Who develops HDL dysfunction?

Learn the specific conditions that exhibit HDL dysfunction

In certain patient populations, inflammation, oxidative stress, and high blood glucose damage the HDL particles, impairing their cardioprotective function. Patients present with normal or high HDL-cholesterol levels, and further evaluation reveals the threatening nature of dysfunctional HDL. Due to the ubiquity and versatility of HDL particles, multiple medical conditions influence their activity. Below are examples of conditions affecting HDL function and the specific HDL mechanisms harmed.

Cardiovascular disease

- Coronary heart disease
- Coronary artery disease
- Acute coronary syndrome
- Hypertension

Metabolic disease

- Obesity
- Metabolic syndrome
- Type 2 diabetes
- Nonalcoholic fatty liver disease
- Polycystic ovary syndrome

Chronic inflammatory and autoimmune disease

- Type 1 diabetes
- Rheumatoid arthritis
- Systemic lupus erythematosus
- Psoriasis
- Periodontitis

Kidney disease

- Chronic kidney disease
- End-stage renal disease

Other conditions

- Cardiac surgery
- Obstructive sleep apnea
- Hyper-homocysteinemia
- Hyper-alphalipoproteinemia
- HIV infection
- Environmental contaminant exposure

Cardiovascular disease

Disease/condition	Evidence of HDL dysfunction
Coronary heart disease[1,2]	• Reduced PON1 activity in HDL • Reduced inhibition of monocyte binding to endothelial cells • Reduced inhibition of oxidation of LDL
Coronary artery disease[3,4,5]	• Reduced PON1 activity in HDL • Increased apoC-III level in HDL • Reduced cholesterol efflux capacity from macrophages • Reduced stimulation of NO production in endothelia cells • Reduced antioxidative capacity in endothelial cells • Reduced VCAM-1 expression in endothelial cells • Reduced inhibition of endothelial-monocyte adhesion • Reduced endothelial repair following carotid artery injury
Acute coronary syndrome[6,7,8,9]	• Reduced PON1 activity in HDL • Increased apoC-III level in HDL • Reduced inhibition of LDL oxidation • Impaired HDL-apoA-I exchange
Hypertension[10]	• Reduced serum PON1 activity • Reduced inhibition of LDL oxidation

apoA-I= apolipoprotein A-I; **apoC-III**= apolipoprotein C-III; **HDL**= high-density lipoprotein; **LDL**= low-density lipoprotein; **NO**= nitric oxide; **PON1**= paraoxonase 1; **VCAM-1**= soluble vascular cell adhesion molecule-1

Metabolic disease

Disease/procedure	Evidence of HDL dysfunction
Obesity[11,12,13,14]	• Reduced PON1 activity in HDL • Increased levels of lipid hydroperoxides in HDL • Increased SAA levels in serum
Metabolic syndrome[15,16]	• Increased triglycerides and decreased cholesteryl esters in HDL • Reduced apoA-I in HDL • Reduced inhibition of LDL oxidation
Type 2 diabetes[17,18,19,20,21]	• Increased MPO activity in HDL • Reduced PON1 activity in HDL • Increased triglycerides in HDL • Reduced stimulation of NO production in endothelial cells • Reduced antioxidative capacity in endothelial cells • Reduced endothelial repair following carotid artery injury • Reduced inhibition of LDL oxidation • Reduced cholesterol efflux capacity • Reduced inhibition of LDL-induced monocyte chemotactic activity in endothelial cells
Nonalcoholic fatty liver disease[22,23]	• Reduced cholesterol efflux capacity • Reduced circulating apoA-I • Reduced circulating preβ1-HDL
Polycystic ovary syndrome[24,25]	• Reduced cholesterol efflux capacity • Reduced circulating apoA-I levels • Increased intrinsic HDL oxidation levels

apoA-I= apolipoprotein A-I; **HDL**= high-density lipoprotein; **LDL**= low-density lipoprotein; **MPO**= myeloperoxidase; **NO**= nitric oxide; **PON1**= paraoxonase 1; **SAA**= serum amyloid A

Chronic inflammatory or autoimmune disease

Disease/condition	Evidence of HDL dysfunction
Type 1 diabetes[26,27,28]	• Reduced PON1 activity in HDL • Glycoxidation in HDL • Reduced ability to counteract oxLDL-mediated actions
Rheumatoid arthritis[29,30,31,32]	• Increased MPO in HDL and plasma • Reduced PON1 activity in HDL • Increased SAA in HDL • Reduced plasma LCAT activity • Reduced cholesterol efflux capacity from macrophages • Reduced inhibition of LDL oxidation
Systemic lupus erythematosus[33,34]	• Reduced inhibition of LDL oxidation • Reduced cholesterol efflux capacity
Psoriasis[35]	• Reduced apoA-I in HDL • Reduced cholesterol efflux capacity
Periodontitis[36,37]	• Reduced production of NO in endothelial cells • Increased production of superoxide in endothelial cells • Reduced serum PON activity • Reduced apoA-I in plasma

apoA-I= apolipoprotein A-I; **HDL**= high-density lipoprotein; **LCAT**= lecithin cholesterol acyltransferase; **LDL**= low-density lipoprotein; **MPO**= myeloperoxidase; **NO**= nitric oxide; **oxLDL**= oxidized LDL; **PON**= paraoxonase; **SAA**= serum amyloid A

Kidney disease	
Disease/condition	**Evidence of HDL dysfunction**
Chronic kidney disease[38]	• Reduced stimulation of NO production in endothelial cells • Reduced endothelial repair following carotid artery injury • Reduced inhibition of endothelial monocyte adhesion • Reduced inhibition of endothelial VCAM-1 expression • Increased superoxide production in endothelial cells
End-stage renal disease[39,40,41,42,43]	• Reduced apoA-I in HDL • Increased triglycerides in HDL • Reduced apoA-II in HDL • Increased apoC-III in HDL • Increased SAA in HDL • Reduced inhibition of LDL oxidation • Reduced cholesterol efflux capacity • Reduced inhibition of oxLDL-stimulated VCAM-1 expression in endothelial cells • Reduced inhibition of oxLDL uptake in monocytes • Reduced inhibition of MCP-1 production in endothelial cells

apoA-I= apolipoprotein A-I; **apoA-II**= apolipoprotein A-II; **apoC-III**= apolipoprotein C-III; **HDL**= high-density lipoprotein; **LDL**= low-density lipoprotein; **MCP-1**= monocyte chemoattractant protein-1; **NO**= nitric oxide; **oxLDL**= oxidized LDL; **SAA**= serum amyloid A; **VCAM-1**= soluble vascular cell adhesion molecule-1

Other conditions

Disease/procedure	Evidence of HDL dysfunction
Cardiac surgery[44]	• Reduced PON1 activity in HDL • Reduced inhibition of LDL-induced monocyte chemotactic activity • Reduced inhibition of MCP-1 expression
Obstructive sleep apnea[45,46]	• Reduced inhibition of LDL oxidation • Reduced cholesterol efflux capacity
Hyper-homocysteinemia[47]	• Reduced cholesterol efflux capacity • Reduced inhibition of IL-6 release from endothelial cells
Hyper-alphalipoproteinemia[48]	• Reduced apoA-I in HDL • Reduced cholesterol efflux capacity
HIV infection[49,50,51,52]	• Reduced PON1 activity in HDL • Reduced LCAT activity in HDL • Reduced inhibition of LDL oxidation

Environmental contaminant exposure

Disease/procedure	Evidence of HDL dysfunction
Exposure to POPs[53]	• POP concentration in HDL associated with higher risk of CVD • PON activity negatively correlated with PCB exposure
Chlorpyrifos (pesticide) spraying use[54]	• Reduced PON activity
Higher ambient air pollution[55-58]	• Impaired cholesterol efflux capacity • Reduced HDL-C and HDL-P • Reduced apoA-I levels • Impaired HDL oxidation index
Heavy metal exposure[59-60]	• Cadmium levels associated with lower PON activity • Mercury levels associated with lower PON activity

apoA-I= apolipoprotein A-I; **HDL**= high-density lipoprotein; **IL-6**= interleukin-6; **LCAT**= lecithin cholesterol acyltransferase; **LDL**= low-density lipoprotein; **MCP-1**= monocyte chemoattractant protein-1; **PON1**= paraoxonase 1; **POPs**= persistent organic pollutants

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