Your Cholesterol Profile

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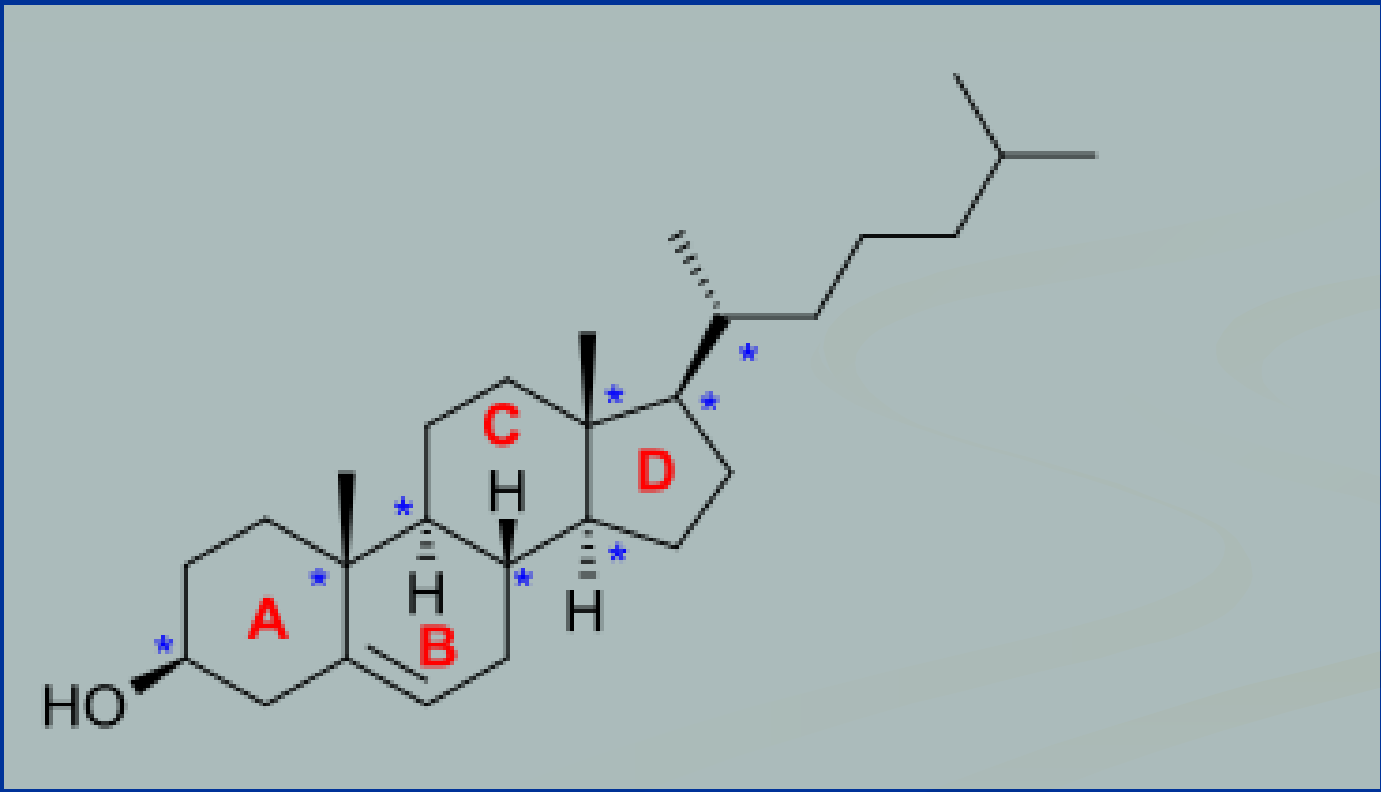
February, 2011

Cholesterol Metabolism

1. Cholesterol is an alicyclic compound with a structure:
   a. Perhydrocyclopentanophenanthrene nucleus of 4 fused rings (5-cholesten-3B-01)

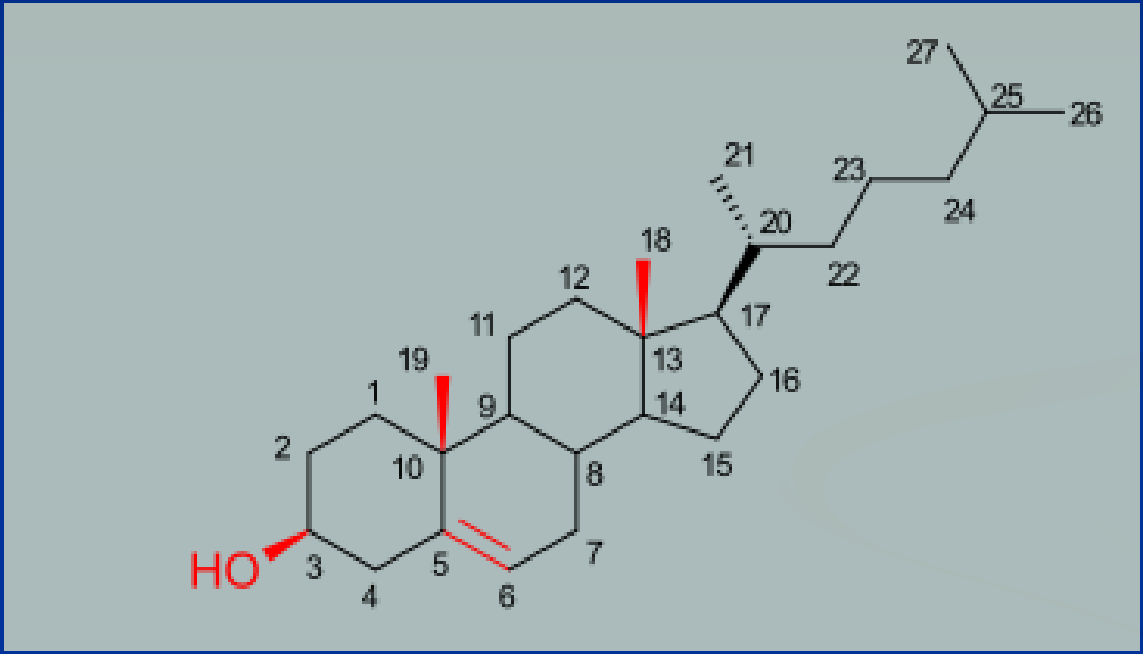


Cholesterol Metabolism

2. Low solubility in water: 0.2mg / 100ml at 250 C
3. Solubility in blood is due to lipoproteins (LDL, VLDL)
4. Total cholesterol
    a. Free 30%
    b. Cholesterol Esters 70% (FA is Saturated or Unsaturated)
        - Long chain FA attached by ester bond to OH group on C-3 on the A-ring (usually linoleic acid) enhances hydrophobiticity.

Cholesterol Metabolism

5. **Structure:**



6. **Bile concentration = 390 mg %**

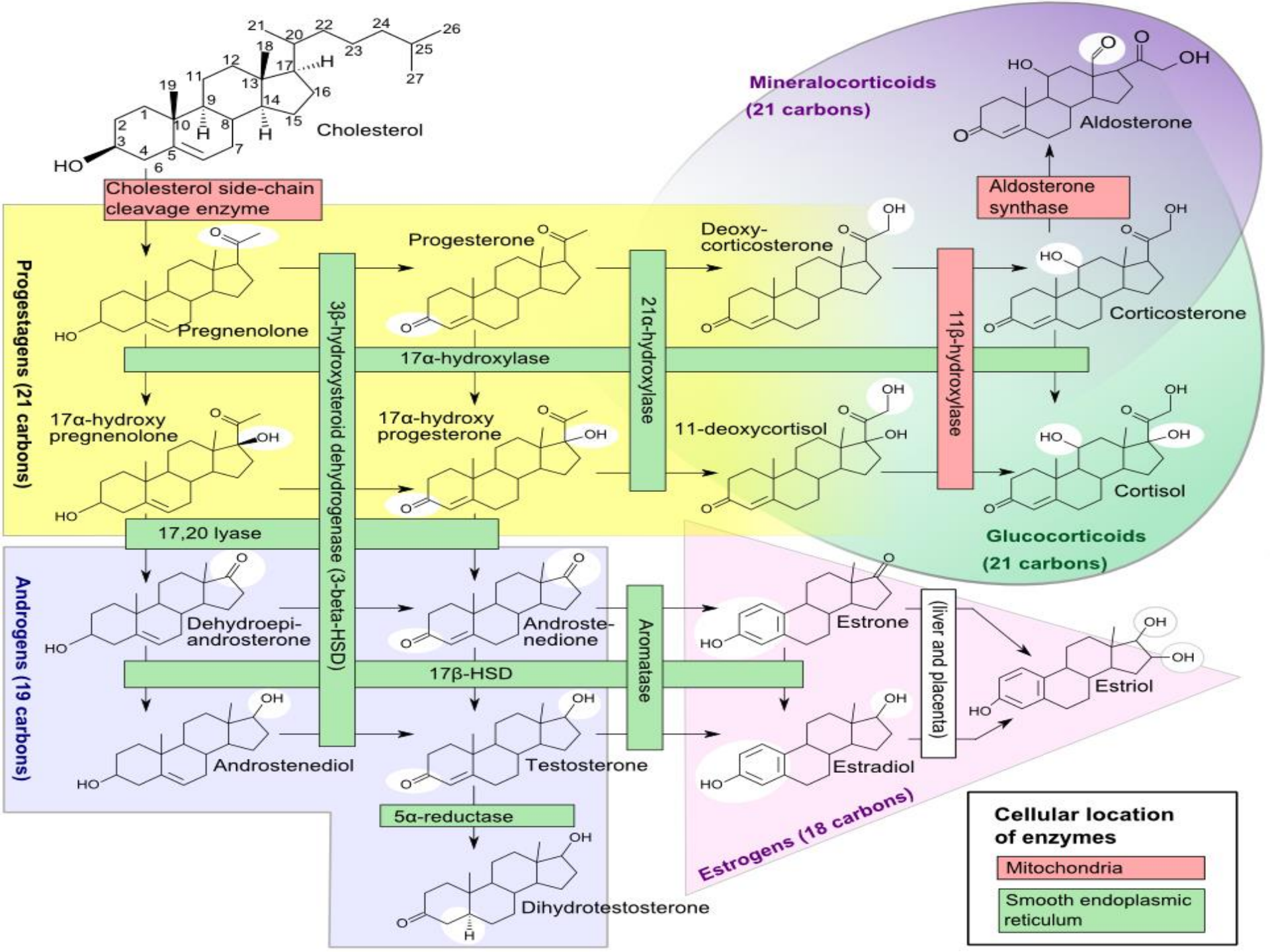
Cholesterol Metabolism

7. **Cholesterol Functions:**
   - **A. Plasma and intracellular membranes (Free Unesterified form)**
   - **B. Myelinated structures of brain and CNS**
   - **C. Inner Mitrochrondrial Membrane**
   - **D. Bile Acids**
   - **E. Steroid Hormones and Sex Hormones**
   - **F. Ergosterol** ----- UV Skin **--> Vitamin D3 (cholecalciferol)**

8. **Synthesis is greatest in:**
   - **– Liver**
   - **– Intestine**
   - **– Adrenal Cortex**
   - **– Reproductive Tissues (Ovary, Testes)**

10/29/84

"Gee ... look at all the little black dots."

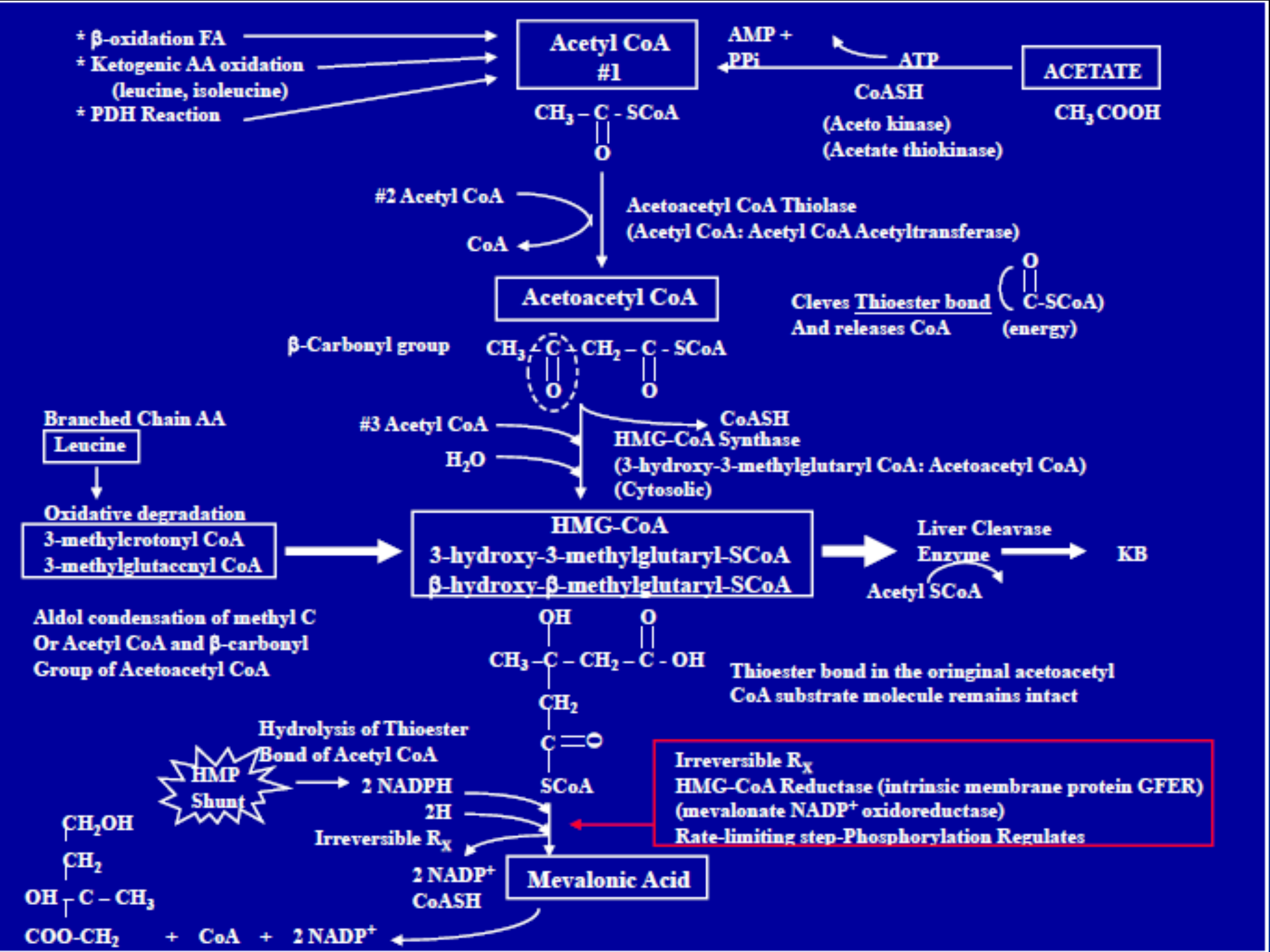

Cholesterol
Cholesterol side-chain cleavage enzyme
Progestagens (21 carbons)
Pregnenolone
Progesterone
Deoxy-corticosterone
Corticosterone
17α-hydroxylase
3β-hydroxysteroid dehydrogenase (3-beta-HSD)
21α-hydroxylase
11β-hydroxylase
Aldosterone synthase
Mineralocorticoids (21 carbons)
Aldosterone
17α-hydroxy pregnenolone
17α-hydroxy progesterone
11-deoxycortisol
Cortisol
Glucocorticoids (21 carbons)
17,20 lyase
Androgens (19 carbons)
Dehydroepi-androsterone
Androste-nedione
17β-HSD
Androstenediol
Testosterone
5α-reductase
Dihydrotestosterone
Aromatase
Estrone
Estradiol
(liver and placenta)
Estriol
Estrogens (18 carbons)
Cellular location of enzymes
Mitochondria
Smooth endoplasmic reticulum

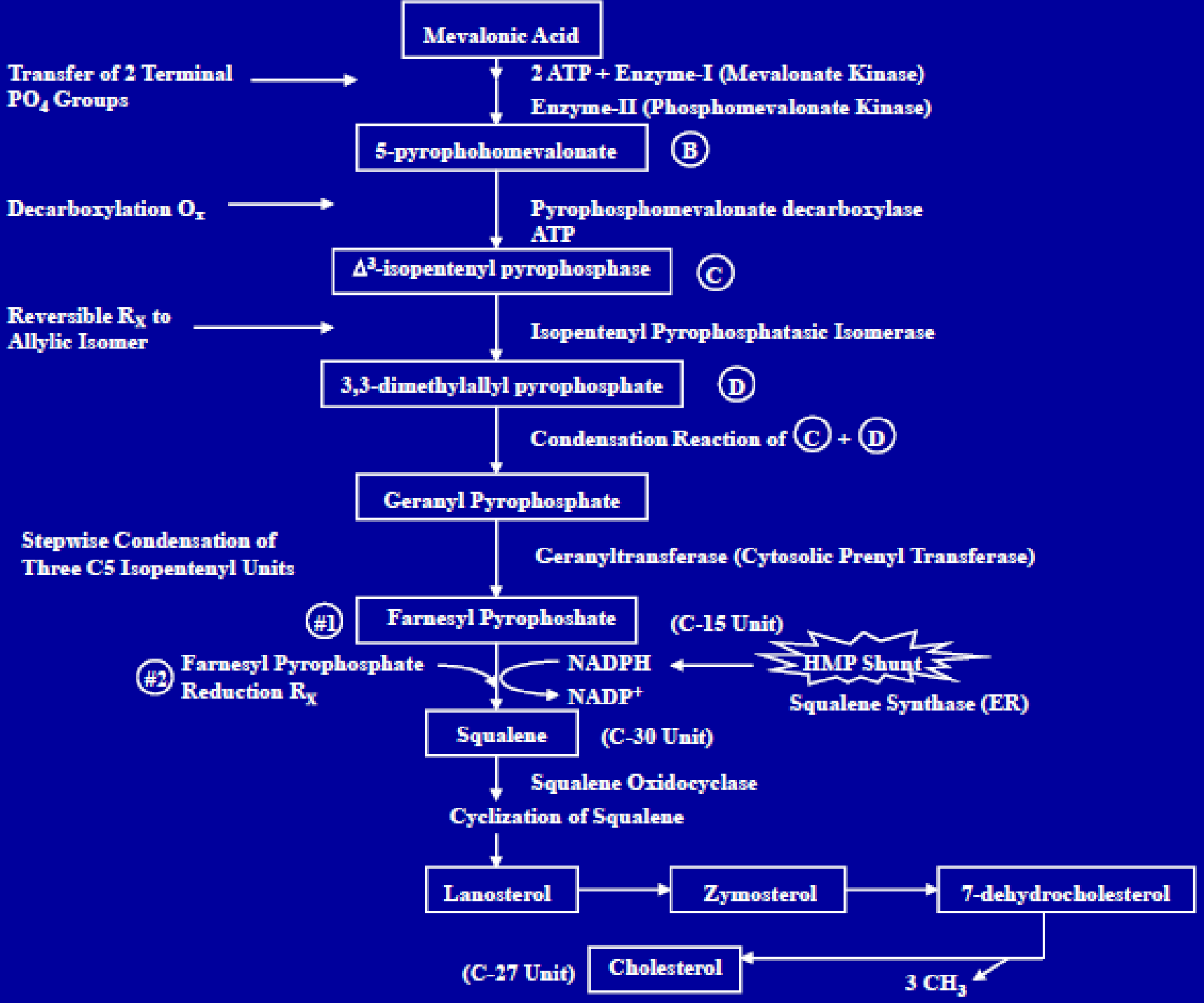
HMG-CoA Reductase Enzyme

1. **Also called mevalonate: NADP+ oxidoreductase (a resident glycoprotein).**
2. **Requires NADPH as reductant -2 moles (4 E-)**
3. **Hydrolysis of thioester bond of HMG-CoA**
4. **Generates a primary alcohol residue : mevalonate**
5. **Irreversible RX**
6. **Produces (R) – (+) mevalonate with 6 C atoms**
7. **Rate limiting step**
8. **Intrinsic membrane protein of the ER (Endoplasmic Reticulum) whose carboxyl terminus extends into the cytosol and carries the enzyme's active site. N-terminus anchors it to ER.**
9. **Phosphorylation regulates activity by AMP activated protein kinase that diminishes its catalytic activity**

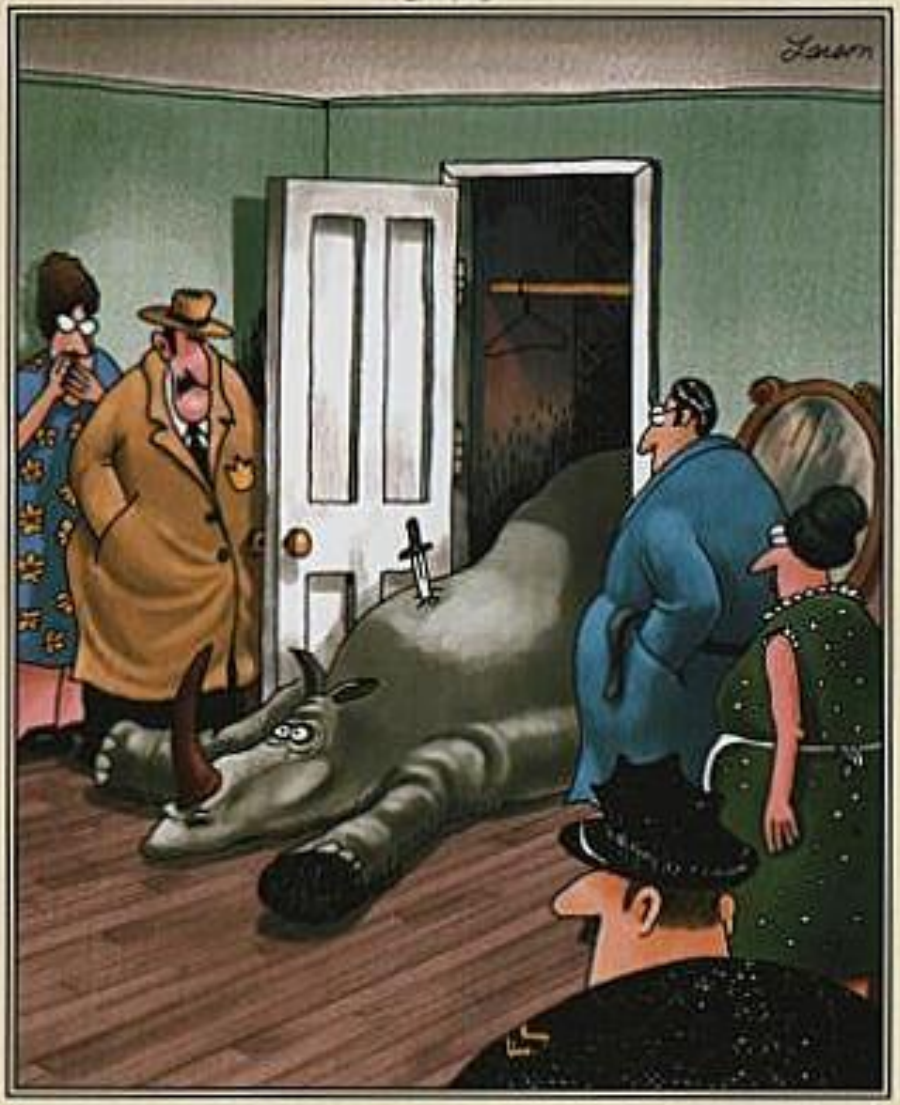
HMG-CoA Reductase Enzyme

10. **Increased intracellular cholesterol stimulates the phosphorylation of HMGCoA Reductase**
11. **Most regulated enzyme known in humans:**
    - **Concentrations of products of mevalonate pathway**
      - **Cholesterol**
      - **Farnesyl Pyrophosphate (FPP)**
        - **Prenylated proteins**
        - **2-cis geranylgeranyl PP (GGPP) → Dolichols**
        - **All-trans geranylgeranyl (GGPP) → Ubiquinone**
      - **Heme**
      - **Selenoproteins**


* β-oxidation FA
* Ketogenic AA oxidation
(leucine, isoleucine)
* PDH Reaction
Acetyl CoA
#1
AMP +
PPi
ATP
ACETATE
CoASH
(Aceto kinase)
(Acetate thiokinase)
CH3 COOH
CH3 – C - SCoA
O
#2 Acetyl CoA
CoA
Acetoacetyl CoA Thiolase
(Acetyl CoA: Acetyl CoA Acetyltransferase)
Acetoacetyl CoA
Cleves Thioester bond
And releases CoA
C-SCoA)
(energy)
β-Carbonyl group
CH3 – C – CH2 – C - SCoA
Branched Chain AA
Leucine
#3 Acetyl CoA
H2O
CoASH
HMG-CoA Synthase
(3-hydroxy-3-methylglutaryl CoA: Acetoacetyl CoA)
(Cytosolic)
Oxidative degradation
3-methylcrotonyl CoA
3-methylglutaccnyl CoA
HMG-CoA
3-hydroxy-3-methylglutaryl-SCoA
β-hydroxy-β-methylglutaryl-SCoA
Liver Cleavase
Enzyme
KB
Acetyl SCoA
Aldol condensation of methyl C
Or Acetyl CoA and β-carbonyl
Group of Acetoacetyl CoA
CH3 – C – CH2 – C - OH
CH2
C
SCoA
Thioester bond in the oringinal acetoacetyl
CoA substrate molecule remains intact
Hydrolysis of Thioester
Bond of Acetyl CoA
HMP
Shunt
2 NADPH
2H
Irreversible RX
Irreversible RX
HMG-CoA Reductase (intrinsic membrane protein GFER)
(mevalonate NADP+ oxidoreductase)
Rate-limiting step-Phosphorylation Regulates
CH2OH
CH2
OH – C – CH3
COO-CH2
2 NADP+
CoASH
Mevalonic Acid
+ CoA + 2 NADP+


Mevalonic Acid
Transfer of 2 Terminal PO4 Groups
2 ATP + Enzyme-I (Mevalonate Kinase)
Enzyme-II (Phosphomevalonate Kinase)
5-pyrophohomevalonate
B
Decarboxylation Or
Pyrophosphomevalonate decarboxylase
ATP
Δ3-isopentenyl pyrophosphase
C
Reversible RX to Allylic Isomer
Isopentenyl Pyrophosphatasic Isomerase
3,3-dimethylallyl pyrophosphate
D
Condensation Reaction of C + D
Geranyl Pyrophosphate
Stepwise Condensation of Three C5 Isopentenyl Units
Geranyltransferase (Cytosolic Prenyl Transferase)
#1
Farnesyl Pyrophoshate
(C-15 Unit)
#2
Farnesyl Pyrophosphate Reduction RX
NADPH
NADP+
HMP Shunt
Squalene Synthase (ER)
Squalene
(C-30 Unit)
Squalene Oxidocyclase
Cyclization of Squalene
Lanosterol
Zymosterol
7-dehydrocholesterol
(C-27 Unit)
Cholesterol
3 CH3

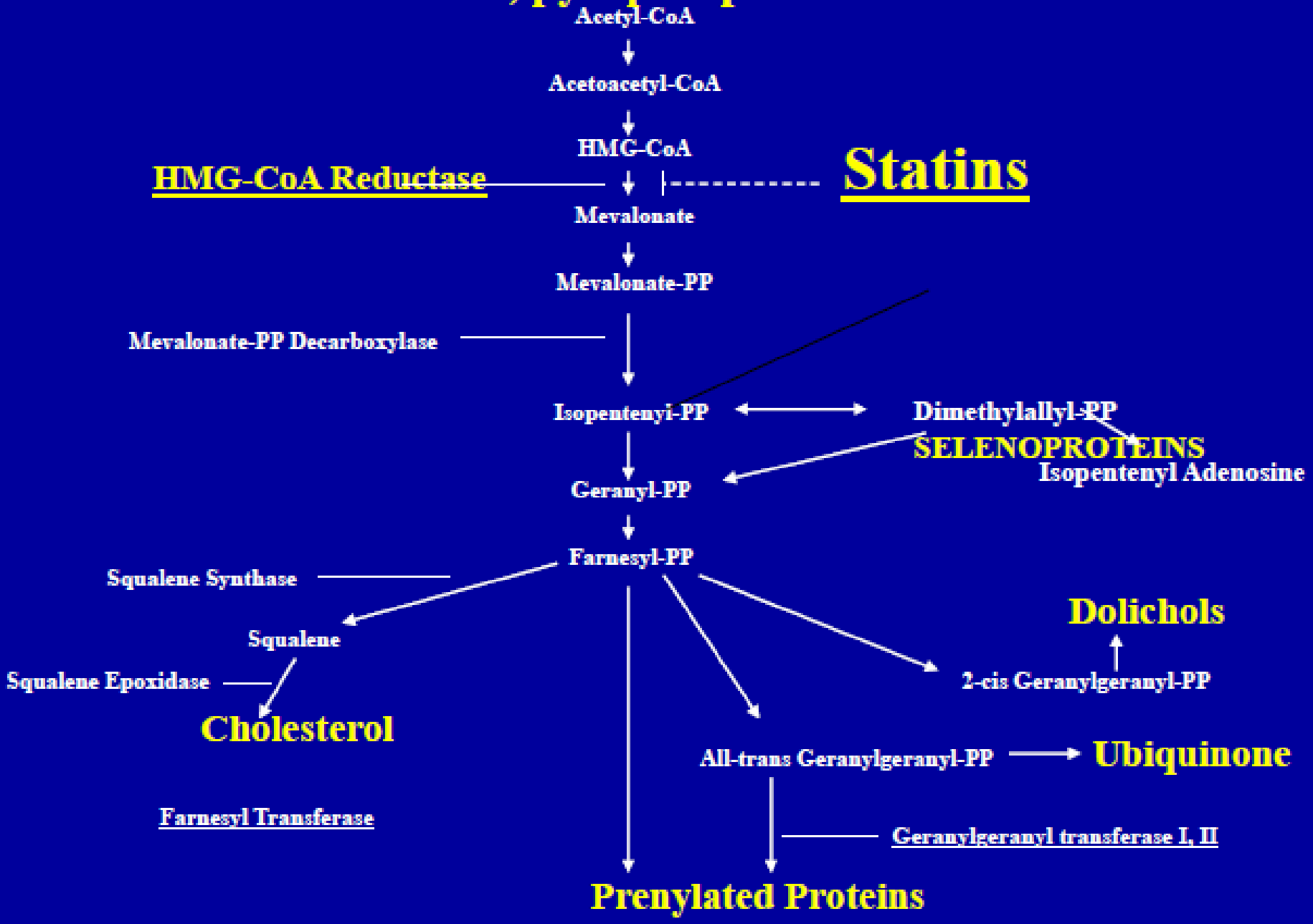
3/18/83



"Blast! Up to now, the rhino was one of my prime suspects."

The Mammalian Cell Mevalonate Pathway

PP, pyrophosphate

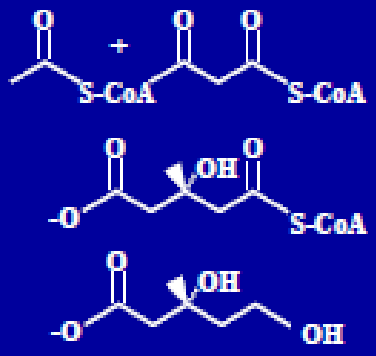


SELENOPROTEINS, STATINS AND MYOTOXICITY

- Selenoproteins and selenocysteine play an important role in development, metabolic homeostasis and antioxidant defense. There are 25 selenoproteins.
  1. Thyroid metabolism: deiodinases T4→ T 3
  2. Glutathione peroxidases (GPx): Antioxidant defense
  3. Thioredoxin reductases (TrxR): Cell redox regulation
  4. Myocyte regeneration
  5. Anti-viral defense
  6. Lymphocyte activation

Sec-tRNA regulates the expression of all selenoproteins. It is post-transcriptionally modified to be functional by isoprenylation of adenosine, which requires IPP and Mevalonate.

Biological Actions of Isoprenoids and Cholesterol



Acetyl-CoA + Acetoacetyl-CoA

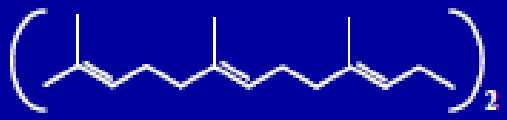
HMG-CoA

HMG-CoA Reductase

Statins

Mevalonate

↓ PI3-Kinase/Protein kinase Akt → ↓ eNOS
↓ BMP-2/Bone formation
↓ Angiogenesis



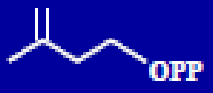
Farnesyl-PP

Dolichol
Haem
Ubiquinone
Ras

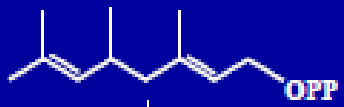
↑ Cellular Growth
↑ Proliferation

Squalene

+ Isopentenyl-PP



Geranylgeranyl-PP



RhoA

Rac 1

Cdc-42

↓ eNOS, ↓ t-PA

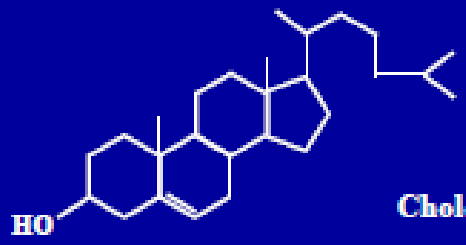
↑ PAI-1, ↑ ET-1

↑ Proliferation and Migration

↑ NAD(P)H Oxidase

↑ Oxidative stress

↓ Actin cytoskeleton



Cholesterol

Lipoprotein
Vitamin D
Bile acids
Steroid hormones

3/14/83

"Okay! Now don't move, Andy! ... Here comes Mom!"

Advanced Testing for Cardiovascular Risk

The New Gold Standard for Lipoprotein Analysis

Evolution of Lipoprotein Testing

"The Lipid Panel"

Total Cholesterol = VLDL + LDL + HDL

Friedewald Equation: VLDL = TG/5

Calculated LDL = TC – (HDL + TG/5)

Direct LDL is Better

Consensus Statement of the American Diabetes Assoc. & American College of Cardiology

Apo B 100 (est. of non-HDL Particles) is Better Yet

Lipoprotein Particles Predict Risk Better than Cholesterol

Lipoprotein Particle Numbers by Subgroup is Best

Separation by Density

Centrifuge Tube with Mixture of Serum, Gradient and Dye

Intense Gravitational Force

600,000 G's

Density (g/ml)

1.000

1.006

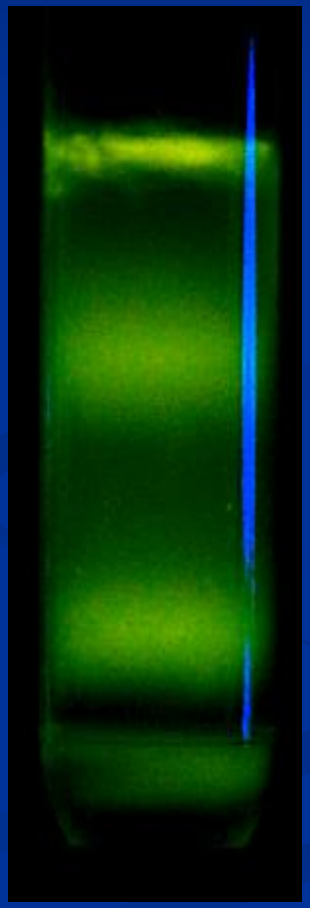
1.030

1.063

1.100

1.300

Separated Lipoproteins



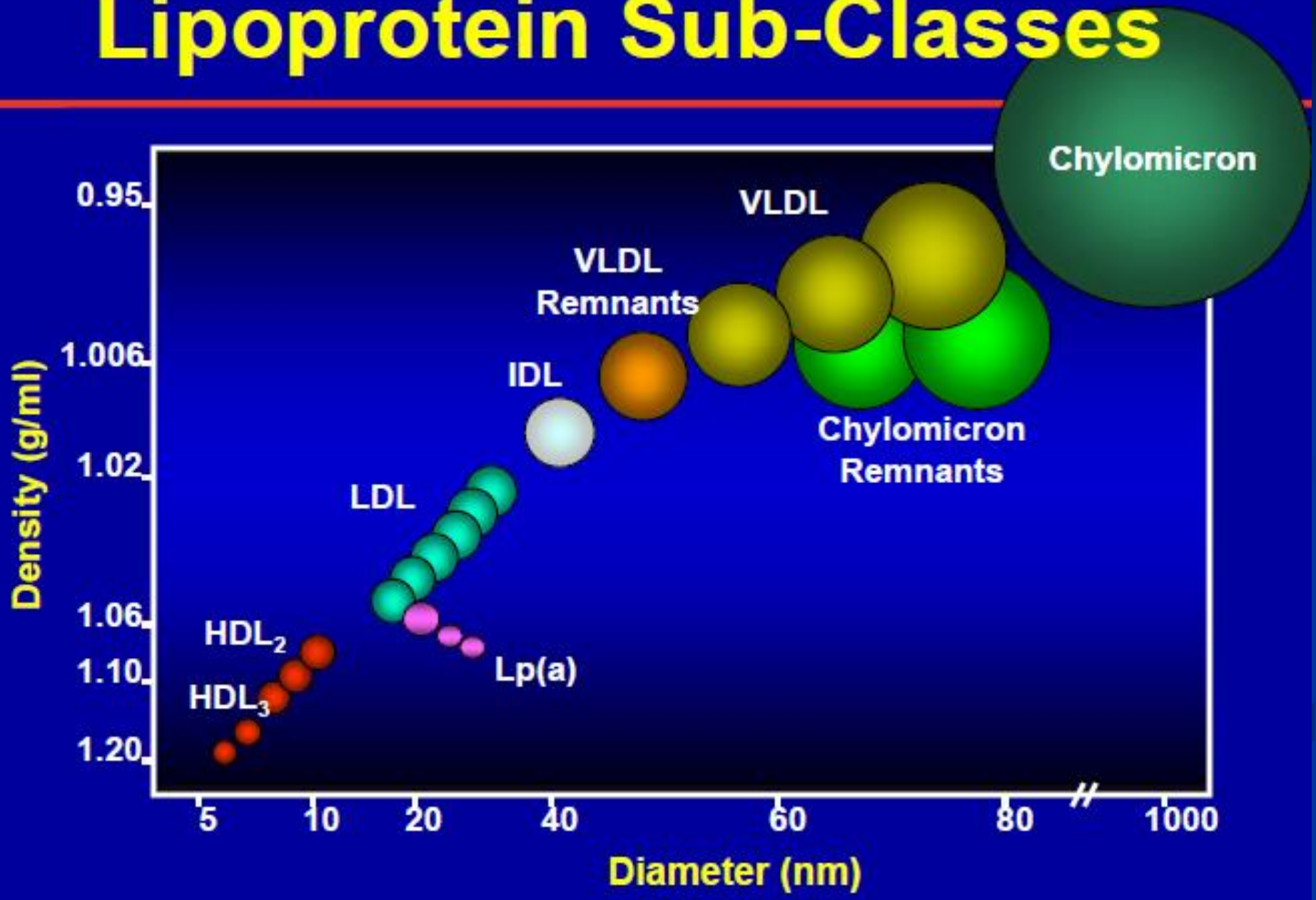
VLDL

LDL

HDL

Proteins

Lipoprotein Sub-Classes



1/11/83

"Well, look who's here. ... God's gift to warthogs."

NCEP Guidelines for Cardiovascular Disease

NCEP - ATP III

- 50% of at Risk Individuals are Not Identified
- 50% of Heart Attack Victims have Normal Cholesterol
- NCEP Identified a Number of New Lipoprotein Risk Factors – To Help Assess Those at Risk

NCEP New Lipoprotein Risk Factors

RLP (Remnant Lipoprotein)

- High in 20% of population
- One of the Most Atherogenic Lipoproteins
- Skips Oxidation Step in Forming Plaque

Small Dense LDL – High in 25% of population

- 3-fold Greater Risk of CVD than Buoyant LDL
- Penetrates Arterial Endothelial Lining Easily
- Less Recognized by LDL Receptors therefore Increases

Lp(a) - High in 20% of population

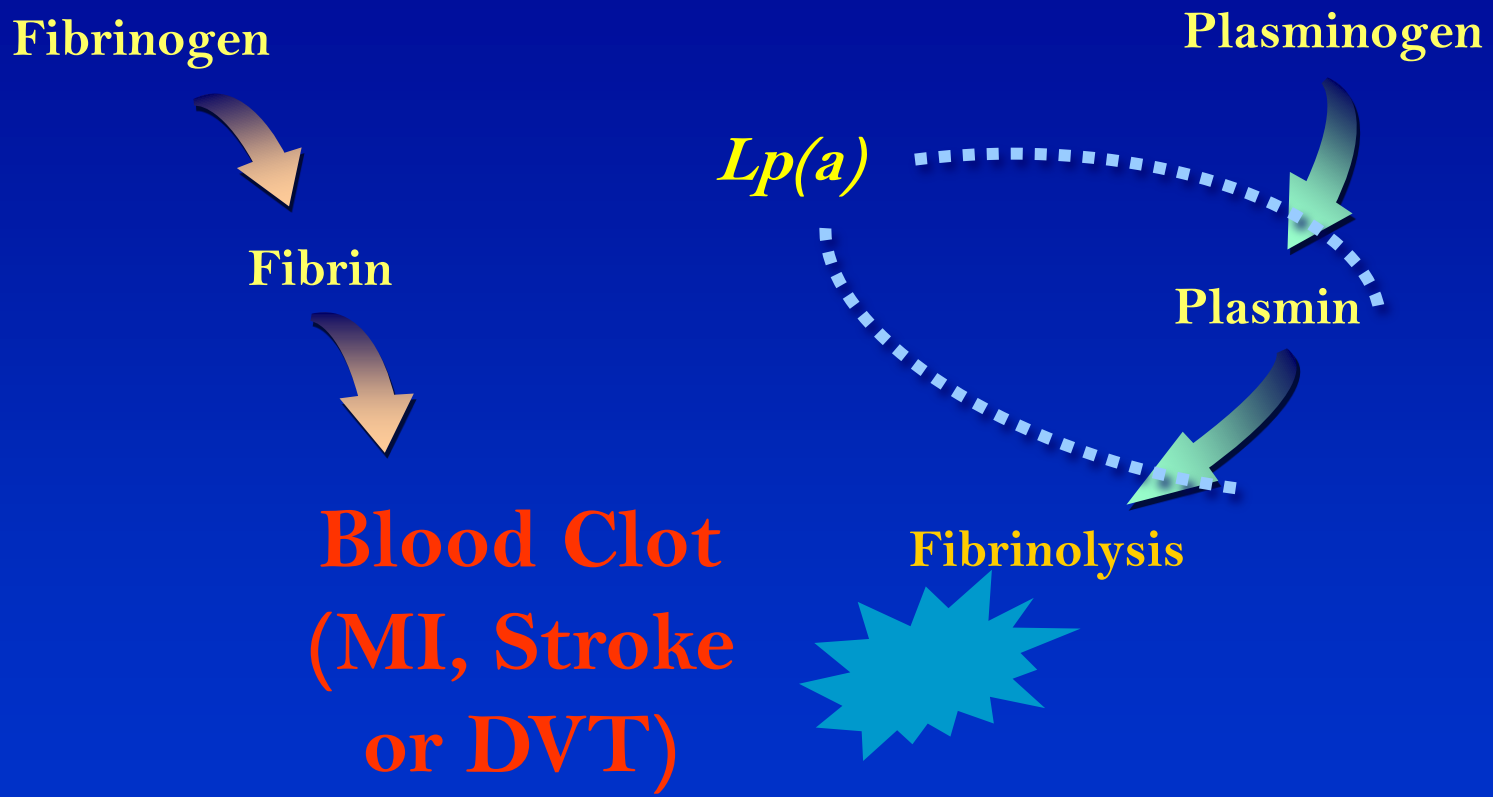
- Small Particles that are Easily Oxidized
- Competes with Plasminogen, Prevents Fibrinolysis

HDL 2b & 3 – Low in 20% of population

- HDL 3 Picks Up Excess Cholesterol and Becomes HDL 2b in Reverse Cholesterol Transport

Lp(a) Competes with Plasminogen and Prevents Fibrinolysis

Many of the over 40 genetic variations of Lp(a) mimic plasminogen



Possible Antithrombotic Therapy Indicated

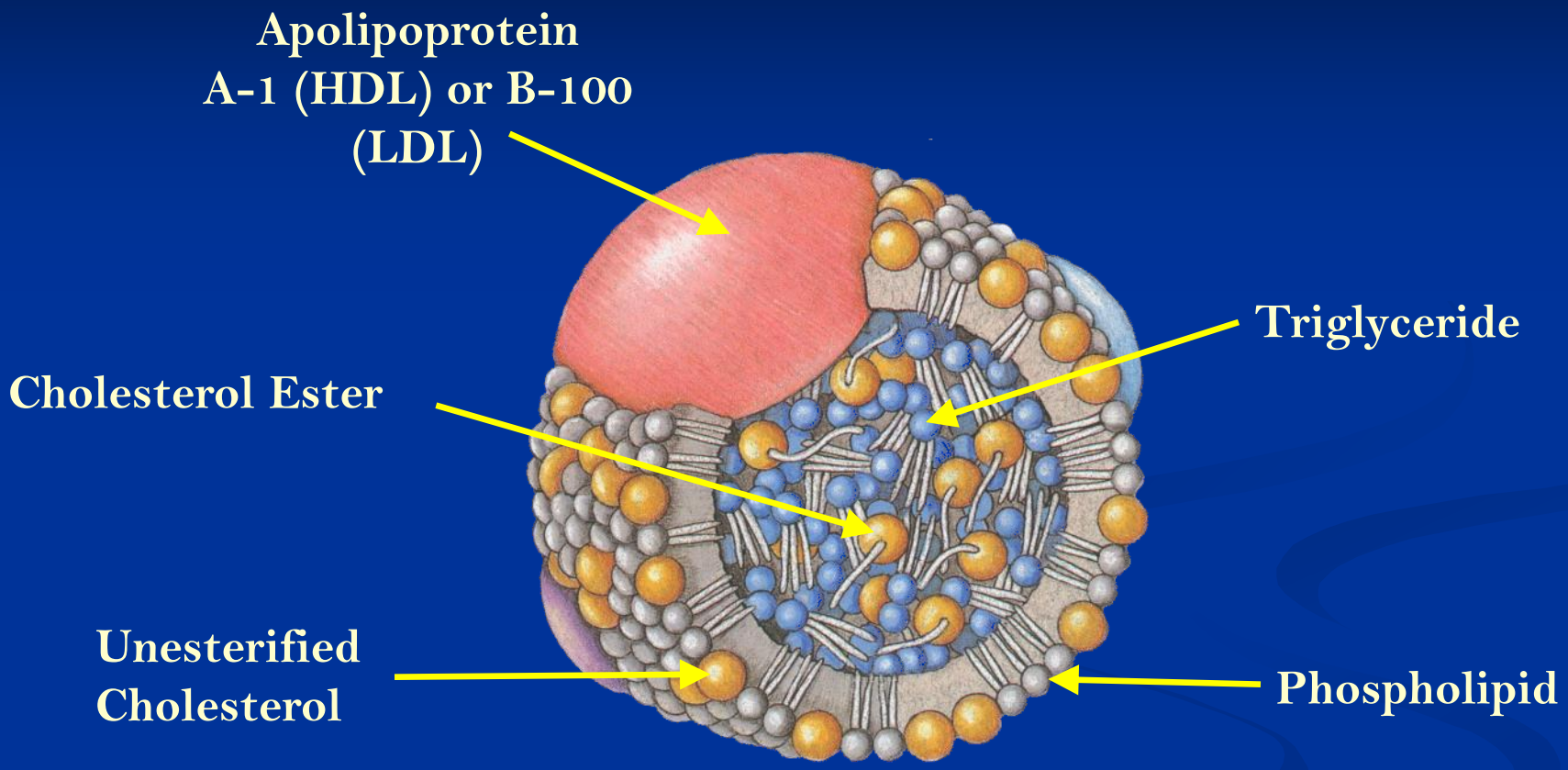
Advanced Lipoprotein Testing

To Determine the NCEP New Risk Factors Lipoprotein Subgroup Information is Needed:

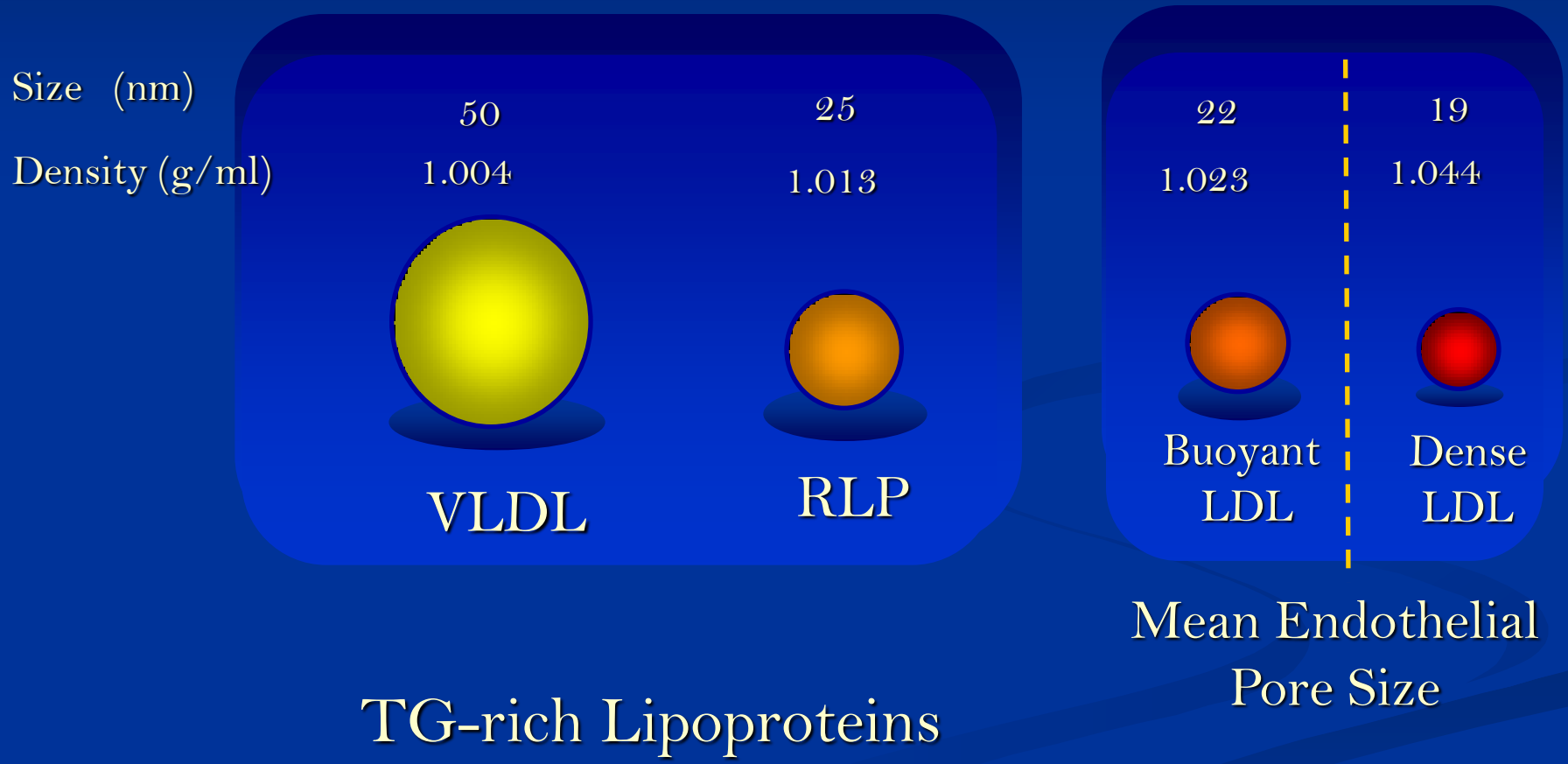
What are Lipoproteins and their Subgroups?

How do they Cause Cardiovascular Disease?

Lipoprotein Particles



Atherogenic Particles



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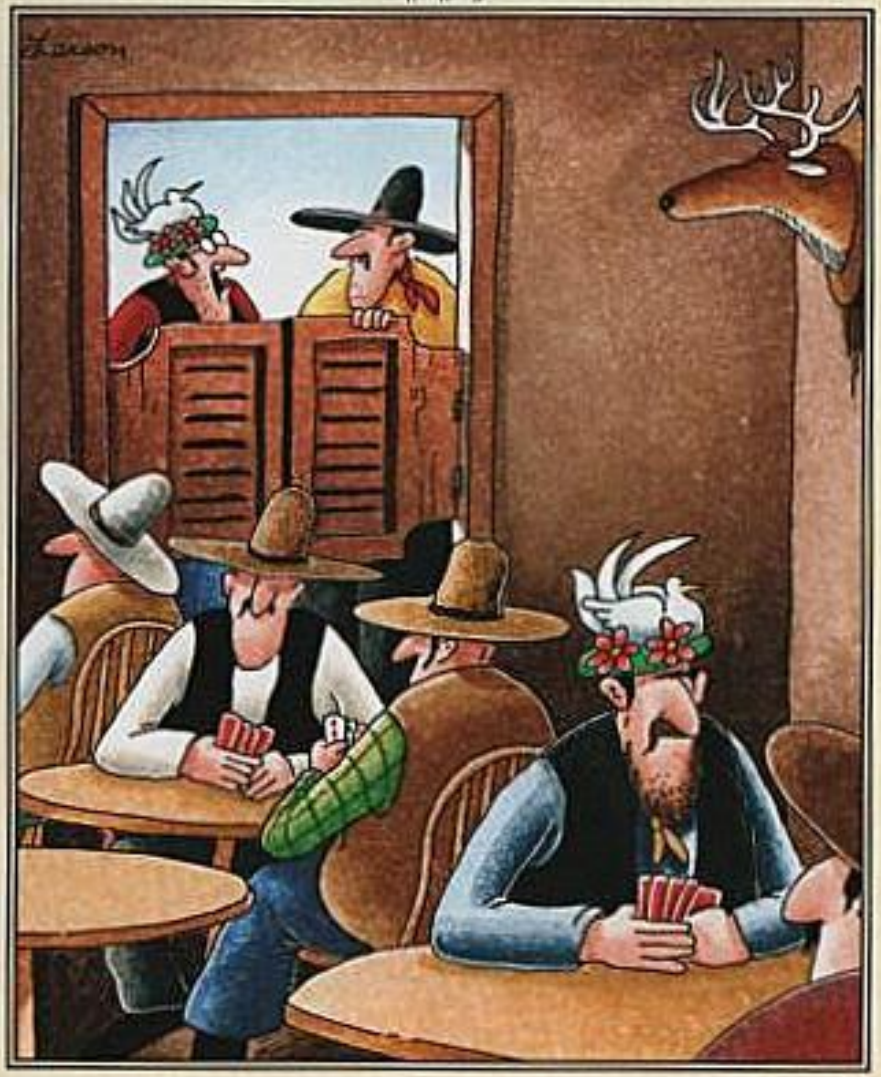
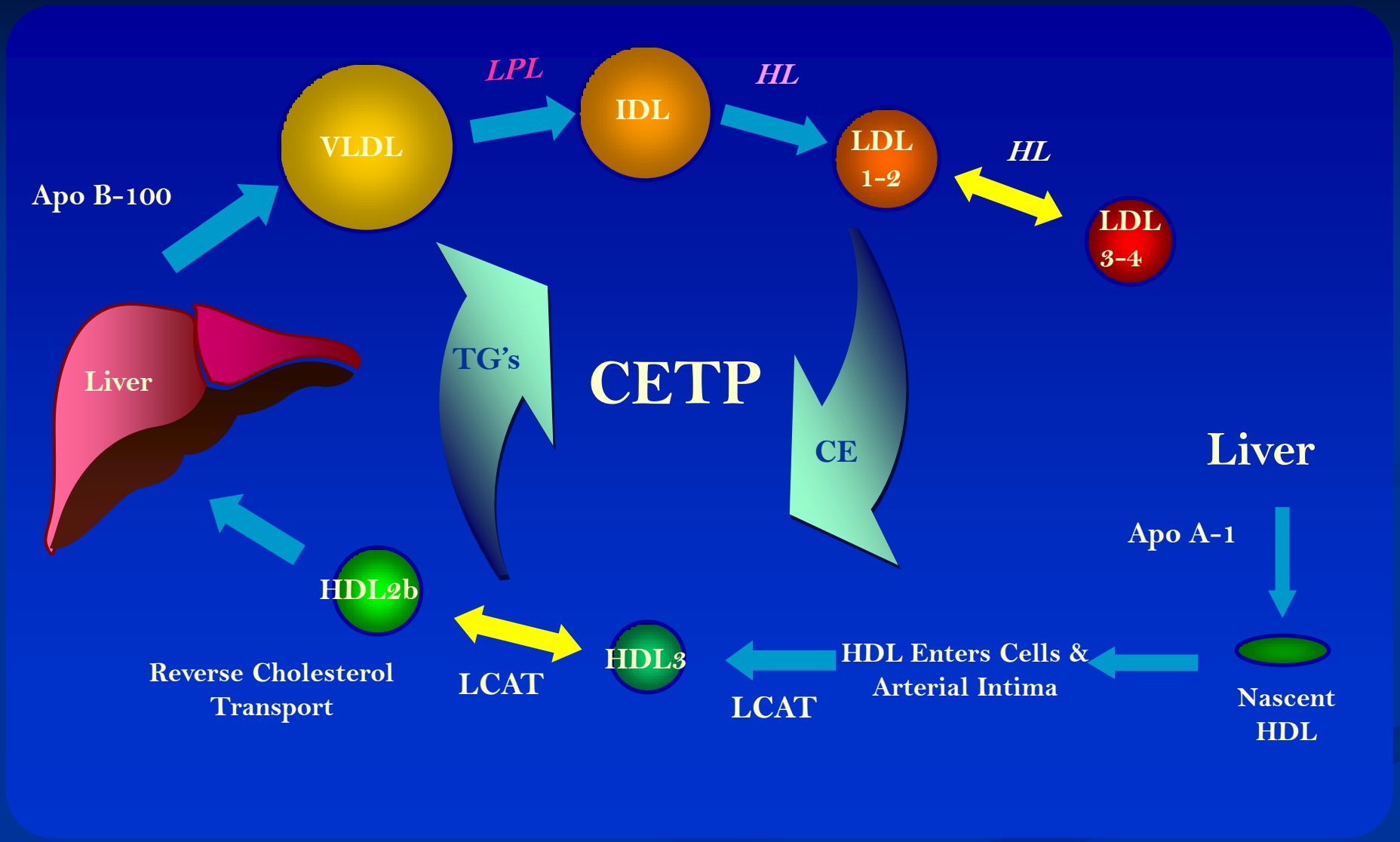


"I just *can't* go in there, Bart! ... Some feller in there and I are wearin' the same kind of hat!"

CETP in Cholesterol Metabolism



Brewer HB et al. *Am J Cardiol* 2003;92:10K-16K.

BALANCE LDL-C LEVELS

- Human infants have LDL-C of 40 to 60 mg%
- Primates have LDL-C of 60 mg%
- South American Paleolithic tribes have LDL of 60mg %
- RCCT with statins demonstrate reductions in CHD, MI, ischemic CVA, CHF, CRI and other CVD with LDL reductions to 60mg%.
- What level of LDL-C is too low for normal cellular function vs. the level that increases CV risk?

1/12/83

LDL Particle Number

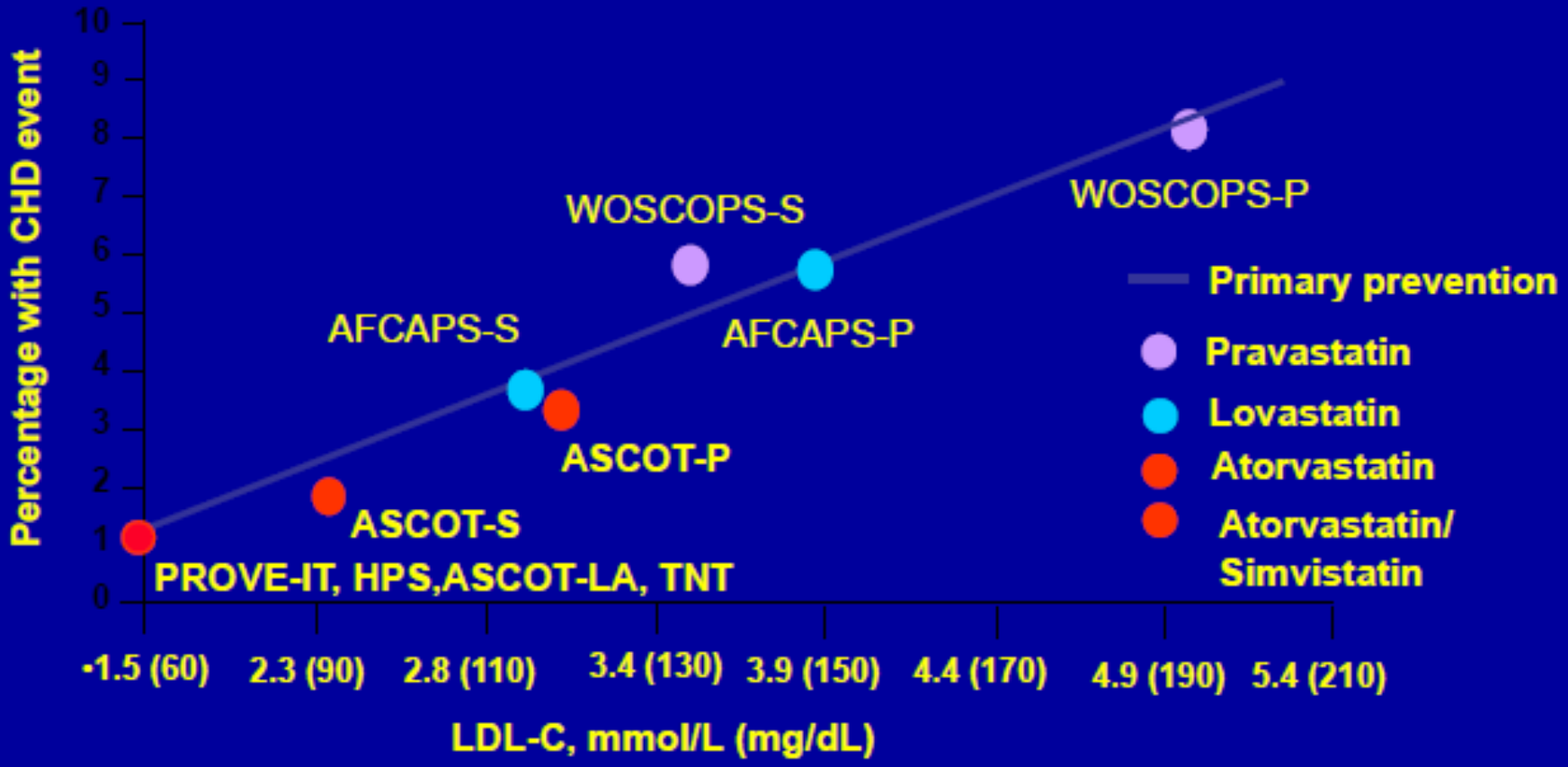
- LDL particle number drives the CVD risk
- Direct measurement of LDL is of no value
- APO B is highly correlated with CVD risk and highly correlated with LDL particle number.
- If HDL is less than 50 mg % then the LDL particle number increases faster that LDL. If the TG is over 125 mg% then the LDL particle number increases faster than the LDL.
- Statins are not effective in reducing LDL particle number, LDL size or APO B
- Statin trials reduce CV risk the same degree independent of LDL

OXIDIZED LDL (and other modified LDL) IS ATHEROGENIC

Dietary fat intake determines susceptibility of LDL to oxidation (oxLDL)

1. oxLDL is taken up by macrophages to form foam cells
2. Autoantibodies to oxLDL in humans
3. oxLDL in human atherosclerotic lesions is the same as in vitro oxLDL
4. Stimulates the AT1R and induces hypertension

Landmark Statin Trials: LDL-C Levels vs Events



S = Statin-treated; P = Placebo-treated

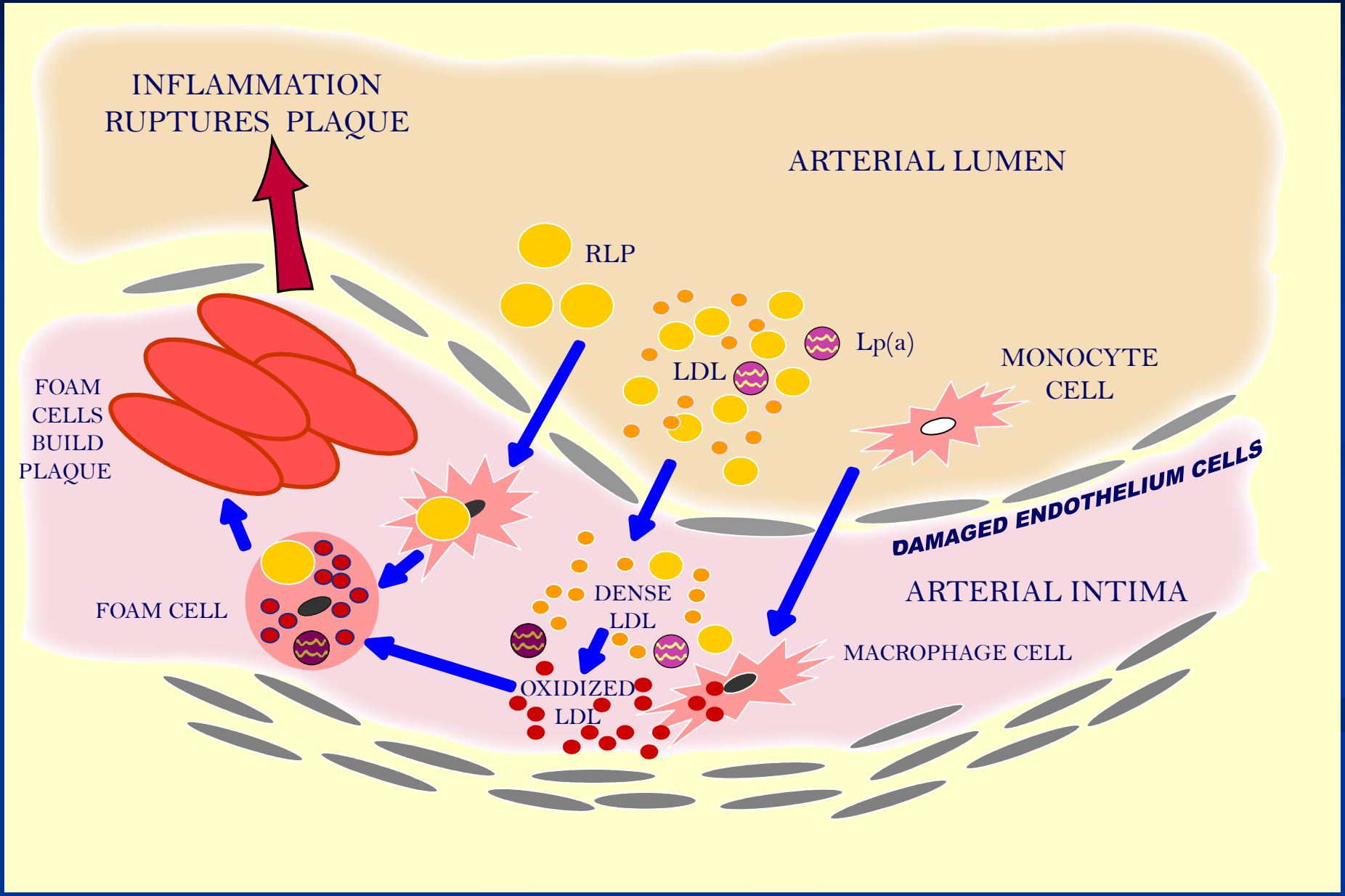
Modified from Kastelein JJP. *Atherosclerosis*. 1999;143(suppl 1):S17-S21.

Statin Trials: Cholesterol Treatment Trialists Collaborators

- 90,056 subjects with 14 trials over 4.7 years with average LDL of 148 mg %
- All cause mortality reduced by 12% ($p < 0.0001$)
- CHD/MI and CVA(ischemic) mortality reduced by 19% ($p<0.0001$) regardless of HDL or TG levels
- Equal benefit at all levels of LDL
- LDL particle number and size drive CV risk more than any other parameter.
- No increased risk of cancer

Lancet 2005; 366:1267-78

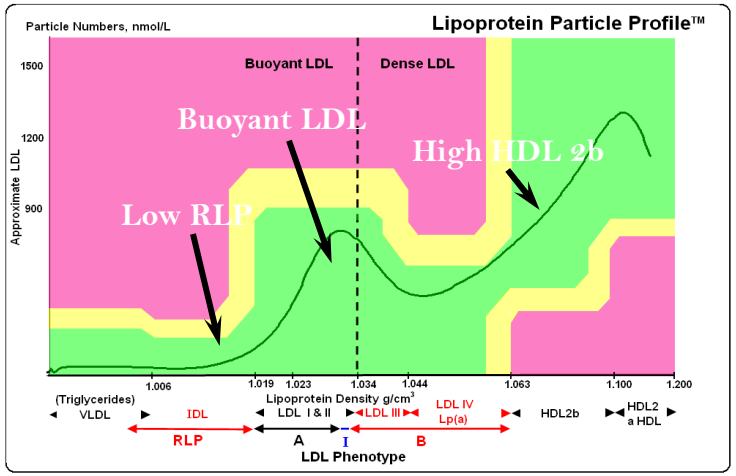
Atherosclerotic Plaque Formation



LPP showing NCEP's New Lipoprotein Risk Factors

Healthy Profile

	Value	NCEP Value	Alert (Notes Page 3)
Total Cholesterol	177	<200	
LDL	96	<100	Above Optimal
HDL	73	>40	Health Factor
Triglycerides (calculated)	47	<150	



Lipoprotein Particle Numbers (nmol/L)

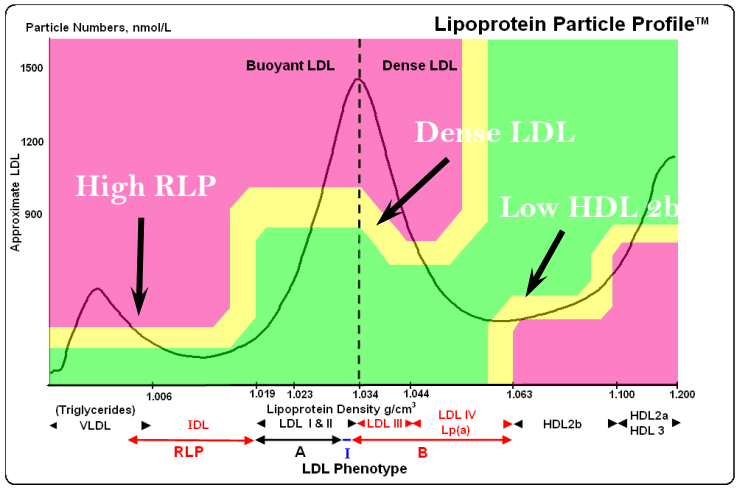
	Value	Reference Value	Alert (Notes Page 3)
VLDL	29	<115[2]	
LDL Total	715	<900[1,2]	
RLP (Remnant Lipoprotein)	40	<150[2]	
Dense LDL III	162	<300[2]	
Dense LDL IV and/or Lp(a)	79	<125[2]	
HDL Total	11676	>7000[2]	Health Factor
Buoyant HDL 2b	3660	>1800[2]	Health Factor (17)

Lipid Group and Non-Lipid Risk Factors

	Value	Reference Value	Alert / Phenotype
Metabolic Syndrome Traits	0.0	0 to 3[3]	None (18)
LDL Mean Density / Phenotype	1.031	<1.033[2]	Buoyant LDL, Type A (19)
HDL Mean Density	1.094	<1.110[2]	

Atherogenic Profile

	Value	NCEP Value	Alert (Notes Page 3)
Total Cholesterol	269	<200	High (2)
LDL	187	<100	Very High (5)
HDL	34	>40	Low (6)
Triglycerides	186	<150	Borderline High (7)



Lipoprotein Particle Numbers (nmol/L)

	Value	Reference Value	Alert (Notes Page 3)
VLDL	180	<115[2]	High (10)
LDL Total	1394	<900[1,2]	High (11)
RLP (Remnant Lipoprotein)	178	<150[2]	High (12)
Dense LDL III	425	<300[2]	High (13)
Dense LDL IV and/or Lp(a)	128	<125[2]	Borderline High (14)
HDL Total	6095	>7000[2]	Low (15)
Buoyant HDL 2b	1417	>1800[2]	Low (15)

Lipid Group and Non-Lipid Risk Factors

	Value	Reference Value	Alert / Phenotype
Metabolic Syndrome Traits	3.0	0 to 3[3]	Metabolic Syndrome (18)
LDL Mean Density / Phenotype	1.034	<1.033[2]	Dense LDL, Type B (21)
HDL Mean Density	1.099	<1.110[2]	

3/1/83

"Not too close, Higgins. ... This one's got a knife."

Treatment of Dyslipidemia

NIACIN (VITAMIN B3)

- Lowers TC, APO B, TG, LDL, small dense LDL, shifts LDL B to LDL A and reduces Lp(a)
- Reduces LDL particle number
- Inhibits LDL oxidation
- Increases HDL especially HDL 2b
- Modulates TG lipolysis in adipose tissue
- Increases APO B degradation
- Reduces fractional catabolic rate of HDL- APO A1
- Reduces HDL-APO A1 uptake
- Fibrinolysis, inhibits platelet function
- Inhibits cytokines, CAM's
- Potent antioxidant

Treatment of Dyslipidemia

NIACIN

- RCCT show reduction in CHD, MI, CVA and CV events of 26% and total mortality of 11% over 6 years
- Average changes in lipids in the dose range of 1 to 4 grams per day:

TC	20 – 25% decrease
LDL	10 – 25% decrease
TG	20 – 25% decrease
HDL	15 – 35% increase

Adverse Effects: hyperglycemia, hyperuricemia and gout, hepatitis, flushing, rash, pruritus, hyperpigmentation, hyperhomocysteinemia, gastritis, PUD, bruising, SVT and palpitations

Treatment of Dyslipidemia

CHINESE RED YEAST RICE (MONASCUS PURPUREUS)

- **Lipid Effects**: "Statin Like" at 2400 mg at night
  - Reduce LDL ~ 22%
  - Reduce TC ~ 17%
  - Reduce TG ~ 12%
  - HDL - No change
- **Monacoline** are active ingredients, which inhibit cholesterol synthesis via HMG-CoA reductase (also omega 3 FA, isoflavones, plant sterols)

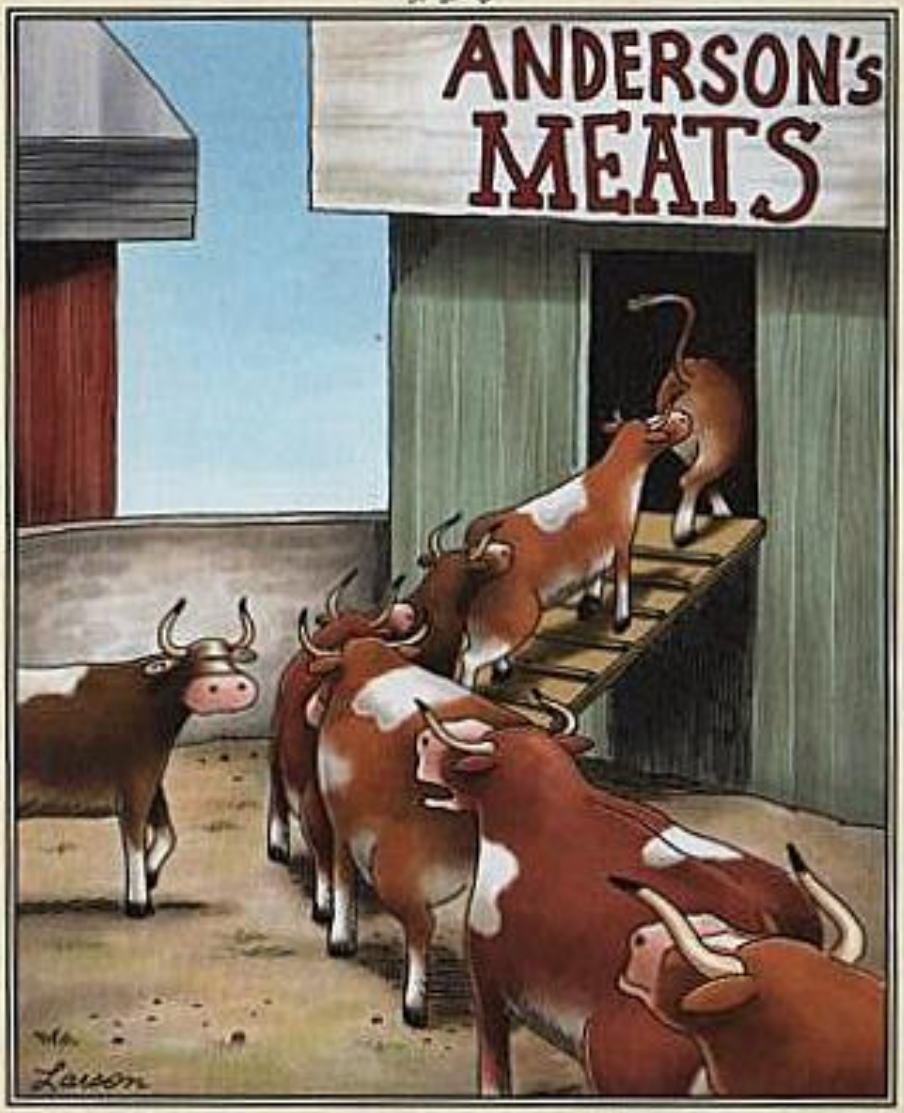
Treatment of Dyslipidemia

CHINESE RED YEAST RICE (MONASCUS PURPUREUS) (continued)

- Citrinin – Toxic fermentation byproduct (mycotoxin from penicillium and aspergillus) may induce renal failure and is mutagenic in animals
- Dose: 2.4 gms / day (= 7 mg Lovastatin) Dose range is 2.4 to 4.8 gms per day at night . Standardize to .4 HMG CoA reductase inhibitors with .3 from lovastatin equivalents This is about 7.2 mg of lovastatin and decreases LDL about 30 mg % over placebo

(Am J Clin Nutr 1999; 69:231)
(Altern Ther Women's Health 2001; 53)
(J Altern Complement Med 2001; 7:133)
(J Nutr Biochem 2003; 14:312
Annals Int Med 2009;150:830

5/13/83



"Hey! You! ... No cutting in!"

Treatment of Dyslipidemia

MARINE OMEGA 3 FATTY ACIDS

- Observational studies in Inuit Eskimos
- RCCT: Reduce CVD, CHD, MI, CVA
  - DART: 29% reduction in mortality in 2 years in 2,033 men post MI with fatty fish or fish oil supplements
  - GISSI: Prevenzione Trial – 11,324 patients for 3.5 years given EPA / DHA had 20% decrease in total mortality, 30% decrease in CV deaths and 45% decrease in sudden death
  - Kuopio Heart Study in Finland: Men with the highest quintile of omega 3 FA intake had 44% decrease in fatal or nonfatal CHD compared to lowest quantile ($p = 0.014$)
  - Reduces CHD progression and CABG occlusion

Treatment of Dyslipidemia

Japan EPA Lipid Intervention Study (JELIS trial)

- 18,645 patients
- Randomized to statin plus 1.8 grams of EPA/DHA vs statin alone
- 19 % RRR in major coronary events and non fatal MI

Lancet 2007;369:1090
Atherosclerosis 2008; 200: 135

Treatment of Dyslipidemia

MARINE OMEGA 3 FATTY ACIDS (continued)

- Mechanisms:
  - Dose related reduction in VLDL 50% TG 45% but little change in TC, LDL APO B or total HDL
  - Increase HDL 2 and increase LDL particle size
  - Anti-inflammatory and anti-thrombotic
  - PPAR agonist
  - Improve heart rate variability, lowers HR
  - ↑ eNOS / NO and improves ED
  - Reduces BP
  - Reduces atrial fibrillation and arrhythmias
  - Reduces growth of atherosclerotic plaque
  - More well-formed fibrous caps and fewer thin wall caps
- Dose: 3 to 4 grams of combined EPA and DHA per day at 3/2 ratio of EPA to DHA
- Balance with GLA at 50 to 90% of the total DHA and EPA and gamma delta Vitamin E at 100 IU to 200 IU per day.

(Acta Med Scand 1980; 208:401)
(Annals 1999; 130:554)
(Lancet 1989; 2:757)
(Circulation 2000; 102:2677)

MPM Middle Path Medicine	Date			
	March of 2010	Aug. of 2010	Nov. of 2010	Feb. of 2011
Total Cholesterol	258	146	167	188
Triglycerides	164	71	73	**233**
HDL	44	50	66	**44**
LDL	181	82	86	97
LDL/HDL	4.1	1.4	1.1	2.2
Trig/HDL	3.7	1.6	1.3	5.3
	*Add Lipitor 20mg and 3g/day Arctic Pure EPA/DHA		*Patient switches to Kirkland Fish Oils	

6/22/83

"Hang him, you idiots! Hang him! ...
'String him up' is a figure of speech!"

Treatment of Dyslipidemia

TOCOTRIENOLS

- Inhibit cholesterol synthesis by post-transcriptionally suppressing HMG-CoA reductase activity by two post-transcriptional actions:
  - Increased controlled degradation of reductase protein
  - Decreased efficiency of translation of HMG-CoA reductase MRNA.

Metabolized by successive beta oxidation and then catalyzed by the cytochrome P450 enzymes CYP 3A4 and CYP 4F2

Treatment of Dyslipidemia

TOCOTRIENOLS
(continued)

Lipid Reductions

12 weeks diet + TRF_{25} ($p < 0.05$)
(Nutr Biochem 1997; 8:290)

- ↓ TC 17%
- ↓ LDL 24%
- ↓ APO-B 15%
- ↓ PF4 14%
- ↓ TxB 31%
- ↓ Lp(a) 17%
- → HDL
- → APO A-I
- ↓ BS

Treatment of Dyslipidemia

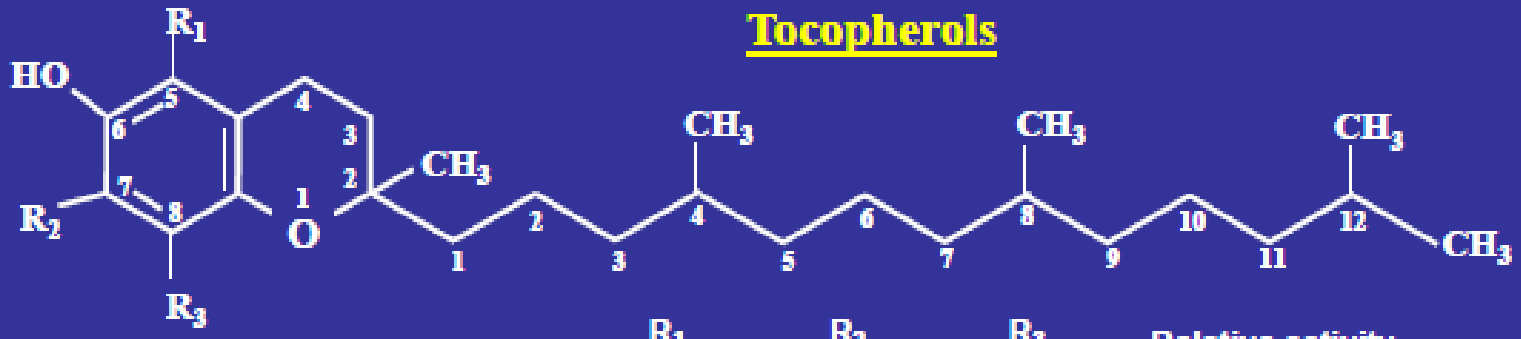
TOCOTRIENOLS
(continued)

Combination of statin and tocotrienols (gamma) is advisable as their mechanism of action on HMG-CoA reductase is different and possibly additive.

J Nutr Biochem 2001; 12:318

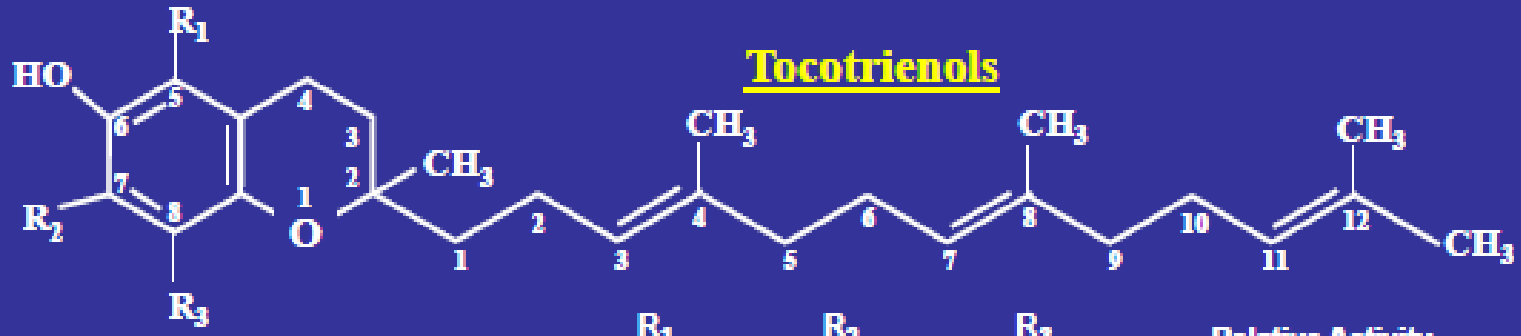
Structure and Activity of Natural Tocopherols and Tocotrienols

Tocopherols



	R_1	R_2	R_3	Relative activity
α-tocopherol	CH_3	CH_3	CH_3	1
β-tocopherol	CH_3	H	CH_3	0.4
γ-tocopherol	H	CH_3	CH_3	0.1 – 0.3
δ-tocopherol	H	H	CH_3	0.01

Tocotrienols



	R_1	R_2	R_3	Relative Activity
α-tocotrienol	CH_3	CH_3	CH_3	0.3
β-tocotrienol	CH_3	H	CH_3	? Insignificant
γ-tocotrienol	H	CH_3	CH_3	? Insignificant
δ-tocotrienol	H	H	CH_3	? Insignificant

Treatment of Dyslipidemia

Tocotrienols reduce carotid artery stenosis progression

- Regression of carotid artery stenosis in 7 of 25 subjects with know cerebrovascular disease over 18 months treated with mixture of tocotrienols.

4/21/83

Suddenly, amidst all the confusion, Fifi seized the controls and saved the day.

Treatment of Dyslipidemia

PANTETHINE VS PANTOTHENIC ACID

- Pantothenic acid is the precursor to Coenzyme A
- Pantethine is the disulfide derivative of pantothenic acid and is metabolized to cystamine (SH)

PANTETHINE: 28 Clinical human trials with 646 patients

- Lowers TC 15% (up to 20.5% at 9 months)

  Lowers LDL 20% and APO B(up to 27.6% at 9 months)
  Increased HDL 8% and APO A-I
  Lowers TG 33%(up to 36.5% at 9 months)

Comparisons to fibrates showed similar reductions in lipids

Reduces lipid deposition and fatty streak formation in aorta and coronary arteries

Reduces intimal thickening in the aorta and coronary arteries.

Reduces peroxidation of LDL-C

Treatment of Dyslipidemia

PANTETHINE

- Inhibit cholesterol synthesis and accelerate FA metabolism in mitochondria
  - Inhibits hepatic acetyl-CoA carboxylase (FA oxidation)
  - Increases CoA in cytoplasm which stimulates the oxidation of acetate at the expense of fatty acid and cholesterol synthesis. Increased Krebs cycle activity .
  - 50% inhibition of FA synthesis and 80% inhibition of cholesterol synthesis.
  - Increases cholesterol esterase activity
  - Inhibits HMG-CoA reductase
- Dose: 300 mg TID or 450 mg BID
- Peak effect is at 4 months in most but may be up to 6-9 months.

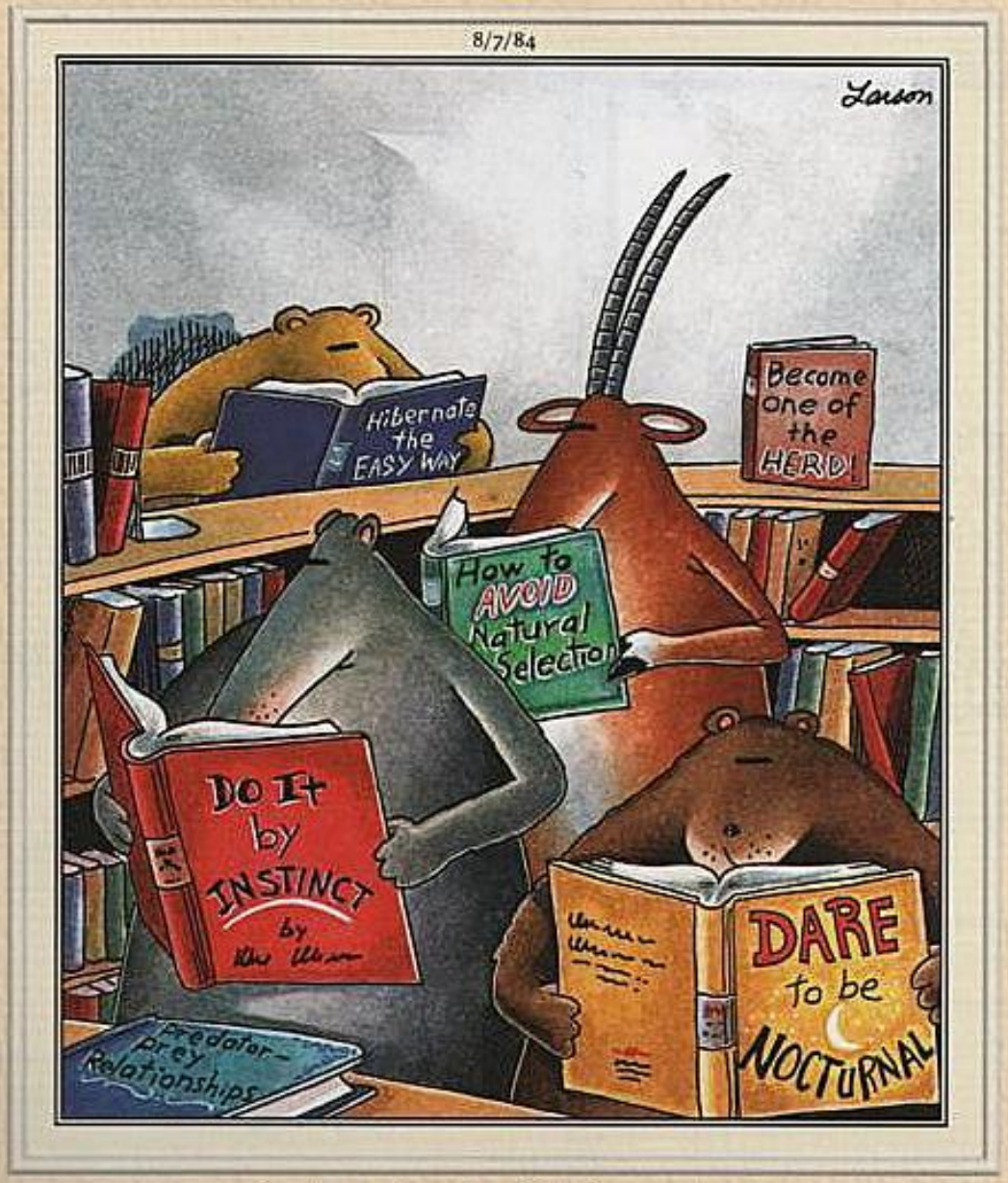
(Atherosclerosis 1984; 501:73)
(Atherosclerosis 1987; 68:41)
(Biochem Biophys Acta 1988; 963:389)
Nutrition Research 2005;25: 319

Lipoprotein Particle Numbers Therapeutic Guidelines

Lipoprotein	Therapeutic Life Style Changes (diet & exercise)	Statins	Niacin	Fibrates	Estrogens	Resins	Absorption Inhibitors	Omega-3's EPA & DHA	Alcohol (moderate)
VLDL (Triglycerides)	♥	♥	♥♥	♥♥	X	X	♥	♥♥	■
RLP (IDL)	♥	♥	♥	♥	X	X	♥	♥♥**	■
LDL I & II - buoyant	♥	♥♥	♥	♥	♥	♥	♥	♥**	■
LDL III - dense	♥	♥**	♥♥	♥	♥♥	♥	♥	■	■
LDL IV or Lp(a)	■	■	♥♥	■	♥	■	■	■	■
HDL 2b - buoyant	♥♥	♥	♥	♥	♥	■	■	■	♥
HDL 2a & 3	♥	♥	♥♥	♥	♥	■	■	■	♥

♥♥ Therapeutic ♥ Beneficial ■ Little or No Effect X Negative Result

*These guidelines provide some of the treatment options available to modify lipoprotein particle numbers determined by the LPP™ test.
**Spectracell Laboratories observed response to treatment.
The National Cholesterol Education Program (NCEP) guidelines provide dosage information on the treatment options.



In the animal self-help section