KRESSER INSTITUTE FOR FUNCTIONAL AND EVOLUTIONARY MEDICINE

Blood Chem Dyslipidemia Review

MISCONCEPTION

- Heart disease is caused by too much “bad” cholesterol.
- LDL-C is the most important marker for heart disease risk and the only one you need to track during treatment.

TRUE CAUSE OF ATHEROSCLEROSIS

The truth is that atherosclerosis is caused by an inflammatory response to sterols in artery walls, and sterols are delivered by lipoproteins. Thus, the number of low-density lipoproteins in the blood, rather than the amount of cholesterol they carry, is a far greater predictor of heart disease risk.

LIPOPROTEIN(A)

- Important marker of cardiovascular disease risk.
- Lp(a) levels are strongly influenced by genetics.
- Important notes on Lp(a):
    - Although observational studies show strong association between Lp(a) and coronary heart disease, there has not yet been an interventional study that has shown that lowering Lp(a) leads to better outcomes.
    - With Lp(a), we can test for particle mass and particle number. The best marker is Lp(a) particle number, and this is expressed in nanomoles per liter, not milligrams per deciliter (mass).
    - Lp(a) particle number in nanomoles per liter, the optimal value is below 75. Intermediate is 75 to 125, and high risk is above 125.
    - In the Copenhagen Heart Study, they found that people with Lp(a) levels above 50 mg/dL had two- to threefold increased risk for heart attack.
    - Lp(a) is the strongest single predictor of coronary heart disease and aortic stenosis, and the association isn’t affected by adjustment for classic risk factors.

The two most important lab markers for assessing CVD risk are LDL-P and Lp(a)-P.

TESTING OPTIONS

1. Add the NMR LipoProfile plus lipoprotein(a) to your case review blood panel.

MODIFIABLE RISK FACTORS FOR HIGH LDL-P

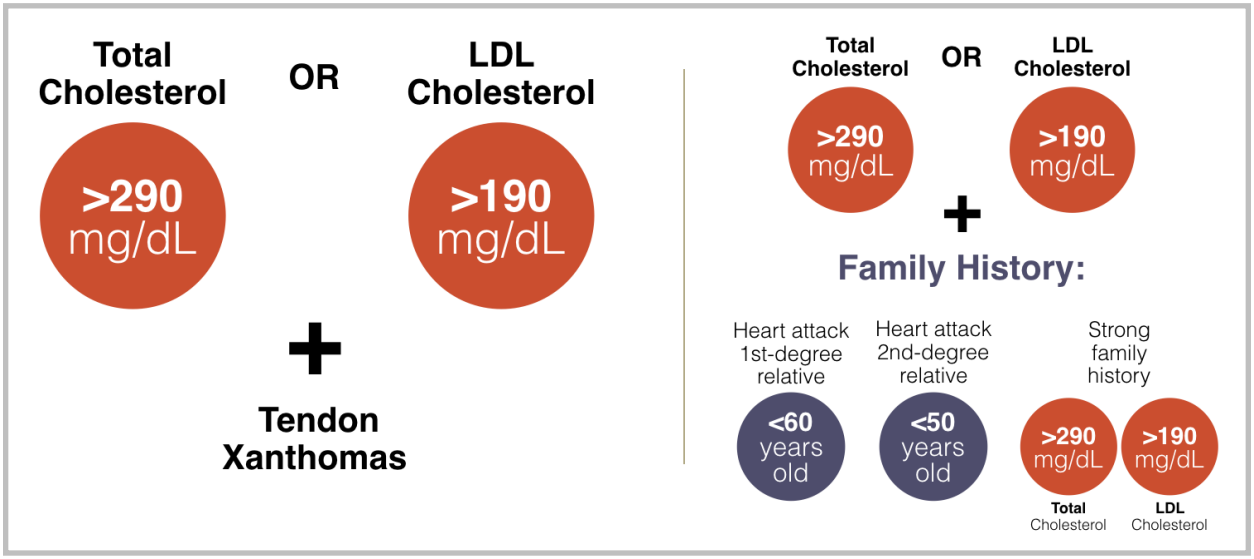
1. Insulin resistance
    a. Note that LDL particles don't just carry cholesterol. They also carry triglycerides, fat-soluble vitamins, and antioxidants, so you can think of LDL as a taxi service that delivers important nutrients to the cells and tissues of the body. An increase in triglycerides, for example, will contribute to increased LDL particles to carry them around.
2. Thyroid hypofunction
    a. It stimulates the expression of HMGCoA reductase, which is an enzyme in the liver involved in the production of cholesterol.
    b. It increases the expression of LDL receptors on the surface of cells in the liver and other tissues. In hypothyroidism, the number of receptors for LDL on cells will be decreased. This leads to reduced clearance of LDL from the blood and thus higher LDL levels.
3. Infection
4. GI pathology
    a. Studies have shown significant increases in LPS-binding protein and thus LDL particles in cases of endotoxins reaching the bloodstream.
    b. Studies have also shown that the gut microbiota disrupts lipid metabolism.
5. Environmental toxicity
    a. Mercury toxicity
    b. Bisphenol A (BPA)
6. HPA axis dysfunction
7. Health diet and lifestyle behaviors

NONMODIFIABLE CAUSES OF HIGH LDL-P

- Familial hypercholesterolemia (FH) involves a mutation of a gene that codes for the LDL receptor or the apolipoprotein B, or apoB protein that decreases p]LD]L particle clearance from the bloodstream.
- Size doesn't matter, at least not as much as number.
    - People with FH have primarily large, buoyant LDL particles and yet are still at a much higher risk for cardiovascular disease.
    - The idea was that small, dense LDL particles were more atherogenic, and large, buoyant LDL particles were protective and nothing to worry about.
    - Studies now show that particle size loses its significance when controlled for particle number. Particle number always trumps particle size as a risk factor.
- Genetics: ApoE and others

- In my experience, genetic testing does not change the treatment plan or outcome.
- My approach has been to address underlying causes, and then if the numbers are still elevated, assume that the remaining influence is genetic.

In the absence of genetic tests, you can use the Simon Broome criteria to diagnosis FH.



Pure hypercholesterolemia equals high total cholesterol, high LDL. Normal triglycerides and HDL.

Dyslipidemia usually involves high triglycerides, low HDL, normal or high total cholesterol, and normal or high LDL cholesterol, and that pattern is caused by metabolic dysfunction, whereas FH and pure hypercholesterolemia are often caused by genetics and other risk factors previously mentioned.

It is possible to have normal and even low total cholesterol and high LDL particle number. This happens most often in patients with metabolic syndrome.

TREATMENT

1. Address underlying mechanisms.
2. Retest and if the numbers are still high, use diet and lifestyle to further lower them.
3. Discuss further treatment options and risk and benefits with the patient.
    a. Family history
    b. Other risk factors for heart disease
    c. Medication options
    d. Supplements

e. Note: We have very little data on the significance of high LDL-P in a population that has no other significant risk factors, is consuming a healthy, nutrient-dense diet, and is living a healthy lifestyle.

DIETARY APPROACHES

- For patients with high LDL-P and normal metabolic function, I suggest a Mediterranean Paleo diet. This is a moderate carbohydrate and moderate fat approach.
- In patients with metabolic syndrome, a lower-carb Paleo approach is often better for lowering LDL-P because the pathology in that case is insulin resistance. Try to promote weight loss and improve insulin sensitivity.
- Other dietary considerations include emphasizing tree nut consumption, ensuring adequate intake of EPA and DHA, consuming fermented foods and fermentable fibers, eating a broad spectrum of colors, and maximizing intake of antioxidant-rich foods.

SUPPLEMENTS

1. **Tocopherols**
    a. The recommended dose is 200 mg of delta and gamma tocotrienols.
2. **Pantethine**
    a. Dose 450 mg twice daily.
    b. Need four to nine months to see significant results
3. **Red yeast rice**
    a. Reduce cholesterol production by inhibiting the HMG-CoA reductase enzyme.
    b. Two capsules of Thorne Coleast-900 contain about 5 mg of lovastatin, similar to taking a very low dose of a statin, but it has much lower side effects.
    c. The brand of red yeast rice is very important. The Thorne product has been shown to have a consistent dose of monacolin K and to be free of citrinin.
4. **CoQ10**
    a. Jarrow QH-Absorb. Dose is 200 mg once a day. Take with a meal that contains fat. Patients may find it to be stimulating; recommend taking the CoQ10 with breakfast.
5. **Glutathione**
    a. Consume at least a cup a day of homemade beef, chicken, or fish stock.
    b. Consume fattier cuts of meat (skin, cartilage and bones as well) rather than only lean cuts to get extra glycine.
    c. Fresh fruits/vegetables and raw dairy are great sources of glutathione.
    d. High-quality, grass-fed, nondenatured whey protein powder.
    e. I prefer liposomal supplement form of glutathione.

6. **Curcurmin and turmeric.** These increase the LDL receptor MRNA.
7. **Fish oil.** For patients who are at risk for heart disease, aim for between 12 and 16 ounces of coldwater fatty fish a week.
8. **Fermentable fibers**
    a. Examples include glucomannan, partially hydrolyzed guar gum, acacia, or others from the gut unit, or just increase intake of these fibers in food.
9. **Probiotics**

TREATMENT MATRIX

Presentation	Diet	Supplements
High LDL-P / Lp(a)-P without **inflammation**	Mediterranean Paleo	Tocotrienols, pantethine, RYR, fiber, probiotics; niacin & L-carnitine (Lp(a)-P)
High LDL-P / Lp(a)-P with **inflammation**	Mediterranean Paleo	Tocotrienols, pantethine, RYR, fiber, probiotics, CoQ10, curcumin, glutathione; niacin & L-carnitine (Lp(a)-P)
High LDL-P/Lp(a)-P with **metabolic syndrome**	Low-carb Paleo	Tocotrienols, pantethine, RYR, fiber, probiotics, CoQ10, curcumin, glutathione; niacin & L-carnitine (Lp(a)-P)
Normal LDL-P/Lp(a)-P with **inflammation**	Paleo	CoQ10, curcumin, glutathione

A note about statins: Most research suggests that the only population for which statins extend lifespan is in middle-aged men with pre-existing heart disease.