Hypertriglyceridemia-induced acute pancreatitis

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INTRODUCTION

Hypertriglyceridemia (HTG) is an important cause of acute pancreatitis [1-3]. Early clinical recognition of HTG-induced pancreatitis (HTGP) is important to provide appropriate therapy and to prevent further episodes [1,2,4-6]. This topic will review the etiology, clinical features, and management of acute HTGP. Long-term therapy of HTG with diet restriction and lipid-lowering medications is discussed separately. (See "Hypertriglyceridemia in adults: Management" and "Lipid management with diet or dietary supplements" and "Management of low density lipoprotein cholesterol (LDL-C) in the secondary prevention of cardiovascular disease".)

EPIDEMIOLOGY

Prevalence — Hypertriglyceridemia-induced pancreatitis (HTGP) causes 1 to 35 percent of all cases of acute pancreatitis and up to 56 percent of pancreatitis cases during pregnancy [1,3-5,7]. There are demographic differences between patients with HTGP and other causes of pancreatitis [8,9]. This was illustrated in a prospective study of 400 consecutive cases of acute pancreatitis. In this study, patients with HTGP were younger in age (44 versus 52 years), predominantly male (65 versus 45 percent), and had a personal history of obesity (57 percent versus 34 percent) or diabetes (38 versus 17 percent) as compared with acute pancreatitis patients without hypertriglyceridemia (HTG) [9].

Risk for and severity of pancreatitis — The risk of acute pancreatitis increases progressively with serum triglyceride levels over 500 mg/dL (5.6 mmol/L), with the risk increasing markedly

with levels over 1000 mg/dL (11.3 mmol/L) [2,10-14]. The risk of developing acute pancreatitis is approximately 5 percent with serum triglycerides >1000 mg/dL (11.3 mmol/L) and 10 to 20 percent with triglycerides >2000 mg/dL (22.6 mmol/L) [15]. In a prospective study of 116,500 individuals with triglyceride levels between 443 mg/dL and 885 mg/dL, the incidence rate of acute pancreatitis was 0.12 percent [16].

The risk of acute pancreatitis also increases with the number of prior episodes of acute pancreatitis. In another large retrospective cohort study of 7,119,195 patients, of whom 4158 (0.058 percent) had one or more episodes of acute pancreatitis in the prior one year, the incidence rate of acute pancreatitis was <1 percent, but increased markedly with each prior episode of acute pancreatitis and at lower triglyceride levels [16].

The degree of triglyceride elevation is associated with the severity of acute pancreatitis [5,8,9,14,17]. However, other factors such as the pancreatic lipase activity, the efficiency of clearing fatty acid (FA) from the serum, and the severity of the underlying pancreatic injury are also likely to influence the severity of acute pancreatitis [8,14,18]. In a retrospective study of 1539 patients with acute pancreatitis, in which 461 (30 percent) had elevated triglyceride levels above 150 mg/dL, the rates of severe acute pancreatitis increased with increasing triglyceride levels [8]. Among 112 patients with severe hypertriglyceridemia (HTG), acute necrotic fluid collections and pancreatic necrosis developed in 32 (29 percent) and 39 (35 percent), respectively [8]. Furthermore, the proportion of patients with persistent organ failure, multiple organ failure, and persistent systemic inflammatory response syndrome increased with the degree of HTG.

ETIOLOGY

Both primary (genetic) and secondary disorders of lipoprotein metabolism are associated with hypertriglyceridemia-induced pancreatitis (HTGP).

Primary hypertriglyceridemia — Familial dyslipidemias are associated with severe hypertriglyceridemia (HTG) and are associated with varying risks of acute pancreatitis [19].

Familial chylomicronemia often presents in infancy. It is caused by a reduction in lipoprotein lipase(LPL) activity either due to deficiencies in the *LPL* gene product or LPL regulators encoded by *APOC2, APOA5, GPIHBP1*, and *LMF1* genes [20] or complex genetic risks [21]. Patients with familial chylomicronemia can present with acute pancreatitis in the absence of an exacerbating condition. The disease frequently manifests early in life, but the diagnosis is often delayed and the median age of diagnosis is 24 years [22]. Patients develop acute pancreatitis that

progresses to recurrent acute pancreatitis and chronic pancreatitis; a subset will develop Type 3c diabetes.

Familial HTG is a rare cause of HTGP because levels of very low-density lipoprotein (VLDL) triglyceride without chylomicrons rarely reach levels at which this risk increases. Familial HTG is a complex genetic disorder in which the interaction of multiple susceptibility genes with environmental components contribute to the phenotype. The pathogenic genetic variants predisposing to HTG do not correlate perfectly with the phenotype, and new genes and variants continue to be recognized [23,24]. Patients usually present with acute pancreatitis in adulthood. HTGP is often precipitated by alcohol and a large fatty meal or initiation of a medication that causes HTG. (See 'Secondary hypertriglyceridemia' below.)

Patients with mixed hyperlipidemia (high chylomicrons and VLDL) have a high risk of acute pancreatitis. However, patients with mixed hyperlipidemia do not have sufficiently elevated serum triglyceride levels to cause acute pancreatitis in the absence of contributing environmental or hormonal factors. This disorder reflects saturation kinetics where LPL-mediated triglyceride removal ensues. However, it is a complex genetic disorder often superimposed with acquired factors affecting VLDL production and secretion or reduction in LPL activity called multifactorial chylomicronemia syndrome (MFCS) [25]. Inherited disorders of lipid metabolism are discussed in detail separately. (See "Familial hypercholesterolemia in adults: Overview" and "Inherited disorders of LDL-cholesterol metabolism other than familial hypercholesterolemia".)

Secondary hypertriglyceridemia — Various conditions can raise triglycerides and lead to HTGP, especially in individuals with underlying genetic risk [26].

- **Diabetes mellitus** – Poorly controlled diabetes mellitus (types 1 and 2) and diabetic ketoacidosis (DKA) can trigger HTGP [1,27-29]. Pancreatitis in DKA usually occurs with severe metabolic acidosis characterized by a low serum pH (<7.1) and high anion gap [29]. Marked elevation of serum triglycerides can occur during episodes of DKA, but this is unusual because free fatty acid (FFA) oxidation and ketone body formation increase more than triglyceride production and VLDL secretion in this setting. However, lack of insulin results in lipolysis in adipose tissue with release of FFAs. Increased delivery of FFAs to the liver can lead to high output of VLDL, which, coupled with the inhibition of LPL in peripheral tissues, results in hypertriglyceridemia. (See 'Insulin' below.)

- **Medications** – Hormone supplementation with oral estrogen and selective estrogen receptor modulator, tamoxifen, can raise serum triglyceride levels [30,31]. Other medications associated with elevated serum triglyceride levels include clomiphene,

immune checkpoint inhibitors, protease inhibitors, antiretroviral agents, propofol, olanzapine, mirtazapine, retinoids, thiazide diuretics, and beta-blockers [32]. (See "Etiology of acute pancreatitis" and "Hypertriglyceridemia in adults: Approach to evaluation", section on 'Etiology'.)

- **Pregnancy** – Although pregnancy causes an increase in serum triglycerides that peaks in the third trimester, the total serum triglyceride level rarely exceeds 300 mg/dL (3.3 mmol/L), a concentration that is not sufficient to cause acute pancreatitis. Cases of nongenetic, nonfamilial pregnancy-induced HTG have been reported but are rare [33]. Most cases of HTGP that occur during pregnancy are attributable to underlying genetic causes of HTG. (See "Familial hypercholesterolemia in adults: Overview" and "Inherited disorders of LDL-cholesterol metabolism other than familial hypercholesterolemia".)

- **Alcohol** – Alcohol may elevate triglyceride levels in patients with an underlying genetic hyperlipidemia [2]. In most other patients, triglyceride elevations with alcohol intake are transient and likely to be an epiphenomenon rather than a cause of pancreatitis [34]. Alcohol, in doses of >60 grams daily, increases serum triglyceride concentrations in a dose-dependent manner [35]. In a study of approximately 8000 males and females, the prevalence of serum triglyceride concentrations above 227 mg/dL (2.5 mmol/L) increased from 8 to 20 percent with an increase in alcohol intake from three to nine or more drinks per day [36]. (See "Etiology of acute pancreatitis", section on 'Alcohol'.)

PATHOGENESIS

Triglycerides themselves do not appear to be toxic. Rather, it is the breakdown of triglycerides into toxic fatty acids (FA) by pancreatic lipases that is the cause of lipotoxicity during acute pancreatitis [37,38]. The severity of acute pancreatitis in patients with hypertriglyceridemia (HTG) is dependent on both the inflammatory response caused by pancreatitis itself, plus the injury caused by lipotoxicity from triglyceride hydrolysis.

In most cases, the HTG is transient and returns to near normal within two to three days, depending on etiology and optimal management [39]. However, severe HTG, plus high lipase levels (>3 times the upper limit of normal) are associated with very high FA levels and can further be complicated by systemic inflammation from acute pancreatitis, direct activation of toll-like receptor (TLR) 2 and TLR4 by free fatty acids (FFAs), and direct lipotoxicity [37,40]. There are no clear biomarkers to determine the effects of lipotoxicity independent of acute pancreatitis with normal triglyceride levels, but several studies have noted a drop in serum calcium levels in more severe cases [40,41].

Pancreatitis does not cause hypertriglyceridemia directly. It is possible that in some patients (body mass index [BMI] >40) the stress of a severe inflammatory response to acute pancreatitis will cause some level of triglyceride increase, but dietary indiscretion prior to the onset of acute pancreatitis cannot be excluded.

CLINICAL FEATURES

Clinical manifestations — The initial presentation of hypertriglyceridemia-induced pancreatitis (HTGP) is similar to that of acute pancreatitis due to other causes, with persistent severe epigastric abdominal pain often radiating to the back, nausea, and vomiting. Most adults with HTGP present with symptoms in the fifth decade of life. However, patients with certain inherited disorders of HTG can develop attacks of acute pancreatitis in early childhood or adolescence. (See "Clinical manifestations and diagnosis of acute pancreatitis", section on 'Clinical features' and 'Primary hypertriglyceridemia' above.)

Physical examination findings suggestive of underlying hypertriglyceridemia (HTG) may be present in patients with HTGP. These include eruptive xanthomas over the extensor surfaces of the arms, legs, buttocks, and back due to persistent hyperchylomicronemia and hepatosplenomegaly from fatty infiltration [42-44]. Lipemia retinalis may be seen in patients with triglyceride concentrations exceeding 4000 mg/dL (45 mmol/L). In this condition, the retinal arterioles and venules, and often the fundus itself, develop a pale pink color due to light scattering by large chylomicrons. Vision is not affected and lipemia retinalis is reversible with reduction of triglyceride levels [42-44].

Laboratory findings — At high triglyceride levels, the serum becomes lactescent (milky coloration) (picture 1). Elevated triglyceride levels can alter routine measurements of sodium, glucose, amylase, and low-density lipoprotein. The excess triglyceride in a serum sample can displace water containing sodium and cause pseudo-hyponatremia [45]. Serum triglyceride levels >500 mg/dL (5.6 mmol/L) may cause a falsely normal amylase level, likely from interference of the calorimetric reading. Serial dilutions of the serum amylase sample can reduce the triglyceride interference [45,46].

DIAGNOSIS

Hypertriglyceridemia-induced pancreatitis (HTGP) should be suspected in patients with acute pancreatitis and risk factors for hypertriglyceridemia (HTG). Serum triglyceride levels >500 mg/dL (5.6 mmol/L) are required for HTG to be considered the underlying etiology of acute

pancreatitis [6]. Serum triglycerides should be measured early in the course of acute pancreatitis, such as in the emergency department or on admission. Early detection of HTG is important for establishing the diagnosis, initiating specific treatments, and improving prognosis, by decreasing the risk of multi-organ dysfunction. Risk factors for HTG include poorly controlled diabetes, alcoholism, obesity, pregnancy, prior pancreatitis, and a personal or family history of HTG [1,2,4,15,47].

Acute pancreatitis by itself does not cause significant HTG. While it is possible that in some patients (eg, body mass index [BMI] >40) the stress of a severe inflammatory response to acute pancreatitis can cause an increase in serum triglycerides, the relation between pre-existing triglyceride levels and reactive mobilization of triglycerides from fat stores, to our knowledge, has not been determined.

The diagnosis of acute pancreatitis in patients with HTG is the same as other etiologies of acute pancreatitis and requires the presence of two of the following three criteria: acute onset of persistent, severe epigastric pain often radiating to the back; elevation in serum lipase or amylase to three times or greater than the upper limit of normal; and characteristic findings of acute pancreatitis on imaging (contrast-enhanced computed tomography, magnetic resonance imaging, or transabdominal ultrasonography). The diagnosis of acute pancreatitis is discussed in detail separately. (See "Clinical manifestations and diagnosis of acute pancreatitis", section on 'Diagnostic evaluation'.)

INITIAL MANAGEMENT

Management of patients with hypertriglyceridemia-induced pancreatitis (HTGP) includes treatment of acute pancreatitis and reduction of serum triglyceride levels with the goal of preventing necrotizing pancreatitis and organ failure. In patients with HTGP, maintenance of triglyceride levels below 500 mg/dL (5.6 mmol/L) may expedite clinical improvement [2]. Our approach to initial therapy for hypertriglyceridemia (HTG) in patients with HTGP is based on the severity of acute pancreatitis and the presence of worrisome clinical features (algorithm 1) [41,48-54].

Assessment for worrisome features — Worrisome features in patients with HTGP include the following:

- Hypocalcemia
- Lactic acidosis

- Signs of worsening systemic inflammation (two or more):
  - Temperature >38.5°C or <35.0°C
  - Heart rate of >90 beats/min
  - Respiratory rate of >20 breaths/min or partial pressure of carbon dioxide ($PaCO_2$) of <32 mmHg
  - White blood cell (WBC) count of >12,000 cells/mL, <4000 cells/mL, or >10 percent immature (band) forms
- Signs of worsening organ dysfunction or multi-organ failure as defined by Modified Marshall scoring system for organ dysfunction (table 1)

General measures in all patients

- **Treatment of acute pancreatitis** — Initial management of a patient with acute pancreatitis consists of supportive care with fluid resuscitation and pain control. The management of acute pancreatitis is discussed in detail separately. (See "Management of acute pancreatitis", section on 'Initial management'.)
- **Dietary fat restriction** — When patients with HTGP can tolerate nutrition by mouth, dietary fat should be severely restricted (<5 percent fat) until triglyceride levels are <1000 mg/dL (11.3 mmol/L) [55]. Fasting triglyceride levels are then mostly, if not entirely, very low-density lipoprotein (VLDL), not chylomicrons. At this point, drugs that lower VLDL triglycerides, eg, fibrates, high-dose omega-3 fatty acids, or high-dose statins, will further lower triglycerides in multifactorial chylomicronemia syndrome (MFCS) <500 mg/dL.
- **Removing secondary causes of HTG** — Medications that can increase triglycerides should be discontinued. (See 'Secondary hypertriglyceridemia' above.)

Additional measures in selected patients

Plasmapheresis — We reserve the use of plasmapheresis in patients with HTGP with worrisome features [56]. (See "Therapeutic plasma exchange (plasmapheresis) with hemodialysis equipment".)

- **Efficacy** – Evidence to support the use of plasmapheresis in patients with HTGP is from observational studies; randomized trials are lacking [54,57-70]. A single session of plasmapheresis has been reported to lower triglyceride levels by 50 to 80 percent. However, studies have not demonstrated an improvement in outcomes in patients with HTGP. One prospective study of plasmapheresis, which examined 60 patients with HTGP who underwent plasmapheresis, found no statistical difference in mortality, systemic, or

local complications between those who received plasmapheresis and historical controls. This was postulated to be related to the delay in initiation of plasmapheresis. However, the benefit of early initiation of plasmapheresis has not been consistently demonstrated [71,72].

Plasmapheresis does not appear to improve outcomes in uncomplicated cases of HTGP [73]. In one study that included 67 patients without multiorgan dysfunction, there was no significant benefit to either mortality or length of stay with the use of adjunct plasmapheresis to medical management, even when patients presented with severely elevated levels of triglycerides.

- **Monitoring and duration of therapy** – In patients treated with plasmapheresis, triglycerides should be measured after each cycle of plasmapheresis [74]. We continue plasmapheresis until triglyceride levels are below <1000 mg/dL (11.3 mmol/L). One series of seven patients with an average triglyceride level of 1407 mg/dL (15.8 mmol/L) reported a decrease in mean triglyceride levels to 683 mg/dL (51 percent) after one plasma exchange session [64]. In another case report, triglycerides were lowered from 2410 (27.2 mmol/L) to 138 mg/dL (1.5 mmol/L) after three days of plasmapheresis alone [69].

Insulin — We administer intravenous (IV) insulin in patients with worrisome features of HTGP in whom plasmapheresis is indicated but is unavailable or cannot be tolerated. As insulin can decrease both triglyceride and glucose levels, we also administer insulin in patients with HTGP with diabetes to manage hyperglycemia, ie, plasma glucose >180 mg/dL [75].

In patients with worrisome features of HTGP, we typically initiate an IV infusion of regular insulin at a rate of 0.1 to 0.3 units/kg/hour while closely monitoring blood glucose levels. In patients with blood glucose levels between 150 and 200 mg/dL, we administer a separate 5 percent dextrose infusion to prevent hypoglycemia due to the insulin infusion. Triglyceride levels should be monitored every 12 hours. Serum glucose should be measured every hour and the insulin/5 percent dextrose infusion should be adjusted accordingly. IV insulin should be stopped when triglyceride levels are <500 mg/dL (5.6 mmol/L).

Many other insulin regimens have been reported to lower triglyceride levels to <500 mg/dL (5.6 mmol/L) over 3.5 to 4 days [51-53,76]. IV insulin may be more effective than subcutaneous insulin in severe cases of HTGP [51,52] and is easier to titrate than subcutaneous administration of insulin [77]. IV insulin as a continuous infusion was found effective in patients with severe HTGP with and without type 2 diabetes mellitus [78].

Insulin decreases VLDL triglyceride production and also lowers serum triglyceride levels by enhancing lipoprotein lipase (LPL) activity, an enzyme that accelerates chylomicron and VLDL metabolism to glycerol and fatty free acids (FFAs) [79,80]. Insulin also inhibits hormone-

sensitive lipase in adipocytes, which is the key enzyme for breaking down adipocyte triglyceride and releasing fatty acids (FAs) into the circulation. Insulin lowers triglyceride levels, but the goal of insulin therapy in severe acute pancreatitis associated with severe HTG is to reverse the stress-associated release of FAs from adipocytes, to promote intracellular triglyceride generation within adipocytes, promote FA metabolism in insulin-sensitive cells, reduce peripheral insulin resistance, and mostly to correct hyperglycemia. In mice, insulin is also shown to reduce the severity of acute pancreatitis and improve recovery [81]. To achieve a reversal in intermediate metabolism in this setting, we use well-established protocols used for diabetic ketoacidosis that maintain high IV insulin levels and protect the patient from hypoglycemia [77].

In patients without worrisome features, in the absence of hyperglycemia, evidence to support the use of insulin is lacking. A retrospective study of patients admitted for HTGP were managed supportively, rendered NPO and IV hydration. Insulin infusion was used only in 12 patients to manage concurrent hyperglycemia [72]. The average triglyceride level decreased from 4018 mg/dL on presentation to 1177 mg/dL within 48 hours, an approximate 70 percent decrease. Moreover, the results were similar for NPO-only and insulin infusion subgroups.

Therapies lacking efficacy

- **Heparin** – We do not use heparin due to the transient nature of reduction of triglyceride levels, potential lipotoxicity from the intravascular release of FFAs from heparin-induced LPL-mediated hydrolysis of triglyceride-rich lipoproteins [82], and an increased risk of bleeding. This degradation contributes to further depletion of plasma stores of LPL and can result in an increase in the level of VLDL and chylomicron triglycerides [83].

SUBSEQUENT MANAGEMENT

Evaluation for modifiable risk factors — Patients with hypertriglyceridemia-induced pancreatitis (HTGP) should be evaluated for secondary causes of hypertriglyceridemia (HTG) [84-89]. For patients with HTG not clearly associated with a secondary cause, family members should be screened with a fasting triglyceride level. (See 'Secondary hypertriglyceridemia' above and "Hypertriglyceridemia in adults: Approach to evaluation", section on 'Clinical manifestations' and "Hypertriglyceridemia in adults: Approach to evaluation", section on 'Etiology'.)

Lipid management — Patients recovering from HTGP require long-term therapy to prevent recurrent acute pancreatitis and to prevent other complications of HTG [10]. This consists of both pharmacologic therapy (eg, oral gemfibrozil 600 mg twice daily) and dietary modification

with restriction of fat content to 10 to 15 percent of the diet and avoidance of concentrated sugars. Other nonpharmacologic interventions include weight loss in patients who are obese, aerobic exercise, avoidance of medications that raise serum triglyceride levels, and strict glycemic control in diabetics. Pharmacologic management of HTG is discussed in detail separately. (See "Hypertriglyceridemia in adults: Management", section on 'Treatment goals' and "Lipid management with diet or dietary supplements" and "Low-density lipoprotein cholesterol lowering with drugs other than statins and PCSK9 inhibitors", section on 'Fibrates' and "Management of low density lipoprotein cholesterol (LDL-C) in the secondary prevention of cardiovascular disease".)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Acute pancreatitis".)

SUMMARY AND RECOMMENDATIONS

- **Epidemiology** – Hypertriglyceridemia (HTG) is one of the most common causes of acute pancreatitis. It is reported to cause 1 to 30 percent of all cases of acute pancreatitis and up to 56 percent of cases during pregnancy. The risk of developing acute pancreatitis is approximately 5 percent with triglycerides >1000 mg/dL (11.2 mmol/L) and 10 to 20 percent with triglycerides >2000 mg/dL (22.6 mmol/L). The degree of triglyceride elevation is also associated with the severity of hypertriglyceridemia-induced pancreatitis (HTGP). (See 'Epidemiology' above.)

- **Etiology** – Primary (genetic) and secondary disorders of lipoprotein metabolism are associated with HTGP. Triglycerides themselves do not appear to be toxic. Rather, it is the breakdown of triglycerides into toxic fatty acids by pancreatic lipases that is the cause of lipotoxicity during acute pancreatitis. (See 'Etiology' above and 'Pathogenesis' above.)

- **Clinical features** – The initial clinical presentation of HTGP is similar to that of acute pancreatitis due to other causes; abdominal pain, nausea, and vomiting are the major complaints. Physical examination findings suggestive of underlying HTG include eruptive xanthomas over the extensor surfaces of the arms, legs, buttocks, and back, hepatosplenomegaly from fatty infiltration, and lipemia retinalis. (See 'Clinical features' above.)

- **Diagnosis** – HTGP should be suspected in patients with acute pancreatitis and risk factors for HTG. Risk factors for HTG include poorly controlled diabetes, alcoholism, obesity, pregnancy, prior pancreatitis, and a personal or family history of HTG. Serum triglyceride levels >500 mg/dL (5.6 mmol/L) are required for HTG to be considered the underlying etiology of acute pancreatitis. (See 'Diagnosis' above.)

- **Initial management**

  - Initial management of patients with HTGP includes treatment of acute pancreatitis, severe dietary fat restriction, and exclusion of culprit medication with the goal of reduction of serum triglyceride levels to <500 mg/dL (5.6 mmol/L) (algorithm 1). (See 'Initial management' above and "Management of acute pancreatitis".)

  - In patients with HTGP (serum triglyceride level >1000 mg/dL plus lipase >3 times the upper limit of normal) **and** worrisome features (hypocalcemia, lactic acidosis, signs of worsening systemic inflammation or organ dysfunction, and/or multi-organ failure), we suggest treatment with plasmapheresis (**Grade 2C**). Triglyceride levels should be monitored every cycle of plasmapheresis. We continue plasmapheresis until triglyceride levels are <500 mg/dL (5.6 mmol/L). (See 'Plasmapheresis' above.)

  - If plasmapheresis is unavailable or is not tolerated, we suggest initiating therapy with intravenous (IV) regular insulin (**Grade 2C**). We administer insulin at a rate of 0.1 to 0.3 units/kg/hour. In patients with blood sugar levels between 150 and 200 mg/dL, we administer IV glucose supplementation with a separate 5 percent dextrose infusion to prevent hypoglycemia. Triglyceride levels should be monitored every 12 hours. Serum glucose should be measured every hour and the insulin/5 percent dextrose infusion should be adjusted accordingly. IV insulin should be stopped when triglyceride levels are <500 mg/dL (5.6 mmol/L). (See 'Insulin' above.)

- **Subsequent evaluation and management**

  - Once triglyceride levels are <500 mg/dL (5.6 mmol/L), patients with HTGP require long-term therapy to prevent recurrent pancreatitis and to prevent other complications of HTG. This consists of both pharmacologic therapy (eg, oral gemfibrozil 600 mg twice daily) and dietary modification (eg, fat- and simple sugar-restricted diet). Other nonpharmacologic interventions include weight loss in patients who are obese, aerobic exercise, avoidance of concentrated sugars and medications that raise serum triglyceride levels, and strict glycemic control in patients with diabetes. (See 'Subsequent management' above.)

- Patients with HTGP should be evaluated for secondary causes of HTG. For patients with HTG not clearly associated with a secondary cause, family members should be screened with a fasting triglyceride level. (See 'Evaluation for modifiable risk factors' above.)

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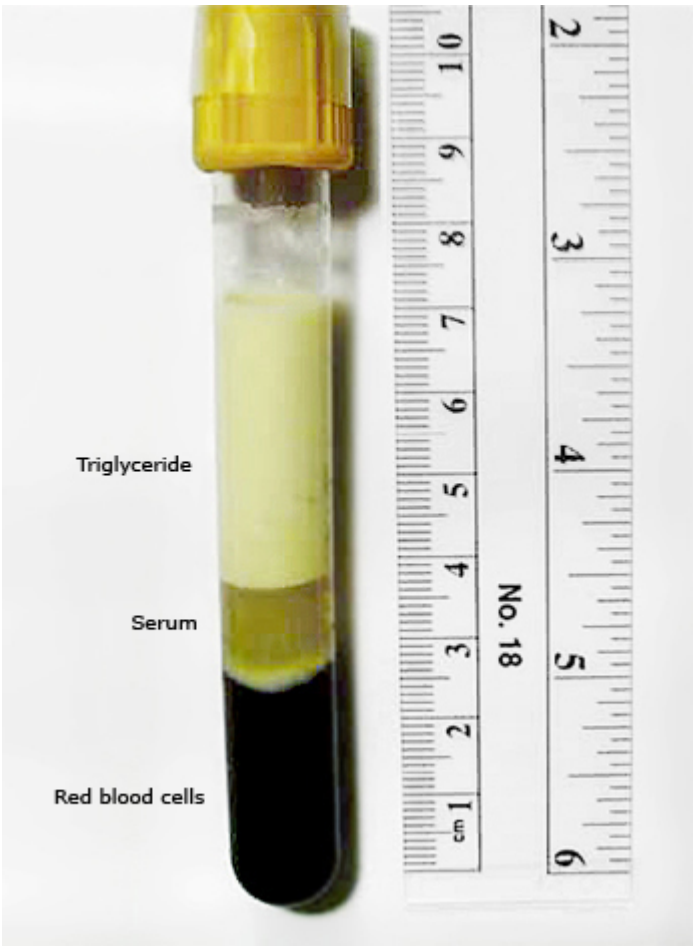
Topic 5655 Version 34.0

GRAPHICS

Blood sample from a patient with a triglyceride level of 1200 mg/dL in a serum separator tube



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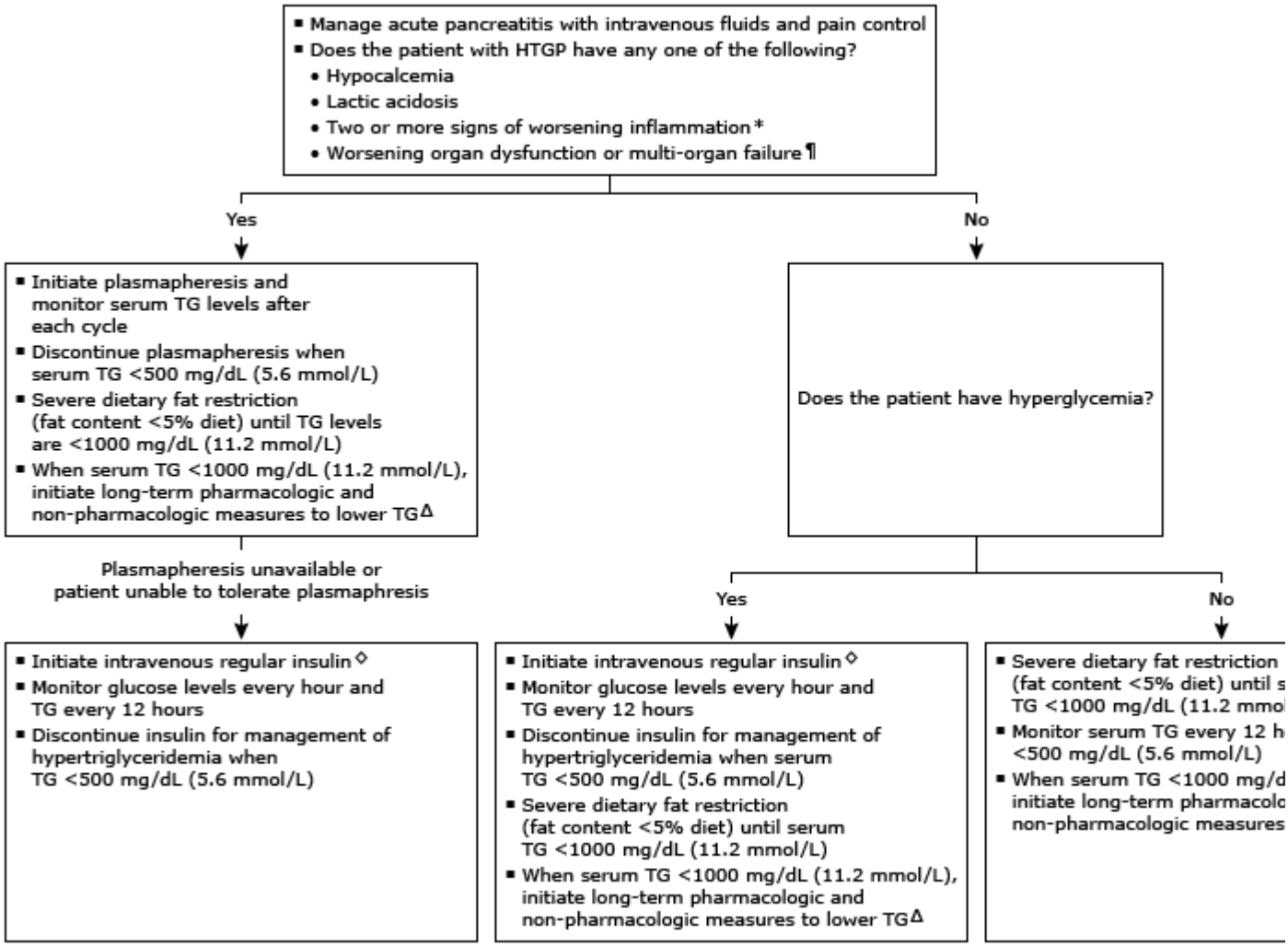
Graphic 58261 Version 5.0

Approach to the management of the adult patient with hypertriglyceridemic pancreatitis



HTGP: hypertriglyceridemic pancreatitis; TG: triglycerides; WBC: white blood cell; $PaCO_2$: partial pressure of carbon dioxide.

* Signs of worsening inflammation include:
- Temperature >38.5°C or <35.0°C
- Heart rate of >90 beats/min
- Respiratory rate of >20 breaths/min or $PaCO_2$ of <32 mmHg
- WBC count of >12,000 cells/mL, <4000 cells/mL, or >10% immature (band) forms

¶ As defined by the modified Marshall scoring system for organ dysfunction. Refer to UpToDate topic on hypertriglycerdemia-induced acute pancreatitis.

Δ Pharmacologic therapy to lower TG levels and dietary fat restriction are needed long-term to prevent recurrences of acute pancreatitis and prevent other complications of hypertriglyceridemia. Other nonpharmacologic interventions include restriction of fat content to 10 to 15% of the diet, weight loss in obese patients, aerobic exercise, avoidance of concentrated sugars and medications that raise serum triglyceride levels, and strict glycemic control in patients with diabetes.

◇ Based on serum glucose levels, intravenous glucose may be necessary in patients being treated with intravenous insulin.

Graphic 133279 Version 2.0

Modified Marshall scoring system for organ dysfunction

Organ system	Score				
	0	**1**	**2**	**3**	**4**
Respiratory (PaO_2/FiO_2)	>400	301-400	201-300	101-200	≤101
Renal*					
(serum creatinine, micromol/L)	≤134	134-169	170-310	311-439	>439
(serum creatinine, mg/dL)	<1.4	1.4-1.8	1.9-3.6	3.6-4.9	>4.9
Cardiovascular (systolic blood pressure, mmHg)¶	>90	<90, fluid responsive	<90, not fluid responsive	<90, pH <7.3	<90, pH <7.2

For nonventilated patients, the FiO_2 can be estimated from below:

Supplemental oxygen (L/min)	**FiO_2 (percent)**
Room air	21
2	25
4	30
6-8	40
9-10	50

A score of 2 or more in any system defines the presence of organ failure.

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* A score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine ≥134 micromol/L or ≥1.4 mg/dL.

¶ Off inotropic support.

Graphic 87718 Version 2.0

Contributor Disclosures

Andres Gelrud, MD, MMSc Consultant/Advisory Boards: AbbVie [Pancreatic exocrine insufficiency]; Ariel [Genetic testing]; National Pancreas Foundation [Ad honorem]. Speaker's Bureau: AbbVie [Pancreatic insufficiency]. All of the relevant financial relationships listed have been mitigated. **Lawrence S Friedman, MD** Other Financial Interest: Elsevier [Gastroenterology]; McGraw-Hill [Gastroenterology]; Wiley [Gastroenterology]. All of the relevant financial relationships listed have been mitigated. **Shilpa Grover, MD, MPH, AGAF** No relevant financial relationship(s) with ineligible companies to disclose.

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Conflict of interest policy

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