National Lipid Association (NLA) Core Curriculum in Clinical Lipidology

1. Selected Lipid Management Recommendations and Guidelines

1.1. General Lipid Recommendations and Guidelines

1.1.1. 2015 National Lipid Association recommendations for patient-centered management of dyslipidemia: Part-1, full report
1.1.2. 2015 National Lipid Association recommendations for patient-centered management of dyslipidemia: Part-2
1.1.3. 2017 Update on the use of PCSK9 inhibitors in adults: Recommendations from an Expert Panel of the National Lipid Association
1.1.4. 2017 American Association of Clinical Endocrinologists and American College of Endocrinology Guidelines for Management of Dyslipidemia and Prevention of Cardiovascular Disease
1.1.5. 2016 ACC Expert Consensus Decision Pathway on the Role of Non-Statin Therapies for LDL Cholesterol Lowering in the Management of Atherosclerotic Cardiovascular Disease Risk
1.1.6. 2016 ESC/EAS Guidelines for the Management of Dyslipidaemias: The Task Force for the Management of Dyslipidaemias of the European Society of Cardiology (ESC) and European Atherosclerosis Society (EAS)
1.1.7. 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Risk in Adults: A Report of the ACC/AHA Task Force on Practice Guidelines
1.1.8. 2004 NCEP ATP III and Update

1.2. Familial Hypercholesterolemia

1.2.1. 2017 Managing the Challenging Homozygous Familial Hypercholesterolemia Patient: Academic Insights and Practical Approaches for Severe Dyslipidemia: A National Lipid Association Masters Summit*
1.2.2. 2016 Defining severe familial hypercholesterolemia and the implications for clinical management: a consensus statement from the International Atherosclerosis Society Severe Familial Hypercholesterolemia Panel
1.2.3. 2015 The Agenda for Familial Hypercholesterolemia: A Scientific Statement from the American Heart Association
1.2.4. 2014 Integrated guidance on the care of familial hypercholesterolemia from the International FH Foundation
1.2.5. 2014 Homozygous familial hypercholesterolemia: new insights and guidance for clinicians to improve detection and clinical management. A position paper from the Consensus Panel on Familial Hypercholesterolaemia of the European Atherosclerosis Society*

1.3. Children and Adolescents

1.3.1. 2016 Screening for Lipid Disorders in Children and Adolescents: US Preventive Services Task Force Recommendation Statement
1.3.2. 2016 Final Recommendation Statement from the U.S. Preventive Services Task Force Lipid Disorders in Children and Adolescents: Screening
1.3.3. 2015 EAS Consensus Statement on Familial Hypercholesterolemia in Children

1.4. Lipid-Altering Drug Safety

1.4.1. 2014 NLA Statin Safety Update
1.4.2. 2007 NLA Safety Task Force: The Non-statins
1.4.3. 2006 NLA Statin Safety Task Force

1.5. Other

1.5.1. 2017 Dietary Fats and Cardiovascular Disease: A Presidential Advisory From the American Heart Association
1.5.2. 2016 Lipids and Bariatric Procedures Part 1 of 2: Scientific Statement from the National Lipid Association, American Society for Metabolic and Bariatric Surgery, and Obesity Medicine Association

1.5.3. 2016 Lipids and Bariatric Procedures Part 2 of 2: Scientific Statement from the American Society for Metabolic and Bariatric Surgery, National Lipid Association, and Obesity Medicine Association
1.5.4. 2013 Chronic Kidney Disease Clinical Practice Guideline for Lipid Management
1.5.5. 2013 Obesity, Adiposity, and Dyslipidemia: A Consensus Statement from the National Lipid Association
1.5.6. 2011 NLA Expert Panel on Biomarkers: Clinical utility of inflammatory markers and advanced lipoprotein testing
1.5.7. 2011 AHA Scientific Statement on Triglycerides and CVD
1.5.8. 2010 EAS Consensus Statement on Lp(a)

2. Lipids and/or Lipid Treatment Targets

2.1. Non–High-Density Lipoprotein Cholesterol (non–HDL-C)

2.2. Low-Density Lipoprotein Cholesterol (LDL-C)

2.3. Apolipoprotein B (apo B)

2.4. LDL Particle Number

2.5. Triglycerides

2.6. High-Density Lipoprotein Cholesterol (HDL-C)

2.7. Lipoprotein (a)

2.8. Chylomicrons

2.9. Very-Low Density Lipoproteins (VLDL)

2.10. Intermediate Density Lipoproteins

2.11. Lipoprotein Remnants (Chylomicron, VLDL, etc.)

3. Non-lipid Biomarkers*

3.1. High Sensitivity CRP

3.2. Interleukin-1

3.3. Pro-BNP

3.4. Cardiac Troponin I and T

3.5. Lp-PLA2

4. Lipid Testing Methodologies

4.1. Fasting vs Non-Fasting Lipid Testing

4.2. Plasma or Serum Cholesterol and Triglyceride Levels [e.g., Automated Enzymatic Analyses Standardized via the Center for Disease Control's (CDC) Lipid Standardization program]

4.3. HDL Cholesterol (e.g., Precipitation and Ultracentrifugation)

4.4. Low-Density Lipoprotein Cholesterol (LDL-C) Levels

4.4.1. Calculated (e.g., Friedewald Equation, Martin-Hopkins Equation)
4.4.2. Direct Measurements (e.g., Ultracentrifugation and Precipitation known as "beta-quantification" or "beta quant")

4.5. Non-High-Density Lipoprotein Cholesterol (e.g., Calculated)

4.6. Apolipoprotein B (apo B) (e.g., Enzyme-linked Immunosorbent Assay)*

4.7. Lipoproteins*

- 4.7.1. Gradient gel electrophoresis*
- 4.7.2. Tube gel electrophoresis*
- 4.7.3. Ultracentrifugation*
- 4.7.4. Vertical auto profile*
- 4.7.5. Nuclear magnetic resonance*

4.8. LDL particle number*

- 4.8.1. NMR*
- 4.8.2. Differential ion mobility analysis*

4.9. Lipoprotein(a) or Lp(a) (e.g., Standardized Immunoassays)*

4.10. Remnant Lipoprotein Particles*

- 4.10.1. Immunoseparation*
- 4.10.2. Vertical auto profile*
- 4.10.3. Calculation method (total cholesterol minus HDL-cholesterol minus LDL-Cholesterol)*

4.11. LDL Particle Size*

- 4.11.1. Segmented gradient gel electrophoresis*
- 4.11.2. Vertical auto profile ultracentrifugation*
- 4.11.3. Nuclear magnetic resonance*

5. Lipoproteins and Lipoprotein metabolism*

5.1. Lipoprotein Structure and Function

5.2. Intestinal Lipid Transport and Chylomicron Formation, Secretion and Catabolism*

5.3. Hepatic Lipid Transport and VLDL Formation, Secretion and Catabolism*

5.4. LDL Receptor Expression, Function and Catabolism (PCSK9)*

5.5. HDL Synthesis, Maturation, Catabolism, Role in Peripheral / Reverse Cholesterol Transport and Non-ASCVD Effects*

5.6. Cholesterol and Bile Acid Metabolism*

5.7. Microbiome

5.8. Intrahepatic Gene Regulation via Nuclear Receptor Factors*

- 5.8.1. LXR
- 5.8.2. FXR
- 5.8.3. PPAR
- 5.8.4. SREBP

6. Vascular Biology*

6.1. Normal Arterial Biology*

6.2. Pathogenesis of Atherosclerosis*

6.3. Thrombosis*

6.4. Inflammation*

7. Atherosclerotic Cardiovascular Disease Risk Assessment

7.1. ASCVD Risk Factors (2014 NLA Recommendations Part 1)

- 7.1.1. Prior or Current Coronary Artery Disease or ASCVD
  - 7.1.1.1. Myocardial Infarction
  - 7.1.1.2. Coronary Stenosis
  - 7.1.1.3. Stroke
  - 7.1.1.4. Carotid Stenosis

- 7.1.1.5. Other Large Artery Atherosclerosis
- 7.1.1.6. Peripheral Vascular Disease
- 7.1.1.7. Aortic Aneurysm

- 7.1.2. Family History of Premature ASCVD
- 7.1.3. High Blood Pressure
- 7.1.4. Cigarette Smoking
- 7.1.5. Diabetes Mellitus
- 7.1.6. Obesity
- 7.1.7. Metabolic Syndrome
- 7.1.8. History of Preeclampsia, Gestational Diabetes, or Pregnancy-induced Hypertension
- 7.1.9. Renal Disease (e.g., Microalbuminuria, Chronic Kidney Disease)
- 7.1.10. Inflammatory Diseases
  - 7.1.10.1. Human Immune Virus
  - 7.1.10.2. Rheumatoid Arthritis
  - 7.1.10.3. Systemic Lupus Erythematosus
- 7.1.11. Solid Organ Transplant

7.2. Subclinical Atherosclerosis Evaluation

- 7.2.1. Coronary Artery Calcium Scoring
- 7.2.2. Coronary Computed Tomography Angiography (CCTA)
- 7.2.3. Carotid Intima-media Thickness and Plaque
- 7.2.4. Ankle-brachial Index

7.3. ASCVD Risk and Other Calculators

- 7.3.1. American College of Cardiology/American Heart Association Atherosclerotic Cardiovascular Disease Risk Estimator
- 7.3.2. Lifetime ASCVD Risk Calculators
  - 7.3.2.1. ACC/AHA Lifetime Risk Calculator
  - 7.3.2.2. Framingham Lifetime Risk Calculator
- 7.3.3. Predominantly US Risk Assessment Calculators / Estimators
  - 7.3.3.1. United States National Heart, Lung, and Blood Institute Framingham Risk Score
  - 7.3.3.2. Multi-Ethnic Study of Atherosclerosis (MESA) 10-Year CHD Risk with Coronary Artery Calcification Risk Score
  - 7.3.3.3. Reynolds Risk Score
  - 7.3.3.4. Strong Heart Study Risk Calculator*
- 7.3.4. Predominantly International Risk Assessment Calculators / Estimators
  - 7.3.4.1. QRISK Risk Calculator*
  - 7.3.4.2. Systemic Coronary Risk Estimation (SCORE)*
  - 7.3.4.3. Prospective Cardiovascular Munster Study (PROCAM)*
  - 7.3.4.4. National Health Service (NHS) Health Check*
- 7.3.5. American College of Cardiology Statin Intolerance App

8. Atherosclerotic Cardiovascular Disease (ASCVD) Risk Categories

8.1. Very-High Cardiovascular Disease Risk

8.2. High Cardiovascular Disease Risk

8.3. Moderate Cardiovascular Disease Risk

8.4. Low Cardiovascular Disease Risk

9. Lipid Treatment Targets, Goals, Thresholds, and Screening

9.1. Definitions

- 9.1.1. Lipid Targets
- 9.1.2. Lipid Goals
- 9.1.3. Lipid Thresholds

9.2. Lipid Screening

9.3. Lipid Treatment Goals and Thresholds

- 9.3.1. Non-HDL-C
- 9.3.2. LDL-C
- 9.3.3. Triglycerides
- 9.3.4. Apolipoprotein B

10. Genetic Dyslipidemias

10.1. Physical Findings

- 10.1.1. Xanthomas
- 10.1.2. Xanthelasma (including Non-Hyperlipidemic Causes)
- 10.1.3. Corneal Arcus
- 10.1.4. Lipemia Retinalis
- 10.1.5. Apple Versus Pear Body Fat Distribution
- 10.1.6. “Test Tube” Blood Appearance

10.2. Hypolipidemias

- 10.2.1. Hypoalphalipoproteinemia Syndromes (deficiencies in APOA1, apoA1milano, ABCA1 (Tangiers), ABCG1, LCAT (Fish Eye Disease)
- 10.2.2. Abetalipoproteinemia (MTP deficiency)
- 10.2.3. Hypobetalipoproteinemias
- 10.2.4. PCSK9 Loss of Function
- 10.2.5. ANGTL 3 Loss of Function

10.3. Major Lipid Associated Genes (GWAS Studies)*

- 10.3.1. LDL - LDLR, APOB, PCSK9, APOB, HMGCR, NPC1L1, LDLRAP1, SORT1, ABCG5/ABCG8, CYP27A1
- 10.3.2. Triglycerides - APOCIII, APOCII, APOA5, LPL, ANGPTL4, ANGPTL3, LMF1, GPIHBP1
- 10.3.3. HDL- ABCA1, ABCG1, LCAT, CETP, SR-B1, LIPC, LPL
- 10.3.4. Lp(a) - LPA

10.4. Hypertriglyceridemia

- 10.4.1. Polygenic
- 10.4.2. Monogenic Hypertriglyceridemia & Familial Hyperchylomicronemia Syndromes (FCS)
  - 10.4.2.1. Lipoprotein Lipase Deficiency
  - 10.4.2.2. APOCII Deficiency
  - 10.4.2.3. GPIHBP1 Deficiency (glycosylphosphatidylinositol anchored high density lipoprotein binding protein 1)
  - 10.4.2.4. LMF1 Deficiency (liase maturation factor)
  - 10.4.2.5. GPD1 Deficiency (glycerol-3-phosphate dehydrogenase 1)
- 10.4.3. Familial Dysbetalipoproteinemia (ApoE II/II or other variants)

10.5. Hypercholesterolemia

- 10.5.1. Homozygous Familial Hypercholesterolemia
- 10.5.2. Heterozygous Familial Hypercholesterolemia
- 10.5.3. Polygenic Hypercholesterolemia
- 10.5.4. Sitosterolemia
- 10.5.5. Autosomal Recessive Hypercholesterolemia
- 10.5.6. Lysosomal Acid Lipase (LAL) Deficiency

10.6. Combined Hyperlipidemia or Mixed Dyslipidemia

10.6.1. Familial Combined Hyperlipidemia
10.6.2. Non-Familial Combined Hyperlipidemia

11. Familial Hypercholesterolemia

11.1. Prevalence

11.2. Genetics and Genetic Testing

11.2.1. LDL Receptor
11.2.2. Defective apo B
11.2.3. PCSK9 Gain of Function

11.3. Diagnostic Criteria

11.4. Relevance of Lipoprotein (a)

11.5. Treatment

12. Secondary Causes of Dyslipidemia

12.1. Lifestyle Related Dyslipidemia Due to Diet, Smoking, Alcohol, or Obesity

12.2. Concomitant Drug-induced Hyperlipidemia

12.3. Diabetes Mellitus and Insulin Resistant States

12.4. Hypothyroidism

12.5. Chronic Kidney Disease (including Nephrotic Syndrome)

12.6. Obstructive Liver Disease (including Primary Biliary Cirrhosis)

12.7. HIV

12.8. Inflammatory Disorders (RA, SLE, Psoriasis)

12.9. Graft Versus Host Disease

12.10. Pregnancy, PCOS, & Menopause

12.11. “Two hit” Genetic and Secondary Dyslipidemias

13. Nutrition and Medical Nutrition Therapy

13.1. Nutrition Science Evidence-Base Related to Blood Lipids and/or ASCVD Risk

13.1.1. Core Metabolic Studies of PUFA-MUFA vs. SFA Feeding
13.1.2. Prospective Cohort Studies of Foods-Nutrients
13.1.3. Randomized Clinical Trials of Whole Diets, Foods-Nutrients

13.2. Foods-Nutrients that Modify ASCVD Risk

13.2.1. Decrease ASCVD Risk:

13.2.1.1. Fruits-Vegetables
13.2.1.2. Beans-Legumes
13.2.1.3. Nuts-Seeds
13.2.1.4. Whole Grains
13.2.1.5. Fish-Seafood
13.2.1.6. Liquid Vegetable Oils High in PUFA-MUFA
13.2.1.7. Alcohol (in Moderation)

13.2.2. Increase ASCVD Risk

13.2.2.1. Solid Fats High in Saturated and Trans-Fats
13.2.2.2. Dietary Cholesterol
13.2.2.3. Processed / Refined Carbohydrates and Added Sugars

13.2.2.4. Processed Meats
13.2.2.5. Sodium

13.2.3. Recommended Whole Dietary Patterns for ASCVD Risk Reduction

13.2.3.1. AHA/ACC Diet Pattern
13.2.3.2. Healthy U.S. Diet Pattern
13.2.3.3. Mediterranean Diet Pattern
13.2.3.4. DASH Diet Pattern
13.2.3.5. Vegetarian-Vegan Diet Pattern
13.2.3.6. Ornish Diet Pattern

13.2.4. Contemporary Nutrition Topics, Controversies and/or Myths

13.2.4.1. Low Fat vs. Higher Fat Diets
13.2.4.2. Ketogenic and Other Popular Diets for Weight loss
13.2.4.3. Specific foods-nutrients (dairy fat, coconut oil, gluten)
13.2.4.4. Nutrition supplements (Omega-3-fatty acids vs. others)

13.2.5. Medical Nutrition Therapy and Therapeutic Diet Interventions

13.2.5.1. For Lowering LDL Cholesterol

13.2.5.1.1. Dietary Saturated Fat Restriction to < 7% of Calories
13.2.5.1.2. Plant Stanols and Sterols
13.2.5.1.3. Soluble Fiber
13.2.5.1.4. Soy Protein

13.2.5.2. For Lowering Moderately Non-HDL-C and Triglycerides

13.2.5.2.1. Dietary Whole Grains and Fiber
13.2.5.2.2. Dietary Sugar Restriction
13.2.5.2.3. Alcohol Restriction

13.2.5.3. For Lowering Very High Triglycerides > 500 mg/dL

13.2.5.3.1. Indication for Hospitalization and Fasting
13.2.5.3.2. Role of IV Insulin in Patients with Type 2 Diabetes Mellitus
13.2.5.3.3. Role of Therapeutic Plasma Exchange
13.2.5.3.4. Role of Enteral or Parenteral Nutritional Support
13.2.5.3.5. Long-term Nutritional Management (Very Low-Fat Diets, MCTs)

13.3. Food Effects on Lipid Levels

13.3.1. Saturated Fats
13.3.2. Processed Carbohydrates
13.3.3. Trans Fats
13.3.4. Polyunsaturated Fats
13.3.5. Monounsaturated Fats
13.3.6. Complex Carbohydrates
13.3.7. Proteins

13.4. Basic Principles of Healthy Nutrition

13.4.1. Saturated Fats and their Replacement

13.4.1.1. Replacing Saturated Fats with Processed or Refined Carbohydrates
13.4.1.2. Replacing Saturated Fats with Mono or Polyunsaturated Fats

13.4.2. Processed or Refined Carbohydrates and Added Sugar
13.4.3. Omega-3 Fatty Acids
13.4.4. Calories
13.4.5. Sodium
13.4.6. Alcohol

13.5. Nutrition therapy of dyslipidemia

13.5.1. Triglyceride-induced Acute Pancreatitis

13.5.1.1. Indication for Hospitalization and Fasting
13.5.1.2. Role of Insulin in Patients with Type 2 Diabetes Mellitus
13.5.1.3. Role of Therapeutic Plasma Exchange
13.5.1.4. Role of Enteral or Parenteral Nutritional Support
13.5.1.5. Dietary Advancement Once Pancreatitis Resolves
13.5.1.6. Long-term Nutritional Management

13.5.2. Elevated Triglyceride Levels without Pancreatitis

13.6. Evidence-based Dietary patterns

13.6.1. Mediterranean Diet
13.6.2. Therapeutic Lifestyle Diet
13.6.3. Dietary Approaches to Stop Hypertension
13.6.4. Ornish Diet
13.6.5. Vegetarian Diet

13.7. Dietary supplements

13.7.1. Efficacy
13.7.2. Safety

13.8. Other Popular Diets

13.8.1. Atkins Diet
13.8.2. Paleo Diet

14. Physical Activity and Lipids

14.1. Dynamic (Aerobic) Exercise and Lipids

14.2. Resistance (Weight Lifting) Exercise and Lipids

14.3. Non-exercise Activity Thermogenesis

14.4. Exercise Prescription

14.5. Physical Activity Goals

14.6. Metabolic Equivalent Tasks

14.7. Tracking

14.7.1. Exercise Logs
14.7.2. Pedometer / Accelerometer
14.7.3. Dynamic Training Metrics (e.g., miles run, laps swam)
14.7.4. Resistance Training Metrics (e.g., muscle circumference measurements, reps, sets)
14.7.5. Percent Body Fat Measurements*

14.7.5.1. Dual-energy X-ray Absorptiometry (DXA)
14.7.5.2. Bioelectrical Impedance*
14.7.5.3. Calipers*
14.7.5.4. Other [Calculated (e.g., U.S. army percent body fat equation), near-infrared interactance, whole-body air displacement plethysmography (BOD POD, underwater weighing] *

15. Obesity, Adiposopathy, Metabolic Syndrome, and Diabetes Mellitus

15.1. Obesity as a Disease

15.2. Adipose Tissue as an Active Endocrine and Immune Organ

15.3. Concomitant Drugs that Affect Weight and Lipid Levels

15.4. Metabolic Syndrome

15.5. Diabetes Mellitus Pharmacotherapy and ASCVD Outcomes

15.6. Weight Loss Effects on Lipid Parameters

15.6.1. Nutrition
15.6.2. Physical Activity
15.6.3. Weight Management Pharmacotherapy
15.6.4. Bariatric Surgery

16. Lipid Pharmacotherapy Safety and Efficacy

16.1. Statins

16.1.1. Mechanism of Action
16.1.2. Lipid Efficacy

16.1.2.1. Intensity of Statin (High, Moderate, and Low)
16.1.2.2. Absolute Versus Percent LDL Cholesterol Reduction

16.1.3. ASCVD Outcomes Efficacy
16.1.4. Safety and Tolerability
16.1.5. Drug Interactions

16.1.5.1. Pharmacokinetics and Pharmacodynamics
16.1.5.2. Drug Metabolism (CYP Enzyme Systems)
16.1.5.3. Transporters
16.1.5.4. Statin Drug Interactions

16.1.6. Statin Intolerance

16.1.6.1. Muscle

16.1.6.1.1. Myalgias
16.1.6.1.2. Myopathy
16.1.6.1.3. Rhabdomyolysis

16.1.6.2. Brain
16.1.6.3. Liver
16.1.6.4. Glucose and Diabetes Mellitus
16.1.6.5. Management of Statin Intolerance

16.2. Fibrates

16.2.1. Mechanism of Action
16.2.2. Lipid Efficacy
16.2.3. ASCVD Outcomes Efficacy
16.2.4. Safety and Tolerability
16.2.5. Drug Interactions

16.3. Omega-3 Fatty Acids

16.3.1. Mechanism of Action
16.3.2. Lipid Efficacy
16.3.3. ASCVD Outcomes Efficacy
16.3.4. Safety and Tolerability
16.3.5. Drug Interactions

16.4. Cholesterol Absorption Inhibitors

16.4.1. Mechanism of Action
16.4.2. Lipid Efficacy
16.4.3. ASCVD Outcomes Efficacy
16.4.4. Safety and Tolerability
16.4.5. Drug Interactions

16.5. PCSK9 Inhibitors

- 16.5.1. Mechanism of Action
- 16.5.2. Lipid Efficacy
- 16.5.3. ASCVD Outcomes Efficacy
- 16.5.4. Safety and Tolerability
- 16.5.5. Drug Interactions

16.6. Bile Acid Sequestrants (Resins)

- 16.6.1. Mechanism of Action
- 16.6.2. Lipid Efficacy
- 16.6.3. ASCVD Outcomes Efficacy
- 16.6.4. Safety and Tolerability
- 16.6.5. Drug Interactions
- 16.6.6. Effect on Glucose Levels

16.7. Niacin

- 16.7.1. Mechanism of Action
- 16.7.2. Lipid Efficacy
- 16.7.3. ASCVD Outcomes Efficacy
- 16.7.4. Safety and Tolerability
- 16.7.5. Drug Interactions
- 16.7.6. Effects on Glucose Levels

16.8. Drugs for Homozygous Familial Hypercholesterolemia

- 16.8.1. PCSK9 Inhibitor (Safety and Efficacy)
- 16.8.2. Lomitapide (Safety and Efficacy)
- 16.8.3. Mipomersen (Safety and Efficacy)

16.9. Investigational Lipid-altering Pharmacotherapy

- 16.9.1. Delivery Modalities (small molecules, prodrugs, anti-sense, monoclonal antibodies, gene therapy)
- 16.9.2. Proprotein Convertase Subtilisin Kexin 9 (PCSK9) Acting Agents (Inclisiran, Vaccines)
- 16.9.3. Adenosine Triphosphate Citrate Lyase Inhibitor (Bempedoic Acid)
- 16.9.4. Dialkyl Ether Dicarboxylic Acid (Gemcabene)
- 16.9.5. Cholesteryl Ester Transfer Protein (CETP) Inhibitors (Dalcetrapib, TA-8995)
- 16.9.6. Antisense Oligonucleotides (ASO's) (apoC3, lipoprotein (a), Angiopoietin-like protein 3)
- 16.9.7. Peroxisome Proliferator Activated Receptor (PPAR) Agents (Pemafibrate, MBX-8025)
- 16.9.8. Adeno-associated Airal (AAV) Vector Gene Therapy (LDL Receptor, Lipoprotein Lipase)
- 16.9.9. High-Density Lipoprotein-mediated Therapy (Reconstituted HDL's, Endothelial Lipase Inhibitors)

17. Lipoprotein apheresis*

17.1. Dextran Sulfate Apo B Lipoprotein Adsorption System (Liposorber)*

17.2. Heparin Extracorporeal LDL Apheresis (HELP)*

17.3. Conventional Plasmapheresis (Plasma Exchange)*

17.4. Efficacy and Safety of Lipoprotein Apheresis*

- 17.4.1. Lipid Effects
- 17.4.2. Safety
- 17.4.3. Evidence of ASCVD Outcomes Benefits
- 17.4.4. Indicated Use
- 17.4.5. Lp(a) Lowering

18. Management of by Age, Race, and Gender

18.1. Dyslipidemia in Children, Adolescents, and Young Adults < 21 Years of Age

- 18.1.1. Lipid Screening
- 18.1.2. ASCVD Risk Assessment
- 18.1.3. Nutrition and Physical Activity
- 18.1.4. Statin Therapy
- 18.1.5. Non-statin Therapy

18.2. Individuals >75 years

- 18.2.1. Risk Assessment
- 18.2.2. Drug Metabolism, Drug Interaction, and Medication Dosing
- 18.2.3. Polypharmacy
- 18.2.4. Concurrent Illnesses, Life Expectancy, and Overall Medical Status (Frailty)
- 18.2.5. Patient Preference

18.3. Asians

- 18.3.1. South Asians Versus Other Asians
- 18.3.2. Metabolic Syndrome & Insulin Resistance
- 18.3.3. Differences in Culture and Nutrition
- 18.3.4. Different Diagnostic Criteria for Waist Circumference and Predisposition for Dysfunctional Adipose Tissue (Adiposopathy)
- 18.3.5. Differences in Lipid Profiles [Lp(a), Non-HDL Cholesterol, HDL Cholesterol, Triglycerides)
- 18.3.6. ASCVD Risk Assessment
- 18.3.7. Statin and Other Lipid-altering Drug Dosing

18.4. African Americans

- 18.4.1. Overall Cardiovascular Disease Risk and Mortality
- 18.4.2. Differences in Culture and Nutrition
- 18.4.3. Differences in ASCVD Risk Factors [Blood Pressure, Lp(a), Triglycerides, HDL Cholesterol]
- 18.4.4. Difference in Statin Safety Measurements (Creatine Kinase)
- 18.4.5. ASCVD Risk Assessment

18.5. Hispanics / Latinos

- 18.5.1. Overall Cardiovascular Disease Risk and Mortality (Hispanic Paradox)
- 18.5.2. Differences in Culture and Nutrition
- 18.5.3. Differences in ASCVD Risk Factors (Triglycerides and HDL Cholesterol)
- 18.5.4. ASCVD Risk Assessment

18.6. Women

- 18.6.1. Risk Assessment
- 18.6.2. Primary and Secondary Prevention
- 18.6.3. Statin Benefits and Risk
- 18.6.4. Other Lipid-altering Drug Benefits and Risk
- 18.6.5. Lipid Drug Administration During Reproductive Years
- 18.6.6. Pregnancy
- 18.6.7. Polycystic Ovary Syndrome
- 18.6.8. Menopause

19. Management of Dyslipidemia in Other Patient Populations

19.1. Human Immunodeficiency Virus (HIV)

- 19.1.1. ASCVD risk – NLA vs. ASCVD vs. DAD Scoring
- 19.1.2. HIV Lipodystrophy
- 19.1.3. Protease Inhibitors and Potential for Drug Interactions
- 19.1.4. Efficacy and Safety of Lipid-altering Drugs
- 19.1.5. Clinical Trials

19.2. Patients with Inflammatory Diseases

19.2.1. ASCVD Risk
19.2.2. Lipid Effects of Anti-inflammatory Drugs
19.2.3. Efficacy and Safety of Lipid-altering Drugs

19.3. Patients with Other Chronic Diseases

19.3.1. Type 1 Diabetes Mellitus
19.3.2. Type 2 Diabetes Mellitus
19.3.3. Metabolic Syndrome
19.3.4. Insulin Resistance
19.3.5. Partial Lipodystrophy
19.3.6. Chronic Kidney Disease
19.3.7. Solid Organ Transplant

20. Lipid Treatment Adherence, Measurement, and Quality Improvement

20.1. Lipid Treatment Performance Measures

20.1.1. Lipid Goals (Absolute Targets % LDL-C Reduction)
20.1.2. Other Lipid Outcome Measures

20.2. Lipid Treatment Adherence Gaps

20.3. Improving Lipid Treatment Adherence and Gaps

20.3.1. Use of Team-based Care
20.3.2. Use of Behavior Change Techniques
20.3.3. Use of Health IT (System, Provider and Patient-level Tools)

21. Consultative Issues in Clinical Lipidology

21.1. Clinical Management of Homozygous FH*

21.1.1. Diagnosis

21.1.1.1. Family History
21.1.1.2. Lipid Levels
21.1.1.3. Physical Findings

21.1.2. Diagnostic Criteria
21.1.3. Genetic Screening
21.1.4. Cascade Screening
21.1.5. Lifestyle Intervention
21.1.6. When to Start Lipid-altering Drug Therapy
21.1.7. Choice of Lipid-altering Drug Therapy
21.1.8. Treatment in Women

21.1.8.1. Child-bearing Potential
21.1.8.2. Pregnancy
21.1.8.3. Breast Feeding

21.1.9. LDL Apheresis

21.2. Clinical Management of Heterozygous FH

21.2.1. Diagnosis

21.2.1.1. Family History
21.2.1.2. Lipid Levels
21.2.1.3. Physical Findings

21.2.2. Diagnostic Criteria
21.2.3. Genetic Screening
21.2.4. Cascade Screening
21.2.5. Lifestyle Intervention
21.2.6. When to Start Lipid-altering Drug Therapy

21.2.7. Choice of Lipid-altering Drug Therapy

21.2.7.1. Child-bearing Potential
21.2.7.2. Pregnancy
21.2.7.3. Breast Feeding

21.2.8. LDL Apheresis

21.3. Clinical Management of Severe Hypertriglyceridemia

21.3.1. Diagnosis

21.3.1.1. Family History
21.3.1.2. Lipid Levels
21.3.1.3. Physical Findings

21.3.2. Diagnostic Criteria
21.3.3. Genetic Testing
21.3.4. Lifestyle Intervention
21.3.5. When to Start Lipid-altering Drug Therapy
21.3.6. Choice of Lipid-altering Drug Therapy

21.3.6.1. Child-bearing Potential
21.3.6.2. Pregnancy
21.3.6.3. Breast Feeding

21.3.7. Hospitalization Decision

21.4. Clinical Management of Low HDL Cholesterol Levels

21.4.1. Diagnosis

21.4.1.1. Genetic Causes
21.4.1.2. Secondary Causes

21.4.2. Lifestyle Intervention
21.4.3. Drug Therapy

21.5. Clinical Management of Elevated lipoprotein (a)

21.5.1. Family History
21.5.2. Presence or Relative Absence of Other ASCVD Risk Factors
21.5.3. Progressive ASCVD Despite Absence of Substantial Other ASCVD Risk Factors
21.5.4. Racial Considerations
21.5.5. Drug Therapy

22. Evidence Based Medicine, Journal Article Interpretation, and Statistics for the Clinical Lipidologist*

22.1. Clinical Trial Process*

22.1.1. Study Idea or Hypothesis
22.1.2. Protocol Development
22.1.3. Data Management & Statistical Plan
22.1.4. Ongoing Data Collection and Processing with Cleaning & Discrepancy Management – quality control
22.1.5. Data Lock
22.1.6. Transfer for Statistical Analyses
22.1.7. Quality Assurance
22.1.8. Statistical Analyses
22.1.9. Clinical Study Report
22.1.10. Abstract
22.1.11. Manuscript

- 22.2. Study Designs*
  - 22.2.1. Placebo Controlled
  - 22.2.2. Randomized Controlled Trials (RCTs)
  - 22.2.3. Cohort Trials
  - 22.2.4. Observational Studies
  - 22.2.5. Meta-analyses
  - 22.2.6. Hierarchy of Study Design
- 22.3. Clinical trial interpretation*
  - 22.3.1. Primary Outcomes
  - 22.3.2. Secondary Outcomes
  - 22.3.3. Intention to Treat Analysis
  - 22.3.4. Per-protocol or Completer Analysis
  - 22.3.5. Landmark Analysis
  - 22.3.6. Post-hoc and Subgroup Analyses
    - 22.3.6.1. Correction for Multiplicity
    - 22.3.6.2. Bonferroni
    - 22.3.6.3. Stepwise Hierarchical Testing
- 22.4. Statistical and Clinical Significance*
- 22.5. Sample Size and Power Calculations*
- 22.6. Demographics*
- 22.7. Missing Data*
  - 22.7.1. Drug Approval Considerations
  - 22.7.2. Last Observation Carried Forward
- 22.8. Outlying Data*
- 22.9. Data Distribution (Parametric/Normal Versus Nonparametric/Non-normal) *
  - 22.9.1. Parametric/Normal/Gaussian
    - 22.9.1.1. Total and LDL Cholesterol
    - 22.9.1.2. Glucose
  - 22.9.2. Non-parametric/Non-normal/Non-Gaussian *
    - 22.9.2.1. Triglycerides
    - 22.9.2.2. Lp (a)
    - 22.9.2.3. CRP
- 22.10. Data Location (Mean, Median)*
- 22.11. Basic Statistical Tests and Plots*
  - 22.11.1. P-value and Setting Alpha for Statistical Significance
  - 22.11.2. Confidence Intervals
  - 22.11.3. Forest Plots
  - 22.11.4. Kaplan Meier Curve
  - 22.11.5. Waterfall Plots
- 22.12. Event Rates, Relative Risk Reduction (RRR), Absolute Risk Reduction (ARR), Hazard Ratios, Odds Ratios*
- 22.13. Number Needed to Treat (NNT) and Cost-efficacy
- 22.14. Number Needed to Harm (NNH)*
- 22.15. Study Biases and Limitations (e.g., Publication Bias)*

22.16. Interpreting Reviews and Guidelines*

- 22.16.1. Grading of Evidence – AHA/ACC Level of Evidence and Strength of Recommendation
- 22.16.2. GRADE Guidelines

22.17. Clinical Decision Making

- 22.17.1. Patient's Values, Preferences, Beliefs
- 22.17.2. Shared Decision Making
- 22.17.3. Clinical Judgment

22.18. Sentinel and Landmark Clinical Trials

- 22.18.1. Historic
- 22.18.2. Recent
- 22.18.3. Ongoing