Plasmapheresis is an advanced and established extracorporeal therapy in critical care, a process in which plasma, the fluid part of the blood, is separated from blood cells by a device known as a cell separator. In critically ill patients, plasmapheresis is used to remove toxins, medications, destructive antibodies, and clotting factors from the peripheral circulation. During plasmapheresis, a nurse uses a cell separator that either spins the blood to separate the cells from the fluid or filters the blood through a membrane with extremely small pores that allow only the fluid part to pass through. Although in current practice the terms plasmapheresis and therapeutic plasma exchange (TPE) are often used interchangeably, TPE...
Plasmapheresis is being extensively used in autoimmune disease to lower the serum level of autoreactive antibodies. Yeh et al reported that plasmapheresis provided rapid amelioration of clinical weakness in patients with generalized myasthenia by removing pathogenic antibodies to the acetylcholine receptor and decreased the cytotoxic effect of natural killer cells. In addition, a marked reduction in blood total protein, immunoglobulin, cholesterol, fibronectin, and erythrocyte aggregation occurred after plasmapheresis of patients with diabetic retinopathy, leading to improvement of visual function. Plasmapheresis can also be used to lower a harmful level of lipids such as triglycerides.

In the human body, triglycerides constitute 15% to 20% of total body weight and are a major source of energy (9 kcal/g). The triglycerides in the body have 2 sources: exogenous (dietary) and endogenous (produced by the liver). Triglycerides can be secreted into the blood as very low-density lipoprotein (VLDL) and as high-density lipoprotein. VLDL is converted to intermediate-density lipoprotein, which is further broken down into low-density lipoprotein. Although the level of triglycerides varies with age, a “normal” level is less than 150 mg/dL (to convert to millimoles per liter, multiply by 0.0113). In hypertriglyceridemia, the blood level of triglycerides is greater than 500 mg/dL, and elevated plasma concentrations of triglycerides have been linked to several diseases, such as atherosclerosis, stroke, and insulin resistance, thereby increasing the risk for coronary artery disease. The etiology of hypertriglyceridemia includes a high-carbohydrate diet, a high fat diet, obesity, and renal failure. Hypertriglyceridemia can be primary, such as genetically based familial hyperlipidemias, or secondary (due to other diseases or specific conditions), such as that associated with diabetes, alcohol abuse, nephrotic syndrome, hypothyroidism, autoimmune disorders, paraproteinemia, pregnancy, and medications. If severe (triglyceride level >1000 mg/dL), hypertriglyceridemia can have serious medical consequences, such as acute pancreatitis, an acute potentially life-threatening complication.

Conventional management of hypertriglyceridemia includes both nutritional and pharmacological treatments. Nutritional management consists of restriction of carbohydrates and fat in the diet or use of a diet rich in omega-3 fatty acids or both. The main pharmacotherapy for high levels of triglycerides consists of insulin, heparin, omega-3 fatty acids, fibrates, statins, or niacin (nicotinic acid); however, the associated side effects or relatively slow mode of action have adversely affected the use of these agents. Insulin stimulates adipose cells to synthesize and secrete lipoprotein lipase, which degrades triglycerides to glycerol and free fatty acids. The dose of heparin required to release lipoprotein lipase into the circulation is less than the dose required for anticoagulation. Antilipidemic agents for hypertriglyceridemia include fibric acid derivatives,
3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors (statins), and nicotinic acid. Fibric acid derivatives, such as gemfibrozil, reduce triglycerides by as much as 50% by modulating the peroxisome proliferator-activated receptor in the liver, reducing hepatic secretion of VLDL, and increasing the lipolysis of plasma triglycerides. Statins inhibit the rate-limiting step in cholesterol synthesis and reduce hepatic production of VLDL. Nicotinic acid inhibits lipolysis of triglycerides from adipose tissue, decreasing transport of free fatty acids to the liver. Resins that bind bile acids worsen plasma triglyceride concentrations, whereas cholesterol absorption inhibitors (eg, ezetimibe) do not. Clinical practice guidelines suggest that pharmacotherapy should be considered for patients with triglyceride levels greater than 200 mg/dL.

Severe hypertriglyceridemia can also interfere with clinical laboratory tests, making patient care more difficult. The increased level of triglycerides affects not only physiology but also interpretation of laboratory data, especially in metabolic alterations such as diabetic ketoacidosis. Interference by the lipids can lead to inappropriate additional tests, incorrect diagnoses, and treatment with potentially unfavorable outcomes. Preferably, the final concentration of triglycerides for laboratory testing should be less than 1400 mg/dL. Severe lipemia interferes with spectrophotometric and indirect potentiometric laboratory analyses via 2 mechanisms. Lipemic serum creates a turbid analyte, resulting in light scattering by chylomicrons and VLDL particles in spectrophotometric testing. Moreover, in photometric analysis and indirect potentiometry, water displacement by an increase in the nonaqueous phase of the sample results in a false underestimation of electrolyte concentrations. Lipemia interference can be minimized by using direct potentiometry, by reducing the interfering lipid by ultracentrifuging the sample (100 000 g), or by using polymers to precipitate the lipids in the sample. Ultracentrifuging can produce excess heat and cause hemolysis and the release of intracellular potassium. The point-of-care test (iSTAT system, Abbott) commonly used in many intensive care units uses direct potentiometry. With direct potentiometry, the concentration of electrolytes is determined by measuring the electrical potential between 2 chambers without partitioning the sample.

### Table

<table>
<thead>
<tr>
<th>Factor</th>
<th>Normal range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Triglycerides</td>
<td>&lt;150 mg/dL</td>
</tr>
<tr>
<td>Glucose</td>
<td>82-110 mg/dL</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>&lt;240 mg/dL</td>
</tr>
<tr>
<td>Sodium</td>
<td>135-145 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.5-4.5 mmol/L</td>
</tr>
<tr>
<td>Calcium</td>
<td>8.5-10.2 mg/dL</td>
</tr>
<tr>
<td>Phosphate</td>
<td>2.4-4.1 mg/dL</td>
</tr>
<tr>
<td>Bicarbonate</td>
<td>23-32 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>100-111 mmol/L</td>
</tr>
</tbody>
</table>

The values may be slightly different for different laboratories. SI conversion factors: To convert to mmol/L, multiply by 0.0113 for triglycerides, by 0.0555 for glucose, by 0.0259 for cholesterol, by 0.25 for calcium, and by 0.323 for phosphate.

### Case Report

We present a case of a woman with diabetic ketoacidosis complicated by severe hypertriglyceridemia who was successfully treated with TPE when conventional treatments did not sufficiently reduce the high level of triglycerides.

A 63-year-old woman with chronic, poorly controlled diabetes came to the emergency department because she had had a tender mass at the apex of her scalp for 1 week. She was hypertensive and tachycardic, she had polyuria and polydipsia, and her blood glucose level was 559 mg/dL (to convert to millimoles per liter, multiply by 0.0555). She required incision and drainage for the scalp abscess. The results of an initial chemistry panel were uninterpretable because of severe lipemia. Laboratory values obtained after ultracentrifugation of a blood sample revealed hypertriglyceridemia (triglycerides level 10132 mg/dL vs normal level <150 mg/dL), glucose level 559 mg/dL (normal range, 82-110 mg/dL), and an anion gap metabolic acidosis, with bicarbonate 12 mmol/L, consistent with diabetic ketoacidosis. Her cholesterol level was 1051 mg/dL (normal level <240 mg/dL; to convert to millimoles per liter, multiply by 0.0259), confirming the severely elevated triglyceride level (see Table and Figure).

The patient was admitted to the intensive care unit for treatment of diabetic ketoacidosis with severe hypertriglyceridemia. She said she had not had any abdominal pain or nausea. She had no xanthomas and no focal neurological deficits. On hospital day 1, the diabetic ketoacidosis was treated with administration of intravenous physiological...
saline, intravenous infusion of insulin, and replacement of electrolytes (see the Table for normal basal ranges). She was given antibiotics (vancomycin and meropenem) empirically for the scalp abscess pending cultures of blood, wound, and urine specimens. Findings on a chest radiograph were normal, and she did not have biomarkers for cardiac ischemia. Treatment of the diabetic ketoacidosis was complicated by iatrogenic hyperkalemia due to lipemia-associated delay in return of laboratory data. Despite conventional treatment of the severe hypertriglyceridemia with insulin, atorvastatin, and subcutaneous heparin, the level of triglycerides remained markedly elevated (7501 mg/dL vs normal level of <150 mg/dL), causing delayed results of laboratory studies and complications in treatment.

On hospital day 2, a catheter was placed in the right internal jugular vein and TPE was started. The serum level of triglycerides rapidly decreased to 1745 mg/dL in less than 24 hours (see Figure). The marked reduction in triglycerides allowed for timely correction of electrolyte abnormalities of sodium 135 mmol/L, potassium 3.5 mmol/L, calcium 7.2 mg/dL, phosphate 2.4 mg/dL, bicarbonate 26 mmol/L, and chloride 110 mmol/L (see the Table for normal ranges and SI conversion factors). The diabetic ketoacidosis resolved after 35 hours, and treatment was changed to subcutaneous insulin and a fat-free diabetic diet. The patient had no further complications, and she was later transferred from the intensive care unit to the internal medicine service. At 1-month follow-up in the internal medicine clinic, her serum level of triglycerides was 184 mg/dL.

**Discussion**

Increased levels of triglycerides are associated with severe diseases, such as acute pancreatitis and cardiovascular disease. Serum concentrations greater than 1000 mg/dL indicate severe hypertriglyceridemia, which is a marked risk for acute pancreatitis. In fact, severe hypertriglyceridemia is one of the most common causes of acute pancreatitis and accounts for up to 10% of all instances of this pancreatic abnormality. The pathogenesis of hypertriglyceridemia-induced pancreatitis is not fully understood but is thought to be related to premature activation of intrapancreatic trypsinogen. Reducing the serum level of triglycerides to 200 mg/dL or less (close to the normal value) effectively prevents further episodes of pancreatitis. In a comparison between supportive therapy (restriction of oral intake, intravenous fluids, and analgesia) and infusions of insulin plus dextrose for treatment of hypertriglyceridemia-associated pancreatitis, the mortality rate was 11% when the level of triglycerides was more than 877 mg/dL. The hypertriglyceridemia of our patient was mainly due to type 2 diabetes mellitus, a finding in agreement with the review of Watts and Karpe, who reported that elevated plasma levels of triglycerides, in both fasting and postprandial states, was a consistent feature of type 2 diabetes.
Conventional management of hypertriglyceridemia includes both nutritional and pharmacological treatments. Because patients with hypertriglyceridemia are in urgent need of fast, effective lowering of the level of triglycerides to prevent disease complications, further alternative measures must be considered. Plasmapheresis is a successful and responsibly safe alternative for treatment of hypertriglyceridemia resistant to conventional management. According to the American Society of Apheresis and the American Medical Association Council on Scientific Affairs, hypertriglyceridemia is a class III indication for TPE. Treatment is based on removing 2 to 3 L of plasma via filtration and replacing the volume with 5% human albumin with or without fresh frozen plasma. The mechanisms of action are thought to be removal of cholesterol-containing lipoproteins, removal of excess proteases from the plasma, and replacement of consumed protease inhibitors with the donor’s plasma. TPE is relatively safe, with few complications. The most common complications include urticaria (0.7%-12% of cases), paresthesias (1.5%-9%), rigors, headaches (0.3%-5%), hypotension (0.4%-4.2%), muscle cramps (0.4%-2.5%), and catheter-related problems (0.08%-4%). When replacement products include blood products, nurses must be aware of the risks for various transfusion reactions (eg, allergic reactions), bacterial contamination, hypothermia, and transfusion-transmitted diseases. The safety of plasmapheresis for lowering the serum level of triglycerides is indicated by its continual use since its first application in 1978. In addition, Altun et al reported 2 cases of hypertriglyceridemia-induced acute pancreatitis during pregnancy that were successfully treated by using plasmapheresis. Case studies suggest that a single session of TPE may lower the plasma level of triglycerides as much as 70%, producing clear clinical and laboratory improvement.

Several reports document the successful use of TPE in treatment of hypertriglyceridemia. In some instances, TPE for hypertriglyceridemic pancreatitis resulted in improvements in clinical and laboratory findings and patient outcomes. TPE has been effective in acute management of patients with hypertriglyceridemic pancreatitis and acute respiratory distress syndrome, recurrent acute pancreatitis, diabetes-associated severe hypertriglyceridemia, gestational hypertriglyceridemia, and familial hyperlipidemias. In one case, plasmapheresis was used successfully in a child with hypertriglyceridemia, diabetic ketoacidosis, pancreatitis, and acute kidney injury. TPE is also an effective treatment in hypertriglyceridemia associated with ritonavir and with asparaginase chemotherapy for acute lymphocytic anemia in adults and children.

In addition to using TPE, clinicians should treat the underlying cause of the hypertriglyceridemia, which may include diabetes (as in our case), excessive alcohol consumption, and pancreatitis. In our case, a plan of care was created to correct the underlying cause of hypertriglyceridemia, that is, type 2 diabetes mellitus. Furthermore, in our case, care included proper and prompt management of the patient’s diabetic ketoacidosis, because a severe electrolyte imbalance can be fatal. We corrected the diabetic ketoacidosis with fluid replacement and an insulin infusion. Even though TPE is a safe procedure, nurses should be aware of possible plasmapheresis-related complications.

Severe hypertriglyceridemia is one of the most common causes of acute pancreatitis and accounts for up to 10% of all instances of this pancreatic abnormality.
References