MAYO CLINIC LABORATORIES

Lipids and Lipoproteins in Blood Plasma (Serum)

Mayo Clinic Laboratories
Cardiovascular Laboratory Medicine

Guidelines on Lipid Management in Adults

Formal recommendations for the management of dyslipidemia, particularly hypercholesterolemia, have been issued by several organizations. These guidelines share a common goal of improving patient care through standardization and optimization of treatment, however, in some instances there are fundamental differences in the approach. The following is a summary of recommendations for biomarker measurement according to guidelines issued by the National Cholesterol Education Program Third Adult Treatment Panel (NCEP-ATPIII),[1] the American College of Cardiologists/American Heart Association (ACC/AHA),[2] the National Lipid Association (NLA),[3] and Mayo Clinic.[4]

Guideline Commonalities

- Treatment should be guided by patient-specific atherosclerotic cardiovascular disease (ASCVD) risk.
- Basic lipids should be measured:
  - To establish a baseline ASCVD risk
  - Every 4 to 6 years in adults ≥20 years of age and not on treatment
  - Regularly to assess compliance and therapeutic efficacy for patients on lipid-lowering treatment
- Basic lipids include the following measurements:
  - Total cholesterol
  - High-density lipoprotein cholesterol (HDL-C)
  - Triglycerides
  - Low-density lipoprotein cholesterol (LDL-C)
  - Non-high-density lipoprotein cholesterol (Non-HDL-C)
- A treatment plan should be developed utilizing shared decision-making between the patient and their health care provider.

Recommended Biomarkers for Assessment of ASCVD Risk

NCEP-ATPIII (2004)	LDL-C (primary therapeutic target) Non-HDL-C (secondary target in cases of hypertriglyceridemia)
2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol	LDL-C (primary biomarker to assign statin benefit groups) High-sensitivity C-reactive protein (hs-CRP) Coronary artery calcium (CAC) score Ankle-brachial index (ABI)
NLA Recommendations for Patient-Centered Management of Dyslipidemia (2014)	Non-HDL-C (primary therapeutic target), LDL-C (secondary target) Apolipoprotein B (optional target) CAC, hs-CRP, Lipoprotein(a), urine albumin/creatinine ratio (UAC)
Mayo Clinic Preventive Cardiology Task Force	Non-HDL-C (primary biomarker to assign statin benefit groups) hs-CRP, Lipoprotein(a), CAC, eGFR (augment risk assessment)

Recommended Clinical Decision Points for Basic Lipids in Adults

Lipid (mg/dL)	Low	Desirable	Above Desirable	Borderline High	High	Very High
Non-HDL cholesterol	–	<130	130–159	160–189	190–219	≥220
LDL cholesterol	–	<100	100–129	130–159	160–189	≥190
Total cholesterol	–	<200	–	200–239	≥240	–
HDL cholesterol	–	–	–	–	–	–
Men	<40	–	–	–	–	–
Women	<50	–	–	–	–	–
Triglycerides	–	<150	–	150–199	200–499	≥500

Assessing Pediatric Hyperlipidemia

The National Heart, Lung and Blood Institute recommends universal lipid screening for children at ages 9 to 11 and again at ages 17 to 21 with either a fasting lipid profile (total cholesterol, HDL-C, triglycerides, non-HDL-C, LDL-C) or nonfasting lipid profile (total cholesterol, HDL-C, non-HDL-C). If nonfasting non-HDL-C is ≥145 mg/dL, perform a fasting lipid profile.[5]

Mayo Clinic recommends screening of high-risk children >2 years of age with 1 or more of the following criteria:

- Family history of dyslipidemia or premature CVD
- First- or second-degree relative
- Obesity (BMI >95th percentile)
- Hypertension
- Smoking
- Diabetes mellitus
- Chronic inflammatory disease
- Protease inhibitor treatment
- Chronic kidney disease
- Solid organ transplant
- Kawasaki syndrome

Initial testing includes a fasting lipid screen (12-hour fast). Avoidance of high fat food or dairy products 9 to 12 hours prior to testing is encouraged. The National Cholesterol Education Program (NCEP) provides guidance on pediatric lipid levels. Repeat testing is recommended in 3 to 5 years for results in acceptable range and every 1 year for borderline.

Recommended Clinical Decision Points for Lipids and Lipoproteins in Children and Adolescents

Lipid (mg/dL)	Low	Acceptable	Borderline High	High
Total cholesterol	–	<170	170–199	≥200
LDL cholesterol	–	<110	110–129	≥130
Non-HDL cholesterol	–	<120	120–144	≥145
Apolipoprotein B	–	<90	90–109	≥110
Triglycerides				
0–9 years	–	<75	75–99	≥100
10–19 years	–	<90	90–129	≥130
HDL cholesterol	<40	>45	–	–
Apolipoprotein A-1	<115	>120	–	–

Lipoprotein Metabolism Profile

Lipoprotein metabolism profile analysis adds practical information about the etiology of cholesterol and triglyceride elevations. In some patients, increased serum lipids reflects elevated levels of intermediate density lipid (IDL), very low density lipid (VLDL), Lipoprotein(a) (Lp[a]) or even LpX. These elevations can be indicative of a genetic deficiency in lipid processing, nephrotic syndrome, endocrine dysfunction or even cholestasis. Identification of the lipoprotein associated with lipid elevation is achieved using the gold-standard methods which include ultracentrifugation, selective precipitation, electrophoresis, and direct measurement of cholesterol and triglycerides in isolated lipoprotein fractions.

Proper characterization of a patient's dyslipidemic phenotype aids clinical decisions and guides appropriate therapy.

Disorders Identified by Lipoprotein Metabolism Profile

Dyslipidemia	Phenotype	Elevated Lipoproteins	Atherogenic	Primary Disorders
Exogenous hyperlipidemia	Type I	Chylomicrons	–	Lipoprotein lipase deficiency; ApoC-II deficiency
Hypercholesterolemia	Type IIa	LDL	+++	Familial hypercholesterolemia
Combined hyperlipidemia	Type IIb	LDL and VLDL	+++	Familial multiple lipoprotein-type hyperlipidemia
Remnant hyperlipidemia	Type III	IDL (beta-VLDL)	+++	Familial dysbetalipoproteinemia
Endogenous hyperlipemia	Type IV	VLDL	+	Familial hypertriglyceridemia (mild); Tangier disease
Mixed hyperlipemia	Type V	Chylomicrons and VDL	+	Familial hypertriglyceridemia (severe); Familial lipoprotein lipase deficiency

Once a lipoprotein metabolism profile has been obtained, routine repetition of lipoprotein analysis is not necessary; however, reevaluation of the lipoprotein profile would be appropriate after a clinically significant change in either the serum cholesterol or triglyceride concentration.

Lipoprotein(a)

Lp(a), is a complex lipoprotein particle which consists of an ordinary LDL particle combined with an additional protein. As with LDL, Lp(a) contains apolipoprotein B100 (ApoB); however, Lp(a) additionally contains apolipoprotein(a) (Apo[a]), which is covalently linked to ApoB. Apo(a) has a high sequence homology with plasminogen and thus Lp(a) combines elements of lipid transport and coagulation in its structural composition.

The Lp(a) particle has been referred to as "the most atherogenic lipoprotein." Concentrations of Lp(a) particles in the blood can be expressed readily either as concentrations of Lp(a) protein or Lp(a) cholesterol. Studies over the last 3 decades have indicated 2- to 3-fold increased cardiovascular risk in patients with Lp(a) >30 mg/dL or Lp(a) cholesterol >3 mg/dL.

Accurate immunochemical measurement of Lp(a) protein, however, is complicated by a the large number of apo(a) polymorphisms in the general population. The polymorphisms cause a specific protein domain to repeat between 2 and 38 times for a given individual. Consequently, the molecular size of Lp(a) protein varies over a broad range in the population (240-800 kDa), a test result primarily related to the number of molecules of Lp(a) protein in a specimen cannot be expressed accurately or meaningfully in terms of mg protein/dL unless the molecular weight of the Lp(a) protein in that specimen has been determined. An additional related concern is that the degree of atherogenicity of the Lp(a) particle in any specific case might depend on the molecular size of the Lp(a) protein.

Mayo Clinic Laboratories measures and reports Lp(a) cholesterol as part of LMPP / Lipoprotein Metabolism Profile. It is also available as a stand-alone test (LPAWS / Lipoprotein (a) Cholesterol, Serum). The cholesterol content of Lp(a) particles varies little, and Lp(a) cholesterol can be readily quantified. In many cases, we have observed Lp(a) cholesterol to be at levels of 25 to 50 mg/dL and in rare cases as high as 100 mg/dL. Thus, Lp(a) can contain significant proportions of the serum cholesterol. In such cases, knowledge of the concentration of Lp(a) and of the contribution of Lp(a) cholesterol to the serum total cholesterol should be helpful to physicians in their evaluation of cardiovascular risk.

References

1. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report). Circulation 2002;106:3143-3421
2. Stone NJ, Robinson JG, Lichtenstein AH, et al: 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults. a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 2014 Jul 1;63(25 Pt B):2889-2934
3. Jacobson TA, Ito MK, Maki KC, et al: National Lipid Association recommendations for patient-centered management of dyslipidemia. Part 1 – executive summary. J Clin Lipidol 2014;8:473-488
4. Lopez-Jimienez F, Simha V, Thomas RJ, et al: A Summary and Critical Assessment of the 2013 ACC/AHA Guideline on the Treatment of Blood Cholesterol to Reduce Atherosclerotic Cardiovascular Disease Risk in Adults: Filling the Gaps. Mayo Clin Proc 2014;89:1257-1278
5. Expert Panel on Integrated Guidelines for Cardiovascular Health and Risk Reduction in Children and Adolescents: Summary Report. Pediatrics 2011;128:S213-S256