

Nutrition Strategies For Surviving HIV & HAART*

Charlie Smigelski, RD

***Highly Active Antiretroviral Therapy**

Where Nutrition Impacts HIV Infection: practical

~~~~~ Assess Systems ~~~~~

Regular body function: keep
muscles, liver, intestines well.

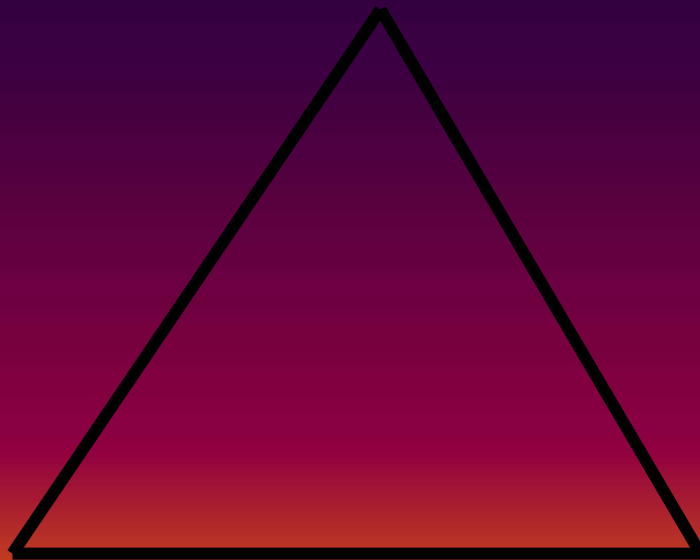
Cope with the hassel of medicines:
diarrhea, fatigue ...

Where Nutrition Impacts HIV Infection: practical

“I am eating up a storm,
but I still can't gain weight ...”

**1. What is the totally best
diet for health & HIV
Infection ?**

The Food Guide Pyramid ?



The Food Guide Pyramid ...

“the best diet advice you can
buy in Congress”

Walt Willett MD

Eat Drink and Be Healthy

**What is the healthiest diet
as we understand it ?.**

When in doubt,

eat Caveman Cuisine

Paleolithic Diet

Genes expect a blend of foods in the diet.

Balanced intake of $n 6$: $n 3$ fats.

Higher amounts of calcium & potassium

Many fruits & veges: vit C & vit E

Low in sodium.

Simopolous Evolutionary aspects of omega-3 fatty acids in the food supply. Prostaglandins Leukot Essent Fatty Acids 1999; 60(5-6):421-9

Paleolithic Diet

	Paleo	Now
Cholesterol	520mg	300mg
Protein	33%	12%
Fat	21%	30%
<i>n6:n3</i> ratio	1.4:1	20:1
Fiber	100gm	30gm
Simopolous:		

**You crawled out of your hut
this morning, and you ..**

**... clobbered a fish, grabbed
some mussels, and nibbled
nuts and seeds and berries, ...**

**... out of your hut this
morning, you ..**

... protein ... fruit ... nuts

.... add leaves and roots ...

(nice weather)

Caveman Breakfast

Fish/mussels

moldy fruit/berries

Walnuts

Sunflower seeds

leaves/shoots

Soy/Whey Protein

& banana smoothie

Walnuts

Sunflower seeds

(juice)

Caveman Lunch

Tuna White beans Romaine Olives
an orange and some yogurt

Cottage Cheese Humus Raw veges
red grapes and cashews

Caveperson Supper

Salmon Green Peas Carrots Pignolis

Chicken Sw. Potato Gr. beans Almonds

Pork loin Black beans Spinach Walnuts

Caveman Cuisine

Proteins

tuna

cod

salmon

sardines

blue fish

chicken

Veges

spinach

carrots

broccoli

kale

tomatoes

cabbage

Fruits

orange

banana

berries

melons

apricots

peaches

Starches

lentils

black beans

chick peas

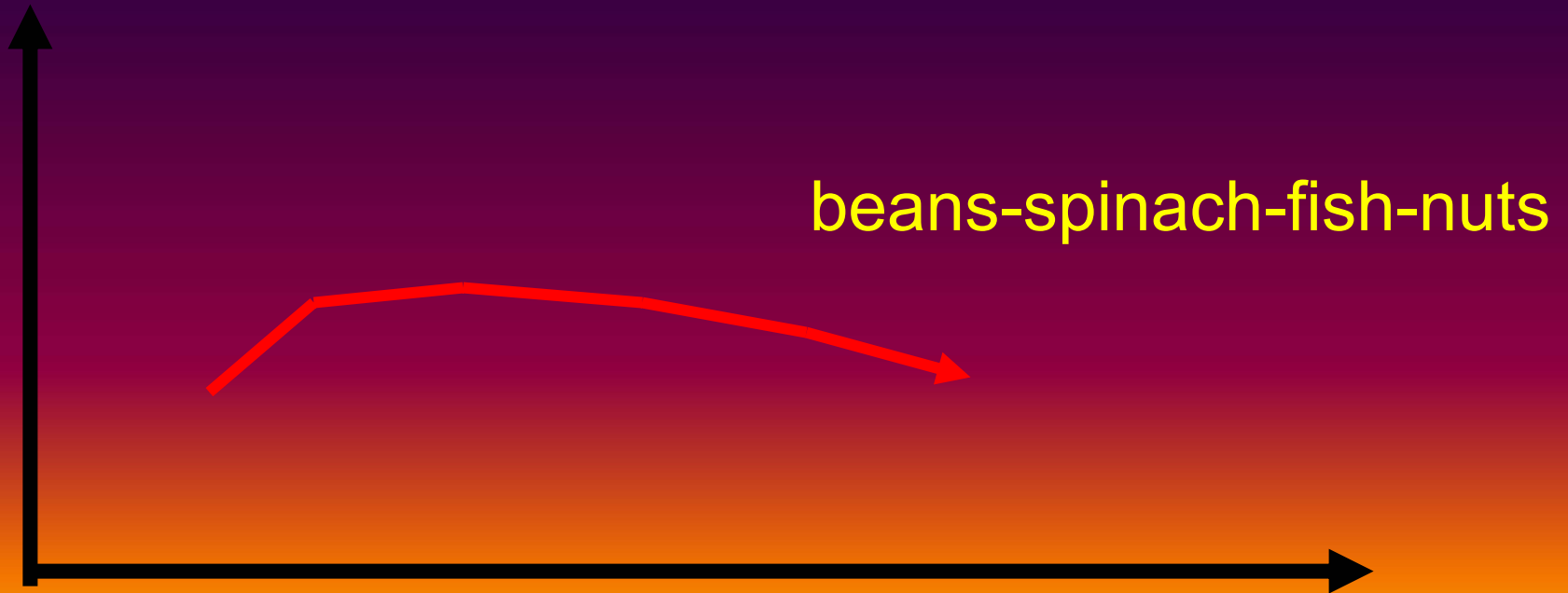
humus

peas

potato

Med-High Protein, Medium Fat, Medium Carb. Diet

modest blood sugar curves



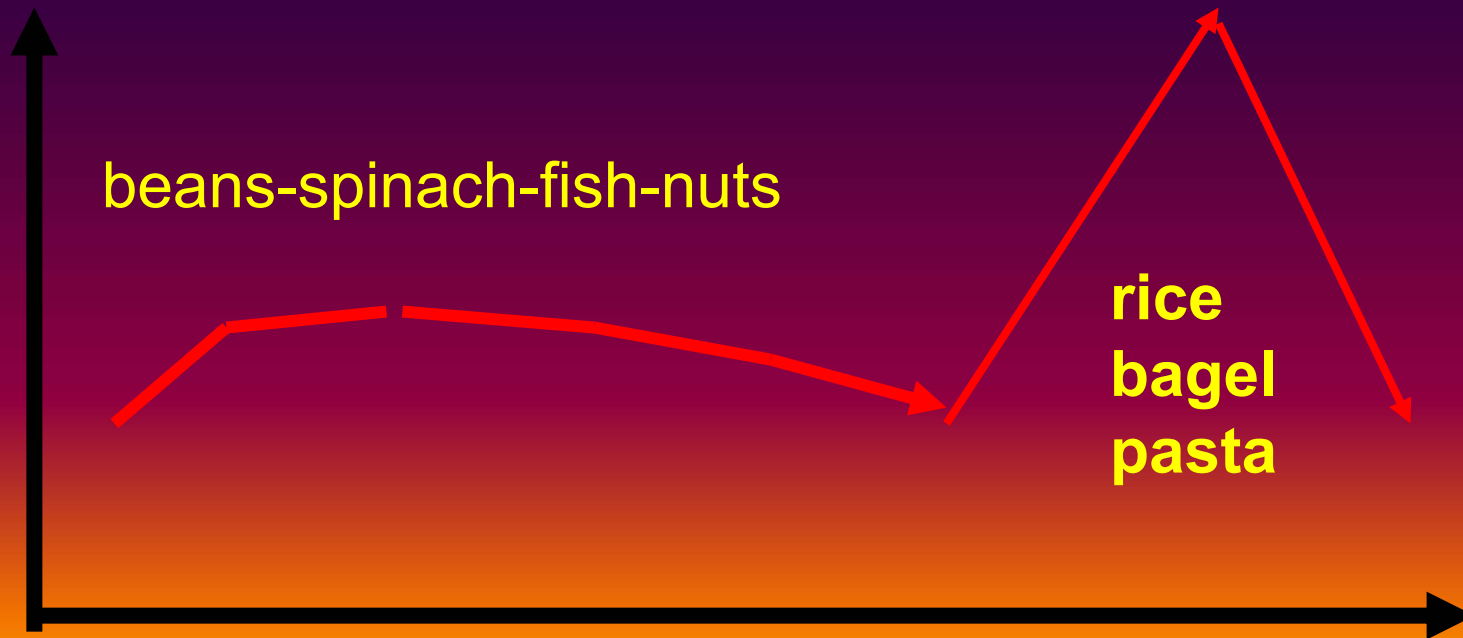
Caveman Cuisine

Grains are a modern invention

metabolisms under stress might not cope
with them well

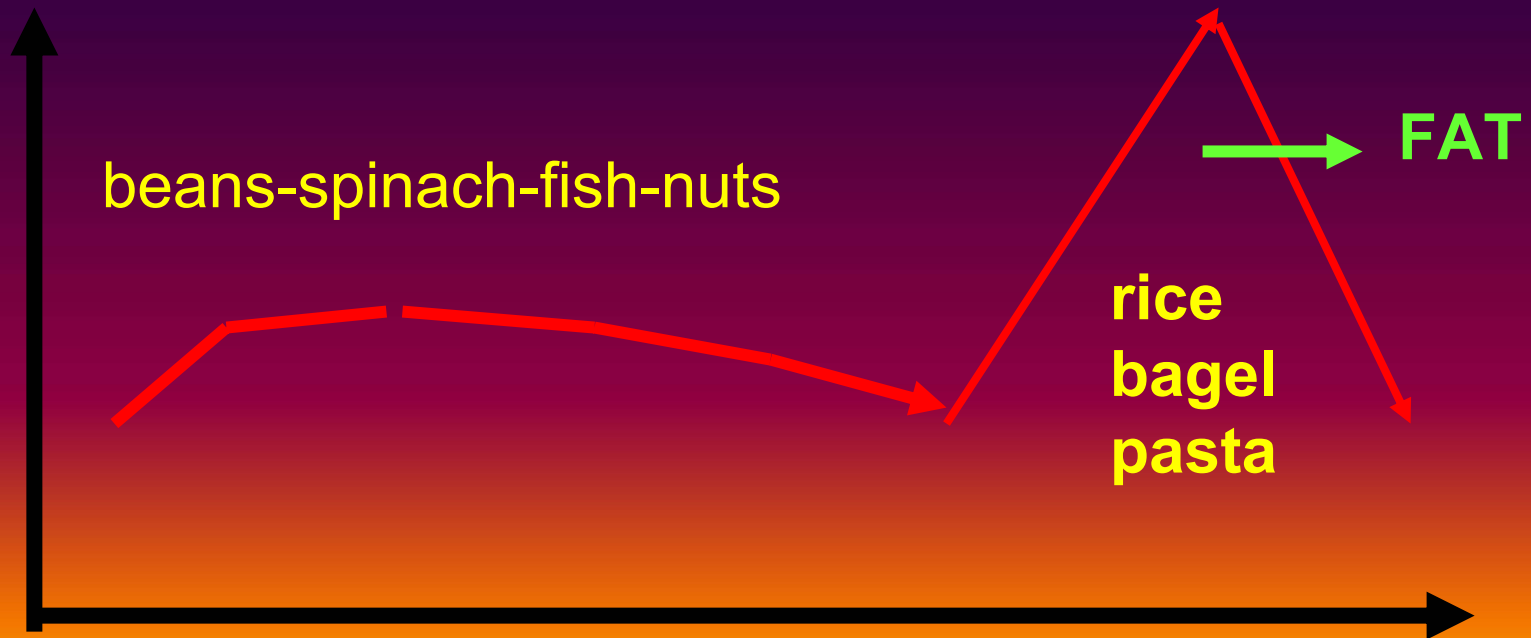
Cereal Toast Poptart Bagel or Cinnabun

& spiked & crashed your blood sugar



Cereal Toast Poptart Bagel or Cinnabun

& spiked & crashed your blood sugar



Where Nutrition Impacts HIV Infection: practical

“I am eating up a storm,
but I still can't gain weight ...”

Where Nutrition Impacts HIV Infection: practical

~~~~~ Assess Systems ~~~~~

Regular body function: keep
muscles, liver, intestines well.

Cope with the hassel of medicines:
diarrhea, fatigue ...

Abnormalities of Intestinal Architecture in HIV infection

crypt changes

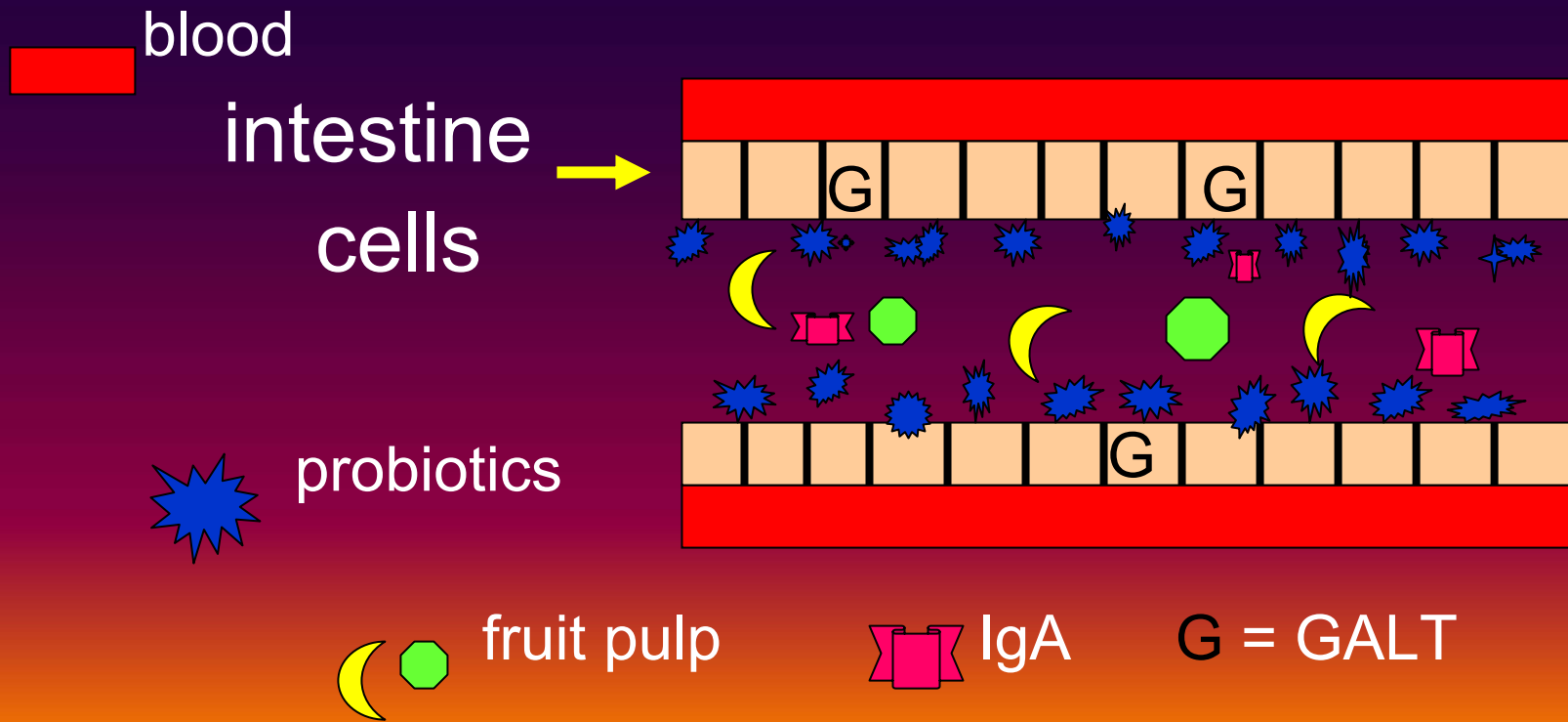
Am J Gastroenterol 2000 95(12):3482-89.

Diarrhea and Abnormalities of Gastrointestinal Function in a Cohort of Men and Women with HIV infection

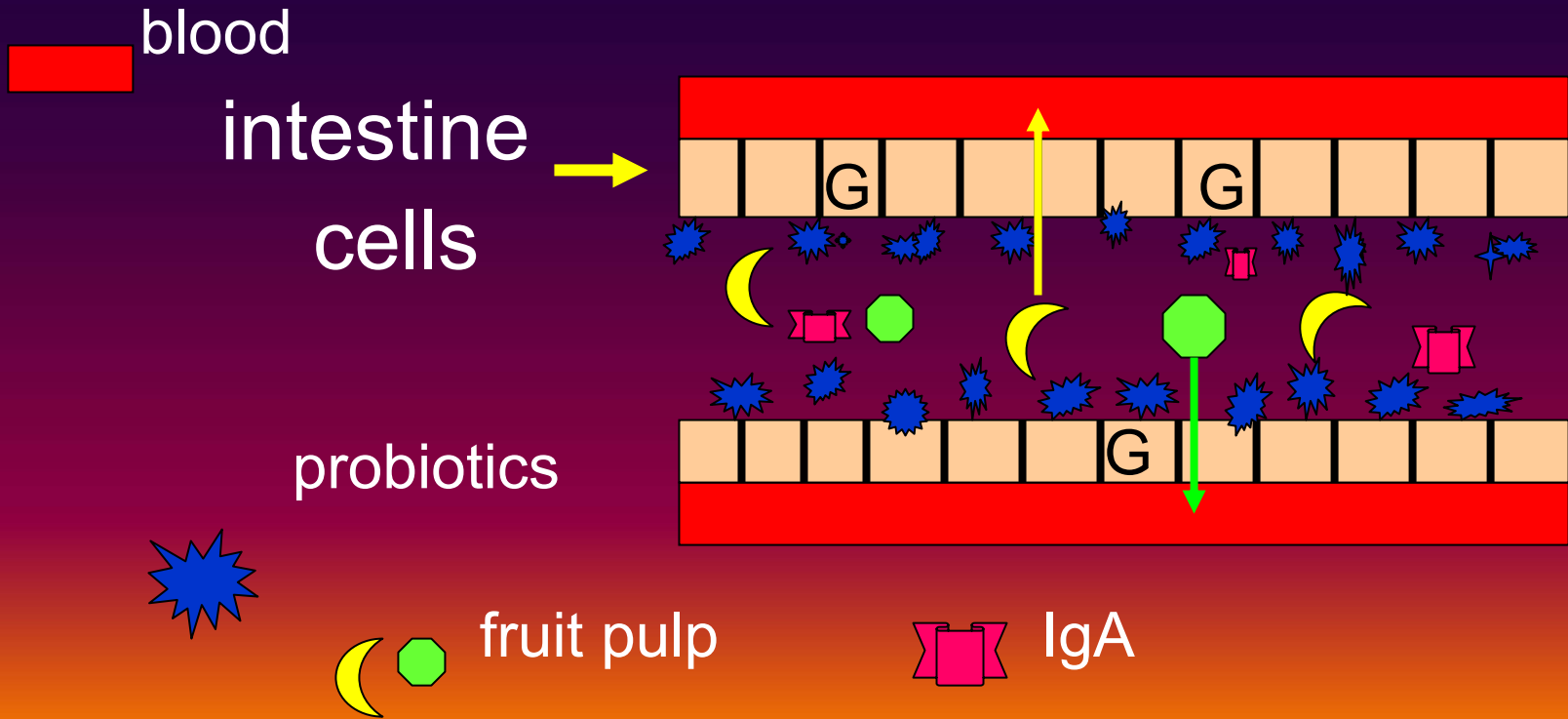
**80% of 671 people in NFHL study
47.7 low D-xylose absorption**

Gorbach Am J Gastroenterol 2000 95(12):3482-89.

Practical Nutrition: Think about Gut ecology ...



Leaky gut



Diarrhea: remedy

Muscles >> L-glutamine >> Gut Repair

Econutrition and Health Maintenance

A New Concept to Prevent GI Inflammation, Ulceration, and Sepsis

Luminal nutrition:	Small intestine 50%
	Large intestine 80%
Surface area:	Tennis court (250m ²)
Fuel source:	PROBIOTICS

(Bengmark Clinical Nutrition 1996, 15:1-10.)

Diarrhea: remedy

Glutamine powder 5-10 grams/day

Acidophilus pills 1-2 /day

Fiber pill: Fibercon or Citrucel

Imodium: 1/day

(less wheat: pasta, bagels, bread)

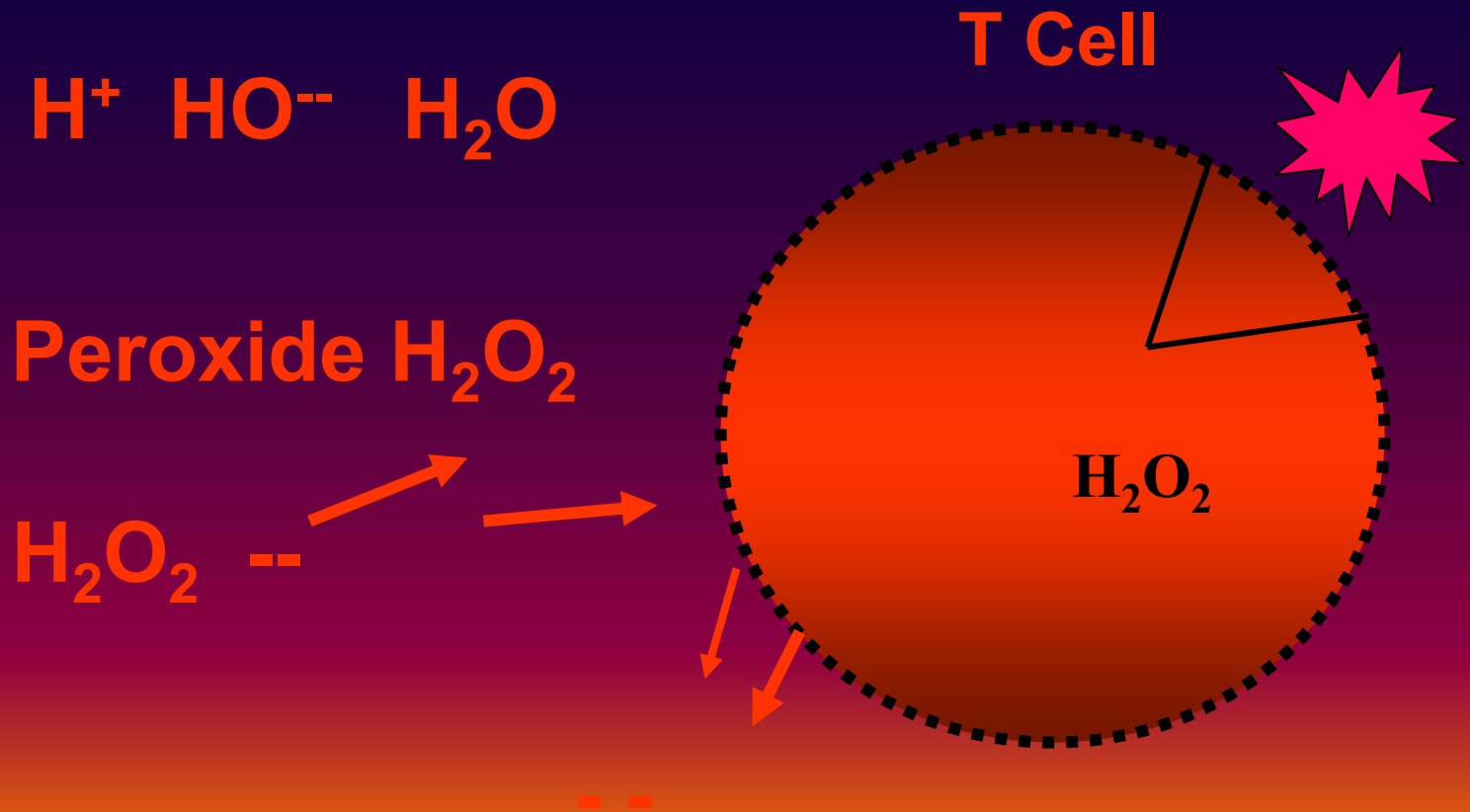
Where Nutrition Impacts HIV Infection: practical

“I am eating up a storm,
but I still can't gain weight ...”

Where Nutrients Impact HIV Infection: science

- Replace lost CD4 cells
- Reduce Oxidative Stress
- Reduce side effects of HAART

Oxidative Stress



Oxidative Stress

Random Oxygen Species ROS

Stray Electrons (Rust Corrosion)

Induce cytokines: IL₁ IL₂ (Th1)

IL₄ IL₅ IL₆ (Th2)

TNF_a **wasting**

NF_kB grow HIV

Massive Loss of Sulfur in HIV Infection

- Malorni W, Rivabene R, Lucia BM, et al. The role of oxidative imbalance in progression to AIDS: effect of the thiol supplier N-acetylcysteine. *AIDS Res Hum Retroviruses*. 1998;14:1589-1596.
- Walmsley SL, Winn LM, Harrison ML, Uetrecht JP, Wells PG. Oxidative stress and thiol depletion in plasma and peripheral blood lymphocytes from HIV-infected patients: toxicological and pathological implications. *AIDS*. 1997;11:1689-1697

Massive Loss of Sulfur in HIV Infection

**Sulfur loss in asx HIV+ people
10 grams a day
versus usual 3 /day**

HAART therapy not sulfur-sparing

W. Droge AIDS Res & Hum Retrovirol

2000 16:203-209.

Antioxidant Status

	<u>HIV-</u>	<u>HIV+ II</u>	<u>HIV+ IV</u>
tocopherol	31.1	26.8	18.6 yM/l
carotenoids	1.79	0.94	0.42 mg/l
zinc	12.3	10.47	0.87 yM./
selenium	0.96	0.93	0.59 yM/l
<u>GPx</u>	375	310	238 mU/ml

Favier et al. Chemico-Biol Interact 1994; 91:165-180.

HIV Mortality Associated With Selenium Deficiency

Nutritional Deficiency and Survival cox

Vit A	3.23 (1.1-9.48)
Vit B12	8.33 (1.69-41.1)
Zinc	2.91 (1.04-8.18)
Selenium	19.9 (5.52-71.9)

Baum MK, et al. JAIDS Hum Retrovirol 1997; **15**:370-374.

Glutamine Increases BCM

	Placebo	Gln/Antiox
Weight	71.7 _± 11.2	68.3 _± 8.3
gain	71.9 _± 11.2	70.6 _± 4.6
BCM	28.4 _± 6.0	26.9 _± 4.4
gain	28.8 _± 6.1	28.6 _± 4.6*
avg. gain		1.8 kg

Shabert/Wilmore Nutrition 1999 15:860-64. *p<0.001

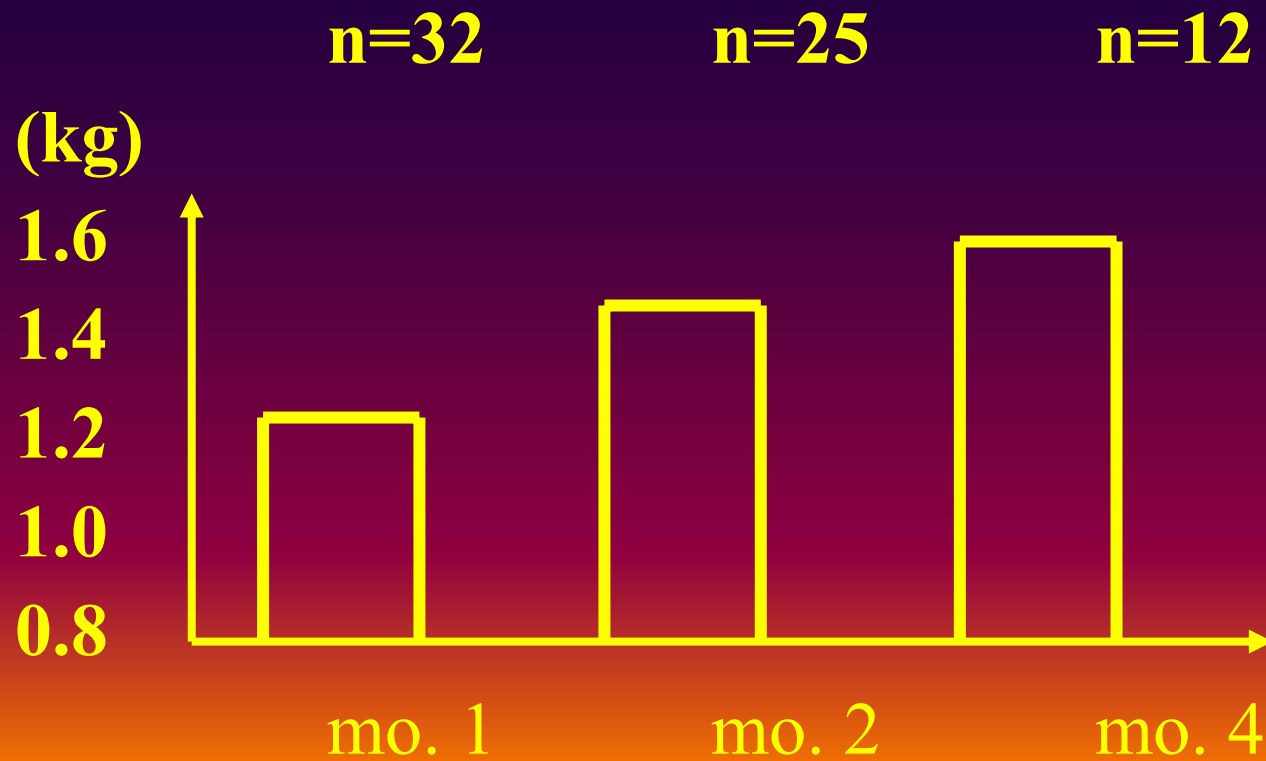
JM Kinney International Award Nutrition 2001 17:206-210.

Changes in Body Cell Mass

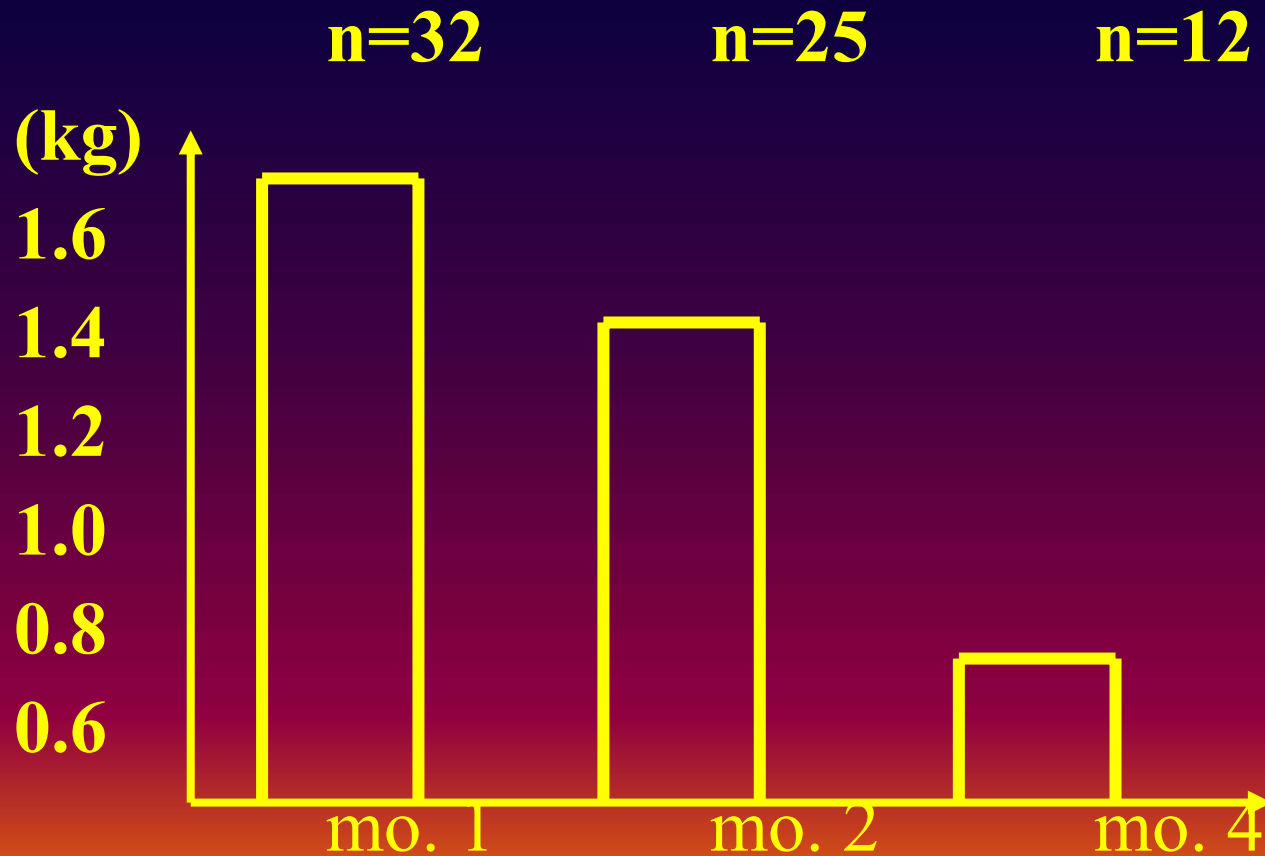
Oxandrolone 20 mg per day

A Fisher, M Abbaticola, Cannes, France 1997
2nd International Conference on Nutrition-HIV
Infection

Mean change BCM

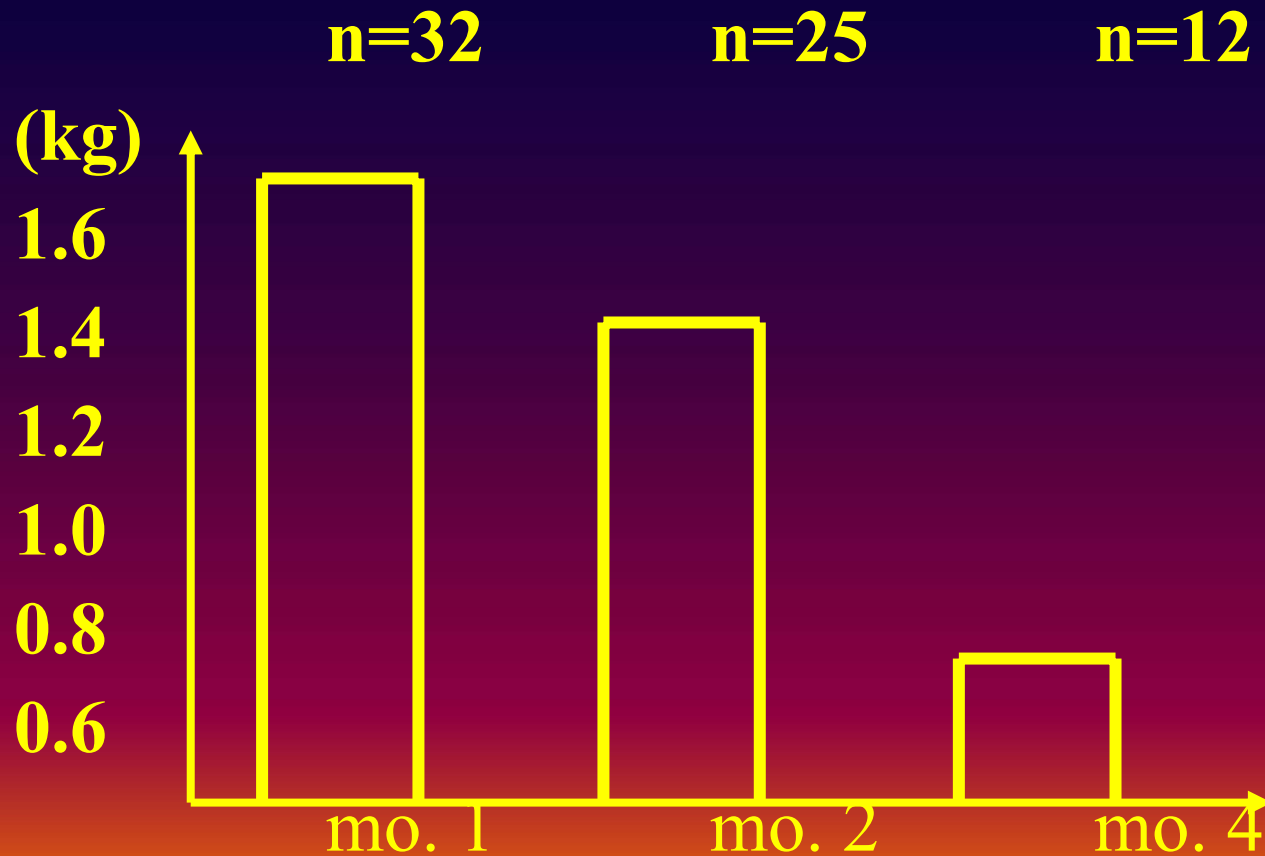


Kilogram change BCM



Fisher/Abbaticola, 1997

L-glutamine 20 grams/d for 1 mo.



Fisher/Abbaticola, 1997

Changes in Body Cell Mass

<u>Time</u>	<u>Weight</u>	<u>BCM</u>	<u>Fat</u>
Baseline	68.44	24.15	14.48
Month 1	72.63	25.89	16.22
Month 2	72.17	26.34	15.38
Month 4	74.04	27.02	15.96

Fisher/Abbaticola, 2nd International Conference on Nutrition-HIV Cannes 1997

Glutathione deficiency linked to impaired survival

Oral administration of NAC:

% survival 2-3 years (CD4<500)

NAC 60%

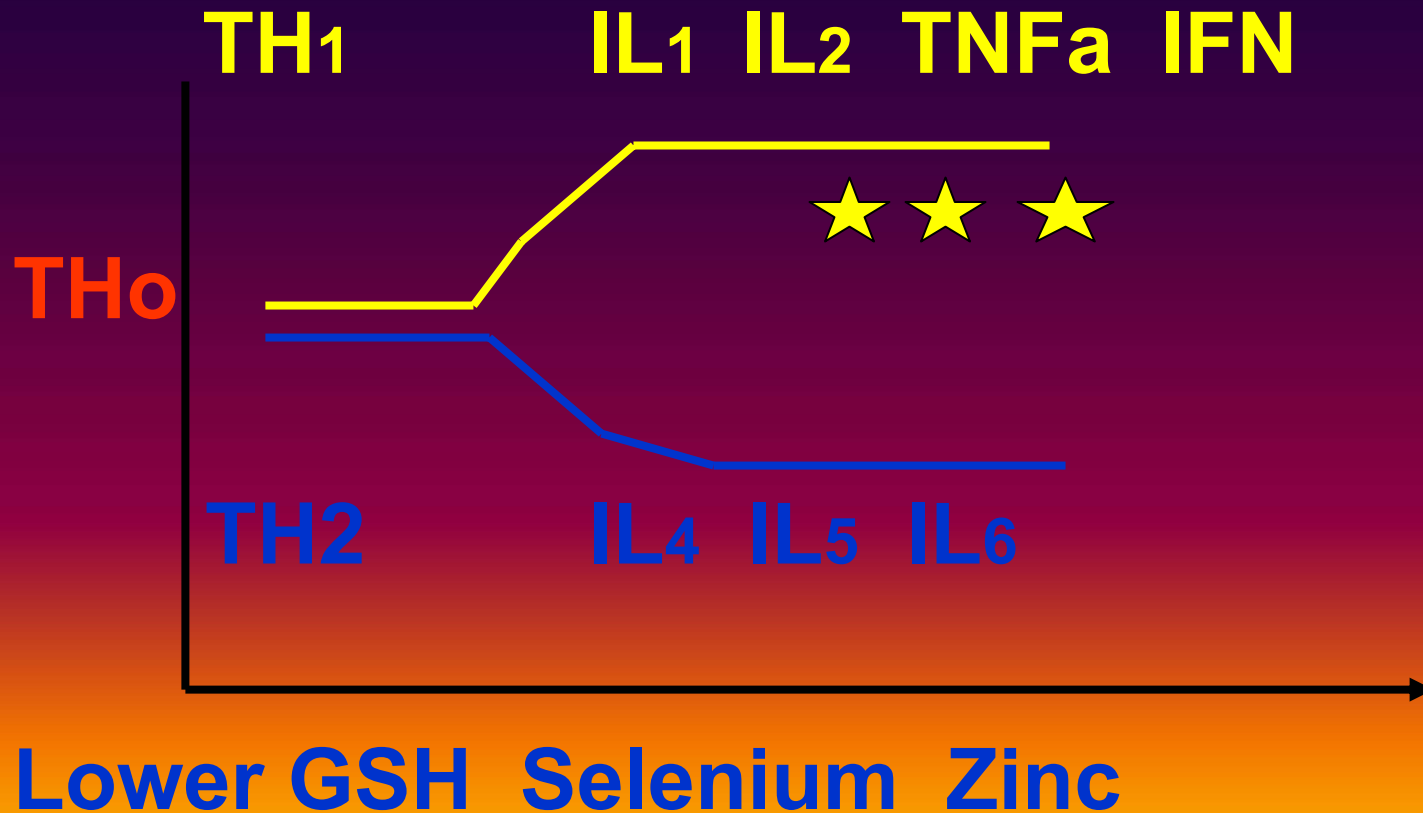
--- 40%

GSH deficiency is due to a shortage of
cysteine availability

Herzenberg Proc Nat Acad Sci USA 1997 94:1967

Jahoor Am J Physiol 1999 276: E205-211.

IMMUNOLOGY



Cellular Dysmetabolism: The Dark Side of HIV-1 Infection

Apoptosis	High
Oxidant Stress	Yes
Mitochondrial Toxicity	Yes
Liver enzymes	Elevated
*Cytokines	Th1->Th2

Famularo, Moretti, Marcellini, Alesse, DeSimone.

J Clin Lab Immunol 1996;48:123-32.

Increased serum IFNa in HIV associated lipodystrophy synd.

Three parameters: IFN-a, insulin, and cortisol:DHEA ratio aggregated to form the best model for hyperlipidemia associated with anti-retroviral therapy.

Eur J Clin Investig. 2002; 32(1):43-50 Christeff, Melchior, et al.

Increased serum IFNa in HIV associated lipodystrophy synd.

	<u>20 HIV-</u>	<u>15 LD-</u>	<u>27 LD+</u>
IFNa (p<0002)	3.85	9.80 (p<.0002)	18.4
IL ₆	2.4	7.05 (p<.0008)	7.4
TNFa	4.0	5.65 (p<0.04)	8.1 (NS)
Cortisol:DHEA		16.5	35.0 (p<.001)

Eur J Clin Investig. 2002; 32(1):43-50 Christeff, Melchior, et al.

Effects Of IFN- α On Metabolism

1. Hepatic lipogenesis & TG pdn.
2. Decreases adipose LPL activity
3. Increases adipose lipolysis

Cellular Dysmetabolism: The Dark Side of HIV-1 Infection

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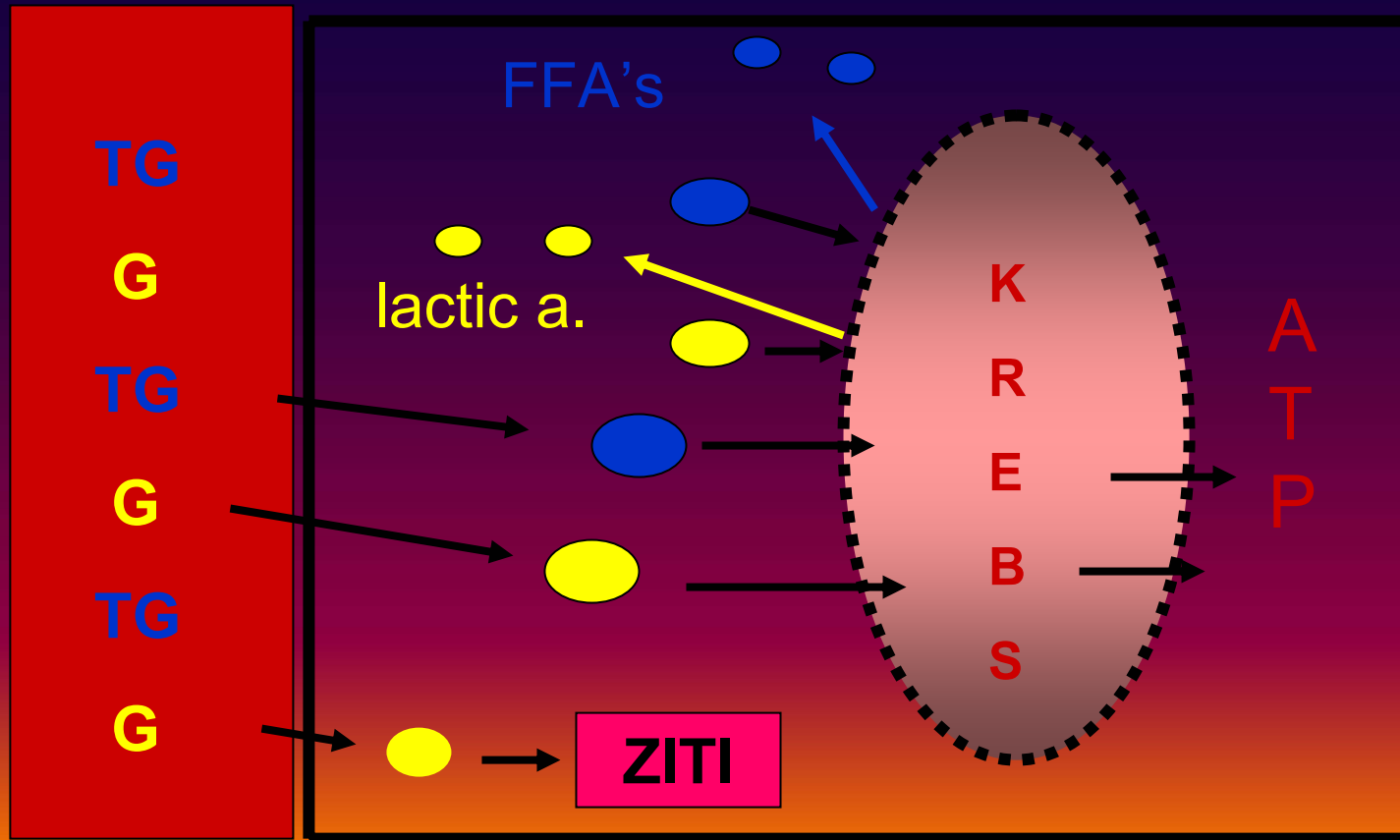
J Clin Lab Immunol 1996;48:123-32.

Zidovudine-induced experimental myopathy: dual mechanisms of mitochondrial damage.

A short-term mechanism that affects the respiratory chain; and a long-term mechanism that alters *mtDNA*, altering protein synthesis.

J Neurol Sci 1999; 166(2): 131-40.

Making Energy: ATP



AZT: Oxidative Damage to Muscle Mitochondria

Urinary excretion of 8-oxo-dG:

(8-oxo-7, 8-dihydro-2' deoxyguanosine)

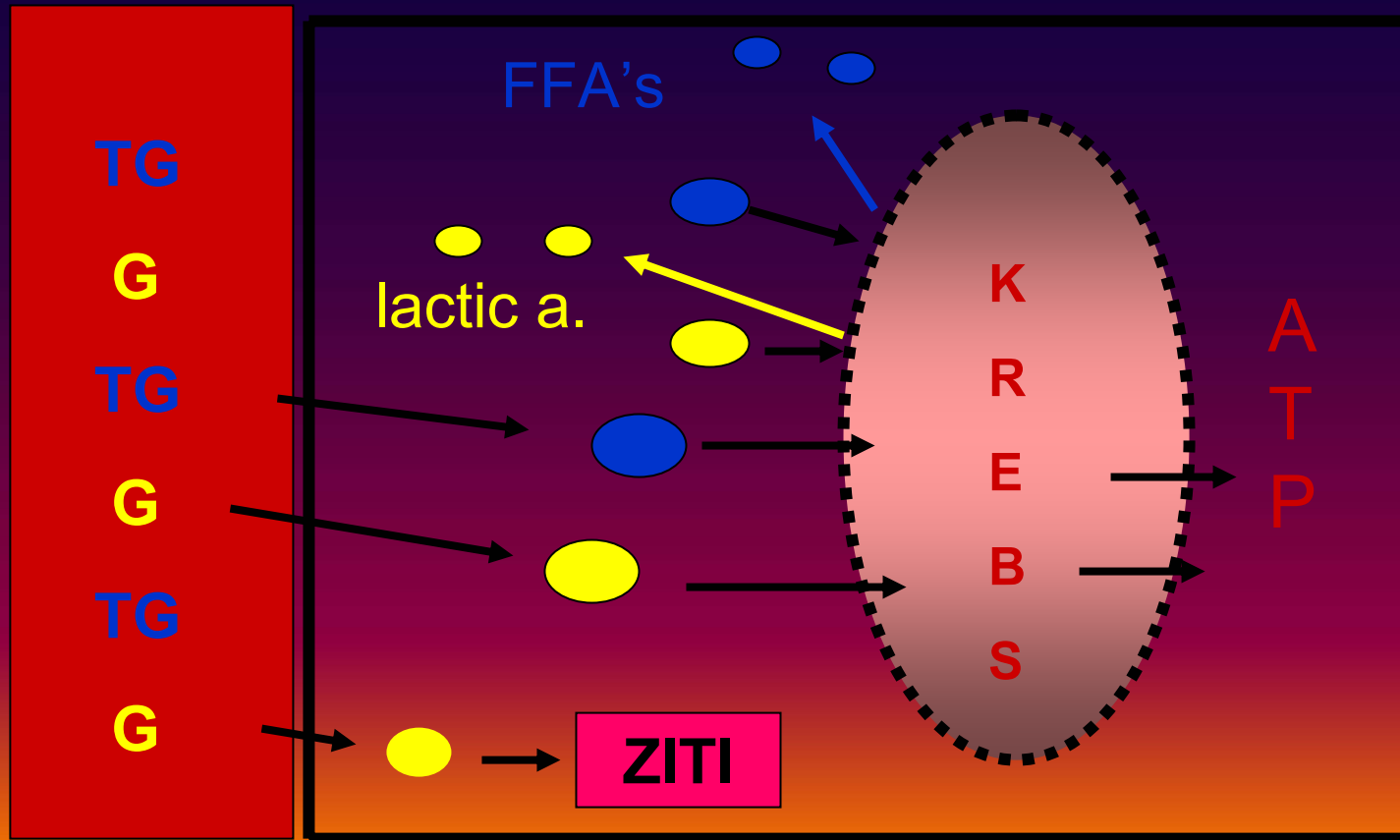
355_±100 pmol/kg/d (HIV/AZT)

182_±29 (HIV alone)

110_±79 with Tx vit C & vit E

J Clin Invest 1998; 102(1): 4-9.

Making Energy: ATP



Lipodystrophy Syndrome

Modest elev. Cholesterol

Very high TG's

Low HDL

Dry itchy skin

Abdominal fat - paunch

Thinning arms/legs

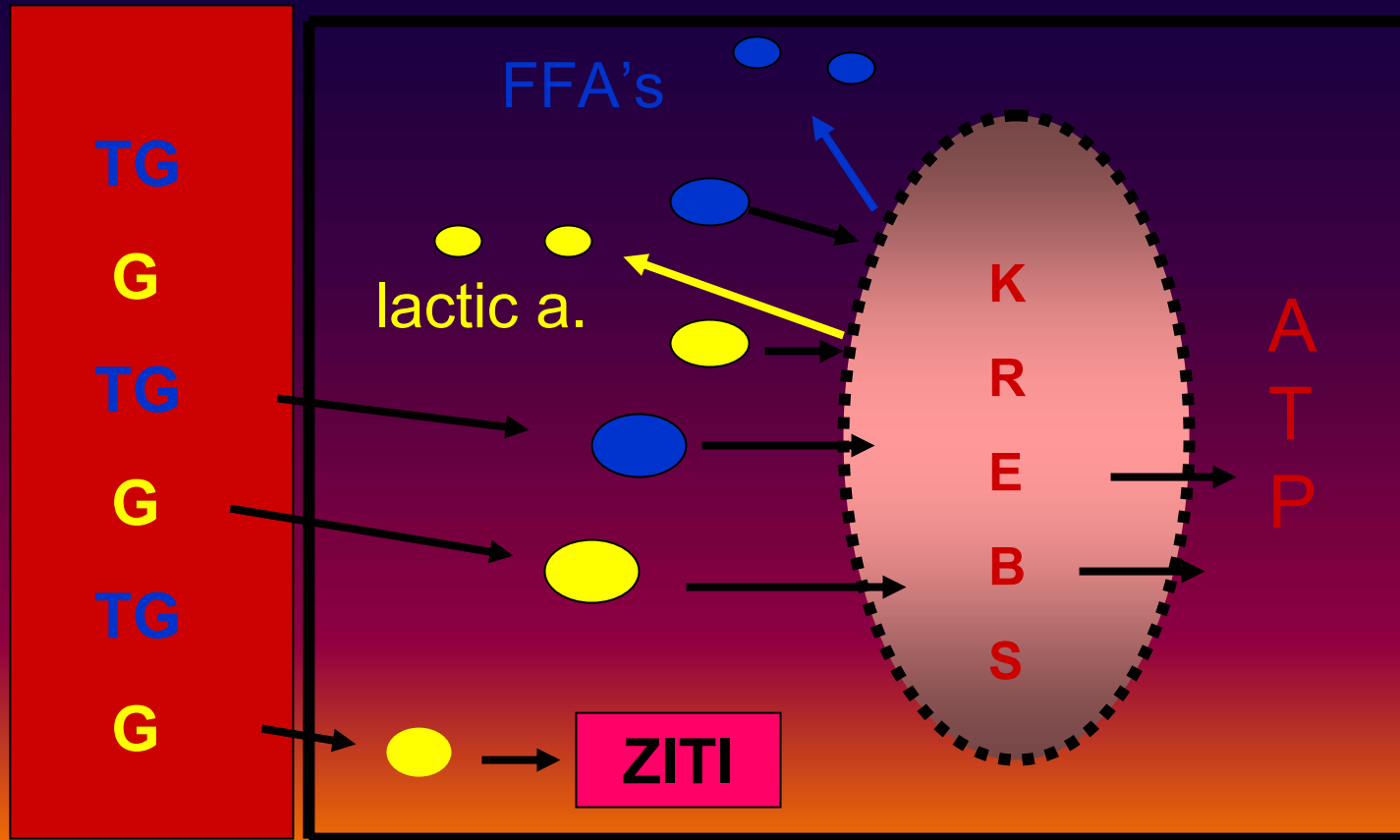
Breast swelling

Buffalo hump

Effects Of IFN- α On Metabolism

1. Hepatic lipogenesis & TG pdn.
2. Decreases adipose LPL activity
3. Increases adipose lipolysis

Making Energy: ATP



Carnitine Intervention

3 g a day L-carnitine to Rx elev. TG's

16 ppl 7.2 yrs Rx CD4 218_±210

Day 1	5.67 _± 1.78	(nml 0.5-2.0)
1 mo	3.43 _± 1.27	(39%)
2 mo	4.08 _± 1.93	(28%)
last	3.70 _± 2.50	(35%)

Loignon/Toma AIDS 2001 15(9):1194-5

Insulin Resistance

plasma \uparrow FFA's impairs insulin signal.

muscle \uparrow FFA's impairs insulin signal (Glucosamine path)

TNF_α reduces Insulin receptor phosphorylation

Fasting Hyperinsulinemia in HIV+ Men: relationship to body composition, gonadal function and PI use

Hadigan, CorcoranGrinspoon

J Clin Endocrinol Metab 2000 85(1):35-41

Fasting insulin levels:

50 HIV+ men

16.6 ± 1.8

20 Framingham

10.4 ± 0.8 microU/mL

Higher Insulin correlated with:

**lower free testosterone & LBM,
and higher BMI**

Fatty acids, triglycerides and syndromes of insulin resistance

“strong relationships between the fatty acid composition of structural membrane lipids and insulin action.... Good insulin action is associated with increased proportion of *n*-3 fatty acids”

Prostaglandins Leucotrienes and Ess Fatty Acids 1997; 57:379-85

Improved Insulin Sensitivity and Body Fat Distribution in HIV-Infected Patients Treated With Rosiglitazone: A Pilot Study

Gelato, Mynarisk et al

... JAIDS 2002; 31:163-170.

Improved Sensitivity ?!?

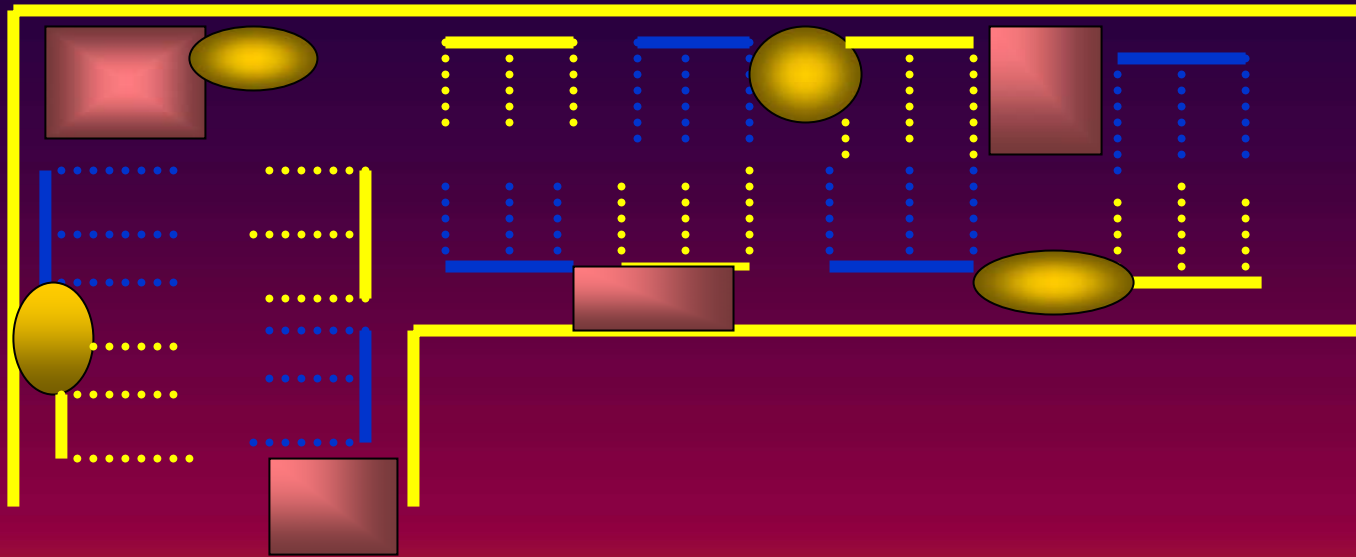
<u>Pt.</u>	<u>Age</u>	<u>CD4</u>	<u>BMI</u>	<u>TG₁</u>	<u>TG₂</u>
1.	52F	700	28.3	437	258
2.	39M	650	28.0	315	193
3.	30F	952	20.4	375	404
4.	49F	341	34.6	174	410
5.	39F	370	20.4	244	187

Improved Insulin Sensitivity

<u>Pt.</u>	<u>Age</u>	<u>CD4</u>	<u>BMI</u>	<u>TG₁</u>	<u>TG₂</u>
6.	33F	637	20.8	669	1548
7.	44M	303	31.8	148	342
8.	39M	39	26.3	356	645
9.	(fine print) ??	Dropped d/t liver problems)			
	TG's	5 of 8 rose	133	\pm 118	$p = .30$

You are what you eat

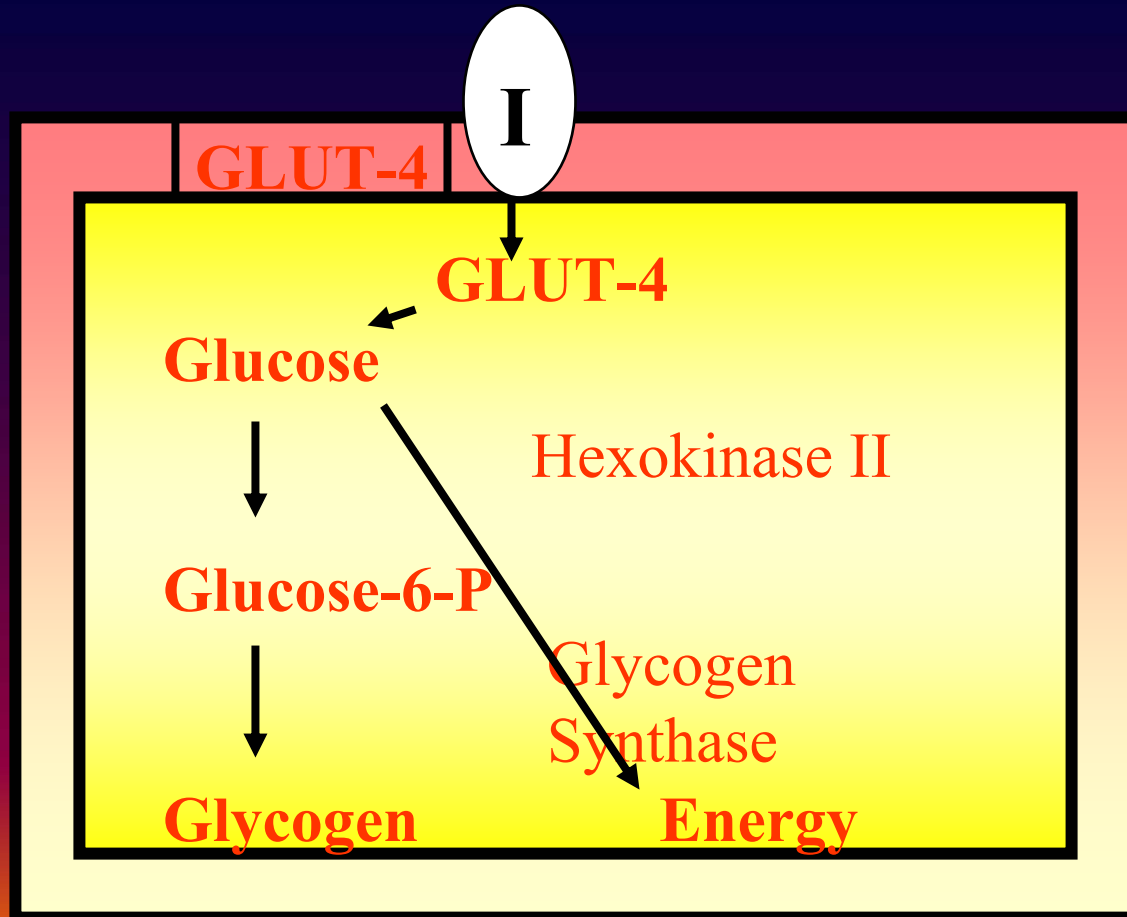
Lipid Bi-layer and dietary fats



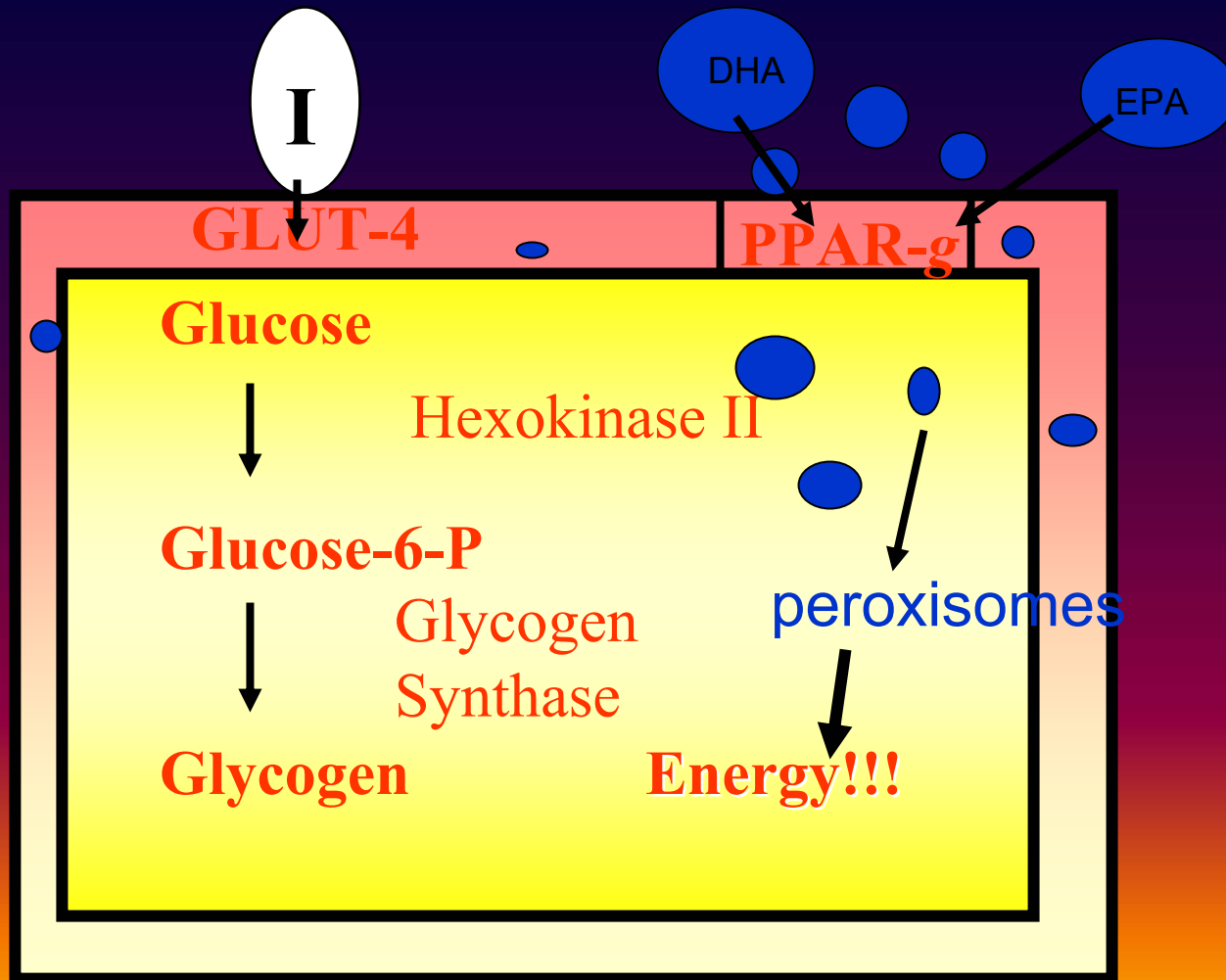
Rehabilitation: *N* 3 fats restore ideal function

www.omegabrite.com Andrew Stoll

Insulin Action on Cells



EPA/DHA Action on Cells



Essential Fatty Acid Deficiency

Plasma Lipids changes:

- + free fatty acids**
- ++ triglyceride**
- + total cholesterol**
- + phospholipids**
- extrahepatic LPL**

(J Lipid Res 1990 31(11):2009.)

Caveman Fats & Hormones

N-6

LA- corn oil

GLA-primrose

AA arachidonic

(COX/Vioxx)

Prostaglandins/PGE₂

D-6*

D-5

D-4

N-3

ALA flax walnuts

--

EPA

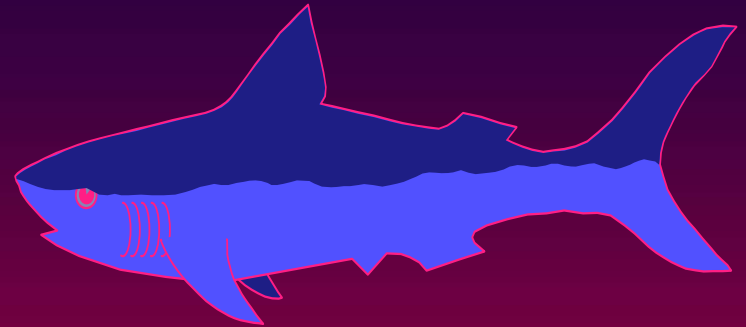
DHA fish oils

***Delta 6 Delta 5 Delta 4 desaturase enzyme**

Omega 3 Fatty Acids

- Fish Oils
- 10% Flax Seeds
- Wheat Germ
- Walnuts
- Purslane
- (Borage Oil)

Rx 2-3 gms/d



Fish Oil vs Olive Oil in UC

18 gm/day 18 Maxepa Pills vs Olive Oil

20 ppl Age 32 – 79

15-30 mg prednisolone 0-20 after

PGE₂ 25.1 (4.7 SEM) 10.8 (2.6) ng/mg prot

TxB₂ 10.3 (1.4 SEM) 6.4 (1.0) ng/mg prot

Hillier 1991 *Gut* 32:1151-1155.

Omega 6 Fatty Acids

Gamma Linolenic

- **Evening Primrose Oil**
- **(Borage Oil)**
- **(Black Currant Oil)**

Raise HDL's

Rx Dry Skin

2 grams/day



Modulation of cytokine production in vivo by dietary essential fatty acids in patients with colorectal cancer - Horrobin

“no significant alteration in total cytokine concentrations in the first 2 months, but reaching minimum levels at 6 months.

GLA *n*-6 Supplement

Impr. Muscle Strength

Impr. Tendon Reflexes

Impr. Sensation (arm/leg)

(Deterioration on placebo)

DM Care 1993 16(1):8-15



Fatty acids, triglycerides and syndromes of insulin resistance

“strong relationships between the fatty acid composition of structural membrane lipids and insulin action.... Good insulin action is associated with increased proportion of *n*-3 fatty acids”

Prostaglandins Leucotrienes and Ess Fatty Acids 1997; 57:379-85

Lipoprotein composition

Triglycerides = VLDL

Triglyceride 60%

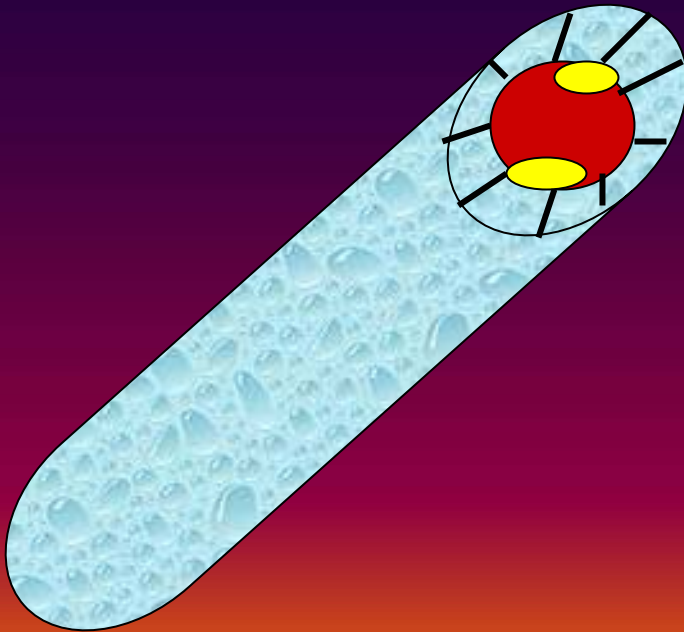
Cholesterol 10%

Phospholipid 18%

Protein 10%

(Apolipo .B100, CI, CII, CIII)

HAART & Blood Vessels



C-reactive protein

Homocysteine

Oxidants

PI's

Nucleosides

Nitric Oxide

**Poster 692-T: Sutliff et al.
Seattle: 9th Retrovirus 2002**

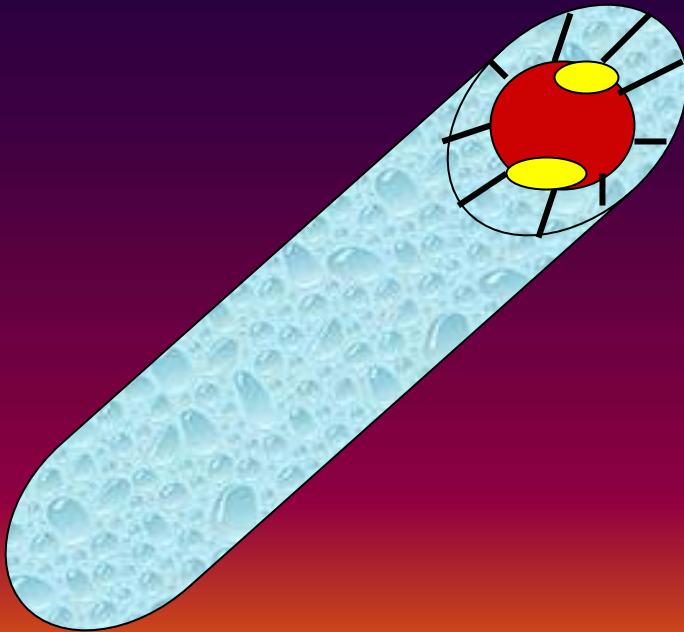
AZT increases endothelial super-oxide generation which results in abnormal endothelium-dependent relaxation.

**... generation of ROS ...
availability of NO ... impaired
relaxation**

**Abstract 29: Sosman et al.
SF: 7th Retrovirus & OI's 2000**

**Endothelial Dysfunction is
associated with the use of
Human Immunodeficiency Virus
Protease Inhibitors.**

HAART & Blood Vessels



C-reactive protein

Homocysteine

Oxidants

PI's

Nucleosides

Nitric Oxide

Beyond Lipids--the role of the endothelium in coronary artery disease.

NO dilation, anti-clotting, LPL activity

Aengevaeren WR. *Atherosclerosis* 1999; 147
Suppl.S11-S16.

Lyon Diet Heart Study

Cretan - Mediterranean Diet vs NCEP1
(fruits-veges-mono fat/olive oil)

ALA: leafy veges, purslane, nuts, legumes
& margarine w/ 4.8% ALA

At 27 months, 76% reduction relative risk
of in fatal and non-fatal MI's

No differences in Chol TG HDL !!

Circulation 1999; 99:779-785.

Lyon Diet Heart Study

Cretan - Mediterranean Diet vs NCEP1

Fatal MI	3	16
Non-fatal MI	5	17

(70% drop in death rate)

(4 yr data)... 56% drop in cardiac deaths

61% drop in cancer deaths

Circulation 1999; 99:779-785.

Where Nutrients Impact HIV Infection: **practical**

- Food: help, not hassle the body
- Nutrients: reduce HAART toxicity
- Supplements: fix metabolism

How Supplements are Useful in HIV Disease

- Replace lost CD4 cells
- Clear Random Oxygen Species
- **Reduce side effects of medicines**



Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil

B: Muffin and Coffee

L: rice, beans, salad

Sn: granola bar; 1-2 Qts. Juice/day

D: chicken leg, rice, beans

Works 2 jobs, more coffee

5'7" 141 lbs

Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil

5'7" 141 lbs

CD4+ - 675; VL = undetectable

Chol 342

TG's 1,980

HDL 42

Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil

Chol 342 TG's 1,980 HDL 42

- 
- 1.
 - 2.
 - 3.
 - 4.

Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil

Chol 342 TG's 1,980 HDL 42

1. Food:

2.

3.

4.



Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil

Chol 342 TG's 1,980 HDL 42

1. Food: Protein-Fruit Smoothie,
Fish, Beans, Solid Fruits,
Balance Bar, Seltzers, rice

2.

3.

4.

Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil

Chol 342 TG's 1,980 HDL 42

1. Food: Protein-Fruit Smoothie,

2. ?????

3.

4.

Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil

Chol 342 TG's 1,980 HDL 42

1. Food: Protein-Fruit Smoothie,
2. Fish Oils 3 gms/day
- 3.
- 4.



Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil

Chol 342 TG's 1,980 HDL 42

1. Food: Protein-Fruit Smoothie,
2. Fish Oils 3 gms/day
3. ???
- 4.



Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil


Chol 342 TG's 1,980 HDL 42

1. Food: Protein-Fruit Smoothie,
2. Fish Oils 3 gms/day
3. Carnitine: 330mg 9/day 30d
- 4.




Quiz: 41 yo Latino male Combivir, Kaletra, Gemfibrozil

Chol 342 TG's 1,980 HDL 42

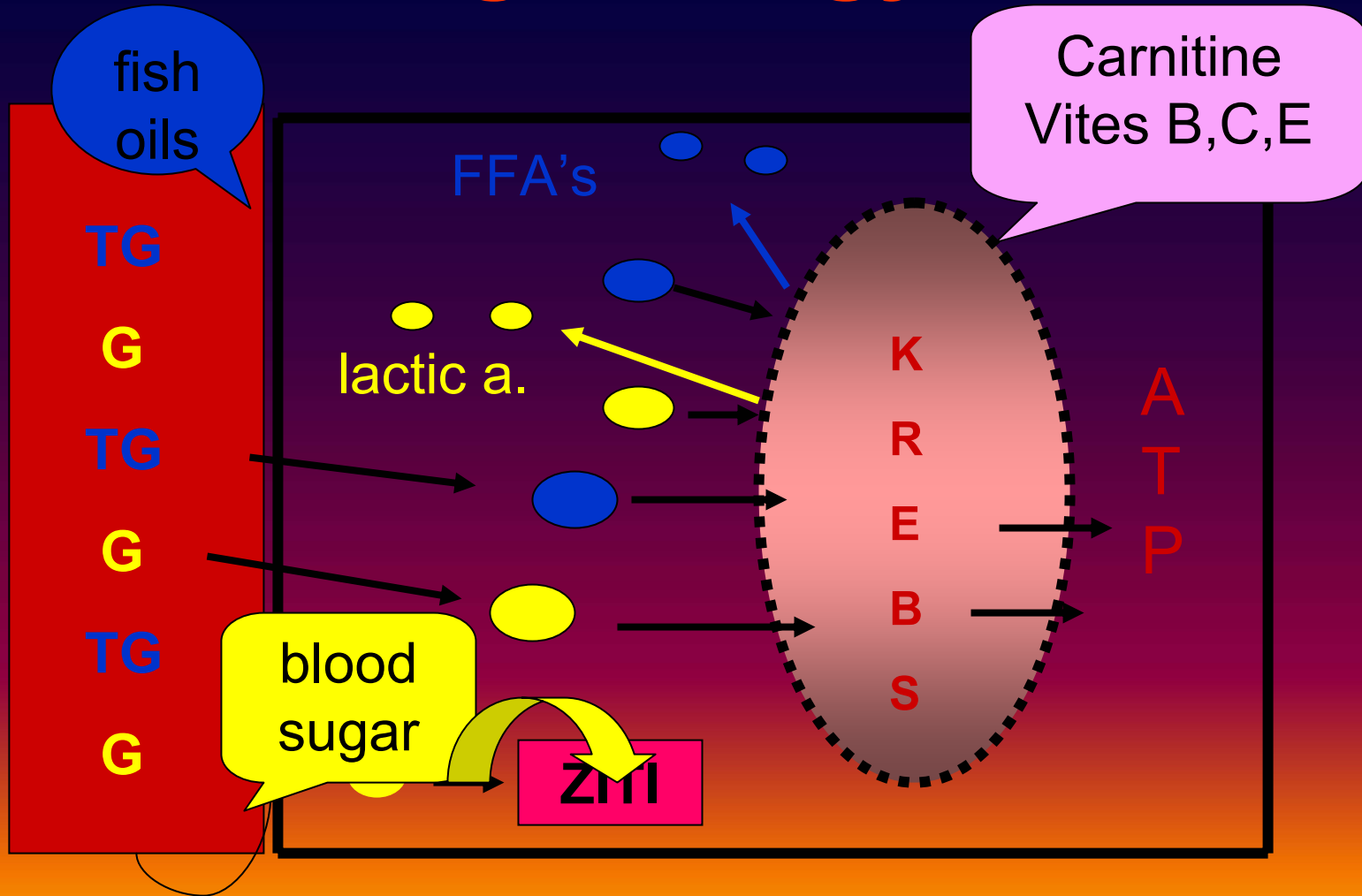
- 
1. Food: Protein-Fruit Smoothie,
 2. Fish Oils 3 gms/day
 3. Carnitine: 330mg 9/day 30d
 4. Antioxidant vitamin: 2/day

Chol 342 TG's 1,980 HDL 42

- 
1. Food: Caveman breakfast etc.
 2. Fish Oils 3 gms/day
 3. Carnitine: 330mg 9/day 30d
 4. Antioxidant vitamin: 2/day

Chol 221 TG's 420 HDL 38

Making Energy: ATP



Rx Elevated SGOT/SGPT

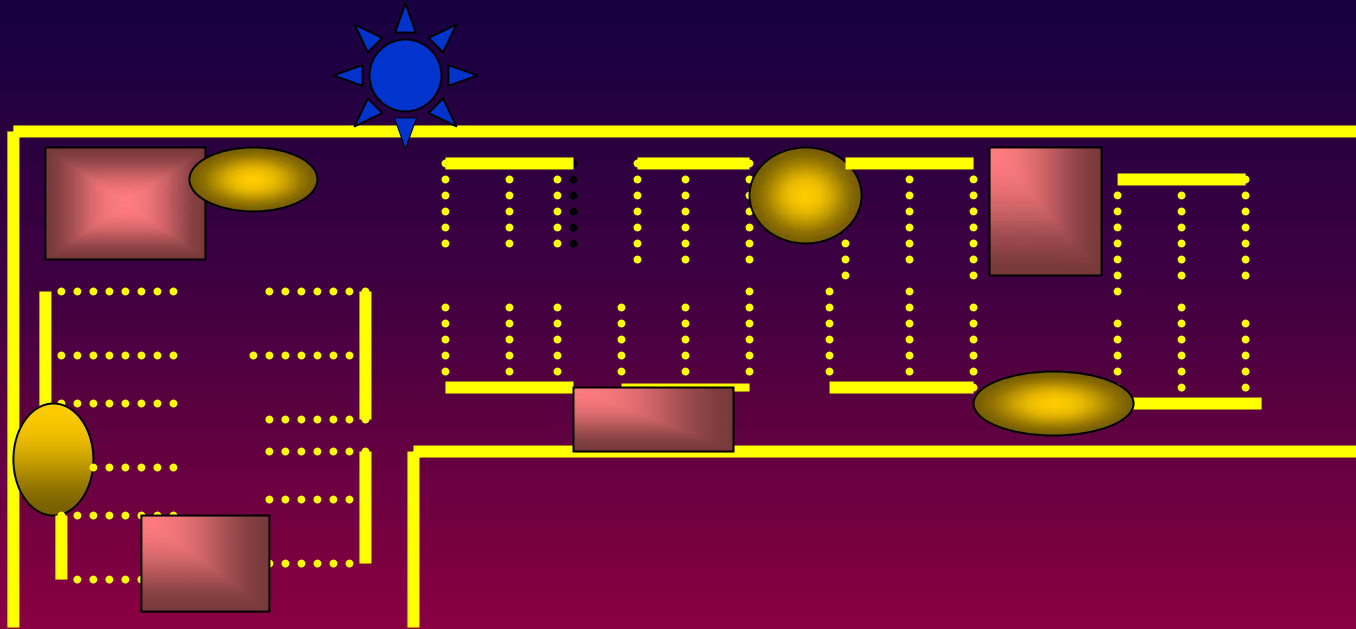
L-glutamine 5-10 gm/day

&

Nutrivir 80 grams / day

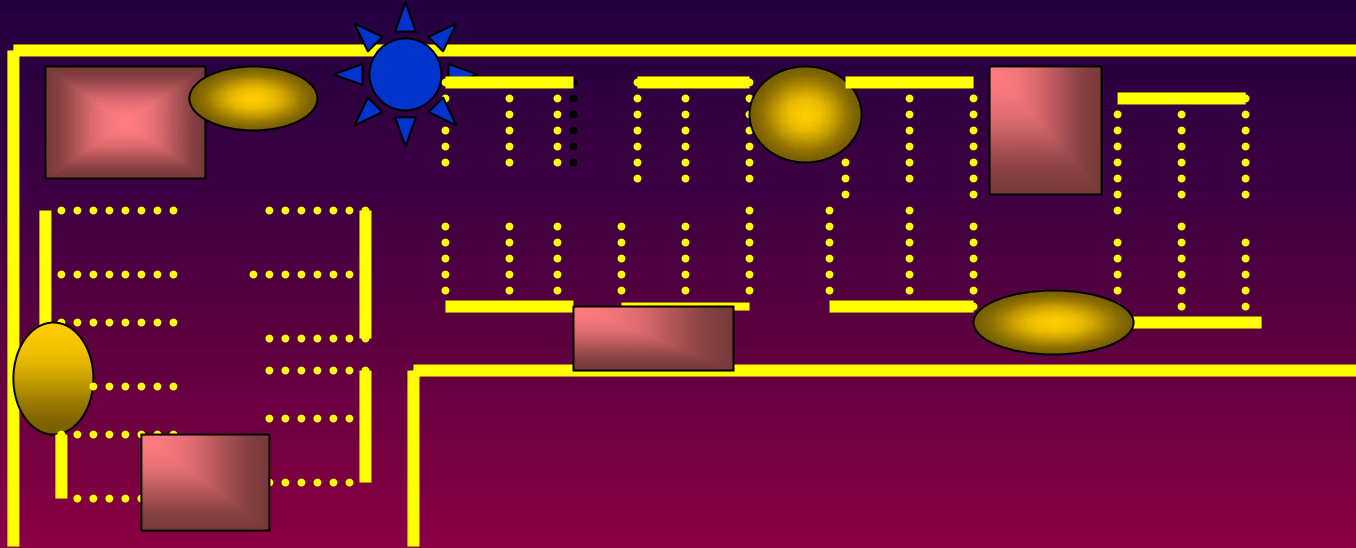
www.bionxs.com

How membranes function....



the message; and how well it's received.

insulin TNFa T-gel AZT
Avandia, corn oil, fish oil



Thanks for your attention

Charlie Smigelski, RD

www.eatupbooks.com