TG AWARE

Research advances are revealing how genetics and lifestyle affect triglyceride (TG) metabolism and may provide better tools for reducing the complications of severe HTG.[1]

People with severe hypertriglyceridemia (sHTG) – defined as plasma TG > 500 mg/dL – and especially those with TG > 880 mg/dL are at increased risk for acute pancreatitis. Reducing TG levels to < 500 mg/dL is recommended by multiple medical societies and clinical practice guidelines, including the AHA, ACC, ESC, EAS, NLA, AACE, ACE, and the Endocrine Society.*[2-7]

There are many potential causes of sHTG, and they are classified as either primary causes or secondary causes.[1]

The complex etiology of sHTG

In most people with sHTG, elevated triglyceride levels are caused by a complex mix of factors including genetic variations acting in combination with secondary factors such as diet, lifestyle, medications, and other medical conditions *(see Figure 1 on following page)*.[1]

Secondary causes are important contributors to elevated TG levels, and many secondary causes are targets for clinical intervention.[1] When pharmacotherapy is needed, it may involve agents such as fibrates, statins, niacin, or omega-3 fatty acids.[1]

* AHA, American Heart Association; ACC, American College of Cardiology; ESC, European Society of Cardiology; EAS, European Atherosclerosis Society; NLA, National Lipid Association; AACE, American Association of Clinical Endocrinologists; ECE, American College of Endocrinology.

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Figure 1: Selected Secondary Causes of sHTG

- Diet
- Alcohol consumption
- Obesity
- Metabolic syndrome, insulin resistance, diabetes mellitus
- Hypothyroidism
- Pregnancy
- Renal disease
- Paraproteinemia
- Systemic lupus erythematosus
- Sedentary lifestyle
- Medications (numerous medications increase TG levels)

Familial Chylomicronemia Syndrome (FCS)

A small percentage of people with sHTG have Familial Chylomicronemia Syndrome (FCS), an autosomal recessive condition caused by homozygous or compound heterozygous variants in the genes that control the activity of lipoprotein lipase (LPL).[1, 9, 10] Genes identified to date include LPL itself (accounting for about 80% of cases), APOC2, APOA5, GPIHBP1, LMF1, GPD1, and CREB3L3.

LPL resides on the surface of vascular endothelial cells and is responsible for hydrolysis of triglyceride-rich lipoproteins (chylomicrons and very low-density lipoprotein). Activity of LPL is crucial for the clearance of triglyceride-rich lipoproteins from the bloodstream.[1,9] Gene variants associated with FCS reduce the synthesis or activity of LPL, leading to accumulation of triglyceride-rich lipoproteins in the blood.[9]

Elevated TG levels in people with FCS are often refractory to traditional pharmacotherapy because the effectiveness of those agents largely depends on a functional lipolytic pathway.[9]

Diagnosis and Genetic Testing for FCS

FCS can be identified on the basis of clinical criteria, but genetic testing may be used to confirm a clinical diagnosis.[9]

The FCS Genetic Testing Program offers confidential genetic testing for people suspected of having FCS

Available for people who meet both of the following criteria:

- At least 2 consecutive fasting TG levels > 750 mg/dL (8.4 mmol/L) at the time of screening
- No secondary causes or medical conditions known to cause hypertriglyceridemia

The program also offers education on FCS and genetic counseling.
For more information or questions, please call **GeneMatters at +1 888.478.1494**.

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