

Pathophysiology of lipid metabolism

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Keystones

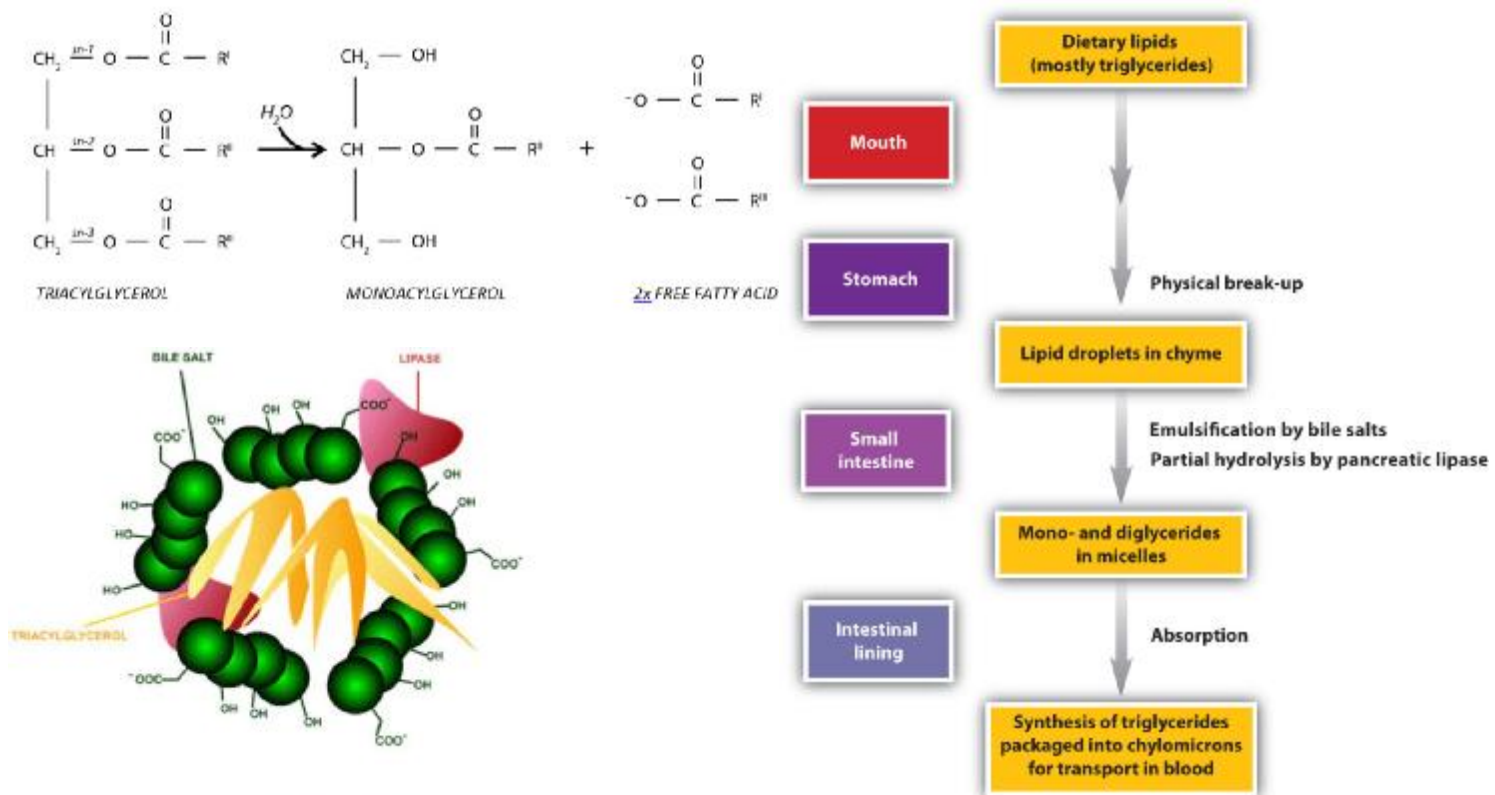


- Dyslipidemias
- Atherosclerosis
- Obesity



GOOD FATS	BAD FATS
MONOUNSATURATED FATS (OMEGA-9) Monounsaturated fats are liquid at room temperature and naturally occur in many foods.	TRANS FATS Most trans fats are artificially produced as a result of partial hydrogenation, which is a process used to convert liquid oil to a solid.
POLYUNSATURATED FATS (Omega-3) Polyunsaturated fats also are liquid at room temperature and naturally occur in many foods.	SATURATED FATS Saturated fats are typically solid at room temperature and naturally occur in foods such as meat.

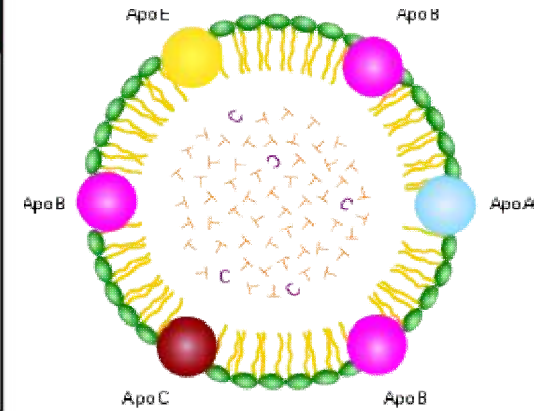
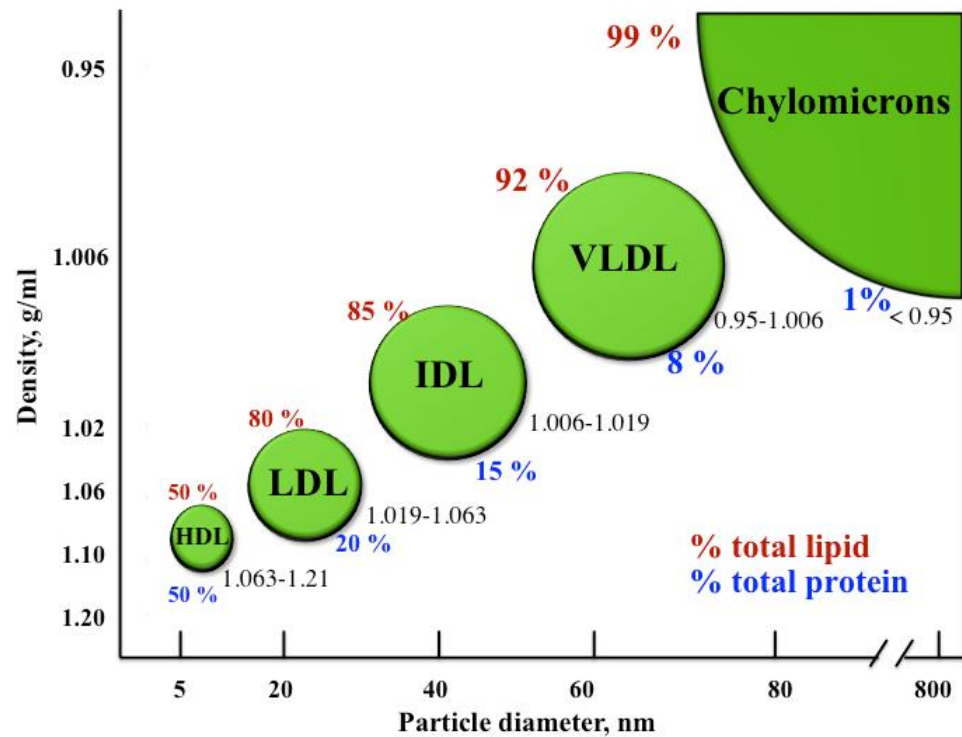
Digestion and Absorption



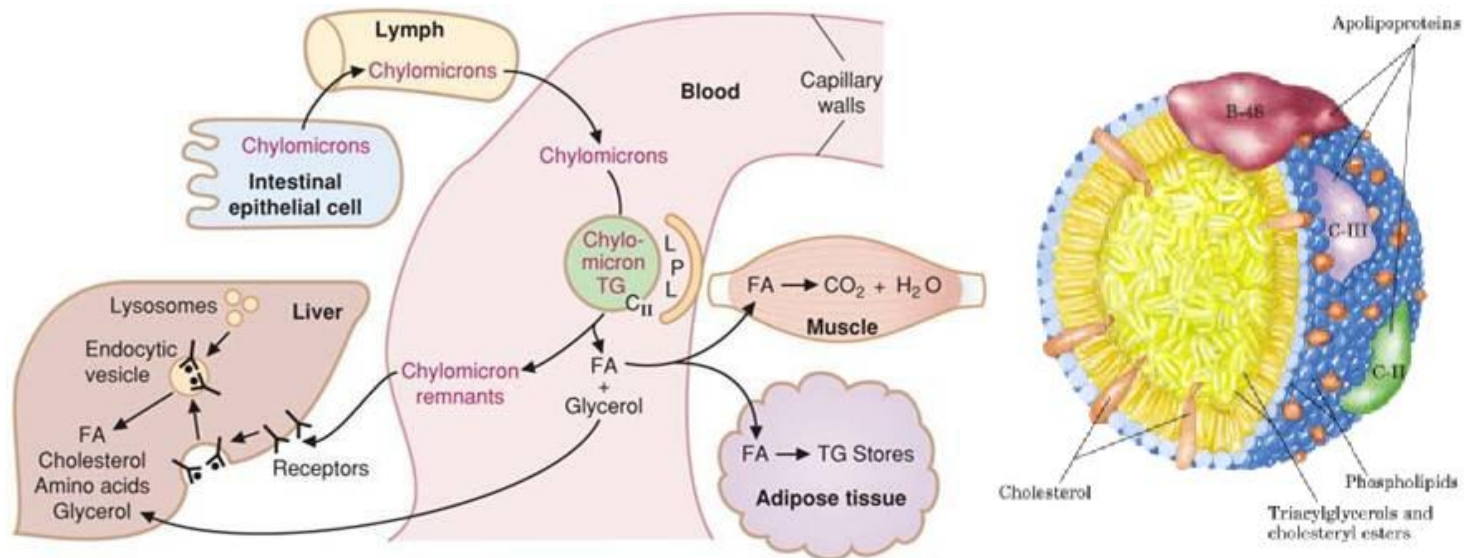
What may go wrong?

- Insufficient bile in duodenum (cholecystitis, cholelithiasis)
- Insufficient pancreatic lipase in duodenum (pancreatitis)
- Food, rich in Ca^{2+} and Mg^{2+} salts
- Stomach hyperacidity (decreased lipase activity)
- Increased intestinal passage
- Hyponatremia, e.g. Addison's disease (α -GlyceroP)
- Hypoproteinemia, hypovitaminosis A, B, C (decreased chylomicron synthesis)

Further logistics

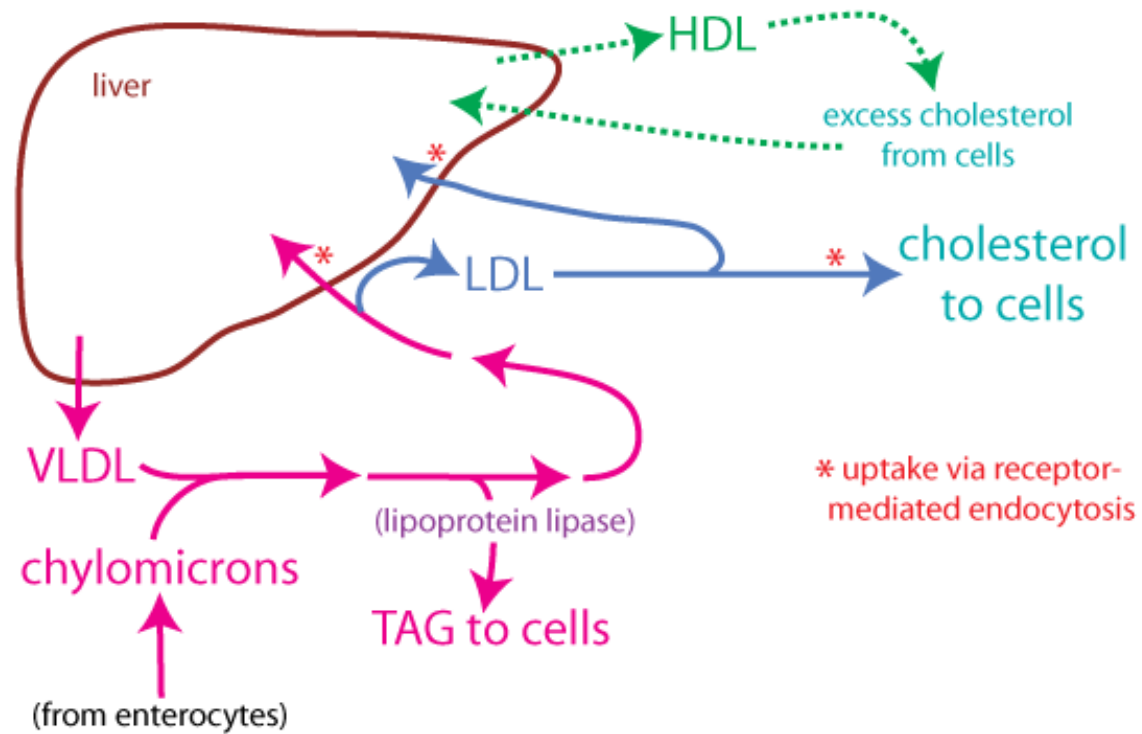


How the lungs digest lipids... and more



The Lipoprotein Lipase (LPL) requires ApoC-II as a co-factor

Liver Almighty



Under Apo-control

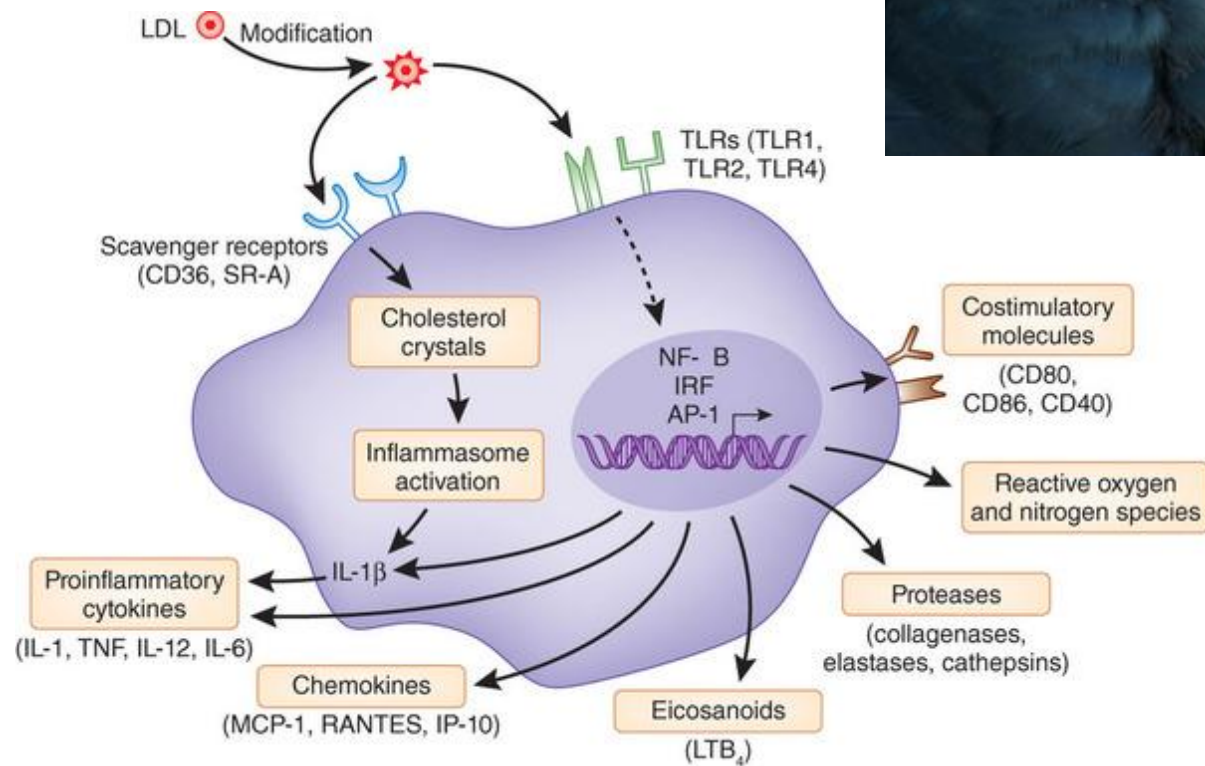
Ø ApoA – Activates Lecithine-Cholesterol Acyl-Transferase (LCAT)

Ø ApoB – Binding to cellular receptors

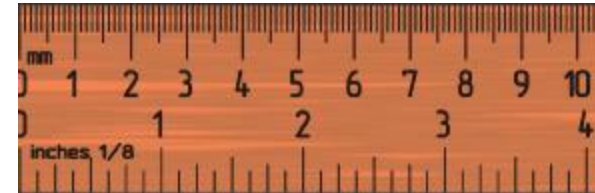
Ø ApoC – Activates LPL

Ø ApoE – Binding of other lipoproteins to LDL

Scavengers



Lipid metrics



	Optimal	Borderline	High
TC mg/dL	<200	200 - 239	>239
TC mmol/l	<5.2	5.3 - 6.2	>6.2

	Ideal	Intermediate	High
LDL-C in mg/dL	<130	130 - 159	>159
LDL-C in mmol/l	<3.36	3.36 - 4.11	>4.11

	High risk	Intermediate	Protective
HDL-C in mg/dL	<40	40 - 60	>60
HDL-C in mmol/dl	<1.03	1.03 - 1.55	>1.55

		Optimal	Moderate	High
Total/HDL ratio	Men	<3.5	3.5 - 5.0	>5.0
	Women	<3.0	3.0 - 4.4	>4.4
LDL to HDL ratio		<2.5	2.5 - 3.3	>3.3
HDL to LDL ratio		>0.4	0.4 to 0.3	<0.3
TG to HDL ratio		<2	2 - 3.8	>3.8

“Keep your
cholesterol ratio
5-to-1 or lower”.

AHA

A blood too fat

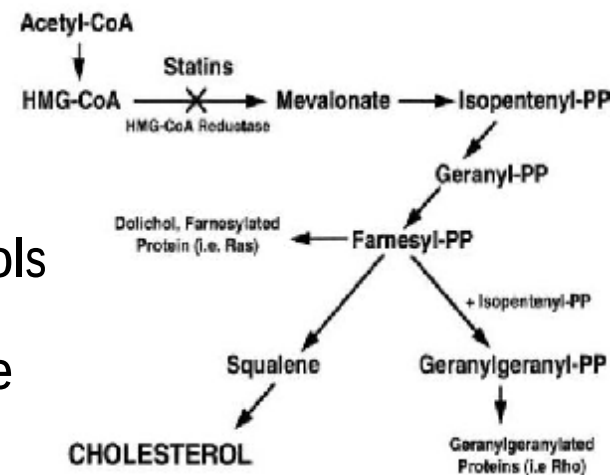
Phenotype/ relative frequency	Lipoprotein(s) elevated	Serum Chol. Conc.	Serum TG Conc.	Etiology
I <1%	Chylomicrons	Normal to #	####	Deficiency in LPL or apoCII
IIa 10%	LDL	##	Normal	↓ or no functional LDL-R
IIb 40%	LDL and VLDL	##	##	Overproduction of VLDL by liver
III <1%	IDL	##	###	Abnormal apoE
IV 45%	VLDL	Normal to #	##	Overproduction and/or impaired catabolism of VLDL
V 5%	VLDL and chylomicrons	# to ##	####	Increased production or decreased clearance of VLDL and chylomicrons

Acquired hyperlipemias

LPL - inhibitors

- NaCl
- Biliary salts (cholestasis)
- Pancreatic LPL-inhibitor
- Circadian genes

Hypoalbuminemia



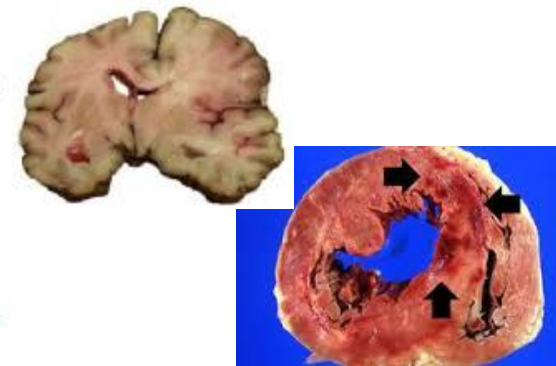
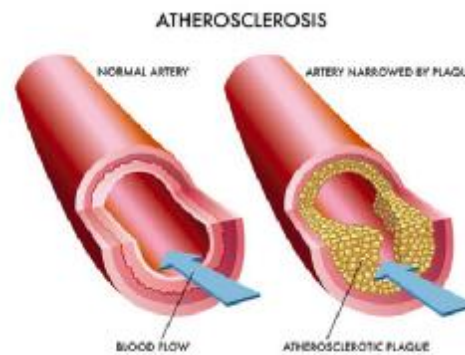
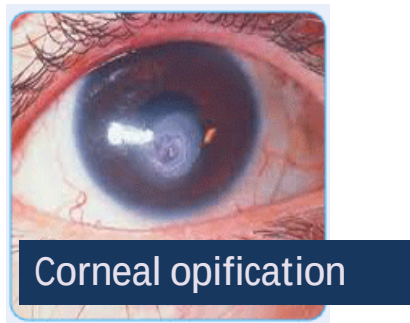
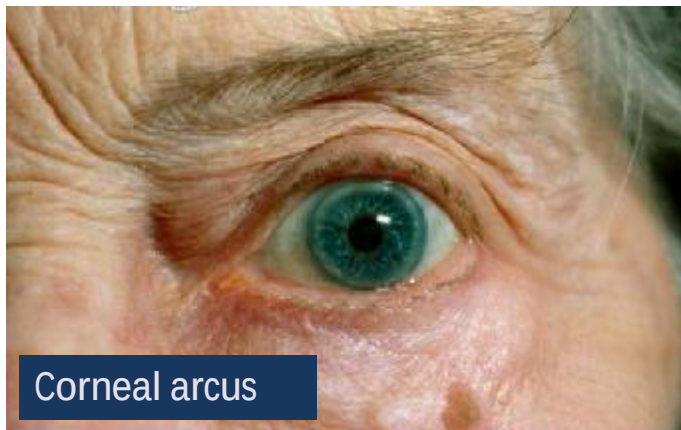
Low HDL is even worse

Independent predictor of CAD!

Causes:

- Insulin resistance
- Physical inactivity
- Diabetes mellitus type 2
- Smoking
- High CH intake
- Drugs (anabolic steroids, contraceptives, β -blockers, diuretics)

Look at the cholesterol... it matters!



Atherosclerosis

Definition and risk factors

- **Modifiable**

- Diabetes mellitus
- Dyslipoproteinemia
- Tobacco smoking
- C-reactive protein
- Vitamin B6 deficiency
- Hypothyroidism

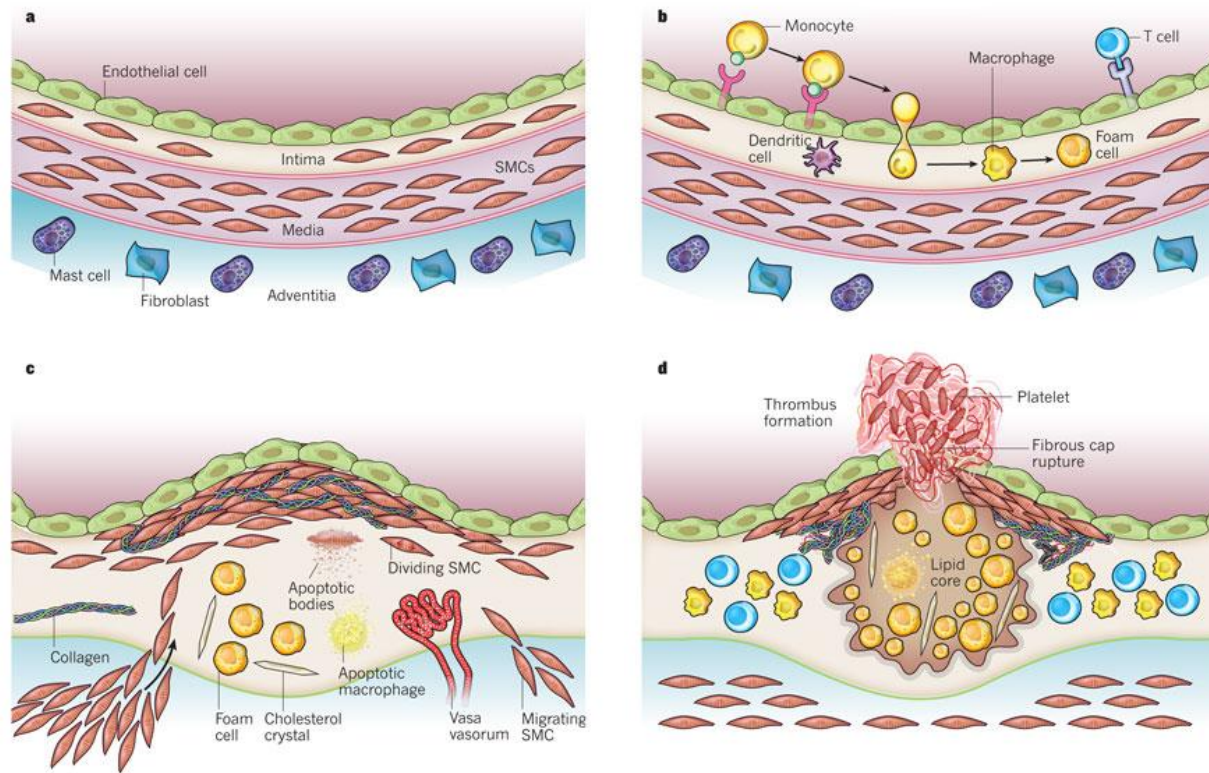
- **Nonmodifiable**

- Advanced age
- Male sex
- Genetics

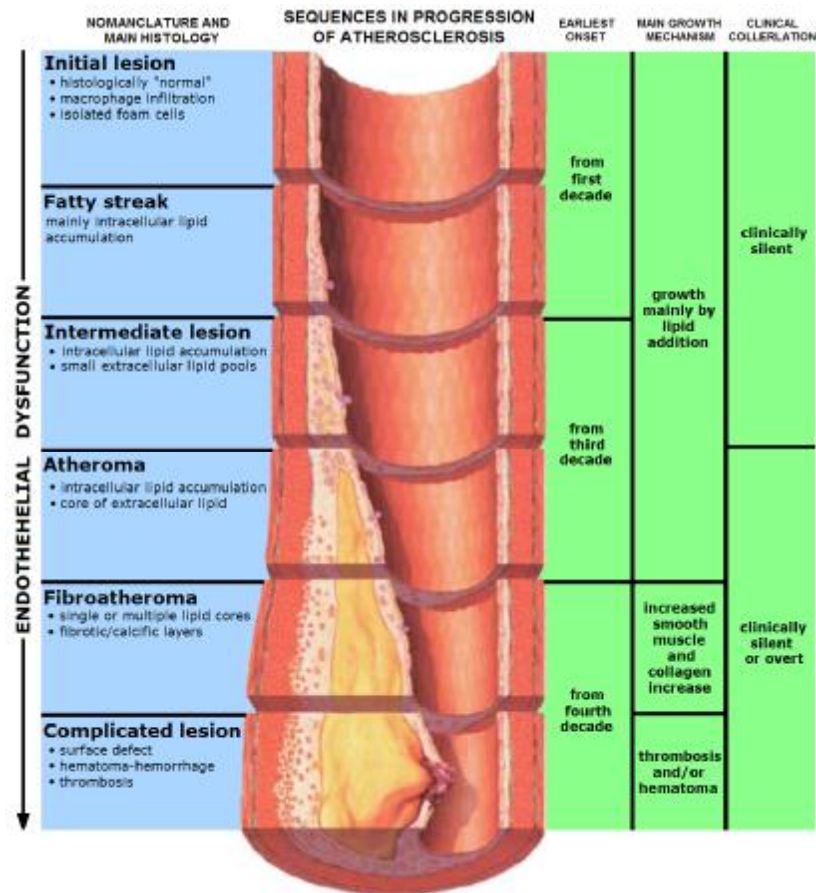
- **Uncertain**

- Obesity
- Postmenopausal estrogen deficiency
- Saturated fat
- Trans fat
- High carbohydrate intake
- Short sleep duration
- Chlamydia pneumoniae

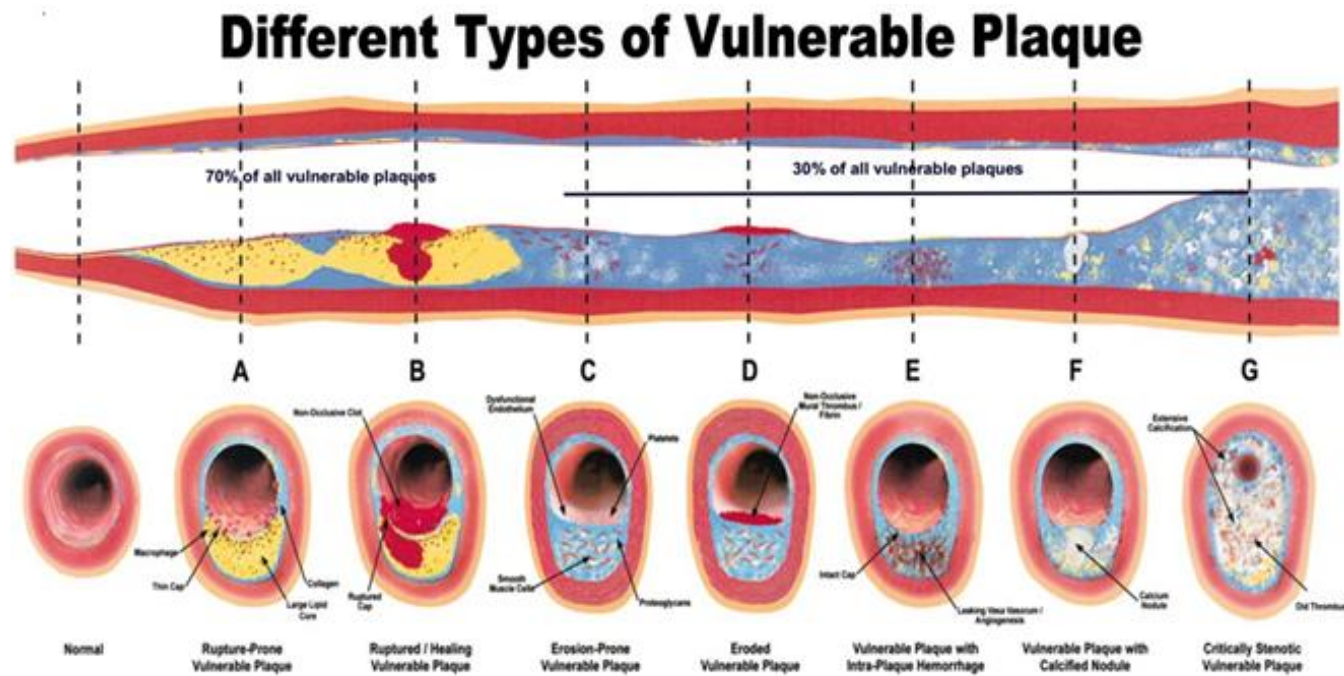
Step by step



From cradle to grave



Sometimes it gets complicated



Nature Reviews | Immunology

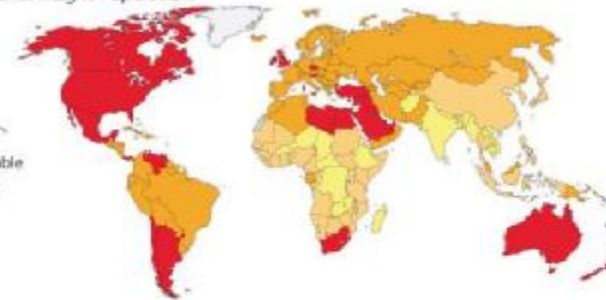


KEEP
CALM
AND
SAY NO TO
JUNK FOOD!

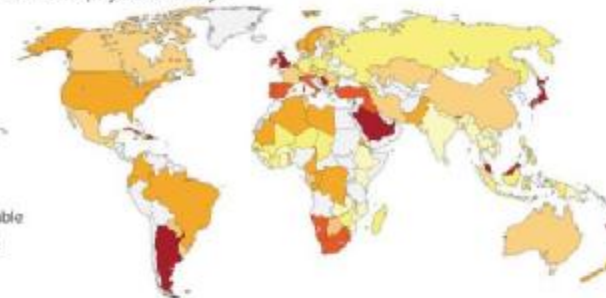
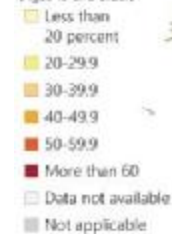
Etiology

- Ø Genetic predisposition
 - ü Monogenetic
 - ü Polygenetic
- Ø Maternal diabetes during pregnancy
- Ø Age
- Ø Lifestyle
 - ü Sedentary
 - ü Overeating/ Junk food
 - ü Smoking cessation
 - ü Socio-economic status
- Ø Medical treatment
- Ø Viruses?

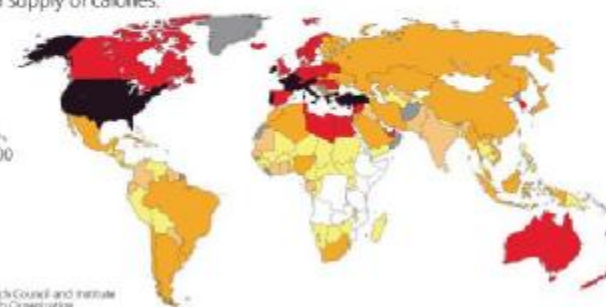
Percentage of Overweight Population:
(Ages 20 and older)



Prevalence of insufficient physical activity:
(Ages 15 and older)

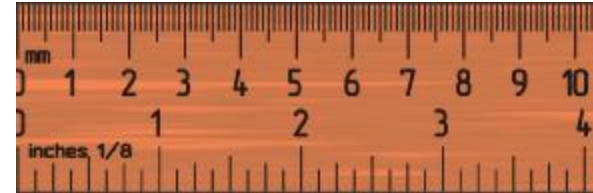


Daily per capita supply of calories:



Sources: National Research Council and Institute of Medicine, World Health Organization

Obesity metrics



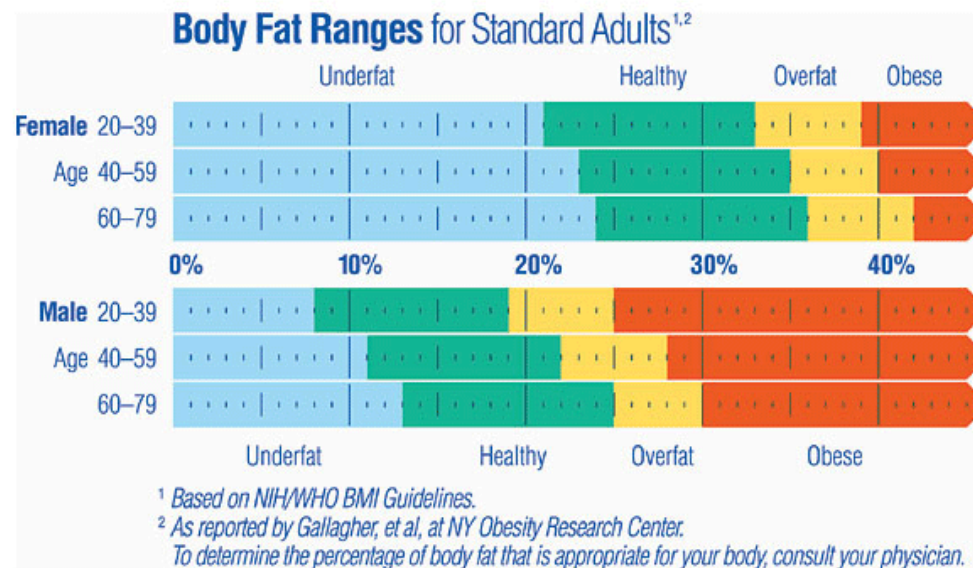
Obesity is a medical condition in which excess body fat ...

How is body fat percentage measured?

- Ø Underwater weighing
- Ø Whole-body air displacement plethysmography
- Ø Dual energy X-ray absorptiometry
- Ø Bioelectrical impedance analysis
- Ø Skinfolds



Birthdays come with an extra... fat



Lower basal metabolic rate
 Lower muscle mass

Insulin resistance
 Sedentarism

Types of obesity



Life issue vs Wife issue

© ADAM, Inc.

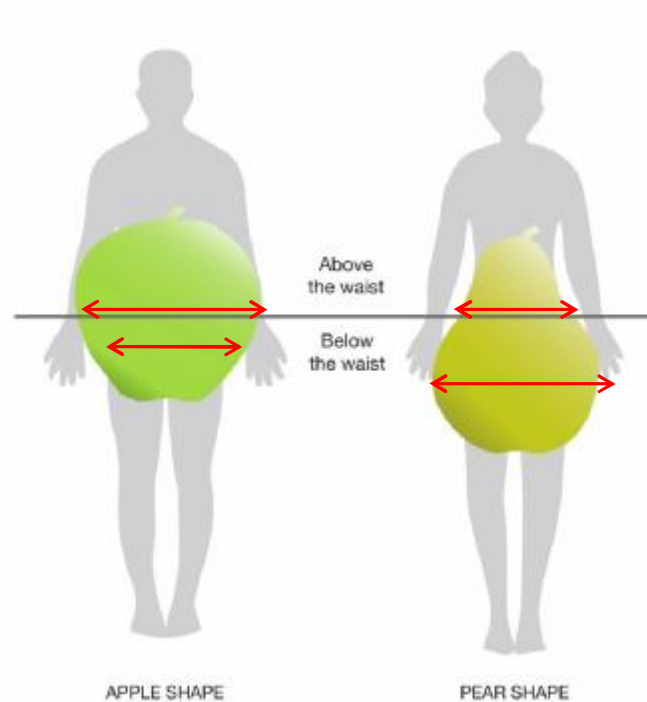
Ø30% less Ins-R

Ø"Active fat"

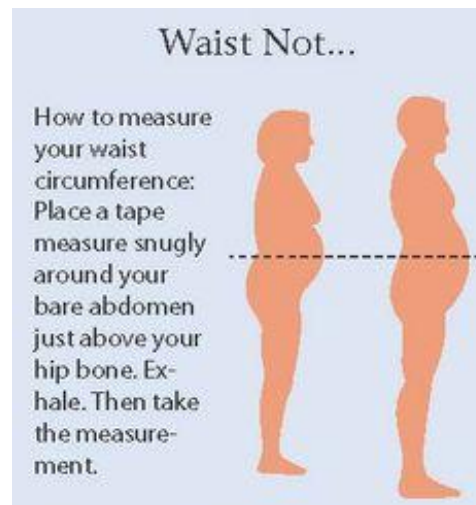
FOFI
FOTI
TOFI
TOTI



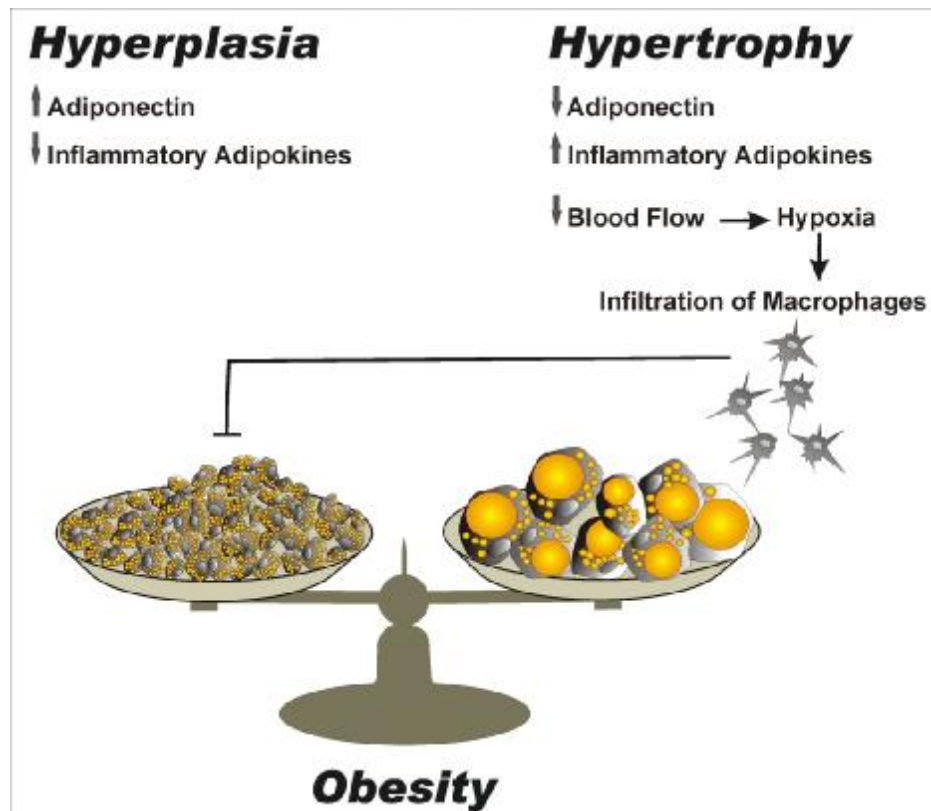
Some more metrics



	Males	Females
Waist	>94 cm	>80 cm
Waist/Hip ratio	>0.90	>0.85
Shirt size	>43 (XL)	



Too many or too big



Classification

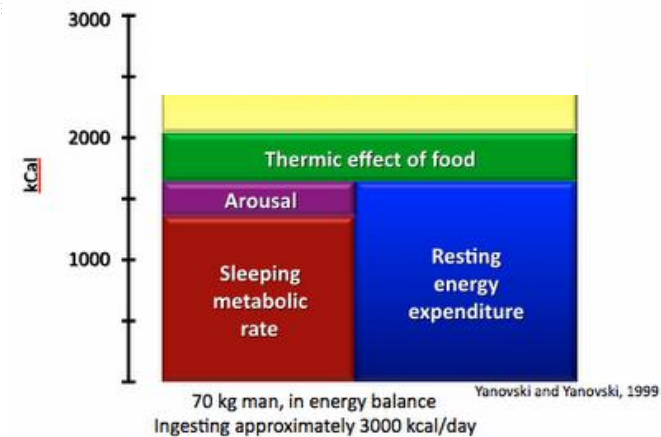
- Primary
 - Alimentary
 - Regulatory
 - Metabolic
- Secondary
 - Endocrine
 - Iatrogenic

Alimentary...not elementary

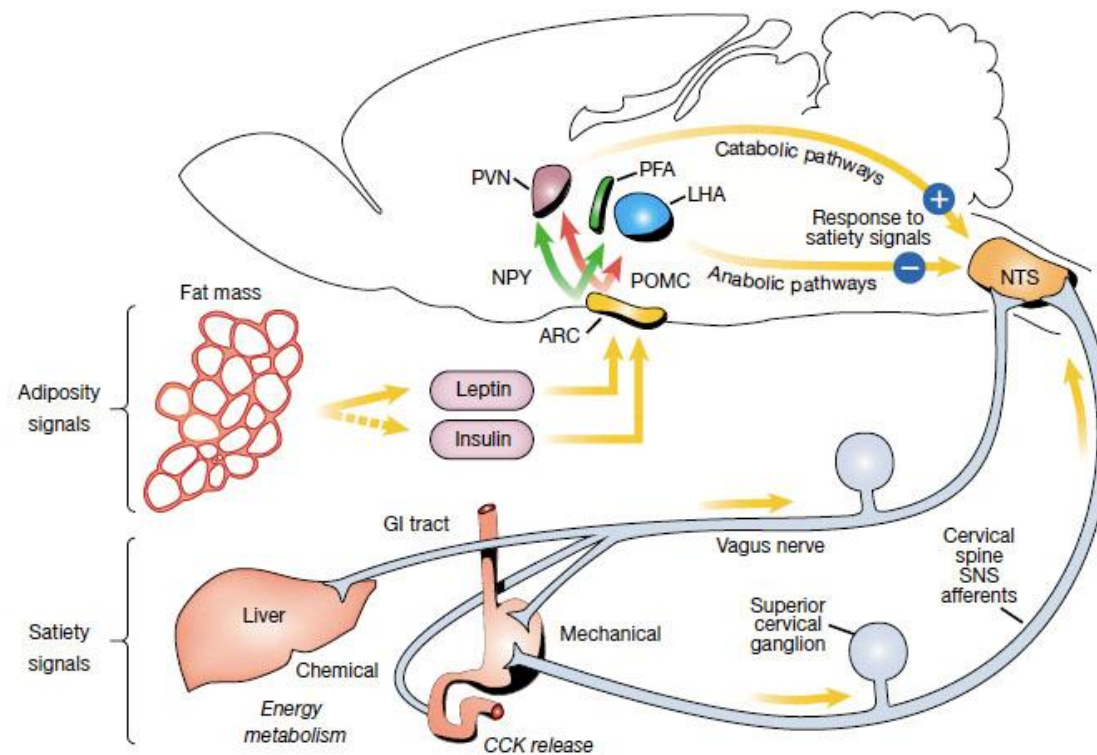
Energy
input



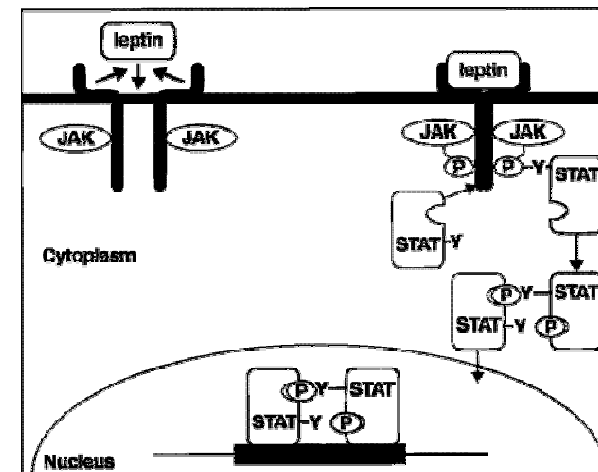
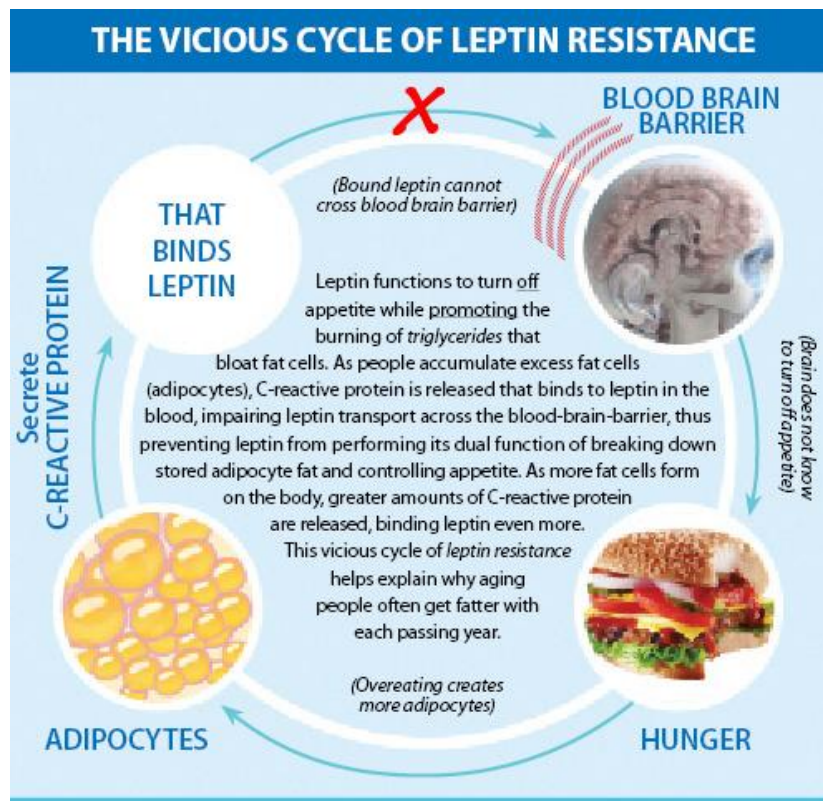
Energy
expenditure



Hunger or Appetite



Leptin resistance



Metabolic obesity

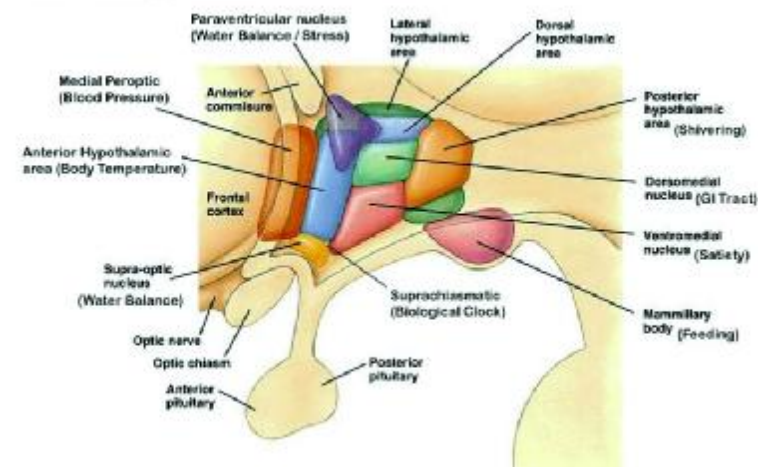
- Ø Decreased Basal Metabolic Rate (BMR)
- Ø Tendency towards lipogenesis
- Ø More efficient E- production
- Ø More efficient energy expenditure

Regulatory obesity

Hypothalamic damage

- Ø Tumor
- Ø Trauma
- Ø Haemorrhage
- Ø Infection

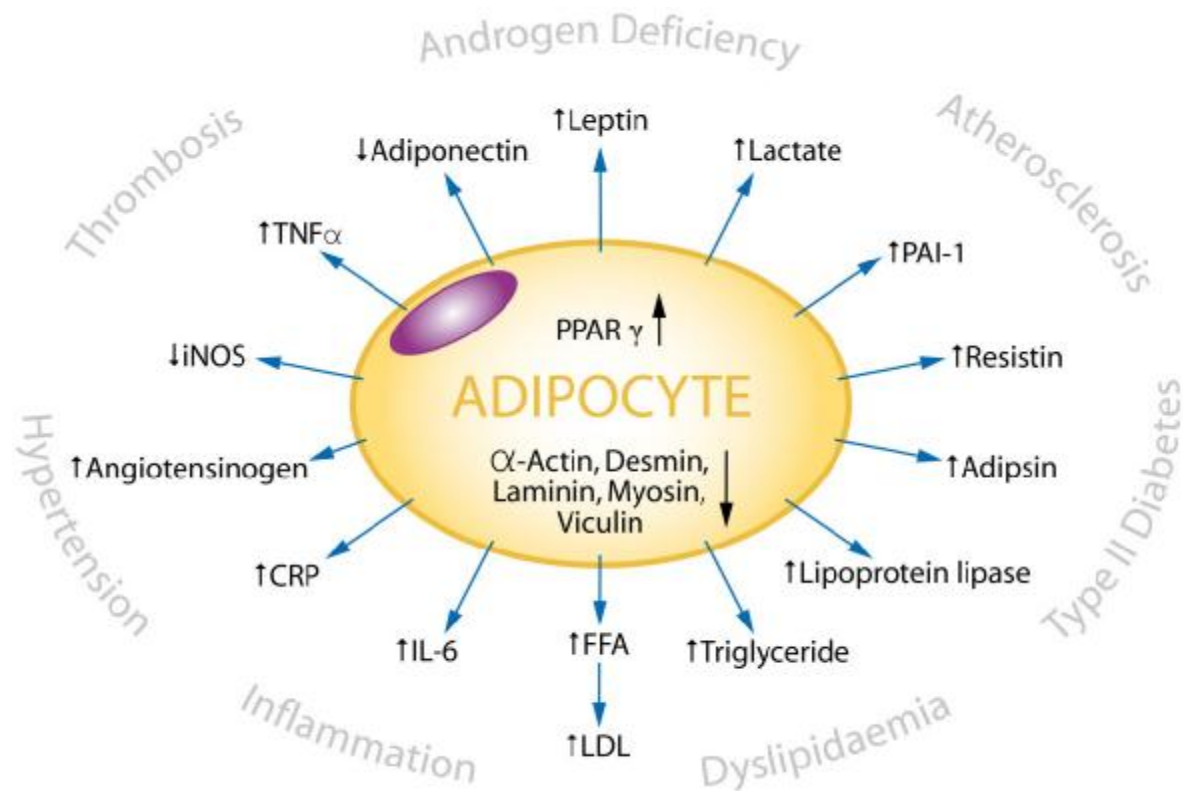
► Nuclei of the Hypothalamus

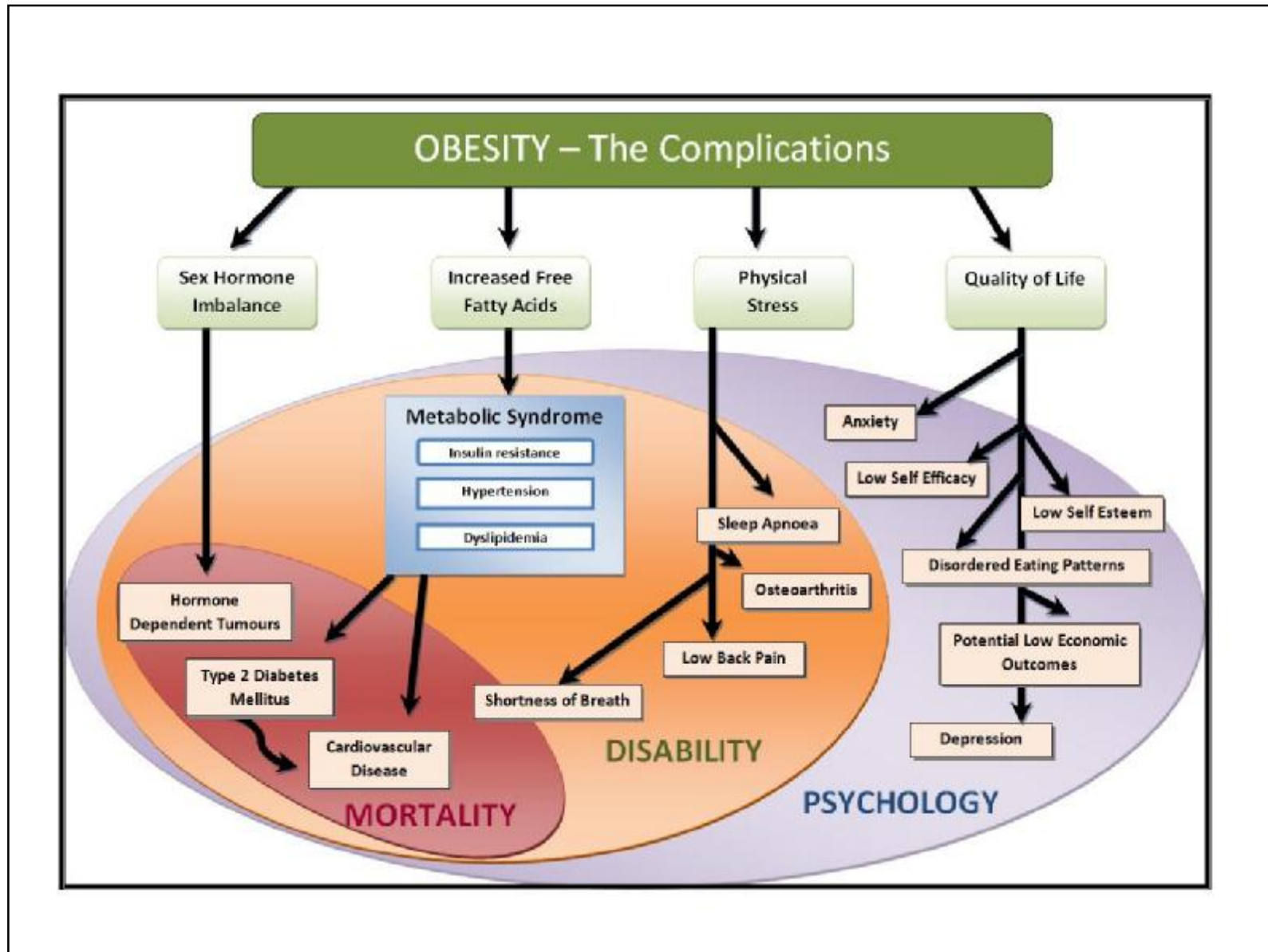


Secondary obesity

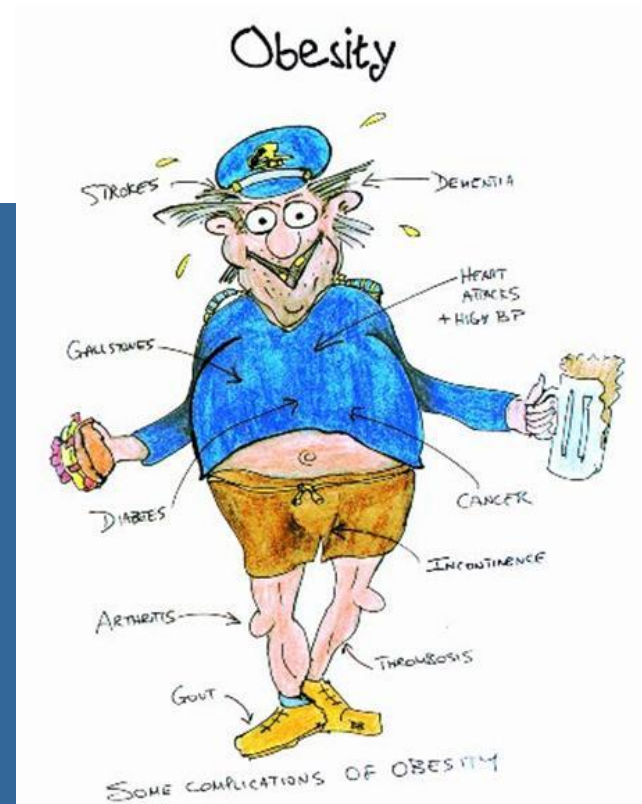
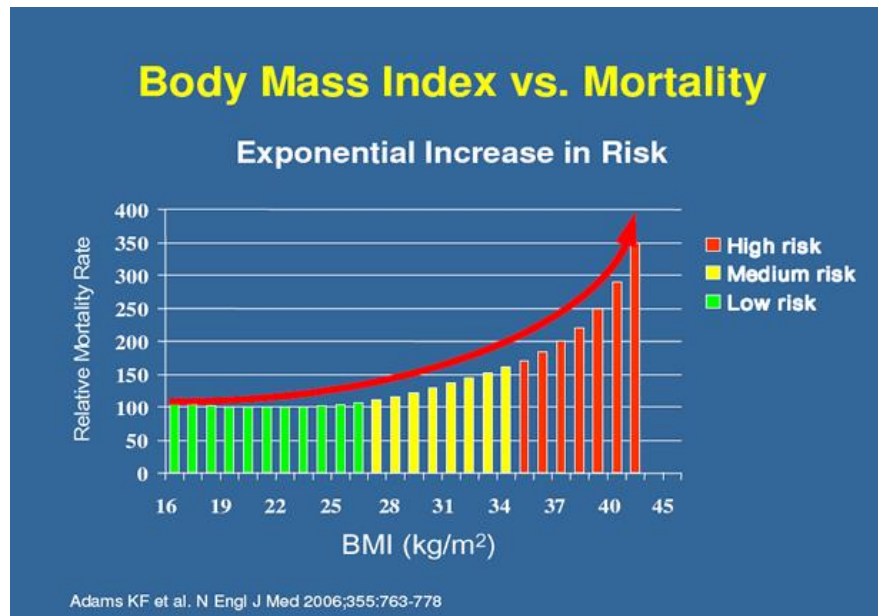
- Endocrine
 - Hypogonadism
 - Hypothyroidism
 - Adreno-genital syndromes
 - Hyperglucocorticism
 - Polycystic ovaries (PCOS)
 - Pregnancy (progesterone, leptin)
- Iatrogenic
 - CS, Antidepressants ...

The Endocrine Adipocyte





Morbidity and mortality



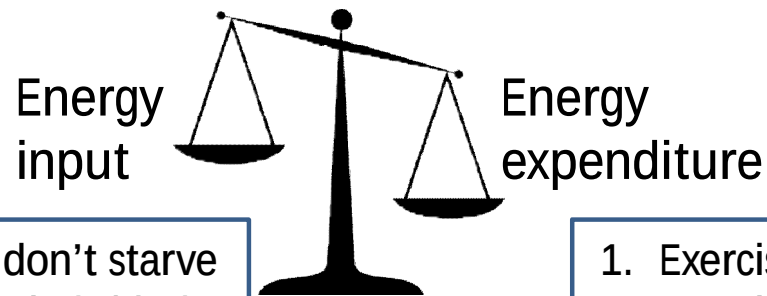
The Metabolic Syndrome

MS components	ATPIII [3]	IDF [4]
To be diagnosed as MS:	3 or more components	central obesity plus at least two other components
Waist circumference	≥ 88 cm	≥ 80 cm
blood pressure	SBP ≥ 130 or DBP ≥ 85 mmHg or Taking hypertension medication	Same as ATPIII criteria
serum glucose level	≥ 6.1 mmol/L or taking diabetes medication	≥ 5.6 mmol/L or taking diabetes medication
serum triglyceride level	> 1.70 mmol/L	> 1.70 mmol/L or taking abnormal lipid medication
HDL-cholesterol	< 1.29 mmol/L	< 1.29 mmol/L

Add-ons

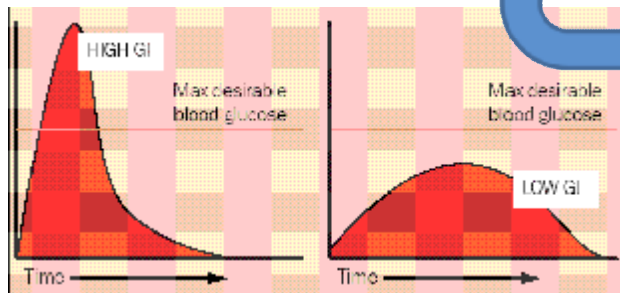
- Hyperuricemia
- Obstructive Sleep Apnea
- hsCRP
- PCOS

Tilt the scales

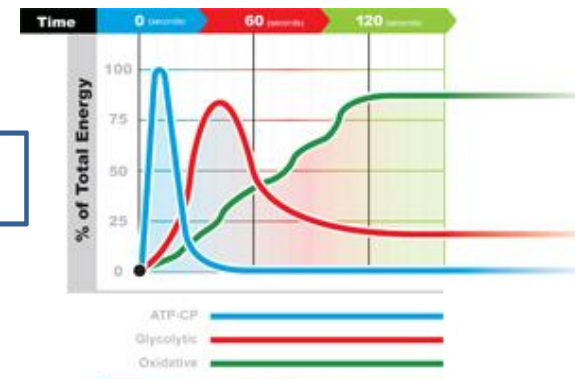


1. Eat less, but don't starve
2. Frequent meals (5/day)
3. More fibers
4. Less CH with high GI

1. Exercise more (5x45)
2. Exercise aerobic



\$Insulin



Giuseppe Arcimboldo

