Sex and Gender Differences

LIPIDS AND LIPOPROTEINS

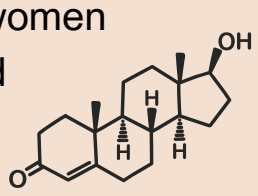
Lipids are fat molecules and combine with proteins to transport fat and cholesterol throughout the body.

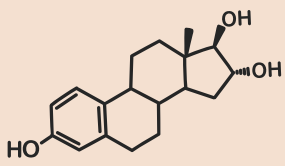
Abbreviations: HDL-C (high-density lipoprotein cholesterol); LDL-C (low-density lipoprotein cholesterol); TG (triglycerides)

Hormonal Basis for Sex Variation

Estrogen, testosterone, and other sex hormones regulate lipid metabolism in the liver.

- **Puberty:** HDL-C decreases by 10 mg/Dl due to testosterone
- **Adult men:** HDL-C is 10 mg/dL lower than in adult women
- **Pregnancy:** higher estrogen levels lead to increased LDL-C, HDL-C, and TG
- **Menopause:** Small increase in LDL-C





- **Oral estrogen** (e.g., some oral contraceptives): can affect lipids based on route and formulation
- **Polycystic Ovarian Syndrome**: higher testosterone levels lead to increased TG and decreased HDL-C
- **Male hypogonadism**: Increased LDL-C and TG
  - May correct with testosterone replacement
- **Anabolic steroid use**: Very low HDL-C
- **Gender Affirming Hormone Therapy (HT)**
  - Feminizing HT: decreased LDL-C, increased TG, increased HDL-C
  - Masculinizing HT: increased LDL-C, increased TG, decreased HDL-C

Prevalence

	Males	Females
LDL-C ≥ 130 mg/dL (Ideal LDL < 100 mg/dL)	27.4%	28.1%
HDL-C < 40 mg/dL	26.6%	8.5%
Ideal TG < 150 mg/dL	Mean TG 100.6 mg/dL	Mean TG 86.8 mg/dL

Ideal HDL-C depends on sex
Females ≥ 50mg/dL
Males ≥ 40mg/dL

Clinical Presentation

- **Dyslipidemia** is **usually asymptomatic**
- Hypercholesterolemia can lead to: angina, myocardial infarction, ischemic stroke
- Hypertriglyceridemia can lead to pancreatitis
- **Women** have a **higher incidence of metabolic syndrome:** Elevated TG, decreased HDL-C

In both sexes, there is a **positive correlation** between LDL-C elevation and ASCVD, the leading cause of death in the U.S. Women have an onset of ASCVD **10 years later** than men.

Treatment

- Statins are contraindicated in pregnancy
- Statin treatment:
  - Similar LDL-C reduction (unless affected by hormone therapy)
  - Similar reduction in risk of ASCVD
  - Females are less likely to be offered despite being eligible
  - Females are less likely to receive dosing at the guideline-recommended intensity
  - Females are at a higher risk of myopathy as a side effect
  - Males are more likely to achieve recommended lipid levels
- Alternative medications available: bile acid sequestrants, cholesterol absorption inhibitors, PCSK9 inhibitors, fibrates

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SEX and GENDER HEALTH COLLABORATIVE of the American Medical Women's Association

To learn more or get involved, visit **amwa-doc.org/sghc** or email us at **sghc@amwa-doc.org**

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Definitions & Disclaimers References