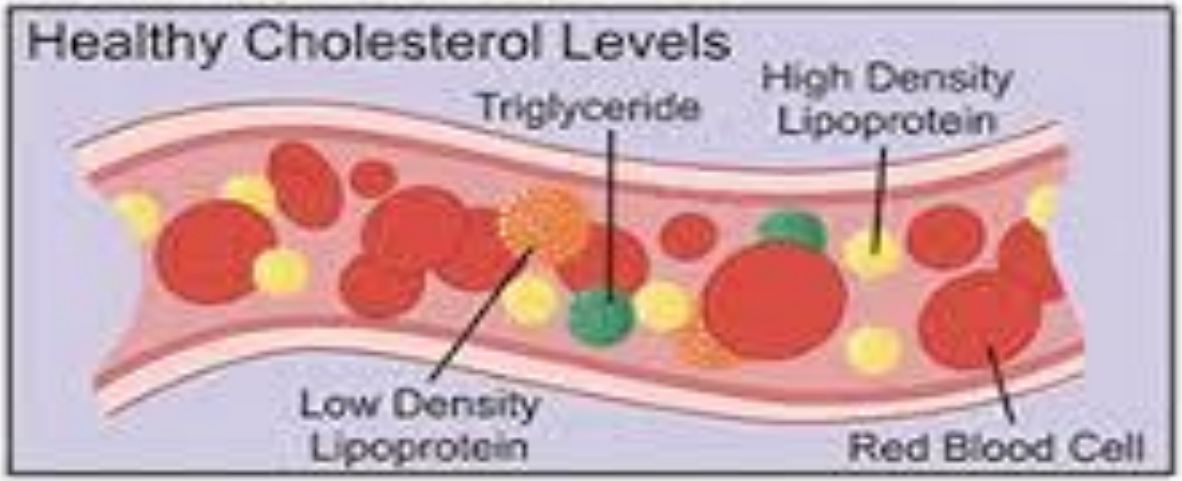
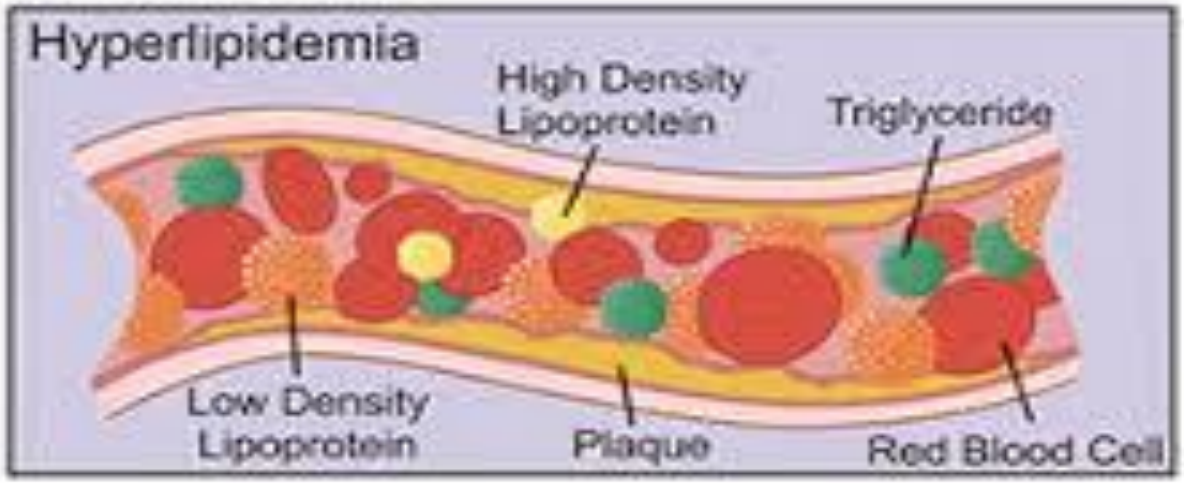
# Hyperlipidemia



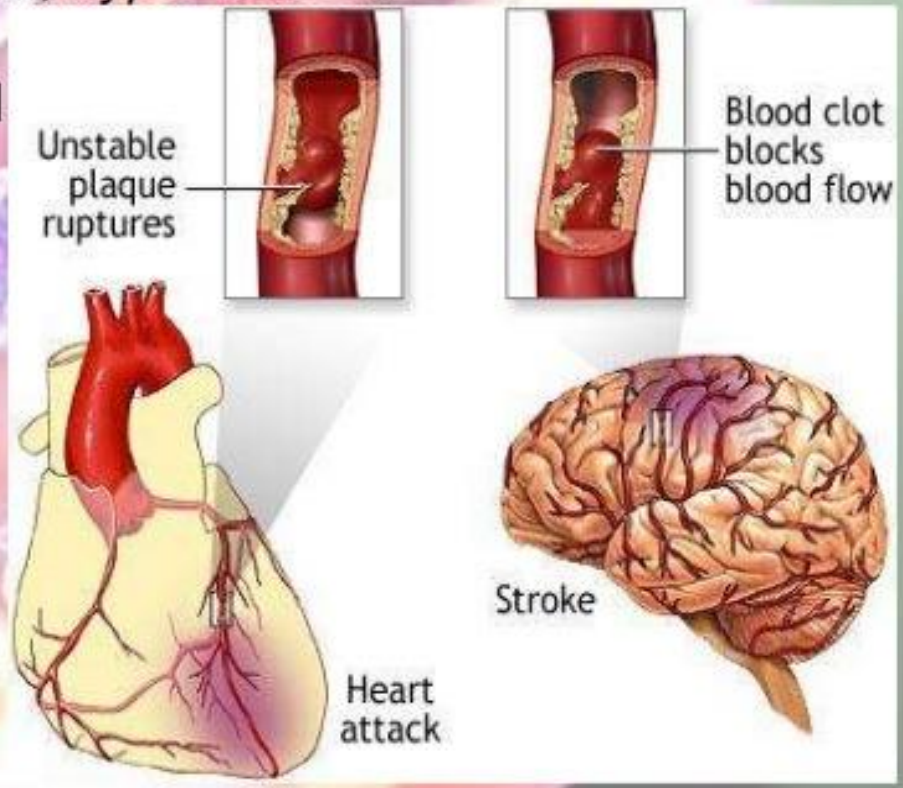

# INTRODUCTION

- **Hyperlipidemia Hyperlipoproteinemia** means abnormally increased plasma lipoproteins-one of the risk factors for atherosclerosis (deposition of fats at walls of arteries, forming plaque)

- **Other risk factors**-*Cigarette smoking, Diabetes*, another source of oxidative stress. Also, obesity and, *hypertension*.

- ***Hyperlipemia*** denotes increased levels of triglycerides.

- Such abnormality is extremely common in general population, regarded as highly modifiable risk factor for cardio vascular diseases, due to influence of cholesterol.

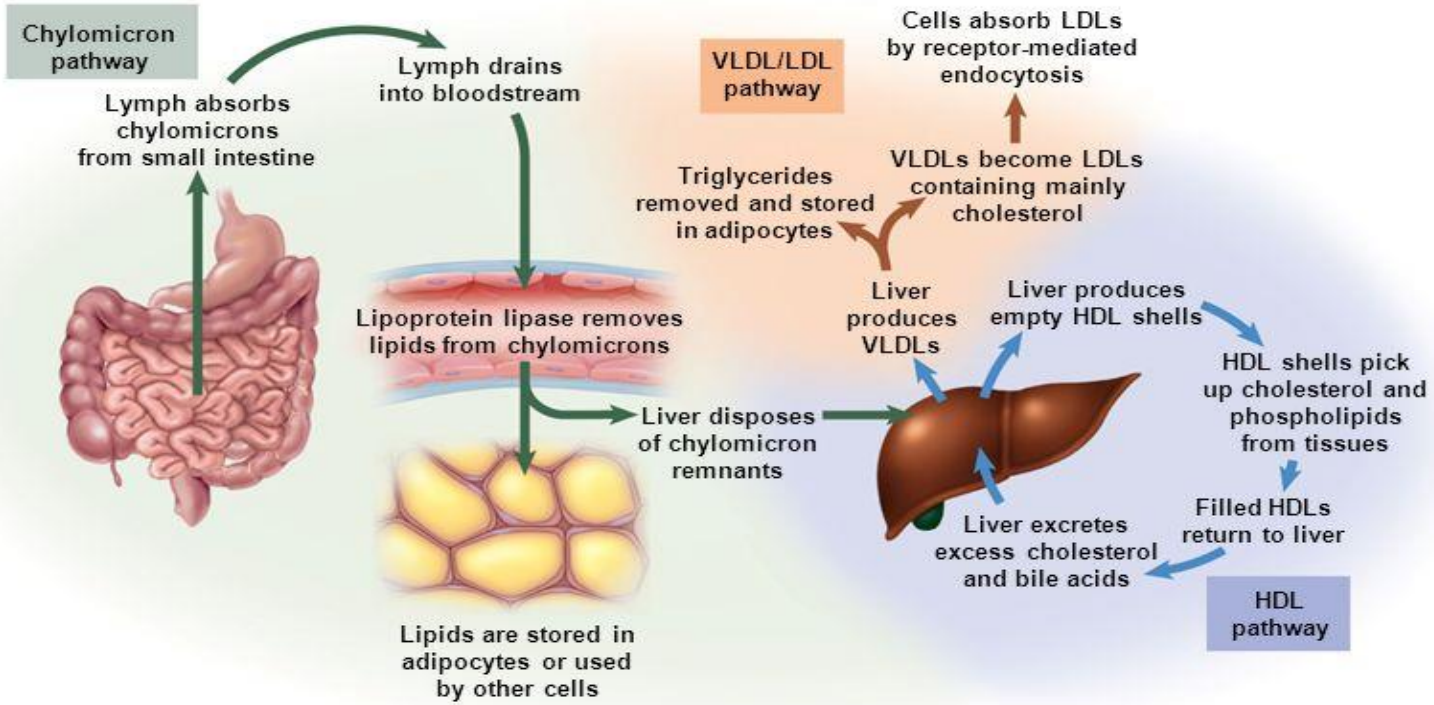


# The story of lipids

- Chylomicrons transport fats from the intestinal mucosa to the liver
- In the liver, the chylomicrons release triglycerides and some cholesterol and become low-density lipoproteins (LDL).
- LDL then carries fat and cholesterol to the body's cells.
- High-density lipoproteins (HDL) carry fat and cholesterol back to the liver for excretion.

# Lipoprotein Processing Pathways






(b) Lipoprotein-processing pathways

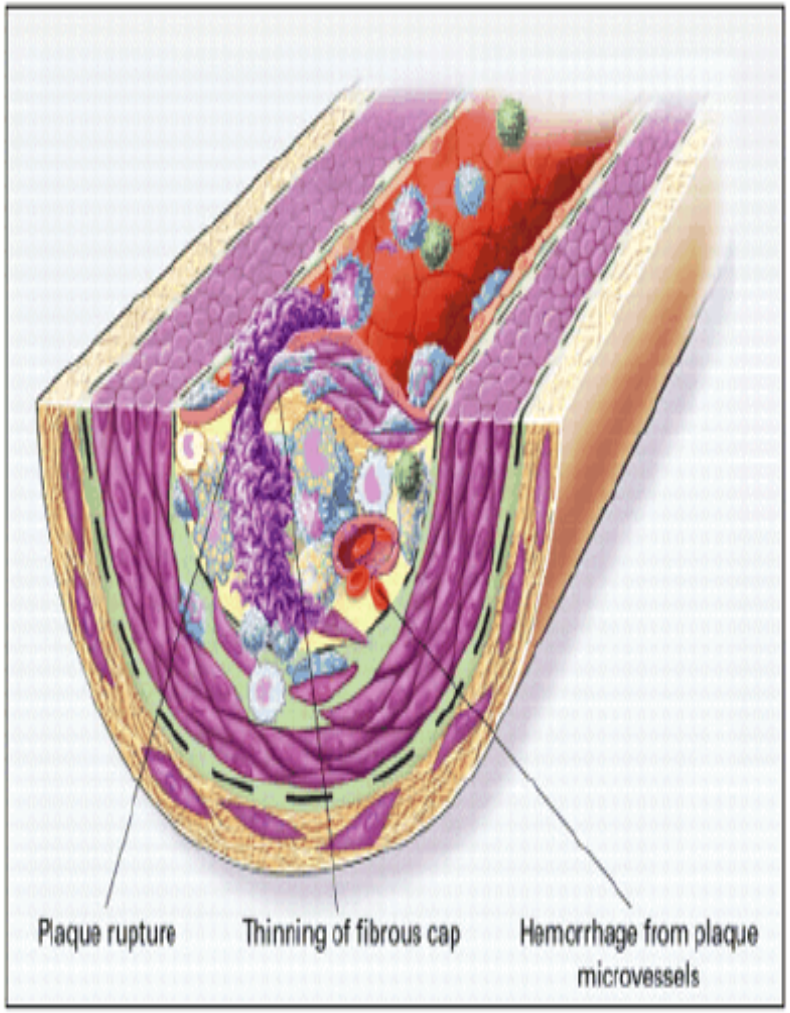
Figure 26.2b

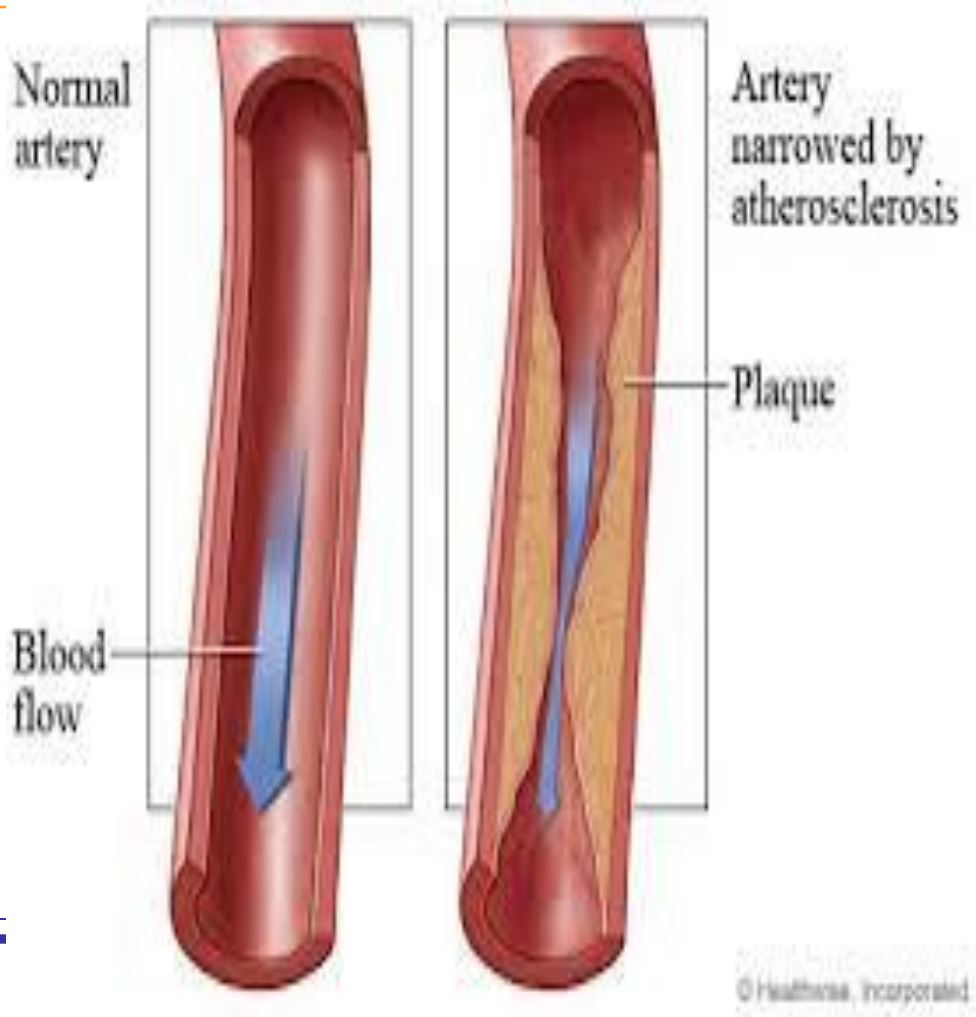
26-30

# The story of lipids (cont.)

- When oxidized LDL cholesterol gets high, atheroma formation in the walls of arteries occurs, which causes atherosclerosis.
- HDL cholesterol is able to go and remove cholesterol from the atheroma.
- Atherogenic cholesterol → LDL, VLDL, IDL

# Atherosclerosis



# Causes of Hyperlipidemia

1. Diet
2. Hypothyroidism
3. Nephrotic syndrome
4. Anorexia nervosa
5. Obstructive liver disease
6. Obesity
7. Diabetes mellitus
8. Pregnancy
9. Acute hepatitis
10. Systemic lupus erythematousus (SLE)
11. AIDS (protease inhibitors)

# Dietary sources of Cholesterol

| Type of Fat | Main Source | Effect on Cholesterol levels |
|---|---|---|
| **Monounsaturated** | Olives, olive oil, canola oil, peanut oil, cashews, almonds, peanuts and most other nuts; avocados | Lowers LDL, Raises HDL |
| **Polyunsaturated** | Corn, soybean, safflower and cottonseed oil; fish | Lowers LDL, Raises HDL |
| **Saturated** | Whole milk, butter, cheese, and ice cream; red meat; chocolate; coconuts, coconut milk, coconut oil , egg yolks, chicken skin | Raises both LDL and HDL |
| **Trans** | Most margarines; vegetable shortening; partially hydrogenated vegetable oil; deep-fried chips; many fast foods; most commercial baked goods | Raises LDL |

# Hereditary Causes of Hyperlipidemia

- Familial Hypercholesterolemia
  - Codominant genetic disorder, coccurs in heterozygous form
  - Occurs in 1 in 500 individuals
  - Mutation in LDL receptor, resulting in elevated levels of LDL at birth and throughout life
  - High risk for atherosclerosis, tendon xanthomas (75% of patients), tuberous xanthomas and xanthelasmas of eyes.
- Familial Combined Hyperlipidemia
  - Autosomal dominant
  - Increased secretions of VLDLs
- Dysbetalipoproteinemia
  - Affects 1 in 10,000
  - Results in apo E2, a binding-defective form of apoE (which usually plays important role in catabolism of chylomicron and VLDL)
  - Increased risk for atherosclerosis, peripheral vascular disease
  - Tuberous xanthomas, striae palmaris

# Checking lipids

- Nonfasting lipid panel
  - measures HDL and total cholesterol
- Fasting lipid panel
  - Measures HDL, total cholesterol and triglycerides
  - LDL cholesterol is calculated:
    - LDL cholesterol = total cholesterol – (HDL + triglycerides/5)

# When to check lipid panel

- Two different Recommendations
  - Adult Treatment Panel (ATP III) of the National Cholesterol Education Program (NCEP)
    - Beginning at age 20:  obtain a fasting (9 to 12 hour) serum lipid profile consisting of total cholesterol, LDL, HDL and triglycerides
    - Repeat testing every 5 years for acceptable values
  - United States Preventative Services Task Force
    - Women aged 45 years and older, and men ages 35 years and older undergo screening with a total and HDL cholesterol every 5 years.
    - If total cholesterol > 200 or HDL <40, then a fasting panel should be obtained
    - Cholesterol screening should begin at 20 years in patients with a history of multiple cardiovascular risk factors, diabetes, or family history of either elevated cholesteral levels or premature cardiovascular disease.

# Goals for Lipids

- LDL
  - < 100 →Optimal
  - 100-129 → Near optimal
  - 130-159 → Borderline
  - **160-189→ High**
  - ≥ 190 → Very High
- Total Cholesterol
  - < 200 → Desirable
  - 200-239 → Borderline
  - **≥240 → High**
- HDL
  - **< 40 → Low**
  - ≥ 60 → High
- Serum Triglycerides
  - < 150 → normal
  - 150-199 → Borderline
  - **200-499 → High**
  - ≥ 500 → Very High

# Determining Cholesterol Goal (LDL!)

- **Look at JNC 7 Risk Factors**
  1. **Cigarette smoking**
  2. **Hypertension** (BP ≥140/90 or on anti-hypertensives)
  3. **Low HDL cholesterol** (< 40 mg/dL)
  4. **Family History of premature coronary heart disease (CHD)** (CHD in first-degree male relative <55 or CHD in first-degree female relative < 65)
  5. **Age** (men ≥ 45, women ≥ 55)

# Determining Goal LDL

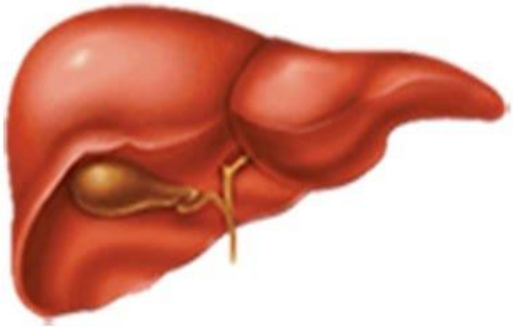
6. CHD
7. CHD Risk Equivalents:
   - Peripheral Vascular Disease
   - Cerebral Vascular Accident
   - Diabetes Mellitus

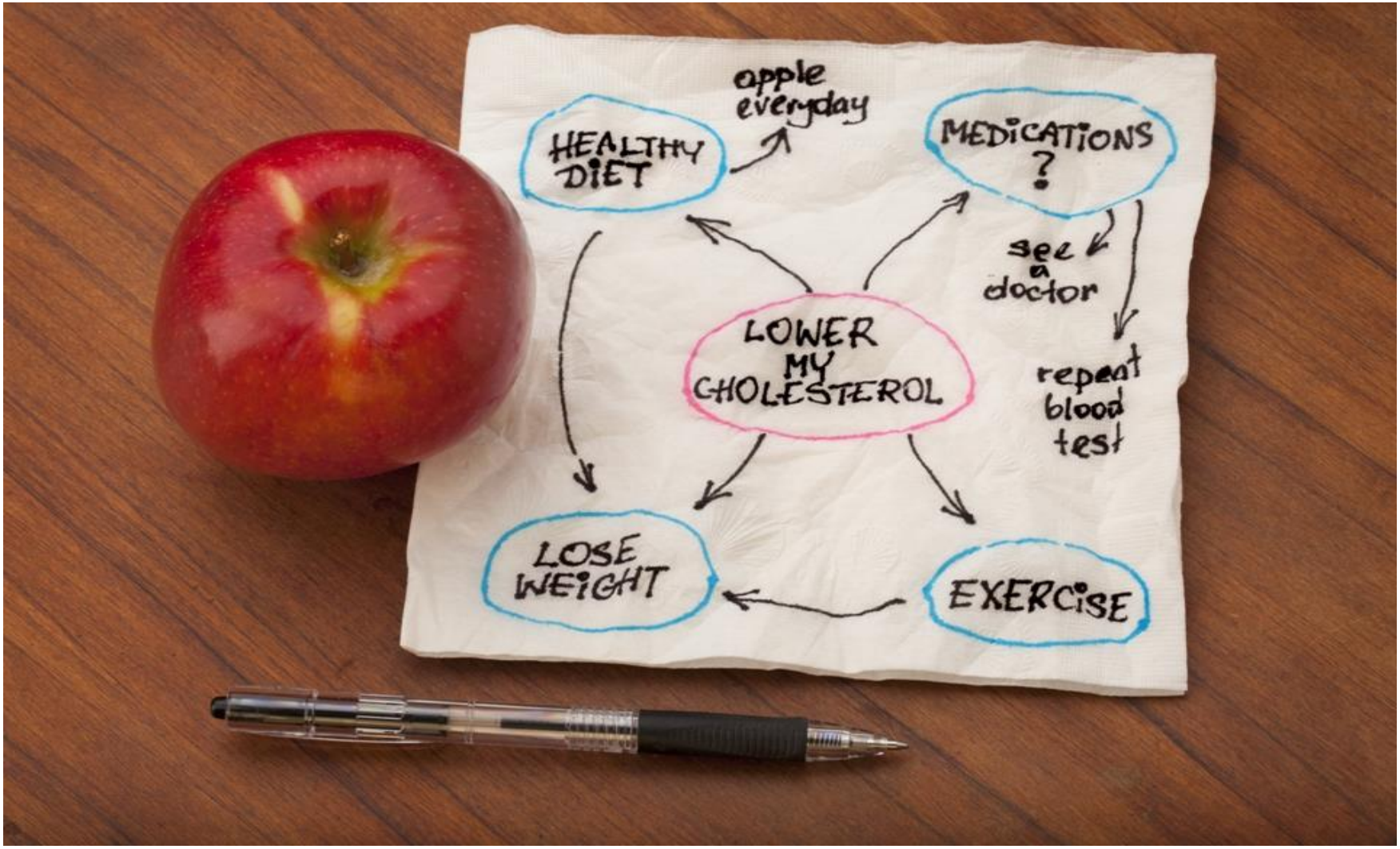
# LDL Goals

- 0-1 Risk Factors:
  - **LDL goal is 160**
  - If LDL ≥ 160: Initiate TLC (therapeutic lifestyle changes)
  - If LDL ≥ 190: Initiate pharmaceutical treatment
- 2 + Risk Factors
  - **LDL goal is 130**
  - If LDL ≥ 130: Initiate TLC
  - If LDL ≥ 160: Initiate pharmaceutical treatment
- CHD or CHD Risk Equivalent
  - **LDL goal is 100 (or 70)**
  - If LDL ≥ 100: Initiate TLC and pharmaceutical treatment

# Importance of Cholesterol

If you somehow removed all Cholesterol, the body would melt & disappear
Liver makes 75% of body's Cholesterol. Brain is made of Fat & Cholesterol




apple everyday
HEALTHY DIET
MEDICATIONS ?
see a doctor
LOWER MY CHOLESTEROL
repeat blood test
LOSE WEIGHT
EXERCISE

# Treatment of Hyperlipidemia

- Lifestyle modification
  - Low-cholesterol diet
  - Exercise

# Medications for Hyperlipidemia

| Drug Class | Agents | Effects (% change) | Side Effects |
|---|---|---|---|
| HMG CoA reductase inhibitors | Lovastatin<br>Pravastatin | **↓LDL (18-55),**↑ HDL (5-15)<br>↓ Triglycerides (7-30) | Myopathy, increased liver enzymes |
| Cholesterol absorption inhibitor | Ezetimibe | ↓ LDL( 14-18), ↑ HDL (1-3)<br>↓Triglyceride (2) | Headache, GI distress |
| Nicotinic Acid | | ↓LDL (15-30), **↑ HDL (15-35)**<br>**↓ Triglyceride (20-50)** | Flushing, Hyperglycemia, Hyperuricemia, GI distress, hepatotoxicity |
| Fibric Acids | Gemfibrozil<br>Fenofibrate | ↓LDL (5-20), ↑HDL (10-20)<br>**↓Triglyceride (20-50)** | Dyspepsia, gallstones, myopathy |
| Bile Acid sequestrants | Cholestyramine | ↓ LDL<br>↑ HDL<br>No change in triglycerides | GI distress, constipation, decreased absorption of other drugs |

# TLC

Lower your cholesterol, decrease risk for heart disease, and lose weight with the Therapeutic Lifestyle Changes (TLC) Diet, a weight-loss program created by the National Institute of Health (NIH) and endorsed by the American Heart Association. Following the TLC Diet is simple -- you'll cut back on saturated fats, incorporate more fiber into your diet, and add regular exercise into your daily routine to get your health back on track.

How It Works:

First, know why you're starting the TLC Diet to help determine your daily caloric intakes. If the objective is to lower LDL cholesterol, men should consume 2,500 calories per day and women should consume 1,800 calories per day. If the objective is to lower LDL cholesterol and lose weight, men should consume 1,600 calories per day and women should consume 1,200 calories per day.

# There are a few rules from NIH you'll need to follow each day when keeping to your calorie count:

1. Consume less than 7 % of your daily calories from saturated fat.
2. Consume less than 200 mg a day of cholesterol.
3. Consume 25-35 % of your daily calories from total fat (including the saturated fat calories).
4. Eat two grams per day of plant stanols or sterols if you want to lower LDL cholesterol. You can find these in things like orange juice, cereal, and granola bars.
5. Eat 10-25 grams per day of soluble fiber found in things like nuts, seeds, beans, and lentils if you want to lower your LDL cholesterol.

6. Eat no more than five ounces of meat, preferably skinless chicken or fish.
7. Eat two to three servings of low-fat or fat-free dairy per day.
8. Eat three to five servings of vegetables, dry beans, or peas per day.
9. Eat two to four servings of fruit per day.
10. Eat six or more servings of breads, cereals, or grains per day.
11. Eat no more than two egg yolks per week, including the yolks in baked goods and cooked or processed foods.
12. Plus, you should have 30 minutes of moderate-intensity exercise every day


What You Need to Know About
PLANT STEROLS & STANOLS
SPARKPEOPLE


12:00
100%
Ounce ⇆ Gram
1 oz. = 28.3495 g
1 g = 0.0353 oz.
1
2
3
4
5
6
7
8
9
0
•
C

Cutting out bad fat from your diet will help to lower your cholesterol, since fat, especially saturated and trans fat, increases your LDL (bad cholesterol) which increases risk for heart disease. Plus, consuming more soluble fiber is also beneficial, as it can help reduce your risk for heart disease and fills you up so that you'll eat fewer calories. Overall, eating a healthier diet and getting active for 30 minutes each day will improve your health and help you lose weight.

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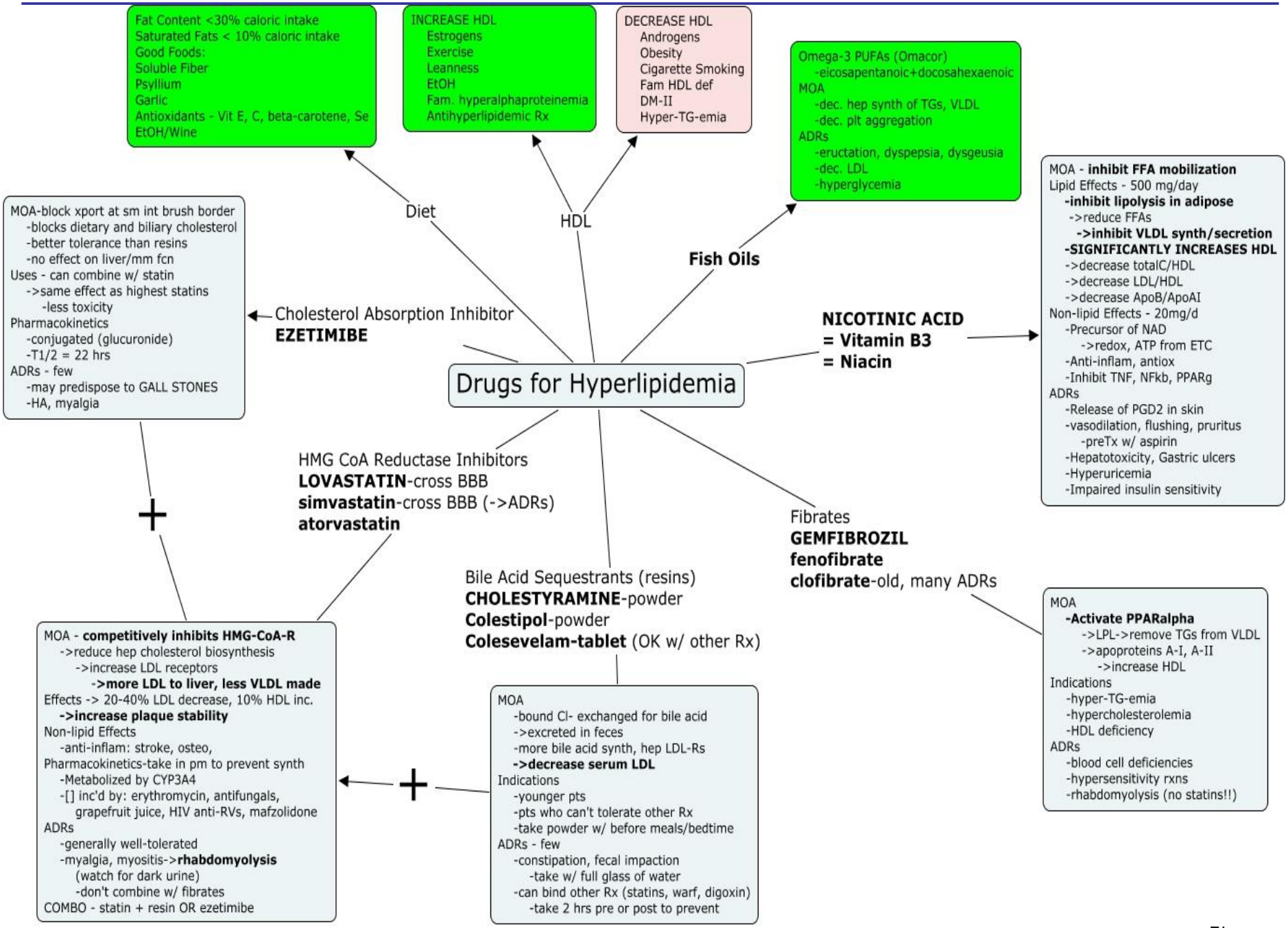
Fat Content <30% caloric intake
Saturated Fats < 10% caloric intake
Good Foods:
Soluble Fiber
Psyllium
Garlic
Antioxidants - Vit E, C, beta-carotene, Se
EtOH/Wine
INCREASE HDL
Estrogens
Exercise
Leanness
EtOH
Fam. hyperalphaproteinemia
Antihyperlipidemic Rx
DECREASE HDL
Androgens
Obesity
Cigarette Smoking
Fam HDL def
DM-II
Hyper-TG-emia
Omega-3 PUFAs (Omacor)
-eicosapentanoic+docosahexaenoic
MOA
-dec. hep synth of TGs, VLDL
-dec. plt aggregation
ADRs
-eructation, dyspepsia, dysgeusia
-dec. LDL
-hyperglycemia
Diet
HDL
Fish Oils
MOA-block xport at sm int brush border
-blocks dietary and biliary cholesterol
-better tolerance than resins
-no effect on liver/mm fcn
Uses - can combine w/ statin
->same effect as highest statins
-less toxicity
Pharmacokinetics
-conjugated (glucuronide)
-T1/2 = 22 hrs
ADRs - few
-may predispose to GALL STONES
-HA, myalgia
Cholesterol Absorption Inhibitor
EZETIMIBE
MOA - inhibit FFA mobilization
Lipid Effects - 500 mg/day
-inhibit lipolysis in adipose
->reduce FFAs
->inhibit VLDL synth/secretion
-SIGNIFICANTLY INCREASES HDL
->decrease totalC/HDL
->decrease LDL/HDL
->decrease ApoB/ApoAI
Non-lipid Effects - 20mg/d
-Precursor of NAD
->redox, ATP from ETC
-Anti-inflam, antiox
-Inhibit TNF, NFkb, PPARg
ADRs
-Release of PGD2 in skin
-vasodilation, flushing, pruritus
-preTx w/ aspirin
-Hepatotoxicity, Gastric ulcers
-Hyperuricemia
-Impaired insulin sensitivity
NICOTINIC ACID
= Vitamin B3
= Niacin
Drugs for Hyperlipidemia
HMG CoA Reductase Inhibitors
LOVASTATIN-cross BBB
simvastatin-cross BBB (->ADRs)
atorvastatin
Bile Acid Sequestrants (resins)
CHOLESTYRAMINE-powder
Colestipol-powder
Colesevelam-tablet (OK w/ other Rx)
Fibrates
GEMFIBROZIL
fenofibrate
clofibrate-old, many ADRs
MOA - competitively inhibits HMG-CoA-R
->reduce hep cholesterol biosynthesis
->increase LDL receptors
->more LDL to liver, less VLDL made
Effects -> 20-40% LDL decrease, 10% HDL inc.
->increase plaque stability
Non-lipid Effects
-anti-inflam: stroke, osteo,
Pharmacokinetics-take in pm to prevent synth
-Metabolized by CYP3A4
-[] inc'd by: erythromycin, antifungals,
grapefruit juice, HIV anti-RVs, mafzolidone
ADRs
-generally well-tolerated
-myalgia, myositis->rhabdomyolysis
(watch for dark urine)
-don't combine w/ fibrates
COMBO - statin + resin OR ezetimibe
MOA
-bound Cl- exchanged for bile acid
->excreted in feces
-more bile acid synth, hep LDL-Rs
->decrease serum LDL
Indications
-younger pts
-pts who can't tolerate other Rx
-take powder w/ before meals/bedtime
ADRs - few
-constipation, fecal impaction
-take w/ full glass of water
-can bind other Rx (statins, warf, digoxin)
-take 2 hrs pre or post to prevent
MOA
-Activate PPARalpha
->LPL->remove TGs from VLDL
->apoproteins A-I, A-II
->increase HDL
Indications
-hyper-TG-emia
-hypercholesterolemia
-HDL deficiency
ADRs
-blood cell deficiencies
-hypersensitivity rxns
-rhabdomyolysis (no statins!!)