LEARNING OBJECTIVES

By the end of the lecture the student should be Able to know:

- Lipids and cardiovascular diseases
- Production of VLDL, LDL, HDL
- Atherosclerosis and lipid accumulation
- Dyslipidemias and types
- Prevention and treatment of dyslipidemias

LIPID AND CARDIOVASCULAR DISEASES

- Dyslipidemia or abnormal Plasma lipoproteins are major modifiable risk factor for cardiovascular diseases
- Elevated Total Cholesterol (TC)
- Elevated Low-density lipoproteins (LDL)
- Elevated triglycerides (TG)
- Decreased High-density lipoproteins (HDL)

As they contribute to the development of atherosclerosis
LIPIDS AND ATHEROSCLEROSIS

• Not only atherogenic LDL but also IDL lipoproteins (a) and possibly chylomicron remnants contribute to development of atherosclerosis.

• Increased plasma concentration and their reduced diameter favor sub endothelial accumulation of these lipoprotein.

• Following oxidation of these Apo-lipoprotein are no longer cleared by normal mechanism.
• They trigger a self perpetuating inflammatory response and are taken by macrophages to form foam cells, a hallmark of atherosclerotic lesion.

• Conversely HDL removes cholesterol from the tissues to liver, where it is metabolized and excreted in bile.

• Low HDL levels which are often associated with triglyceride elevation also predispose to atherosclerosis.
WHY DO WE CARE?

  - High LDL levels are a leading cause of coronary heart disease (CHD) and should be the main target of any cholesterol lowering regimen.

PRIMARY DYSLIPIDEMIA
ETIOLOGY

- Single or multiple gene mutation – resulting in disturbance of LDL, HDL and triglyceride, production or clearance.
- Should be suspected in patients with:
  - Premature heart disease
  - Family Hx of atherosclerotic
  - Or serum cholesterol level >240mg/dl.
  - Physical signs of hyperlipidemia.

SECONDARY DYSLIPIDEMIA

- Sedentary lifestyle
- Most adult cases of dyslipidemia are secondary in nature in western civilizations
- Excessive consumption of cholesterol – saturated fats and trans-fatty acids.

CAUSES OF SECONDARY HYPERLIPIDEMIA

Moderately Common

- Hypothyroidism
- Pregnancy
- Cholestatic Liver disease
- Drugs
  - Antiretroviral drugs
  - Thiamine diuretics
  - Beta-blockers
  - Hormonal agents

Less common Causes

- Nephrotic Syndrome
- Anorexia
- Porphyria
- Hyperparathyriodism.

SPECIFIC DYSLIPIDEMIAS:
VERY HIGH LDL (> 190MG/DL)

Causes and Diagnosis

- Genetic disorders
  - Monogenic familial hypercholesterolemia
  - Familial defective apolipoprotein B-100 (Apo B)
  - Polygenic hypercholesterolemia
- Family testing to detect affected relatives

SPECIFIC DYSLIPIDEMIAS: ELEVATED TRIGLYCERIDES

Causes of Elevated Triglycerides

- Obesity and overweight
- Physical Inactivity
- Cigarette smoking
- Excess alcohol intake
- High carb. diets
- Several diseases (Type 2 DM, chronic renal failure, nephrotic syndrome)
- Medications (corticosteroids, estrogens, retinoids, higher doses of beta blockers)

SPECIFIC DYSLIPIDEMIAS: LOW HDL

Causes of Low HDL (<40 mg/dl)

- Elevated triglycerides
- Overweight and obesity
- Physical Inactivity
- Type 2 diabetes
- Cigarette smoking
- Very high carb. intakes (>60% energy)
- Medications (some beta blockers, anabolic steroids, progestational agents)
Complications of Dyslipidaemia and subsequent atherosclerosis include:

- Atherosclerosis (Damaging and clogging of arteries)
- Hypertension.
- Heart diseases (Angina, Heart Attacks).
- Stroke
- Eye Damage (Retinopathy).
- Kidney Damage (Nephropathy).
- Fatty Liver

EYE SIGNS IN HYPERLIPIDAEMIA

Corneal arcus

Xanthelasmata

ATP III CLASSIFICATION OF LDL, TOTAL, AND HDL CHOLESTEROL (MG/DL)
LIPID MEASUREMENTS ARE PERFORMED FOR

- Screening for primary or secondary prevention of cardiovascular diseases.
- Investigation of Patients with clinical features of Lipid Disorders.
- Testing relatives of patients with one of the single gene defects Causing dyslipedemia

APPROACH TO DYSLIPIDEMIA

- ATP III Classification of LDL, Total, and HDL Cholesterol
- Major Risk Factors
- Categories of Risk
AHA/ACC GUIDELINES.

• **Class I**
  - lipid profile in all patients should be established (Level of Evidence: B)
  - lipid-lowering therapy before discharge
  - Lifestyle modifications (Level of Evidence: B)
    - daily physical activity
    - weight management
  - Dietary therapy
  - statin should be used that reduces LDL-C to 100 mg/dL AND achieves at least a 30% lowering of LDL-C.25–29 (Level of Evidence: C)
  - triglycerides 200 mg/dL should be treated with statins to lower non–HDL-C to 130 mg/dL.25–27,30 (Level of Evidence: B)
  - triglycerides 500 mg/dL should be started on fibrate therapy in addition to statin

AHA/ACC GUIDELINES.

• **Class IIa**
  - intensification of LDL-C–lowering drug therapy with a bile acid sequestrant
  - to treat very high-risk patients* with statin therapy to lower LDL-C to 70 mg/dL
  - very high risk* and who have triglycerides 200 mg/dL, a non–HDL-C goal of 100 mg/dL is reasonable
  - ezetimibe -for patients who do not tolerate or achieve target LDL-C with statins, bile acid sequestrants,‡ and/or niacin.§ (Level of Evidence: C)
  - For all patients, it may be reasonable to recommend omega-3 fatty acids from fish or fish oil capsules (1 g/d) for cardiovascular disease risk reduction
DIETARY COUNSELLING

• Reduce intake of saturated and trans-unsaturated fat to less than 7-10% of total energy. Reduce intake of cholesterol to <250mg/day.
• Replace source of saturated Fat and cholesterol with lean meat, low fat dairy products, polyunsaturated spreads and low glycemic index carbohydrates.
• Reduce energy dense food e.g fat and soft drinks whilst increasing activity and exercise.
• Increase consumption of cardioprotective and nutrient dense food such as vegetables, unrefined carbohydrates such as vegetables, unrefined carbohydrates, fish, pulses, nuts, legumes, fruit etc.
• Adjust alcohol consumption, reduce intake if excessive or if associated with hypertension, hypertriglyceridermia or central obesity.
• Add supplementary food containing nutrients, such as n-3 fatty acids, dietary fibers, plants sterols.

Table 3: Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals

<table>
<thead>
<tr>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarette smoking</td>
</tr>
<tr>
<td>Hypertension (BP ≥140/90mmHg or on antihypertensive medication)</td>
</tr>
<tr>
<td>Low HDL cholesterol (≤40mg/dL)</td>
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<tr>
<td>Family history of premature CHD (CHD in male first degree relative &lt;55 years; CHD in female first degree relative ≤55 years)</td>
</tr>
<tr>
<td>Age (men ≥45 years; women ≥55 years)</td>
</tr>
</tbody>
</table>

PRIMARY PREVENTION WITH LIPID-LOWERING THERAPY

• The clinical approach to primary prevention is founded on the public health approach that calls for lifestyle changes, including:
  1) reduced intakes of saturated fat and cholesterol, 2) increased physical activity, and 3) weight control
• trials show that Lipid-lowering drugs reduce risk for major coronary events and coronary death even in the short term.
SECONDARY PREVENTION WITH LIPID-LOWERING THERAPY

- Lipid-lowering therapy reduces total mortality, coronary mortality, major coronary events, coronary artery procedures, and stroke in persons with established CHD
- Lipid measures should be taken on admission or within 24 hours.
- Adjustment of therapy may be needed after 12 weeks.
<table>
<thead>
<tr>
<th>Drug Class, Agents and Daily Doses</th>
<th>Lipid/Lipoprotein Effects</th>
<th>Side Effects</th>
<th>Contraindications</th>
<th>Clinical Trial Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMG-CoA reductase inhibitors (statins)*</td>
<td>LDL</td>
<td>↓18-55%</td>
<td>Myopathy</td>
<td>Absolute: • Active or chronic liver disease relative; • Concomitant use of certain drugs</td>
</tr>
<tr>
<td></td>
<td>HDL</td>
<td>↓3-15%</td>
<td>Increased liver enzymes</td>
<td>Relative: • TG &gt;400 mg/dL</td>
</tr>
<tr>
<td></td>
<td>TG</td>
<td>↓7-30%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bile acid sequestrants†</td>
<td>LDL</td>
<td>↓15-30%</td>
<td>Gastrointestinal distress</td>
<td>Absolute: • Diabetes - lipoproteinemia • TG &gt;400 mg/dL</td>
</tr>
<tr>
<td></td>
<td>HDL</td>
<td>↓3-5%</td>
<td>Constipation</td>
<td>Relative: • TG &gt;200 mg/dL</td>
</tr>
<tr>
<td></td>
<td>TG</td>
<td>No change or increase</td>
<td>Decreased absorption of other drugs</td>
<td></td>
</tr>
<tr>
<td>Nicotinic acid‡</td>
<td>LDL</td>
<td>↓5-25%</td>
<td>Flushing</td>
<td>Absolute: • Chronic liver disease • Severe gout</td>
</tr>
<tr>
<td></td>
<td>HDL</td>
<td>↑15-35%</td>
<td>Hyperglycemia</td>
<td>Relative: • Diabetes • Hyperuricemia • Peptic ulcer disease</td>
</tr>
<tr>
<td></td>
<td>TG</td>
<td>↓20-30%</td>
<td>Hyperlipidemia (or gout)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Gastrointestinal distress</td>
<td></td>
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<tr>
<td></td>
<td>Hepatotoxicity</td>
<td></td>
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<tr>
<td>Fibric acids§</td>
<td>LDL</td>
<td>↓4-20%</td>
<td>Dyspepsia, Gallstones, Myopathy</td>
<td>Absolute: • Severe renal disease • Severe hepatic disease</td>
</tr>
<tr>
<td></td>
<td>HDL</td>
<td>(may be increased in patients with high TG)</td>
<td>Unexplained non-CVD deaths in WHO study</td>
<td></td>
</tr>
<tr>
<td></td>
<td>TG</td>
<td>↑10-30%</td>
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<tr>
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<td>↓20-50%</td>
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**HOW TO ACHIEVE LIPID CONTROL RATIO...**

- Simplify medication regimens
- Provide explicit patient instruction
- Reinforce and reward adherence
- Involve patients in their care through self-monitoring
- Increase visits for patients unable to achieve treatment goal