1.0 Basic Properties of Lipids and Lipoproteins

1.1 Lipoprotein Composition and Structure

1.1.1 Major Lipids Carried on Lipoproteins
1.1.2 Apolipoproteins (including naturally occurring sequence variants)
1.1.3 Non-apolipoprotein Proteins Reproducibly Associated with Lipoproteins
1.1.4 Principles of Lipoprotein Structure and Structure Types
1.1.5 Major Lipoproteins and Their Measurement
  1.1.5.1 Chylomicrons and chylomicron remnants
  1.1.5.2 Very Low Density Lipoproteins (VLDL)
  1.1.5.3 Intermediate Density Lipoproteins (VLDL remnants)
  1.1.5.4 Low Density Lipoproteins (LDL)
  1.1.5.5 Lipoprotein (a)
  1.1.5.6 High Density Lipoproteins (HDL) and its subspecies
    1.1.5.6.1 Spheroidal (alpha-migrating) HDL, including differentiation by size
    1.1.5.6.2 Non-spheroidal (pre-beta-migrating) HDL, including differentiation by size and shape
    1.1.5.6.3 HDL carrying versus lacking apo A-II
    1.1.5.6.4 Other HDL subspecies
  1.1.5.7 Major Methods of Lipoprotein Separation and Measurement
    1.1.5.7.1 Lipoprotein Separation by Native Gel Electrophoresis by charge or size
    1.1.5.7.2 Lipoprotein Separation by Ultracentrifugation using gradient or non-gradient (isopycnic) density
    1.1.5.7.3 Lipoprotein Estimation by Nuclear Magnetic Resonance
    1.1.5.7.4 Lipoprotein Separation by Antibodies or by Chemical Precipitation
    1.1.5.7.5 Lipid Measurement for Clinical Lipidology (cholesterol oxidase, etc.)
    1.1.5.7.6 LDL-C Calculation (e.g. Friedewald) vs Direct Measurement
    1.1.5.7.7 Research-Oriented Lipoprotein Measurements (brief overview for the clinician)
    1.1.5.7.8 Issues in validation/repeatability and comparability of various lipid measurement techniques

1.2 Lipoprotein Metabolism

1.2.1 Key Enzymes and Transport Proteins Involved in Lipid and Lipoprotein Metabolism

1.2.1.1 Entercocyte Lipid Absorption and Lipoprotein Production
  1.2.1.1.1 Intestinal absorption of UC and other sterols: Niemann-Pick-C-1-Like 1 (NPC1L1)
  1.2.1.1.2 Intestinal desorption of UC and other sterols: ATP Binding Cassette (ABC) Proteins G5 & G8 (ABCG5/G8)
  1.2.1.3 Cholesterol esterification: Acyl-coenzyme A: cholesterol O-acyltransferase (ACAT)
  1.2.1.4 Triglyceride production: Diacylglycerol acyltransferase 1 (DGAT1)
  1.2.1.5 Chylomicron assembly: Microsomal triglyceride transfer protein (MTP)

1.2.1.2 Hepatic VLDL Production
  1.2.1.2.1 Triglyceride synthesis: Diacylglycerol acyltransferase 2 (DGAT2)
  1.2.1.2.2 VLDL assembly: Microsomal triglyceride transfer protein (MTP)

1.2.1.3 Production of Nascent HDL

1.2.1.4 Lipidation of Nascent HDL
  1.2.1.4.1 PL and UC transfer to Pre-beta-1&2 HDL: ABCA1
  1.2.1.4.2 UC transfer to/from alpha-HDL
    1.2.1.4.2.1 ATP Binding Cassette (ABC) Protein G1 (ABCG1)
    1.2.1.4.2.2 Scavenger Receptor-B1 (SR-B1)

1.2.1.5 Cholesterol Esterification
  1.2.1.5.1 Intraplasma (intra-lipoprotein): HDL Core Creation and HDL & LDL Core Increase--Lecithin cholesterol acyltransferase (LCAT)
  1.2.1.5.2 Intracellular: Acyl-coenzyme A: cholesterol O-acyltransferase (ACAT)

1.2.1.6 Intraplasma Enzymatic Lipoprotein Delipidation (TG and PL hydrolysis)
  1.2.1.6.1 Lipoprotein Lipase (LPL)
  1.2.1.6.2 Hepatic Lipase (HL)
  1.2.1.6.3 Endothelial lipase (EL)

1.2.1.7 Intraplasma lipoprotein remodeling
  1.2.1.7.1 Cholesteryl ester transfer protein (CETP)
  1.2.1.7.2 Phospholipid transfer protein (PLTP)

1.2.1.8 Intracellular processing of non-lipoprotein lipids
  1.2.1.8.1 Cholesteryl-ester Hydrolysis (De-esterification): Cholesteryl-Ester Hydrolase (CEH)
  1.2.1.8.2 Triglyceride lipolysis (FFA release): Hormone Sensitive Lipase (HSL)

1.2.1.9 Extracellular/Extraplasma lipid processing
1.2 Exogenous Apo-B-Containing Lipoprotein Metabolism (Intestinal Lipid Transport)

1.2.1 Enterocyte formation of Chylomicrons

1.2.1.1 Apo B-48 synthesis
1.2.1.2 TG synthesis
1.2.1.3 Cholesterol esterification
1.2.1.4 Chylomicron assembly

1.2.2 Intraplasma TG and PL lipolysis in Chylomicrons and Chylomicron Remnants

1.2.3 Chylomicron Remnant Uptake

1.2.4 Postprandial Lipemia

1.2.5 Endogenous Apo-B-Containing Lipoprotein Metabolism (Hepatic Lipid Transport)

1.2.6 Hepatic VLDL Synthesis and Secretion

1.2.7 Intraplasma Delipidation of VLDL and IDL

1.2.8 LDL Receptor

1.2.9 Structure and Synthesis
1.2.9.1 Mediation of VLDL, IDL and LDL Uptake and Catabolism
1.2.9.2 Processing by PCSK9
1.2.9.3 Processing by LDL-Receptor Adaptor Protein

1.2.10 Other receptors (scavenger receptor, etc.)

1.2.11 Non-receptor-mediated processing of apo-B-containing lipoproteins

1.2.12 Apo-B-containing Lipoprotein Metabolism in Interstitial Space and Peripheral Lymph

1.2.13 HDL Metabolism

1.2.14 Apo A-I synthesis and assembly and secretion of nascent HDL

1.2.15 Intraplasma HDL Particle Interconversion

1.2.16 Formation of discoidal HDL from globular HDL
1.2.17 Formation of spheroidal HDL from discoidal HDL
1.2.18 Remodeling among spheroidal HDL particles
1.2.19 Remodeling of spheroidal/alpha HDL particles to produce pre-beta HDL
1.2.20 Formation of pre-beta HDL from chylomicrons

1.2.17 HDL Metabolism in Interstitial Space and Peripheral Lymph
1.2.18 HDL receptors/binding sites (HB2, Ecto F1-ATPase, cubulin/megalin)

1.2.19 Cholesterol and Bile Acid Metabolism

1.2.20 Regulation of intrahepatic sterol content

1.2.21 Cholesterol synthesis, intermediates, regulation and biomarkers
1.2.22 The special role of HMG-CoA reductase

1.2.23 Extrahepatic cholesterol metabolism

1.2.24 Use in cell membrane structure
1.2.25 Use in steroid hormone synthesis
1.2.26 Regulation of intracellular extrahepatic sterol content

1.2.27 Biliary metabolism in the liver and intestine in the regulation of cholesterol excretion
1.2.28 Cholesterol uptake and excretion by the intestine (trans-intestinal cholesterol excretion, TICE)

1.2.29 Fatty Acid and Triglyceride Metabolism

1.2.30 Fatty acid synthesis and beta oxidation
1.2.31 Fatty acid cycling between the liver and extra-hepatic tissues

1.2.32 Intrahepatic Gene Regulation via Nuclear Receptor Factors

1.2.33 LXN
1.2.34 FXR
1.2.35 HNF-alpha
1.2.36 PPARs, alpha, beta (delta) and gamma
1.2.37 SREBP-1a, SREPP-1c, SREBP-2

1.3 Lipoprotein Function

1.3.1 Normal Function of Chylomicrons and Chylomicron Remnants

1.3.2 Normal Function of VLDL, IDL, and LDL

1.3.3 Pro-atherogenic Effects of Apo B-48 and Apo B-100-Containing Lipoproteins
1.3.3.1 Cholesterol Delivery to Extra-hepatic Tissues
1.3.3.2 Lipid and Protein Modification of Apo-B-Containing Lipoproteins
1.3.3.3 Other pro-atherosclerotic Mechanisms and Effects

1.3.4 HDL Functions Potentially Related to Atherogenesis

1.3.4.1 Reverse Cholesterol Transport
  1.3.4.1.1 Cholesterol efflux from cells: ABC transporters and SR-BI
  1.3.4.1.2 Intraplasma cholesterol transfer
  1.3.4.1.3 Cholesterol delivery to the liver (SR-BI, holoparticle uptake, etc.)
  1.3.4.1.4 Cholesterol delivery to the intestine

1.3.4.2 Antioxidant Activity
1.3.4.3 Anti-inflammatory and Immune Regulatory Activity
1.3.4.4 Anti-apoptotic Activity
1.3.4.5 Pro-endothelial Activity
1.3.4.6 Antithrombotic Activity
1.3.4.7 Dysfunctional HDL (mechanisms: oxidation, nitrosylation, tyrosylation, glycation; results)

1.3.5 HDL Functions Unrelated to Atherosclerosis

1.3.5.1 Anti-infective
1.3.5.2 Anti-diabetic
1.3.5.3 CNS-related
  1.3.5.3.1 Apo E and Alzheimer’s
  1.3.5.3.2 Apo A-IV and satiety

1.4 Lipoprotein metabolism in pregnancy

1.4.1 Role of cholesterol in the developing fetus
1.4.2 Transport from mother to fetus vs. de novo synthesis
1.4.3 Lipoprotein lipid production by the yolk sac
1.4.4 Placental Lipid trafficking
1.4.5 Relation between maternal and fetal cholesterol by gestational age
1.4.6 Maternal cholesterol and triglyceride changes in normo-cholesterolemic and hypercholesterolemic women
1.4.7 Anabolic maternal metabolism during first 2/3 of gestation due to hyperphagia and increased tissue lipogenesis
1.4.8 Catabolic metabolism in last 1/3 of pregnancy, with marked increase in lipolysis rates and rise in maternal free fatty acids and glycerol
1.4.9 Gestational accelerational changes in insulin secretion in late Pregnancy (3-3.5 fold) and 50-70% decrease in insulin sensitivity with concurrent increase in basal hepatic glucose production
1.4.10 Effects of insulin resistance and sex steroids on VLDL metabolism
1.4.11 Effects of adiposity in Pregnancy
1.4.12 Effects of lactation on lipid metabolism and diabetes risk
1.4.13 Effects of excessive and under-nutrition and/or fat consumption on predictive programming of the fetus and consequences for cardiovascular risk later in life

2.0 Pathophysiology and Vascular Biology of Atherosclerosis

2.1 Normal Arterial Biology

2.1.1 Pre-natal development of arteries
2.1.2 Diffuse intimal thickening as post-natal phenomenon
2.1.3 Longitudinal mechanical stress in coronaries and at branch points

2.2 Athero-pathobiology Overview and Stages of Atherogenesis

2.2.1 Diffuse intimal thickening
2.2.2 Fatty streak
2.2.3 Fibrous plaque
2.2.4 Plaque rupture or erosion
2.2.5 Organization of mural thrombus
2.2.6 Calcification
2.2.7 Neovascularization
2.2.8 Foam cell formation

2.3 Artery Wall Cell Physiology and Pathophysiology (Endothelium, Smooth-Muscle Cells, Macrophages, Other Inflammatory Cells)

2.3.1 Lack of lymph vessels in the intima
2.3.2 Retention of LDL
2.3.3 Fusion of LDL to form droplets and vesicles
2.3.4 LDL oxidation and action of phospholipases
2.3.5 Interaction of HDL with macrophages
2.3.6 Endothelium
2.3.7 Smooth muscle cells
2.3.8 Inflammatory cells

2.4 Role of Apo-B-Containing Lipoproteins in Atherogenesis
2.5 Roles of HDL in Atherogenesis (Function and Dysfunction)
2.6 Oxidation in Atherogenesis
2.7 Inflammation in Atherogenesis
2.8 Plaque Stability/Vulnerability

2.8.1 Pathology of Atherosclerosis
2.8.2 Progression to Type I to Type IV Lesions
2.8.3 Characteristics of Vulnerable Plaque
2.8.4 Lipid Core
2.8.5 Fibrous Cap
2.8.6 Vaso Vasorum
2.8.7 Predictors of Plaque Rupture

2.9 Thrombosis, Coagulation, Blood Rheolog & Inflammation
2.9.1 Genetic Causes of Hypercoagulability
2.9.2 Factor V (Leiden) Mutation
2.9.3 Hyperhomocysteinemia
2.9.4 Protein C and S Deficiency
2.9.5 Anti-thrombin III Deficiency
2.9.6 Coagulation Cascade
2.9.7 Platelet Aggregation and Antiplatelet Therapy
2.9.8 Drug Induced Causes of Hypercoagulation
2.9.9 Inflammatory Disorders

2.10 Normolipidemic Arterial Pathology

3.0 Pathophysiology of Genetic Dyslipidemias
3.1 Genetic Dyslipidemias
3.1.1 Familial hypercholesterolemia (FH) and other autosomal dominant hypercholesterolemias
3.1.1.1 LDLR defects – heterozygous and homozygous FH
3.1.1.2 APOB defects – familial defective apo B
3.1.1.3 CSK9 – gain of function (GOF) causing high LDL and loss of function (LOF) mutations causing low LDL
3.1.1.4 Polygenic FH
3.1.2 Autosomal recessive hypercholesterolemia and related
3.1.2.1 LDLRAP1 (LDL receptor associated protein 1) deficiency (previously denoted ARH or ARH1)
3.1.2.2 ABCGS/8 (deficiency of either causes sitosterolemia)
3.1.2.3 CYP27A1 (deficiency causes cerebrotendinous xanthomatosis)
3.1.2.4 CYP7A1 (deficiency causes a rare recessive hypercholesterolemia)
3.1.3 Genetic hypobetalipoproteinemias, and VLDL or chylomicron deficiencies
3.1.3.1 APOB and familial hypobetalipoproteinemia (also rare homozygous forms). APOB mutations that affect the folding of the N-terminus of apo B or its interaction with MTP or that remove the apo B C-terminal lipid binding structures (truncation mutations) cause FHBL.
3.1.3.2 MTP (deficiency causes abetalipoproteinemia)
3.1.3.3 SARA2 (deficiency causes chylomicron retention disease). Encodes Sar1b, a small G-protein that appears to initiate formation of specialized COP-II transport carriers to transport chylomicrons out of the ER. Patients have very low LDL and low HDL as well as very little apo B48 in blood.
3.1.3.4 ANGPTL3 (deficiency causes familial combined hypolipidemia)
3.1.4 Genes identified in GWAS and other studies having common variants with smaller effects on LDL – mechanism and significance
3.1.4.1 APOB (common variants increase or decrease LDL and VLDL)
3.1.4.2 APOE (effects on LDL of common 2/3/4 variants)
3.1.4.3 NPC1L1
3.1.4.4 HMGCR (GOF leads to modest increased LDL and MI risk)
3.1.4.5 SORT1 (sortilin)
3.1.4.6 ANGPTL3 ()
3.1.4.7 TRIB1 (for Tribbles) Trib1 apparently affects mRNA expression of acetyl-CoA carboxylase, fatty acid synthase, and stearoyl-CoA desaturase. In mice, over expression of Trib1 in liver decreased serum cholesterol and triglycerides. Deficiency of Trib1 increases total cholesterol and triglycerides and LDL and VLDL particles.
3.1.5 Hypertriglyceridemias
3.1.5.1 Well-defined chylomicronemia syndromes including LPL deficiency, APOC2 defects, GPIHBP1 deficiency, others
3.1.5.2 Genetics of common type IV and V hyperlipidemia, apo AV, etc.
3.1.5.3 Type III hyperlipidemia (familial dysbetalipoproteinemia), APOE, others
3.1.6 HDL deficiency syndromes
3.1.6.1 APOA1 deficiency
3.1.6.2 Tangier disease and ABCA1, ABCG1
3.1.6.3 LCAT, Others
3.1.7 HDL elevating genes
3.1.7.1 CETP
3.1.7.2 Others

3.2 Secondary Dyslipidemias
3.2.1 Diabetes Mellitus and other Insulin Resistant States
3.2.2 Other Endocrine Disorders
3.2.3 Renal Disorders
3.2.4 Hepatic Disorders
3.2.5 Infectious and Inflammatory Disorders
3.2.6 Diet-induced Dyslipidemias
4.0 Evidence-Based Lipidology

4.1 Framing the question
4.2 Finding the Evidence
  4.2.1 RCTs vs observational studies
  4.2.2 Therapy
  4.2.3 Issues of treatment bias in Pharmaco-epi studies
  4.2.4 Harm
  4.2.5 Prognosis
  4.2.6 Diagnosis
  4.2.7 Evaluating best evidence for internal and external validity
  4.2.8 Determining causality
  4.2.9 Modified Hills criteria
  4.2.10 RCT to prove causality
  4.2.11 Differential Diagnosis
  4.2.12 Diagnostic tests
    4.2.12.1 Multiple testing
    4.2.12.2 Simultaneous
    4.2.12.3 Sequential
  4.2.13 Spectrum bias
  4.2.14 Likelihood ratios
  4.2.15 Composite endpoints
  4.2.16 Interpreting Reviews & Guidelines
    4.2.16.1 Narrative
    4.2.16.2 Systematic
    4.2.16.3 Meta-analysis
  4.3 Applying results to individual patients
  4.4 Reporting bias
  4.5 Meta-analysis - Fixed effects vs. random effects modeling
  4.6 Variability of results
  4.7 Interpreting subgroup analysis
  4.8 Drug class effects
  4.9 Economic analysis
  4.10 Decision analysis
  4.11 Screening vs. diagnosis
  4.12 Grading recommendations
    4.12.1 GRADE
    4.12.2 IOM
    4.12.3 NHLBI
  4.13 Tools for critical review
  4.14 Electronic information capture of literature & EBM resources
  4.15 Integration of evidence, clinical judgment, values and systems
    4.15.1 Necessary Tools for Evidence Based Practice
      4.15.1.1 Types of Study Designs
      4.15.1.2 Hierarchy of Study Designs for Evidence
      4.15.1.3 Bias
        4.15.1.3.1 Selection, Measurement, Confounding
      4.15.1.4 Association vs. Causation
      4.15.1.5 Prevalence vs. Incidence Studies
      4.15.1.6 Hypothesis testing & Significance
      4.15.1.7 Estimation, Bayesian Analysis
      4.15.1.8 Clinical vs. Statistical Significance
      4.15.1.9 Categorical vs. Continuous Outcomes
      4.15.1.10 Measures of Association and Risk difference
      4.15.1.11 Number needed to treat or harm
      4.15.1.12 Indicators of validity in clinical trials
      4.15.1.13 Basic statistical tests

5.0 Identification and Clinical Significance of Cardiovascular Disease Risk Factors

5.1 Global Risk Scoring
5.2 Elevated LDL cholesterol
5.3 Other lipid risk factors
  5.3.1 Hypertriglyceridemia
  5.3.2 Remnant lipoproteins
  5.3.3 Non-HDL cholesterol
  5.3.4 Low HDL cholesterol
  5.3.5 Atherogenic dyslipidemia
5.4 Non-lipid major risk factors
5.4.1 Modifiable risk factors
5.4.1.1 Arterial hypertension
5.4.1.2 Cigarette smoking
5.4.1.3 Type 2 diabetes mellitus
5.4.1.4 Overweight/obesity
5.4.1.5 Physical inactivity
5.4.1.6 Atherogenic diet

5.4.2 Non-modifiable risk factors
5.4.2.1 Advancing age
5.4.2.2 Male gender
5.4.2.3 Family history of premature coronary heart disease

5.5 Other risk markers for CVD
5.5.1 Apolipoprotein B
5.5.2 LDL particle concentration
5.5.3 Lipoprotein (a)
5.5.4 High-sensitivity C-reactive protein
5.5.5 Lipoprotein phospholipase A2
5.5.6 HDL and LDL subfractions
5.5.7 Homocysteine
5.5.8 Impaired fasting glucose
5.5.9 Prothrombotic risk factors
5.5.9.1 Fibrinogen
5.5.9.2 von Willebrand factor antigen
5.5.9.3 Tissue plasminogen activator
5.5.9.4 Plasminogen activator inhibitor-1

5.5.10 Markers of oxidative stress
5.5.10.1 Isoprostanes
5.5.10.2 Myeloperoxidase
5.5.10.3 Paraoxanase
5.5.10.4 Multi-marker profiles

5.6 Subclinical atherosclerosis testing
5.6.1 Coronary calcium scoring
5.6.2 Carotid intima-media thickness
5.6.3 Ankle-brachial index
5.6.4 Standard for evaluation of biomarkers of increased CVD risk

5.7 Clinical disorders associated with increased CVD risk
5.7.1 Hypothyroidism
5.7.2 Chronic kidney disease
5.7.3 Chronic inflammatory states
5.7.4 HIV disease and therapy
5.7.5 Illicit drug use
5.7.6 Depression and anti-depressant therapy
5.7.7 Post-transplant states and therapy
5.7.8 Cushing syndrome and states requiring chronic glucocorticoid therapy
5.7.9 Primary hyperparathyroidism

6.0 Therapeutic Lifestyle Changes
6.1 Dietary Recommendations for Prevention and Treatment of CVD
6.1.1 American Heart Association
6.1.2 National Heart Lung and Blood Institute
6.1.3 US Department of Agriculture and Health and Human Services Guidelines?

6.2 Evidence that Supports Current Dietary Recommendations for Heart Health
6.2.1 Dietary Patterns - Epidemiologic Evidence
6.2.2 Dietary Patterns – Clinical Trial Evidence
6.2.3 Foods to Recommend
6.2.3.1 Fruits and Vegetables
6.2.3.2 Fish, Preferably Oily
6.2.3.3 Fiber-Rich Whole Grains
6.2.3.4 Nuts, Legumes and Seeds
6.2.3.5 Liquid Vegetable/seed/nut/olive Oils
6.2.3.6 Nutrient Dense Foods

6.2.4 Food to Avoid/Limit
6.2.4.1 Sugary Beverages and Added Sugars
6.2.4.2 Processed Meat Products
6.2.4.3 Fatty Red Meats and Full-Fat Dairy Products
6.2.4.4 Salt recommendations
6.2.4.5 Alcohol recommendations

6.2.5 Nutrients to Recommend
6.2.5.1 Soluble Fiber and Insoluble Fiber
6.2.5.2 Omega-3 Fatty Acids
6.2.5.3 Unsaturated Fatty Acids
6.2.5.4 Plant Sterols/Stanols
6.2.5.5 Plant/Lean Protein
6.2.5.6 Calcium and Vitamin D

6.2.6 Nutrients to Avoid/Limit
6.2.6.1 Saturated and Trans Fatty Acids
6.2.6.2 Dietary Cholesterol
6.2.6.3 Simple Carbohydrates
6.2.6.4 What about omega 6 fatty acids

6.3 Diet and Weight Management
6.3.1 Various Weight Loss Diets – Effects on Weight and Lipids/Lipoproteins
6.3.2 Strategies for Achieving Weight Loss – Energy Density, Meal Replacers

6.4 Other Nutrition Strategies
6.4.1 Supplements
6.4.2 New and Emerging Strategies for Heart Health – Probiotics, Gut Microbiome

6.5 Effective Nutrition Dissemination Strategies – Motivational Interviewing, etc.

6.6 Nutrition Resources

6.7 Special diets
6.7.1 Extremely low fat diets for hypertriglyceridemia?
6.7.2 Anorexia nervosa
6.7.3 Gall bladder disease
6.7.4 Liver disease
6.7.5 Pregnancy diets
6.7.6 Diabetic diets
6.7.7 Parenteral nutrition

6.8 Lifestyle Management and CVD Prevention
6.8.1 Overall Diet
6.8.1.1 Saturated and Trans Fatty Acids
6.8.1.2 Plant Sterols/Plant Sterols
6.8.1.3 Soluble Fiber
6.8.1.4 CHO Restriction
6.8.1.5 Alcohol Intake
6.8.2 Physical activity
6.8.2.1 Guidelines on amount and intensity of PA to manage dyslipidemia
6.8.2.2 Inactivity and dyslipidemia
6.8.2.3 Pre exercise program assessment guidelines
6.8.3 Weight loss
6.8.3.1 Intensive lifestyle programs
   6.8.3.1.1 RCT evidence
   6.8.3.1.2 USPSTF recommendations
6.8.3.2 Bariatric Surgery
6.8.4 Principles of behavioral change
6.8.5 Lipoprotein Apheresis
6.8.6 Nutraceuticals that affect lipids
6.8.7 Dietician Referral
6.8.8 Dietary Recommendations for Specific Types of Dyslipidemia

7.0 Treatment of Dyslipidemia

7.1 Evidence Based for Treatment of Dyslipidemia
7.1.1 Clinical Trial Evidence

7.2 Treatment Statements and Guidelines
7.2.1 NCEP III and Updated NCEP III
7.2.2 NCEP IV (when available)
7.2.3 American Heart Association Statement on Primary and Secondary Prevention
7.2.4 American Heart Association Scientific Statement on Triglycerides and Cardiovascular Disease (2011)
7.2.5 ADA/ACC 2008 Consensus Statement: Lipoprotein Management in Patients with Cardiometabolic Risk
7.2.6 International Lipid Guidelines
7.2.7 Other Guidelines

7.3 Pharmacologic Therapy for Dyslipidemia
7.3.1 Current Approved Drugs- Statins, BAS, Fibrates, Nicotinic acid, Cholesterol absorption inhibitors, Prescription omega 3 fatty acids
7.3.2 Mechanisms of Action
7.3.3 Pharmacokinetics and Drug-Drug Interactions
7.3.4 Tolerability
7.3.5 Safety
7.3.6 Lipid Efficacy
7.3.7 CVD Efficacy
7.3.8 Treatment for Prevention of Pancreatitis
7.3.9 Treatment of Specific Types of Dyslipidemia
7.3.10 Combination Therapy- Rationale, Safety, and Efficacy
7.3.11 Newly Approved Drugs
7.3.12 Drugs in development
7.3.13 Medication Adherence
7.3.14 Management of Statin Intolerance

8.0 Consultative Issues in Clinical Lipidology

8.1 Dyslipidemia Management in Diabetes
8.1.1 Dyslipidemia in Type I diabetes
8.1.2 Dyslipidemia in Type II diabetes
8.1.3 Lifestyle management
8.1.4 Pharmacologic management
8.1.5 Potential non-lipid benefits of lipid lowering therapy

8.2 Dyslipidemia Management in Pediatrics
8.2.1 Inherited lipid disorders / mandate for family screening
8.2.2 Growth and development / evolution of dyslipidemia over time; changes at time of sexual development
8.2.3 Lifestyle management appropriate to different stages of development
8.2.4 Pharmacologic management

8.3 Dyslipidemia Management during Reproductive Years
8.3.1 CVD Prevention Guidelines for Women
8.3.2 Dyslipidemia associated with oral contraceptives
8.3.3 Special considerations for statin prescription in relation to fetal safety in women who are not using adequate contraception
8.3.4 Concepts of short-term / lifetime risk
8.3.5 Clinical trial data in women

8.4 Polycystic ovary syndrome
8.4.1 Obesity effects
8.4.2 Metabolic syndrome in the adolescent
8.4.3 Contraceptive effects
8.4.4 Teratogenicity of Lipid lowering drugs for persons at risk for pregnancy including liability

8.5 Dyslipidemia Management during Pregnancy
8.5.1 Normal changes in HDL-C, LDL-C and triglycerides by trimester and postpartum 6 weeks and 12 months
8.5.2 Non-pharmacological and Pharmacological management of elevated LDL and elevated TGs
8.5.3 Severe hypertriglyceridemia management

8.5.3.1 Associations with complications of pregnancy and implications
8.5.3.2 Non-pharmacological & pharmacological management

8.5.4 Management of FH in Pregnancy
8.5.5 Fetal origin hypothesis – Implications of fetal programing for dyslipidemia of Pregnancy
8.5.6 Associations of Lifetime risk of CVD with Obstetrical complications and pre-pregnancy and pregnancy weight gain
8.5.7 Categories of drug safety
8.5.8 Effects of breast feeding on lipoprotein lipid changes
8.5.9 Effects of breast feeding on diabetes risk reduction

8.6 Dyslipidemia Management during menopause transition
8.6.1 Lipid metabolic changes at menopause
8.6.2 Hormone effects on lipid metabolism
8.6.3 Estrogen, Progesterin, Androgen routes and dose effects
8.6.4 Individualizing risk assessment for hormone therapy (HT)
8.6.5 Effects of years since menopause
8.6.6 Contraindications for HT
8.6.7 CVD risks of HT
8.6.8 Gender differences in physical activity
8.6.9 Changes in atherosclerotic burden
8.6.10 Gender differences in CVD risk prediction of LDL, HDL and TG
8.6.11 Gender differences in risk of CVD with smoking
8.6.12 Gender differences in CVD risk prevention for low-dose Aspirin by age
8.6.13 Gender differences in CVD outcomes Diabetic women vs. men
8.6.14 Gender differences in CHD risk of Hypertension
8.6.15 Special contributors to CVD risk in women

8.6.15.1 Depression and other psychological factors
8.6.15.2 Autoimmune disease Lupus, Rheumatoid arthritis
8.6.15.3 Gender disparity in Intensity of CVD risk reduction

8.7 Dyslipidemia Management with aging
8.7.1 Relationship between dyslipidemia and risk among the elderly
8.7.2 Common secondary causes of dyslipidemia in the elderly
8.7.3 Clinical trial evidence for dyslipidemia management
8.7.4 Nutritional management
8.7.5 Drug metabolism in the elderly
8.7.6 Susceptibility to adverse effects

8.8 Dyslipidemia Management in Other Endocrine Disorders
8.8.1 Thyroid disease
8.8.2 Anorexia nervosa
8.8.3 Insulin resistance syndromes

8.9 Dyslipidemia Management in Metabolic Syndrome and Obesity
8.9.1 Characteristics of dyslipidemia in metabolic syndrome and obesity
8.9.2 Lifestyle management
8.9.3 Drug management

8.10 Dyslipidemia Management in Hypertension
8.11 Dyslipidemia management in patients with Liver Disease
8.11.1 Characterize dyslipidemia in various hepatobiliary disorders
8.11.2 Nutritional and lifestyle management
8.11.3 Pharmacological management

8.12 Dyslipidemia management in patients with Renal Disease
8.12.1 Dyslipidemia in CKD and in ESRD
8.12.2 Dyslipidemia in nephrotic syndrome
8.12.3 Clinical trials in CKD
8.12.4 Clinical trials in the dialysis population
8.12.5 Nutritional and lifestyle management
8.12.6 Pharmacological management

8.13 Dyslipidemia management in patients with Lipodystrophy
8.14 Dyslipidemia management in patients with HIV
8.14.1 Lipid manifestations of HIV, prevalence
8.14.2 What do the HIV drugs do to the lipid profile?
8.14.3 Dyslipidemia and CV risk in HIV
8.14.4 Lifestyle approaches to treatment
8.14.5 Special considerations in therapy

8.15 Dyslipidemia management in patients with immune disorders (autoimmune disease and post-transplant)
8.15.1 Dyslipidemia during immunosuppression
8.15.2 Pathophysiology of transplant coronary arteriopathy
8.15.3 Importance of lifestyle measures
8.15.4 Pharmacologic therapy with emphasis on drug interactions

8.16 Coronary and Non-Coronary Arterial Disease Management for the Lipidologist
8.16.1 Refer to the recent ACC guidelines on management of the patient with stable IHD
8.16.2 Refer to PAD guidelines
8.16.3 Emphasize importance of cardiac rehabilitation for CHD patient / exercise for PAD patients / PT for stroke patients
8.16.4 Drug therapy with emphasis of interaction between lipid-lowering agents and cardiovascular drugs

8.17 Gender Considerations in Dyslipidemia Management
8.17.1 CVD outcomes for women vs men
8.17.2 Psychological stressors for men vs women
8.17.3 Rehab considerations
8.17.4 Family issues including cooking and grocery shopping influence on the family

8.18 Racial and Ethnic Considerations in Lipidology
8.18.1 Different lipid phenotypes, basic epidemiology
8.18.2 Special challenges in nutritional management with ethnic foods / cultural barriers
8.18.3 Drug management

8.19 Management of Statin Intolerance/Phobia and Statin Safety Issues
8.19.1 What are people afraid of
8.19.2 FDA advisory on safety of statins in terms of liver issues, no need for regular monitoring
8.19.3 Pathophysiology of muscle side effects with statins
8.19.3.1 Non-statins causes of muscle symptoms
8.19.4 Prevalence of muscle complaints in various databases and pros and cons of these databases
8.19.5 Practical tips on how to deal with this
8.19.5.1 Management algorithm including re-challenge (most are not statin intolerant)
8.19.5.2 Alternate-day dosing
8.19.6 Other side effects
8.19.6.1 Neuro side effect pointing out lack of good data; potential benefit of statins on stroke prevention/preservation of cognition
8.19.6.2 Less depression
8.19.6.3 Renal disease – observation evidence ARF, but no signal from RCTs and benefit in CKD < stage 5/dialysis

8.20 Management of Intolerance and Safety Issues in Non-Statin Drugs
8.20.1 Niacin – glucose issues, gout, hepatic side effects, flushing
8.20.2 Resins – constipation, adsorption of other drugs
8.20.3 Fibrates – increase in creatinine, hepatic side effects, myopathy
8.20.4 Ezetimibe
8.20.5 Supplements

8.21 Adherence to Treatment in Clinical Lipidology
8.21.1 Definition of adherence / compliance
8.21.2 Assessment in studies
8.21.3 Epidemiology of non-adherence
8.21.4 Dealing with the non-adherent patient / non-threatening / motivational interviewing

9.0 Lipid Management Aspects of Cardiovascular Disease Risk Factor Management
9.1 Smoking and dyslipidemia
9.1.1 Smoking and high density lipoprotein cholesterol
9.1.2 Smoking and triglycerides
9.1.3 Smoking and other dyslipidemias
9.1.4 Evidence-based Smoking cessation

9.2 Diabetes mellitus
9.2.1 Dyslipidemia often associated with type 1 diabetes mellitus
9.2.2 Dyslipidemia often associated with type 2 diabetes mellitus
9.2.3 Effect of diabetes medications on lipid levels
9.2.4 Evidence-based diabetes management

9.3 Blood pressure medications and lipid levels
9.3.1 Evidence-based BP management

9.4 Physical Activity (PA)
9.4.1 Effect of aerobic / dynamic exercise on lipid levels
9.4.2 Effect of anaerobic / resistance exercise on lipid levels
9.4.3 Effect of modest increase in physical activity on lipid levels
9.4.3 Evidence-based PA recommendations

9.5 Adiposity and dyslipidemia
9.5.1 The pathogenic potential of adipose tissue, and mechanisms involved in adiposity-related dyslipidemia
9.5.1.1 Adipocyte and adipose tissue anatomic abnormalities leading to dyslipidemia
9.5.1.2 Adipocyte and adipose tissue endocrine abnormalities leading to dyslipidemia
9.5.1.3 Adipocyte and adipose tissue immune abnormalities leading to dyslipidemia
9.5.1.4 Adipocyte and adipose tissue miscellaneous functional abnormalities leading to dyslipidemia
9.5.2 Adiposity and triglycerides
9.5.3 Adiposity and high density lipoprotein cholesterol
9.5.4 Adiposity and low density lipoprotein cholesterol
9.5.5 Adiposity and the metabolic syndrome

9.6 Effect of weight loss by nutritional intervention on lipid levels in overweight or obese patients
9.7 Effect of weight loss by increased physical activity on lipid levels in overweight or obese patients
9.8 Effect of weight loss by weight management drugs on lipid levels in overweight or obese patients
9.9 Effect of weight loss by bariatric surgery on lipid levels in overweight or obese patients
9.9.1 Evidence-based weight loss