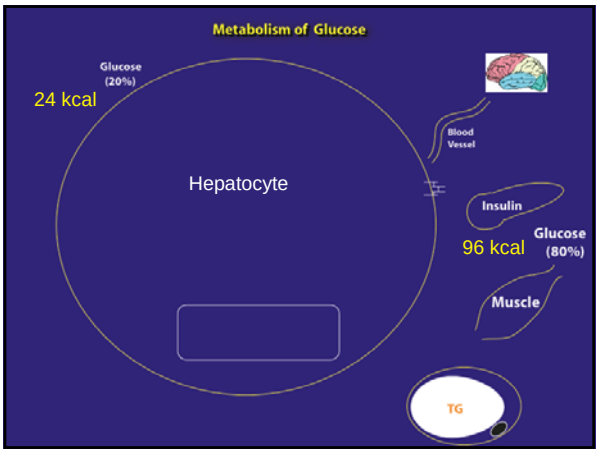
Substitution of trans-fats
- hardening agent, shelf life
- now being removed due to CVD risk

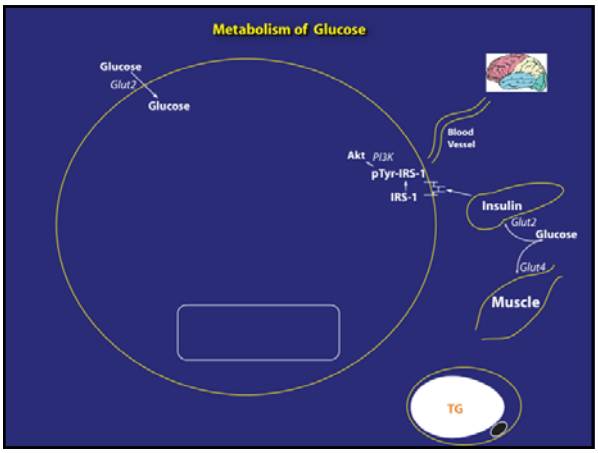
Fructose is not glucose

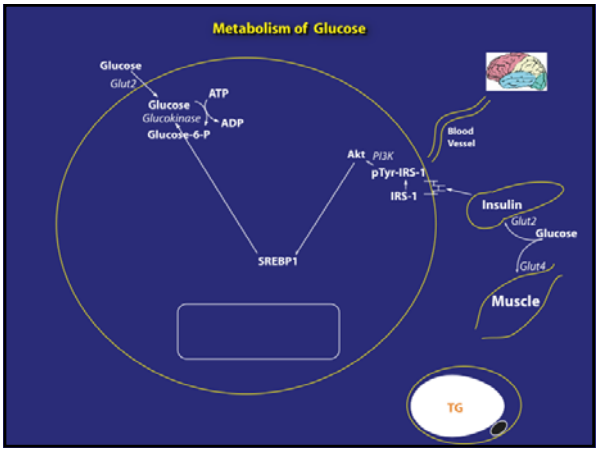
- Fructose is 7 times more likely than glucose to form Advanced Glycation End-Products (AGE's)
- Fructose does not suppress ghrelin
- Acute fructose does not stimulate insulin (or leptin)
- Hepatic fructose metabolism is different
- **Chronic fructose exposure promotes the Metabolic Syndrome**

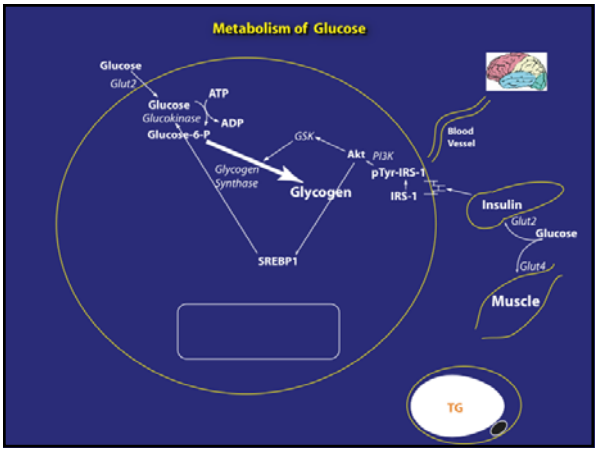
Elliot et al. Am J Clin Nutr, 2002
Bray et al. Am J Clin Nutr, 2004
Teff et al. J Clin Endocrinol Metab, 2004
Gaby, Alt Med Rev, 2005

Le and Tappy, Curr Opin Clin Nutr Metab Care, 2006
Wei et al. J Nutr Biochem, 2006
Johnson et al. Am J Clin Nutr 2007
Rutledge and Adeli, Nutr Rev, 2007
Brown et al. Int. J. Obes, 2008


Metabolism of Glucose
Glucose
(20%)
24 kcal
Hepatocyte
Blood
Vessel
Insulin
Glucose
(80%)
96 kcal
Muscle
TG


Metabolism of Glucose
Glucose
Glut2
Glucose
Blood
Vessel
Akt
PI3K
pTyr-IRS-1
IRS-1
Insulin
Glut2
Glucose
Glut4
Muscle
TG


Metabolism of Glucose
Glucose
Glut2
Glucose
Glucokinase
ATP
ADP
Glucose-6-P
SREBP1
Blood
Vessel
Akt
PI3K
pTyr-IRS-1
IRS-1
Insulin
Glut2
Glucose
Glut4
Muscle
TG


Metabolism of Glucose
Glucose
Glut2
Glucose
Glucokinase
ATP
ADP
Glucose-6-P
GSK
Glycogen
Synthase
Glycogen
SREBP1
Blood
Vessel
Akt
PI3K
pTyr-IRS-1
IRS-1
Insulin
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Glut4
Muscle
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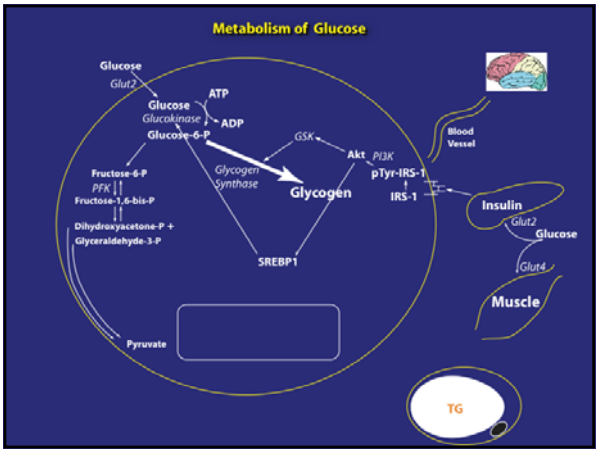
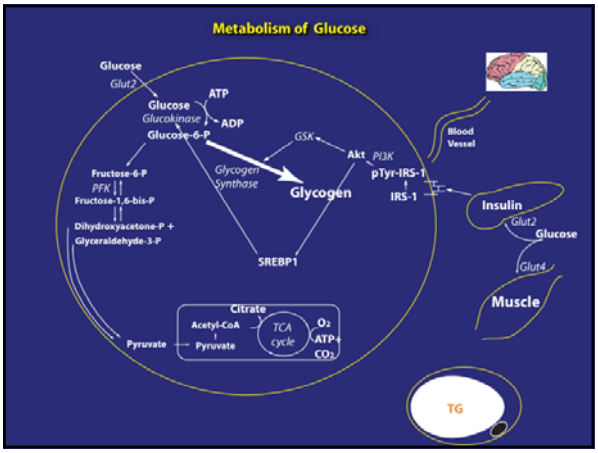
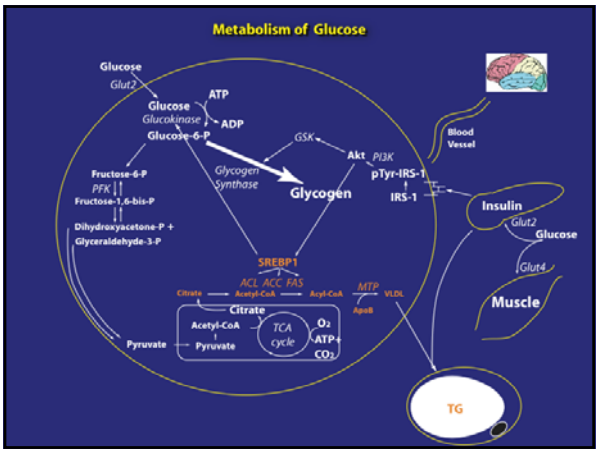
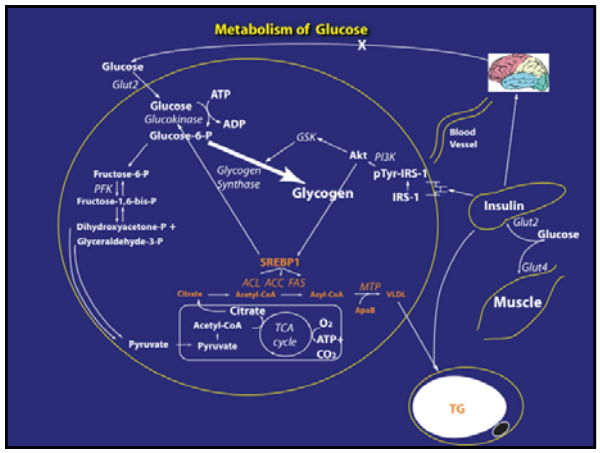

Metabolism of Glucose
Glucose
Glut2
Glucose
Glucokinase
ATP
ADP
Glucose-6-P
Fructose-6-P
PFK
Fructose-1,6-bis-P
Dihydroxyacetone-P +
Glyceraldehyde-3-P
Pyruvate
GSK
Glycogen
Synthase
Glycogen
SREBP1
Blood
Vessel
Akt
PI3K
pTyr-IRS-1
IRS-1
Insulin
Glut2
Glucose
Glut4
Muscle
TG


Metabolism of Glucose
Glucose
Glut2
Glucose
Glucokinase
ATP
ADP
Glucose-6-P
Fructose-6-P
PFK
Fructose-1,6-bis-P
Dihydroxyacetone-P +
Glyceraldehyde-3-P
Pyruvate
GSK
Glycogen
Synthase
Glycogen
SREBP1
Citrate
Acetyl-CoA
Pyruvate
TCA
cycle
O2
ATP+
CO2
Blood
Vessel
Akt
PI3K
pTyr-IRS-1
IRS-1
Insulin
Glut2
Glucose
Glut4
Muscle
TG





Ethanol is a carbohydrate

Ethanol is a carbohydrate

CH_3-CH_2-OH

Ethanol is a carbohydrate

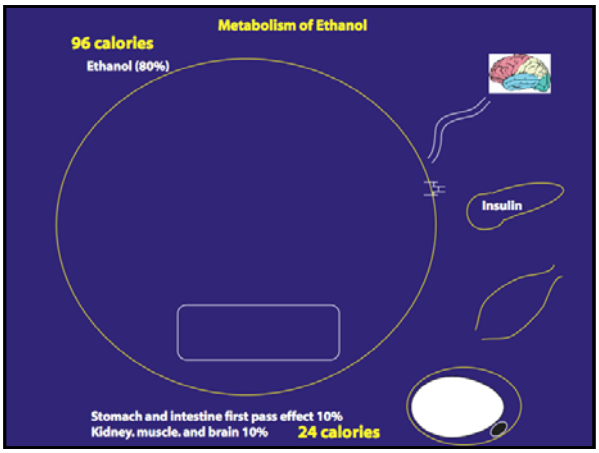
CH_3-CH_2-OH

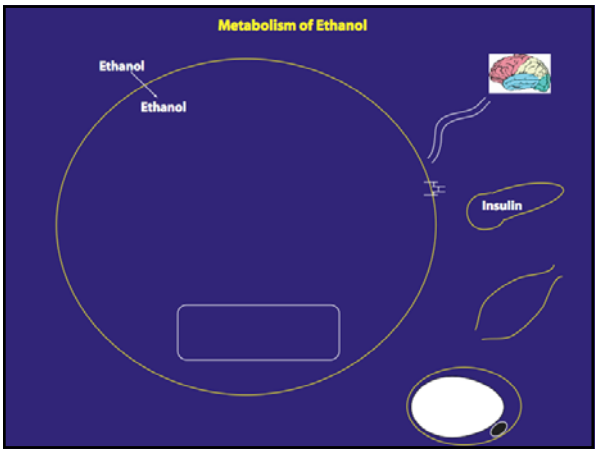
But ethanol is also a toxin

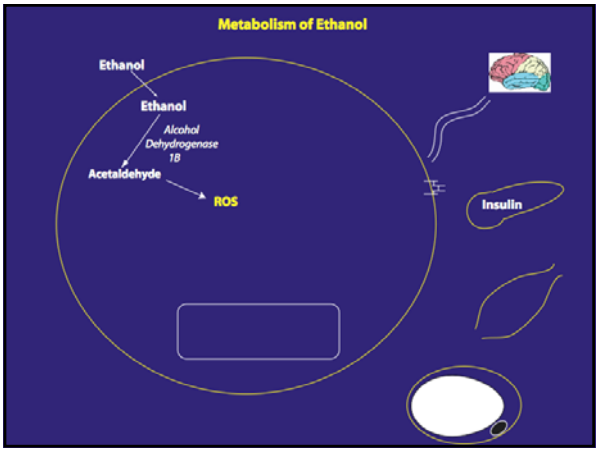
Acute ethanol exposure

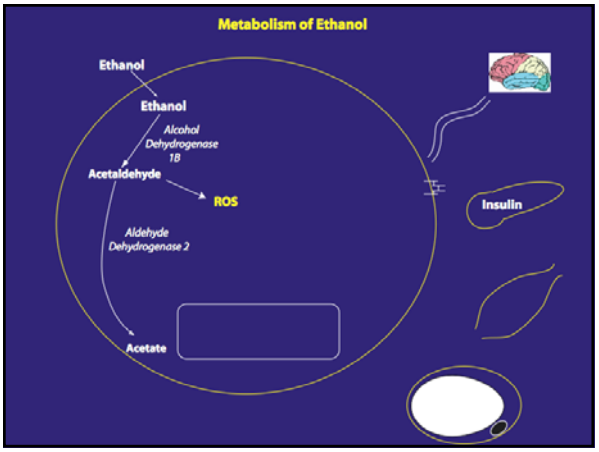
- CNS depression
- Vasodilatation, decreased BP
- Hypothermia
- Tachycardia
- Myocardial depression
- Variable pupillary responses
- Respiratory depression
- Diuresis
- Hypoglycemia
- Loss of fine motor control

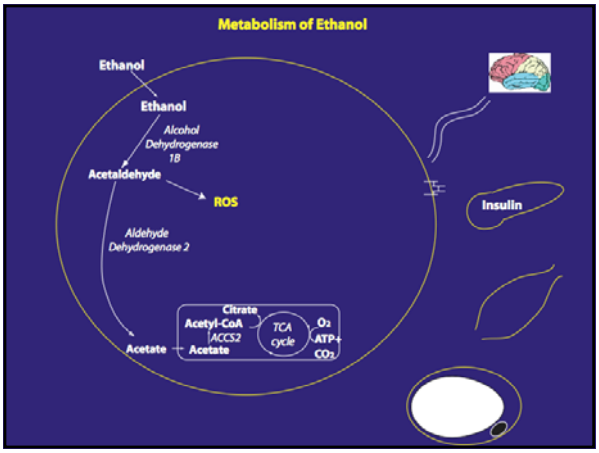
Acute fructose exposure

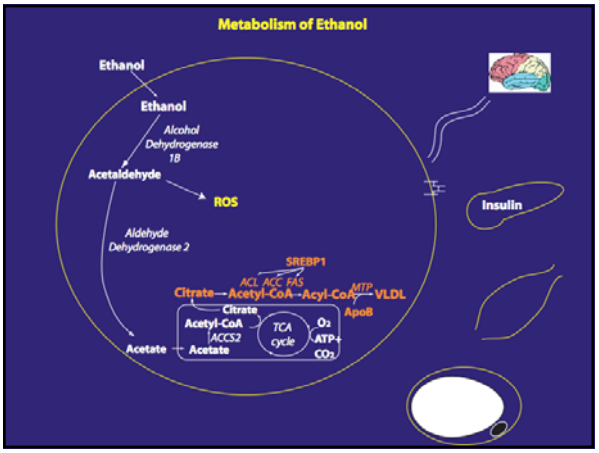

Metabolism of Ethanol
96 calories
Ethanol (80%)
Insulin
Stomach and intestine first pass effect 10%
Kidney, muscle, and brain 10%
24 calories

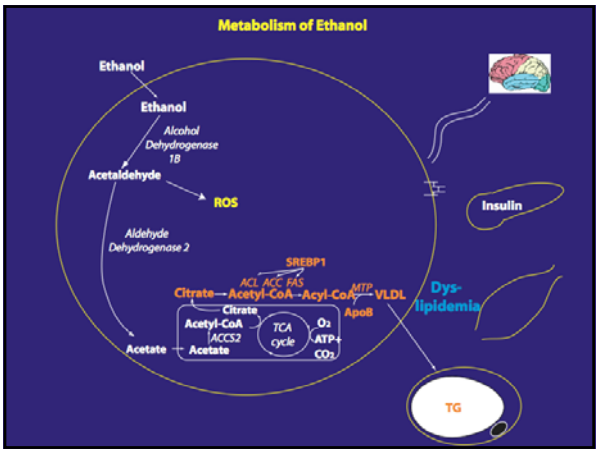

Metabolism of Ethanol
Ethanol
Ethanol
Insulin

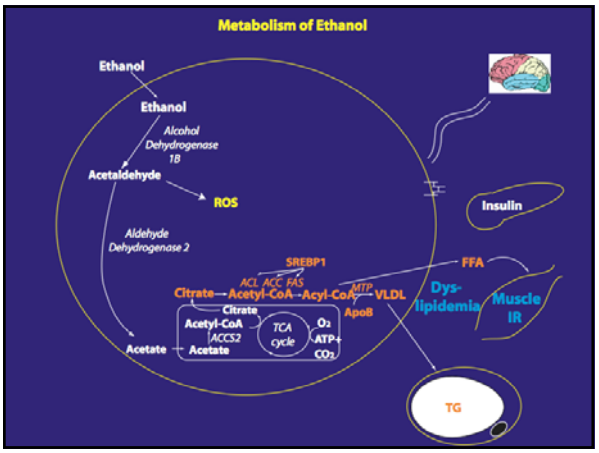

Metabolism of Ethanol
Ethanol
Ethanol
Alcohol Dehydrogenase 1B
Acetaldehyde
ROS
Insulin

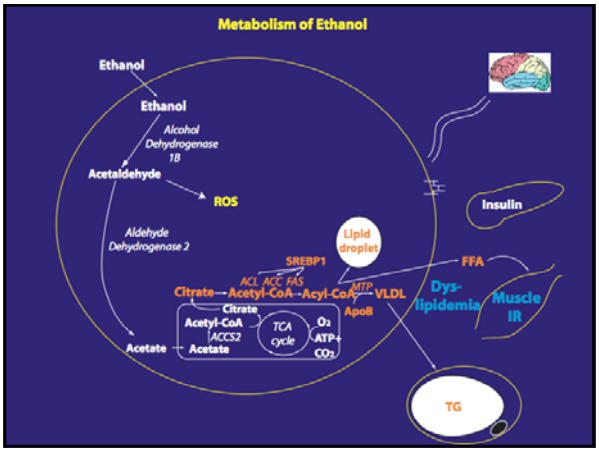

Metabolism of Ethanol
Ethanol
Ethanol
Alcohol Dehydrogenase 1B
Acetaldehyde
ROS
Aldehyde Dehydrogenase 2
Acetate
Insulin

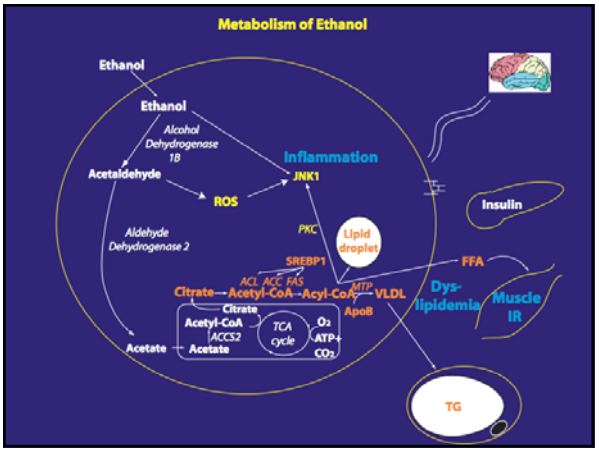

Metabolism of Ethanol
Ethanol
Ethanol
Alcohol Dehydrogenase 1B
Acetaldehyde
ROS
Aldehyde Dehydrogenase 2
Citrate
Acetyl-CoA
ACCS2
Acetate
Acetate
TCA cycle
O2
ATP+
CO2
Insulin

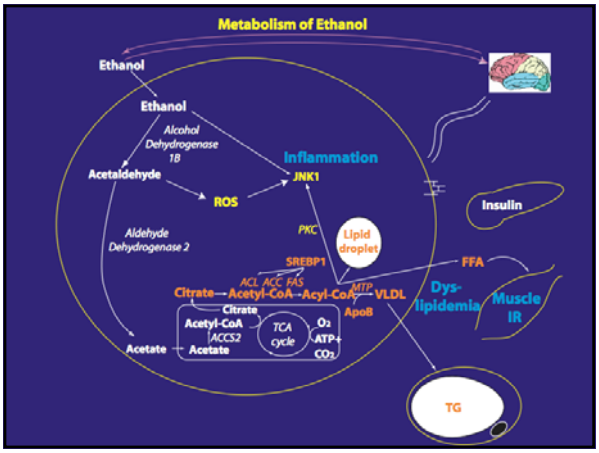

Metabolism of Ethanol
Ethanol
Ethanol
Alcohol Dehydrogenase 1B
Acetaldehyde
ROS
Aldehyde Dehydrogenase 2
SREBP1
ACL ACC FAS
Citrate
Acetyl-CoA
Acyl-CoA
MTP
VLDL
ApoB
Citrate
Acetyl-CoA
ACCS2
Acetate
Acetate
TCA cycle
O2
ATP+
CO2
Insulin

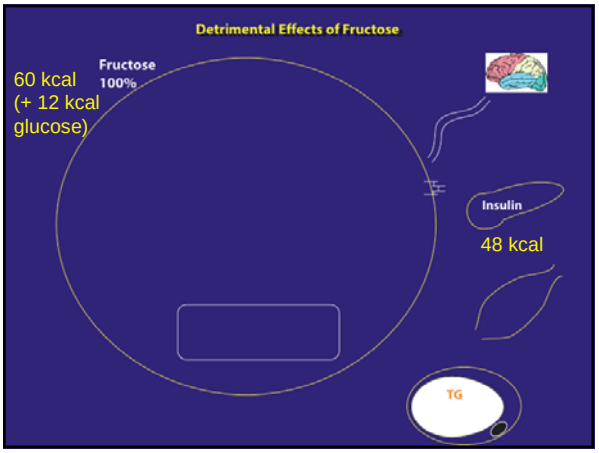

Metabolism of Ethanol
Ethanol
Ethanol
Alcohol Dehydrogenase 1B
Acetaldehyde
ROS
Aldehyde Dehydrogenase 2
Insulin
SREBP1
ACL ACC FAS
Citrate → Acetyl-CoA → Acyl-CoA
MTP
VLDL
ApoB
Dys-lipidemia
Citrate
Acetyl-CoA
ACCS2
Acetate
TCA cycle
O2
ATP+
CO2
TG

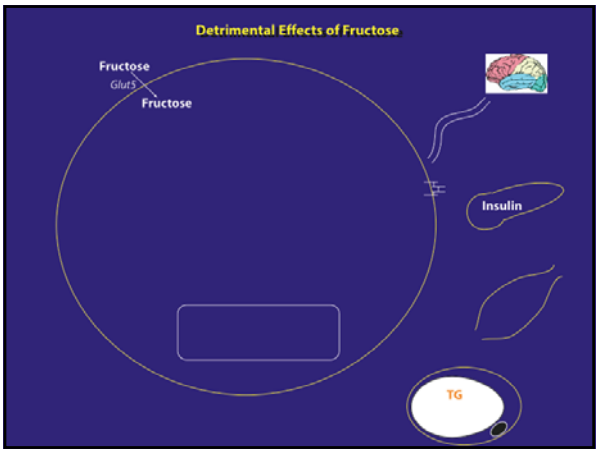

Metabolism of Ethanol
Ethanol
Ethanol
Alcohol Dehydrogenase 1B
Acetaldehyde
ROS
Aldehyde Dehydrogenase 2
Insulin
SREBP1
FFA
ACL ACC FAS
Citrate → Acetyl-CoA → Acyl-CoA
MTP
VLDL
ApoB
Dys-lipidemia
Muscle IR
Citrate
Acetyl-CoA
ACCS2
Acetate
TCA cycle
O2
ATP+
CO2
TG

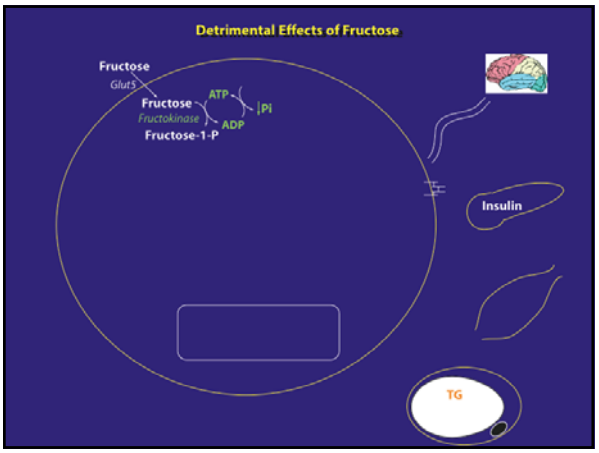

Metabolism of Ethanol
Ethanol
Ethanol
Alcohol Dehydrogenase 1B
Acetaldehyde
ROS
Aldehyde Dehydrogenase 2
Insulin
Lipid droplet
SREBP1
FFA
ACL ACC FAS
Citrate → Acetyl-CoA → Acyl-CoA
MTP
VLDL
ApoB
Dys-lipidemia
Muscle IR
Citrate
Acetyl-CoA
ACCS2
Acetate
TCA cycle
O2
ATP+
CO2
TG

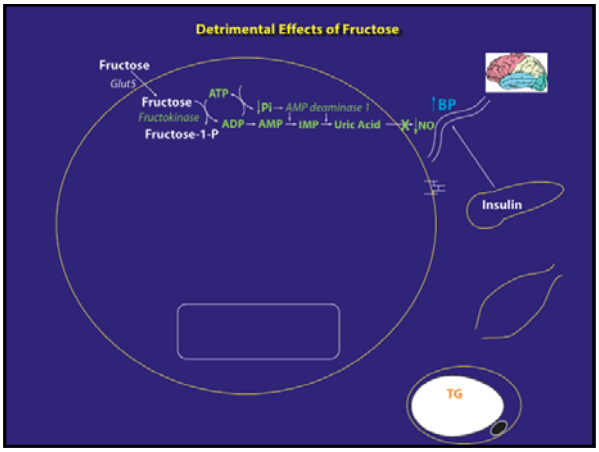

Metabolism of Ethanol
Ethanol
Ethanol
Alcohol Dehydrogenase 1B
Inflammation
JNK1
Acetaldehyde
ROS
PKC
Aldehyde Dehydrogenase 2
Lipid droplet
Insulin
SREBP1
FFA
ACL ACC FAS
Citrate → Acetyl-CoA → Acyl-CoA
MTP
VLDL
ApoB
Dys-lipidemia
Muscle IR
Citrate
Acetyl-CoA
ACCS2
Acetate
TCA cycle
O2
ATP+
CO2
TG

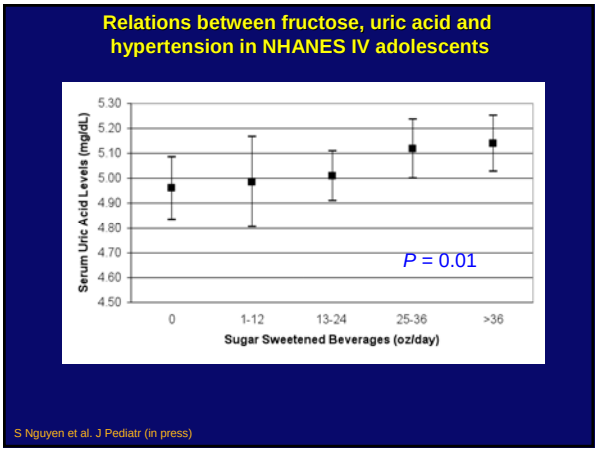

Metabolism of Ethanol
Ethanol
Ethanol
Alcohol Dehydrogenase 1B
Inflammation
JNK1
Acetaldehyde
ROS
PKC
Aldehyde Dehydrogenase 2
Lipid droplet
Insulin
SREBP1
FFA
ACL ACC FAS
Citrate → Acetyl-CoA → Acyl-CoA
MTP
VLDL
ApoB
Dys-lipidemia
Muscle IR
Citrate
Acetyl-CoA
ACCS2
Acetate
TCA cycle
O2
ATP+
CO2
TG

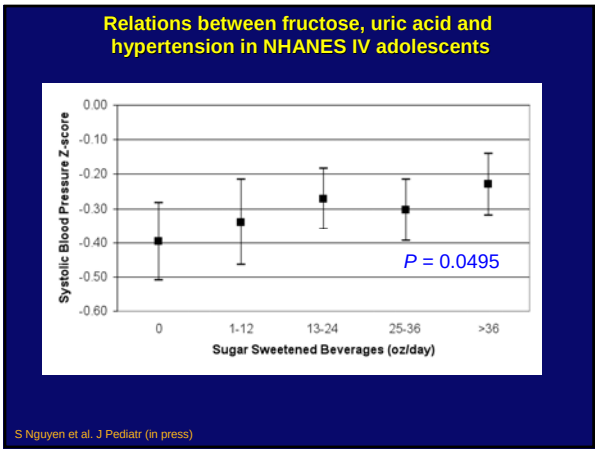

Detrimental Effects of Fructose
60 kcal
(+ 12 kcal glucose)
Fructose
100%
Insulin
48 kcal
TG

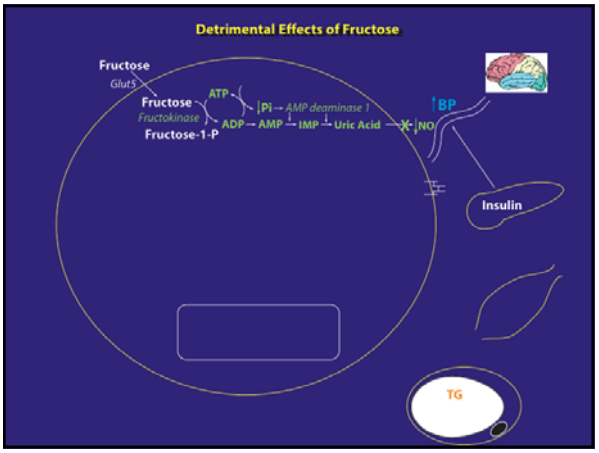

Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Insulin
TG

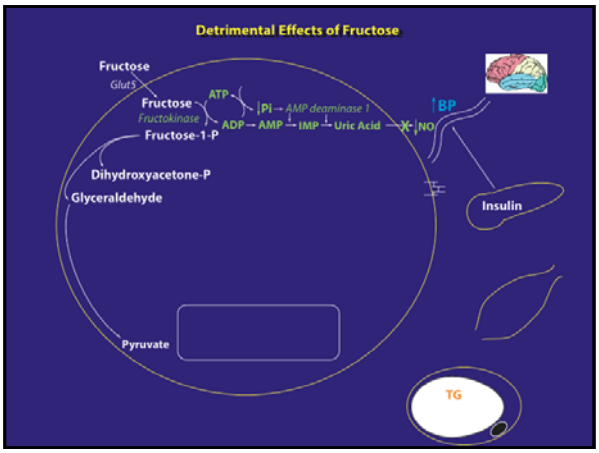

Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
Fructose-1-P
ATP
ADP
Pi
Insulin
TG

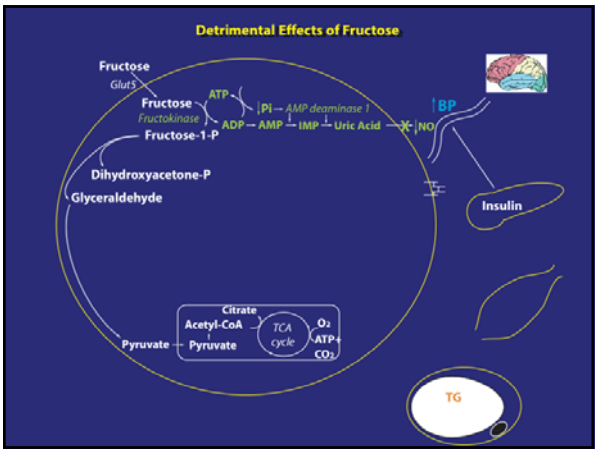

Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
Fructose-1-P
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Insulin
TG

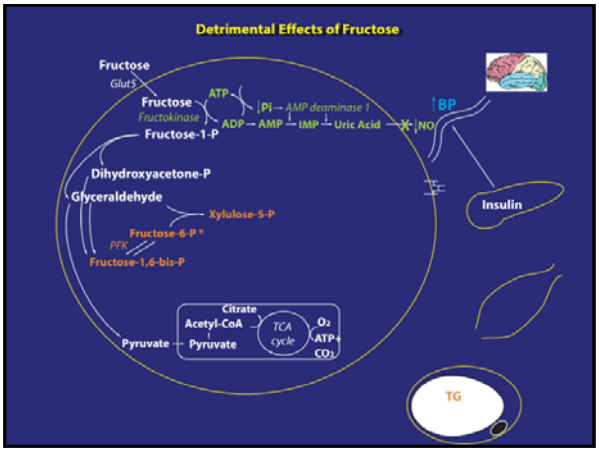

Relations between fructose, uric acid and hypertension in NHANES IV adolescents
Serum Uric Acid Levels (mg/dL)
5.30
5.20
5.10
5.00
4.90
4.80
4.70
4.60
4.50
P = 0.01
0
1-12
13-24
25-36
>36
Sugar Sweetened Beverages (oz/day)
S Nguyen et al. J Pediatr (in press)

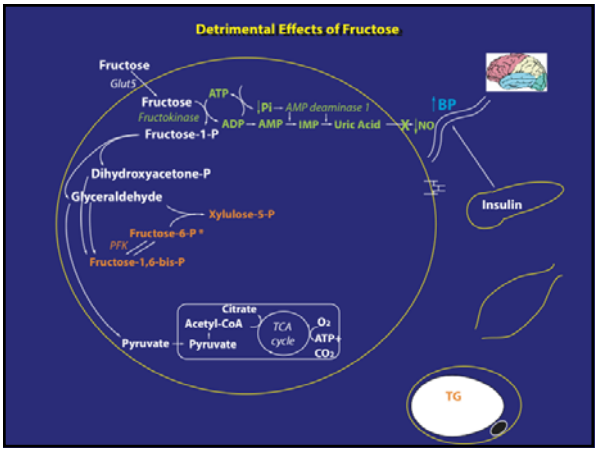

Relations between fructose, uric acid and hypertension in NHANES IV adolescents
Systolic Blood Pressure Z-score
0.00
-0.10
-0.20
-0.30
-0.40
-0.50
-0.60
P = 0.0495
0
1-12
13-24
25-36
>36
Sugar Sweetened Beverages (oz/day)
S Nguyen et al. J Pediatr (in press)

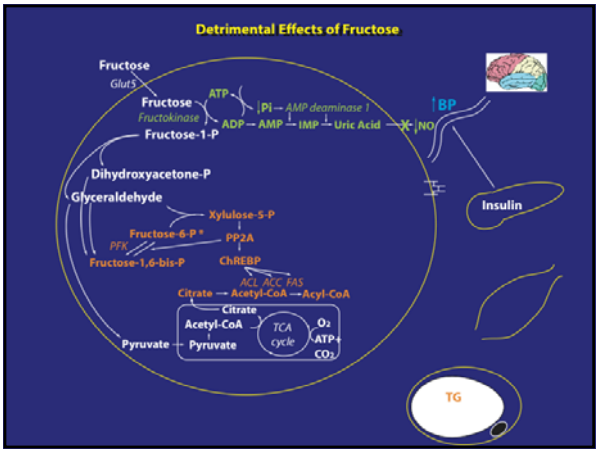

Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
Fructose-1-P
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Insulin
TG

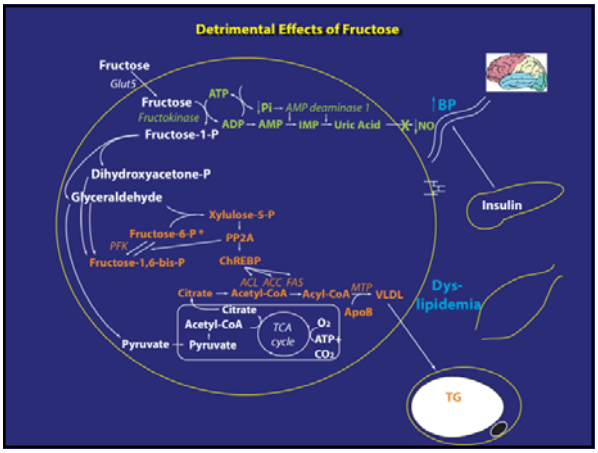

Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
Dihydroxyacetone-P
Glyceraldehyde
Insulin
Pyruvate
TG


Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
Dihydroxyacetone-P
Glyceraldehyde
Insulin
Citrate
Acetyl-CoA
TCA cycle
O2
ATP
CO2
Pyruvate
Pyruvate
TG

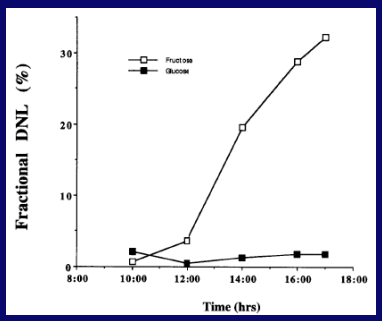

Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
Dihydroxyacetone-P
Glyceraldehyde
Xylulose-5-P
Fructose-6-P *
PFK
Fructose-1,6-bis-P
Insulin
Citrate
Acetyl-CoA
TCA cycle
O2
ATP
CO2
Pyruvate
Pyruvate
TG


Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
Dihydroxyacetone-P
Glyceraldehyde
Xylulose-5-P
Fructose-6-P *
PFK
Fructose-1,6-bis-P
Insulin
Citrate
Acetyl-CoA
TCA cycle
O2
ATP
CO2
Pyruvate
Pyruvate
TG


Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
Dihydroxyacetone-P
Glyceraldehyde
Xylulose-5-P
Fructose-6-P *
PFK
PP2A
Fructose-1,6-bis-P
ChREBP
ACL ACC FAS
Citrate
Acetyl-CoA
Acyl-CoA
Insulin
Citrate
Acetyl-CoA
TCA cycle
O2
ATP
CO2
Pyruvate
Pyruvate
TG

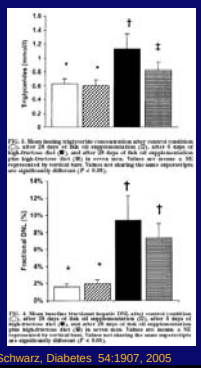

Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
Dihydroxyacetone-P
Glyceraldehyde
Xylulose-5-P
Fructose-6-P *
PFK
PP2A
Fructose-1,6-bis-P
ChREBP
ACL ACC FAS
Citrate
Acetyl-CoA
Acyl-CoA
MTP
VLDL
ApoB
Dys-
lipidemia
Insulin
Citrate
Acetyl-CoA
TCA cycle
O2
ATP
CO2
Pyruvate
Pyruvate
TG

Fructose increases de novo lipogenesis in normal adults



Hellerstein et al. Ann Rev Nutr 16:523, 1996

Fructose increases de novo lipogenesis, triglycerides and free fatty acids in normal adults



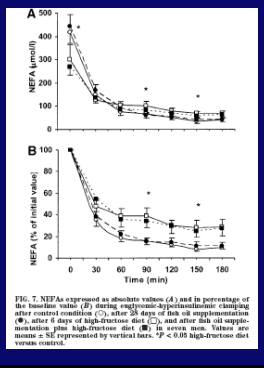
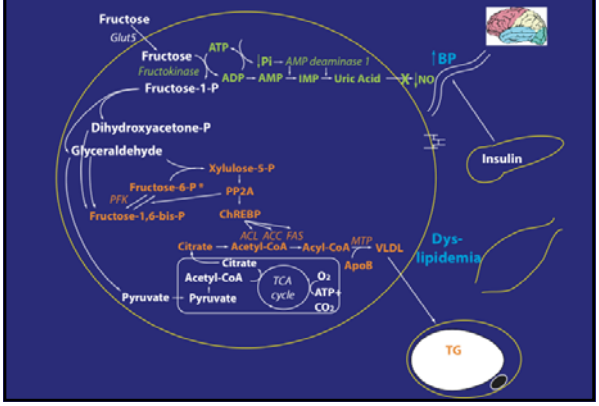


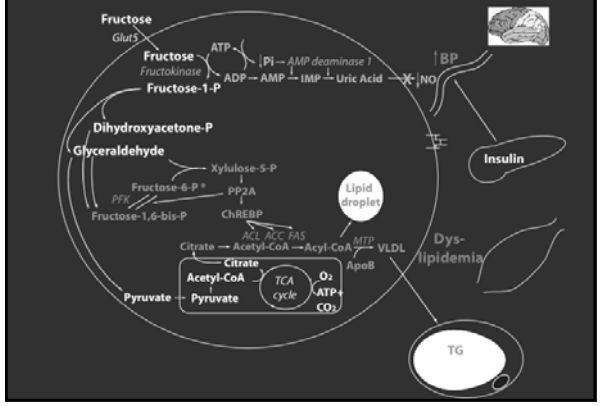
FIG. 7. NEFAs expressed as absolute values (A) and in percentage of the baseline value (B) during euglycemic-hyperinsulinemic clamping after control condition (○), after 28 days of fish oil supplementation (●), after 6 days of high-fructose diet (□), and after fish oil supplementation plus high-fructose diet (■) in seven men. Values are means ± SE represented by vertical bars. *$P < 0.05$ high-fructose diet versus control.

Faeh and Schwarz, Diabetes 54:1907, 2005

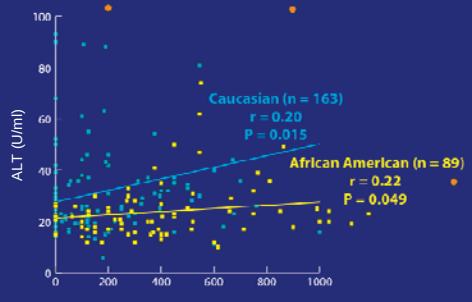
Detrimental Effects of Fructose



Detrimental Effects of Fructose



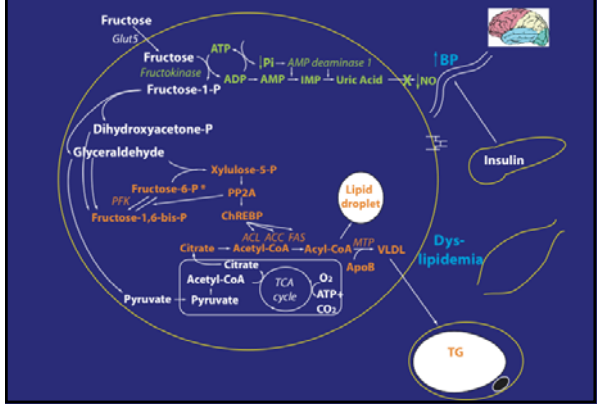
Associations between sugar sweetened beverage consumption and ALT in obese children

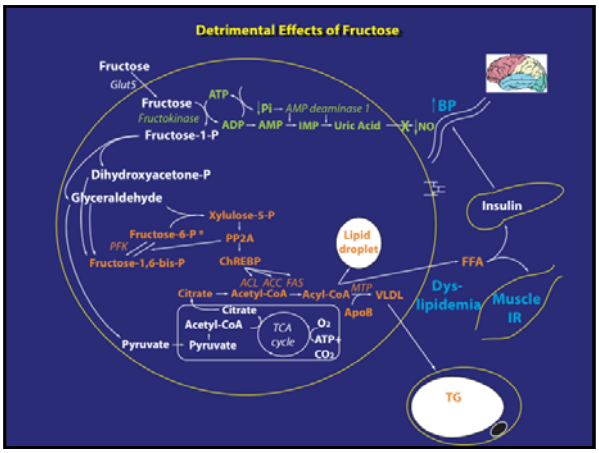


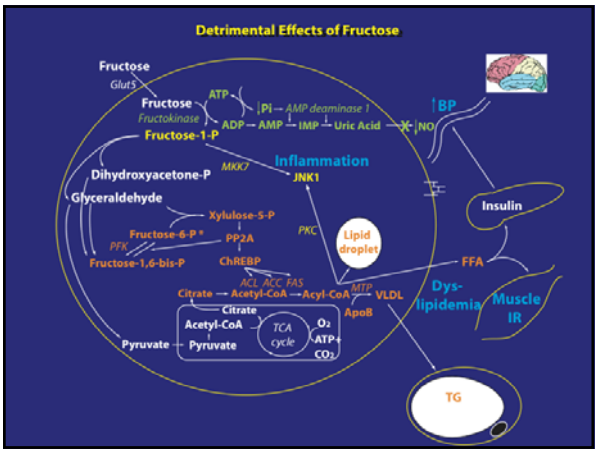
Sugar sweetened beverages (kcal/day)

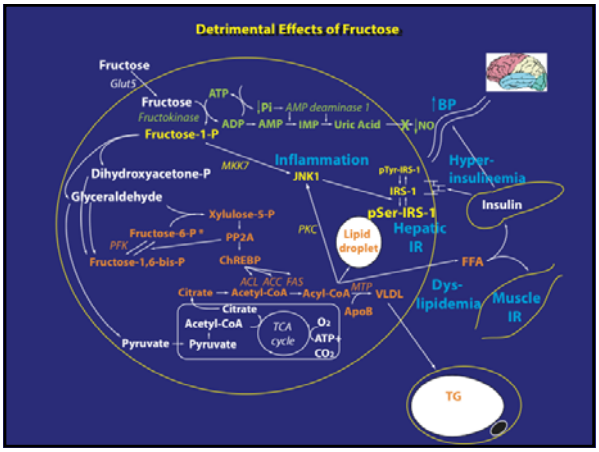
Valente et al. (unpublished)

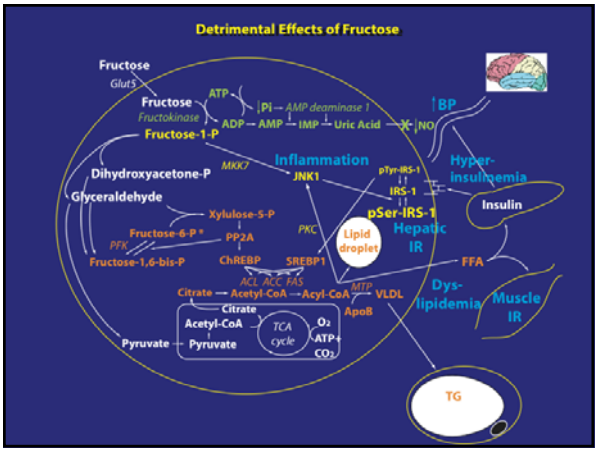
Detrimental Effects of Fructose

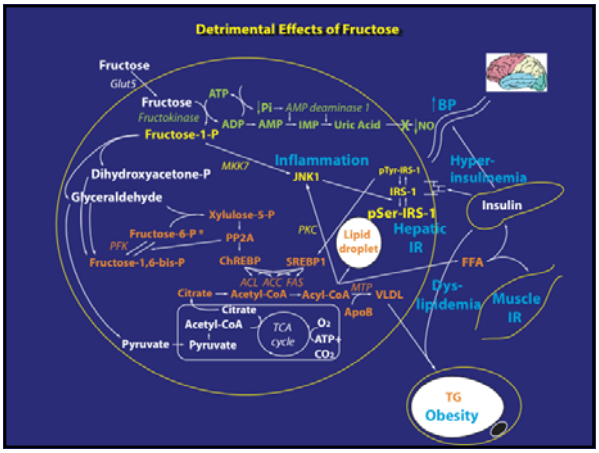



Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
Dihydroxyacetone-P
Glyceraldehyde
Xylulose-5-P
Fructose-6-P *
PFK
PP2A
Fructose-1,6-bis-P
ChREBP
Lipid droplet
Insulin
FFA
ACL ACC FAS
Citrate
Acetyl-CoA
Acyl-CoA
MTP
VLDL
ApoB
Dys-lipidemia
Muscle IR
Pyruvate
TCA cycle
O2
ATP
CO2
TG


Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
MKK7
Inflammation
JNK1
Dihydroxyacetone-P
Glyceraldehyde
Xylulose-5-P
Fructose-6-P *
PFK
PP2A
Fructose-1,6-bis-P
ChREBP
PKC
Lipid droplet
Insulin
FFA
ACL ACC FAS
Citrate
Acetyl-CoA
Acyl-CoA
MTP
VLDL
ApoB
Dys-lipidemia
Muscle IR
Pyruvate
TCA cycle
O2
ATP
CO2
TG


Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
MKK7
Inflammation
JNK1
pTyr-IRS-1
IRS-1
Hyper-insulinemia
Insulin
pSer-IRS-1
Hepatic IR
Dihydroxyacetone-P
Glyceraldehyde
Xylulose-5-P
Fructose-6-P *
PFK
PP2A
Fructose-1,6-bis-P
ChREBP
PKC
Lipid droplet
FFA
ACL ACC FAS
Citrate
Acetyl-CoA
Acyl-CoA
MTP
VLDL
ApoB
Dys-lipidemia
Muscle IR
Pyruvate
TCA cycle
O2
ATP
CO2
TG


Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
MKK7
Inflammation
JNK1
pTyr-IRS-1
IRS-1
Hyper-insulinemia
Insulin
pSer-IRS-1
Hepatic IR
Dihydroxyacetone-P
Glyceraldehyde
Xylulose-5-P
Fructose-6-P *
PFK
PP2A
Fructose-1,6-bis-P
ChREBP
SREBP1
PKC
Lipid droplet
FFA
ACL ACC FAS
Citrate
Acetyl-CoA
Acyl-CoA
MTP
VLDL
ApoB
Dys-lipidemia
Muscle IR
Pyruvate
TCA cycle
O2
ATP
CO2
TG


Detrimental Effects of Fructose
Fructose
Glut5
Fructose
Fructokinase
ATP
ADP
Pi
AMP deaminase 1
AMP
IMP
Uric Acid
NO
BP
Fructose-1-P
MKK7
Inflammation
JNK1
pTyr-IRS-1
IRS-1
Hyper-insulinemia
Insulin
pSer-IRS-1
Hepatic IR
Dihydroxyacetone-P
Glyceraldehyde
Xylulose-5-P
Fructose-6-P *
PFK
PP2A
Fructose-1,6-bis-P
ChREBP
SREBP1
PKC
Lipid droplet
FFA
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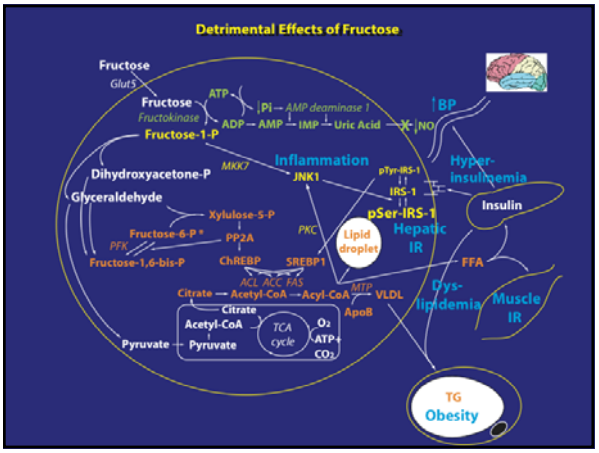
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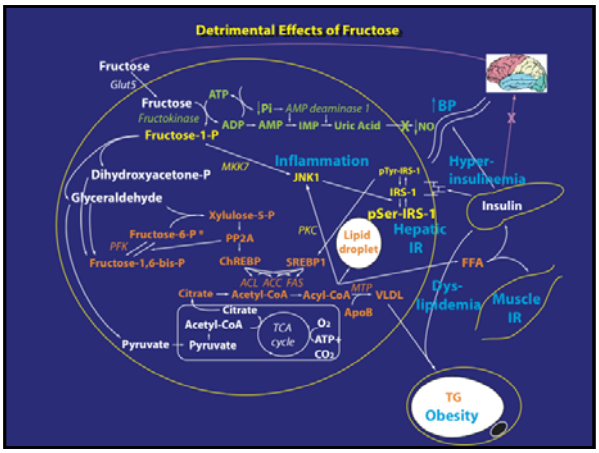

Why is exercise important in obesity?

Because it burns calories?

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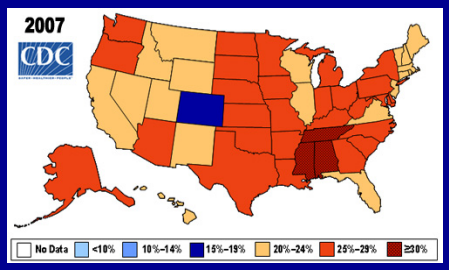
Because it burns calories?

Because it improves skeletal muscle insulin sensitivity

Because it reduces stress, and resultant cortisol release

Because it makes the TCA cycle run faster, and detoxifies fructose, improving hepatic insulin sensitivity

So what's with Colorado?



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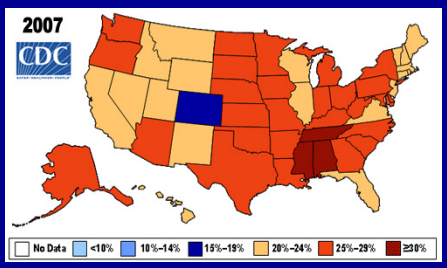

Four factors increase the hepatic TCA cycle

Cold
Altitude
Thyroid hormone
Exercise

Why is fiber important in obesity?

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"When G-d made the poison, he packaged it with the antidote."

Why is fiber important in obesity?

"When G-d made the poison, he packaged it with the antidote."

Fiber:

1. Reduces rate of intestinal carbohydrate absorption, reducing insulin response
2. Increases speed of transit of intestinal contents to ileum, to raise PYY_{3-36}, and induce satiety
3. Inhibits absorption of some free fatty acids to the colon, which are metabolized by colonic bacteria to short-chain fatty acids (SCFA), which suppress insulin

Chronic ethanol exposure

- Hematologic disorders
- Electrolyte abnormalities
- Hypertension
- Cardiac dilatation
- Cardiomyopathy
- Dyslipidemia
- Pancreatitis
- Malnutrition
- Obesity
- Hepatic dysfunction (ASH)
- Fetal alcohol syndrome
- Addiction

Chronic ethanol exposure	Chronic fructose exposure
• Hematologic disorders	
• Electrolyte abnormalities	
• Hypertension	• Hypertension
• Cardiac dilatation	
• Cardiomyopathy	• Myocardial infarction
• Dyslipidemia	• Dyslipidemia
• Pancreatitis	• Pancreatitis (2^o dyslipidemia)
• Malnutrition	
• Obesity	• Obesity
• Hepatic dysfunction (ASH)	• Hepatic dysfunction (NASH)
• Fetal alcohol syndrome	• Fetal insulin resistance
• Addiction	• Habituation, if not addiction

What's the difference?


Calories	150	150
Percent CHO	10.5% (sucrose)	3.6% (alcohol)
Calories from		
fructose	75 (4.1 kcal/gm)	
other carbs	75 (glucose)	60 (maltose)
alcohol		90 (7 kcal/gm)
1st pass GI metabolism	0%	10%
Calories reaching liver	**90**	**92**

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Fructose is a carbohydrate

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Fructose is metabolized like fat

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(corollary: a low fat diet isn't really low fat,
because the fructose/sucrose doubles as fat)

Fructose is a carbohydrate

Fructose is metabolized like fat

Fructose is also a toxin

Summary

- Fructose (sucrose vs. HFCS) consumption has increased in the past 30 years, coinciding with the obesity epidemic
- A calorie is not a calorie, and fructose is not glucose
- You are not what you eat, you are what you DO with what you eat
- Hepatic fructose metabolism leads to all the manifestations of the Metabolic Syndrome:
  - hypertension
  - de novo lipogenesis, dyslipidemia, and hepatic steatosis
  - inflammation
  - hepatic insulin resistance
  - obesity
  - hyperglycemia
  - CNS leptin resistance, promoting reward and continuous consumption
- Fructose is a dose-dependent chronic hepatotoxin (it's "alcohol without the buzz")

Childhood Obesity 2010:
The next generation in prevention and management

- SF Childhood Obesity Task Force
- Sponsored by SF Dept. of Public Health
- Training Day for Childhood Obesity
- Saturday, Feb. 27, 2010, 8AM-5PM
- Milton Marks Auditorium (Civic Center)
- State of the art
- Theory, and tools to use in practice
- CME offered

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- Lorene Ritchie, Ph.D.