51-year-old Woman consulted for Hypertriglyceridemia

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Endorama
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History of Present Illness

- Patient is a 51-year-old woman with past medical history significant for cognitive delay, dyslipidemia, diabetes mellitus type 2, and hypothyroidism who presented to outpatient clinic for consultation on hypertriglyceridemia.
- Caregivers were concerned about her weight, which has been fluctuating. Currently, she is described to be hungry all the time, although her weight in clinic was 95.3 pounds.
- Caregivers were also concerned about her “bone health” although there was no history of fractures.

History of Present continued

- Diet:
  - Breakfast: waffles, pancakes, oatmeal, cold cereal, yogurt
  - Lunch: deli sandwich, cream cheese
  - Dinner: lasagna, pizza, chicken, occ. fish
  - Snacks: applesauce, sugar free pudding, apples, vegetables
  - Desserts: angel food cake, birthday cake
  - Beverages: diet soda, coffee
- Exercise:
  - Walk 30 minutes once a week
  - Water aerobics once a week
  - Bowling on Saturdays

History continued

- Past Medical History:
  - Hypertriglyceridemia
  - Dyslipidemia
  - Diabetes mellitus type 2
  - Hypothyroidism
  - Cognitive delay
- Allergies: Penicillin

History cont.

- Medications:
  - Aspirin 81 mg QDay
  - Atenolol 25 mg QDay
  - Lovaza 2 g BID
  - Metformin 500 mg QDay
  - Levothyroxine 125 mcg QDay
  - Alprazolam 1 mg QHS
  - Asenapine 10 mg QHS
  - Ocuvite one tablet daily
  - Tab-a-vite tab/iron one daily
  - Docusate 100 mg BID
  - Fluticasone 50 mcg 2 sprays daily
  - Tylenol PRN
  - Naproxen 220 mg BID PRN
  - APAP/codeine PRN
  - Bacitracin PRN
  - Genaton Suspension PRN
  - Guaifenesin Syrup DM PRN
  - Hem-Prep cream PRN
  - Loperamide PRN
  - Prochlorperazine 10mg PRN
  - Pseudoephedrine 30 mg PRN
  - Throat Lozenges PRN

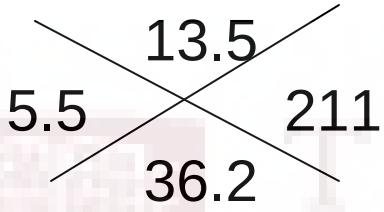
History continued

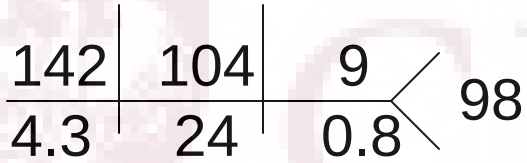
- Social History:
  - Has 2 state caregivers.
  - Lives at Elmwood Home with 4 other women.
  - Meals are provided.
  - The refrigerator and cabinets are locked at night.
- Family History:
  - Mother and father both deceased with history of coronary artery disease.
  - Brother died at a young age from myocardial infarction.
- ROS:
  - No abdominal pain, nausea/vomiting, bowel problems.
  - Erratic chest pain occurring once a month.
  - No dyspnea on exertion.
  - Chronic knee and hip pain.

Physical Exam

- Vitals: 61.5 inches tall, weight is 43.2 kg or 95.2 pounds, BMI 17.7 kg/m^2, blood pressure 124/76, pulse is 53, POC glucose 95 (fasting)
- General: reasonably well-appearing woman in no acute distress.
- HEENT: Pupils are equal, round, and reactive to light. Extraocular muscles intact. There is no xanthelasmas. No arcus senilis. Ophthalmoscopic exam did not reveal obvious lipemia retinalis. Oropharynx is clear. She has moist mucous membranes. Tonsils are pink.
- Neck: No thyromegaly, no thyroid nodularity. No palpable lymphadenopathy in the neck.
- Respiratory: Clear to auscultation bilaterally.
- Cardiovascular: Regular rate and rhythm, S1 and S2. No murmurs, rubs, or gallops.
- Abdomen: soft, nontender, nondistended with normoactive bowel sounds.
- Skin: Only remarkable for obvious lack of sun exposure. No eruptive xanthomas.
- Extremities: No xanthomas of tendons.
- Neuro: Cranial nerves II-XII intact. Deep tendon reflexes 2+ bilaterally upper and lower extremities. No insight. Can answer direct questions but requires refocusing. Able to give a pretty good history.

Laboratory Data





- Ca 9.2

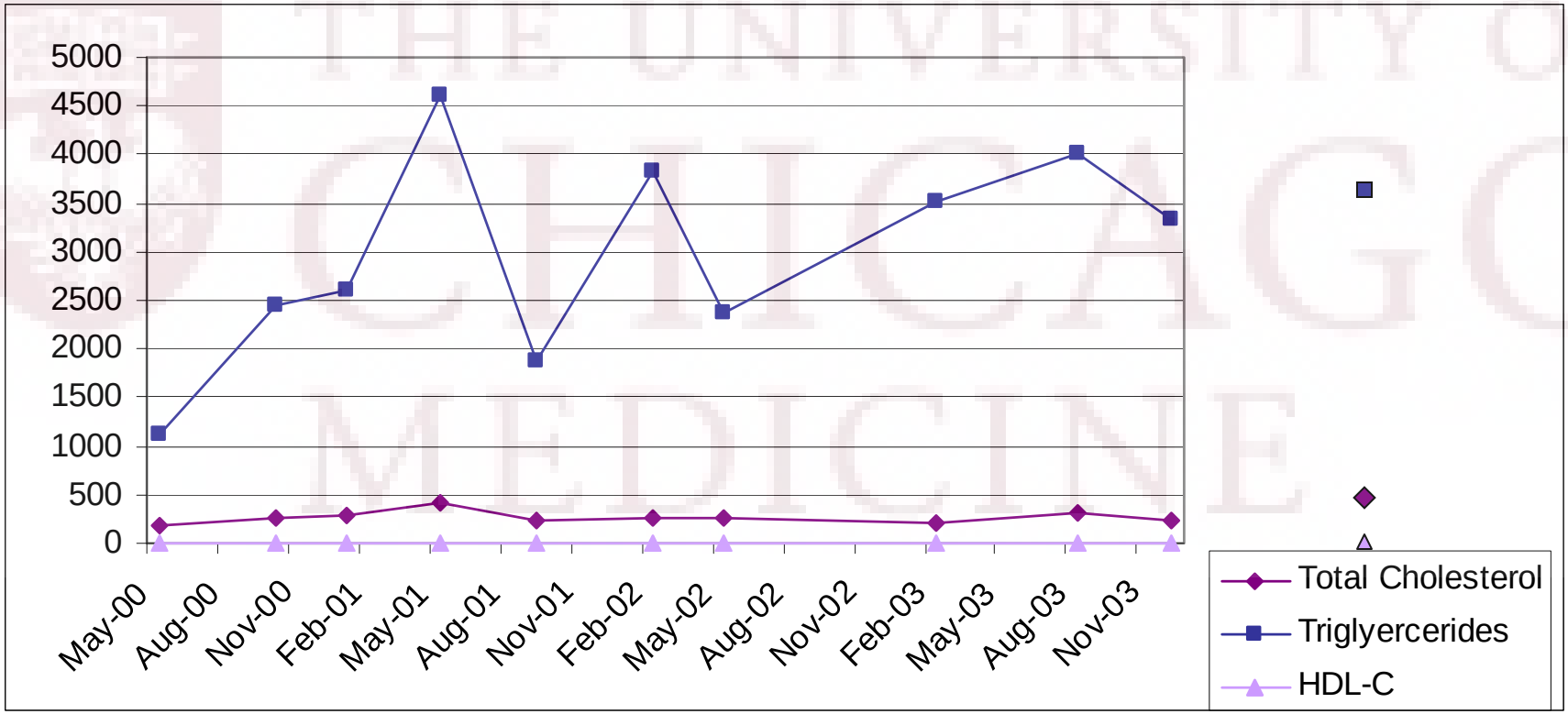
- Albumin 3.7, total protein 8.1
- Total bili 0.1, alk phos 162, AST 39, ALT 12
- Lipase 5

- Total cholesterol 522
- HDL-C 44
- Direct LDL-C <3
- Triglycerides 3610
- Apolipoprotein A-1 could not be performed.
- Apoljpoprotein B-100 53 mg/dL (goal < 80)

- Apolipoprotein E isoform 2/3

- HgbA1c 5.2%
- Urine albumin:creatinine 4.7

Cholesterol History

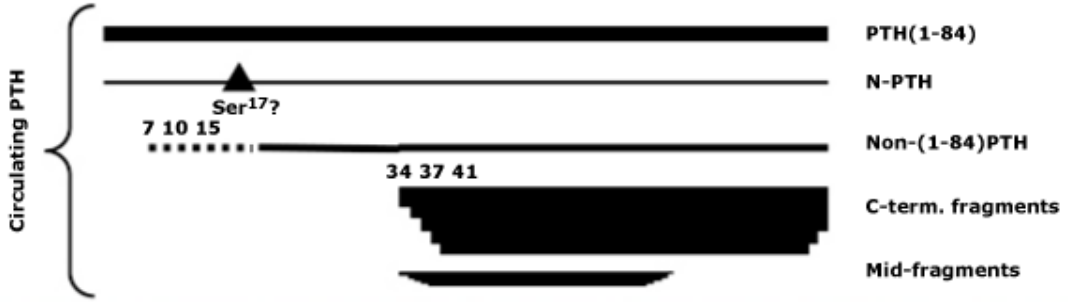


Laboratory Data

- TSH 2.44
- fT4 0.72
- PTH 56 (15-75)
  - Ca 9.2
- 25 OH vitamin D 9

- TSH 3.60
- fT4 0.87
- PTH 173
- 25 OH vitamin D 9

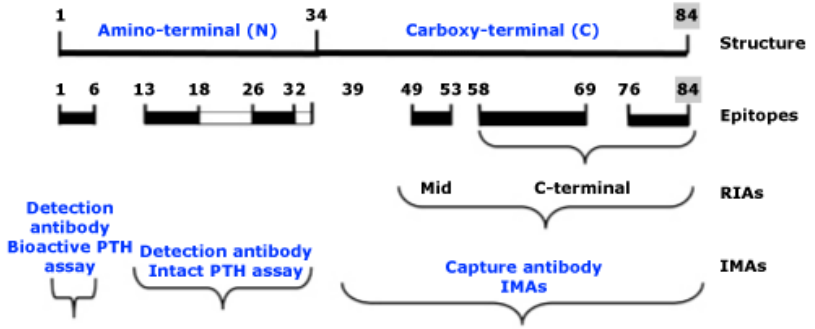
PTH



- PTH 1-84, biologically active hormone
  - 5-30%
  - Half-life of 2-4 minutes
- C-terminal fragments
  - 70-95%
  - Half-life 5-10x longer than PTH 1-84, cleared by kidneys
- N-terminal fragments
  - Small percentage

Fuleihan and Juppner. UpToDate. Parathyroid hormone assays and their clinic use.

PTH assays



- 1st generation assay: radioimmunoassay
  - Measures predominantly PTH fragments
  - Polyclonal abs against epitopes in the mid- or C-terminal portion.
- 2nd generation assay, intact PTH assay: immunometric
  - Measures PTH 1-84 and other large C-terminal PTH fragments
  - Capture antibody against C-terminal portion (39-84) and detection antibody against N-terminal portion (13-34)
- 3rd generation assay, bioactive PTH 1-84 assay: immunometric
  - Measures only PTH 1-84
  - Capture antibody against C-terminal portion and detection antibody against N-terminal portion (1-4)

Fuleihan and Juppner. UpToDate. Parathyroid hormone assays and their clinic use.

What factors can interfere with PTH measurement?

- Renal failure
  - Increased due to presumed decrease in breakdown and clearance by the kidney
- Heterophile antibodies
  - Falsely elevated
  - Usually a problem in patients treated with drugs containing non-human antibodies
- Rheumatoid factor
- Hemolysis
  - Release of proteolytic enzymes from erythrocytes
- Insufficient filling of EDTA tubes
- Medications:
  - Increase: ?propofol
  - Decrease: alteplase, biotin, ?propofol

Rodgers and Lew. Endocr Pract. 2011 Mar-Apr;17 Suppl 1:2-6.
Glendenning et al. Clin Chem. 2002 Mar;48(3):566-7.
Schiller et al. Nephrol Dial Transplant. 2009 Jul;24(7):2240-3.
Sippel et al. Surgery. 2004 Dec;136(6):1138-42.
Meany et al. Clin Chem. 2009 Sep;55(9):1737-9.

Assessment & Plan

- Hypertriglyceridemia: Hyperchylomicronemia
  - Thought to be due to homozygous lipoprotein lipase deficiency and/or apoCII deficiency
  - Lovaza 2 gram BID
  - Very low fat diet (<10% of total calories)
    - Fats from medium chain fatty acids (coconut oil and palm kernel oil)
- Diabetes mellitus type 2: metformin
- Hypothyroidism:
  - Increase levothyroxine to 137 mcg daily given profound hypertriglyercidemia
- Elevated PTH:
  - On ultracentrifuged specimen
  - Possibly due to vitamin D deficiency and likely low dietary calcium intake
  - Ergocalciferol 50,000 IU weekly x 12 weeks + vitamin D3 2000 IU daily
  - Calcium carbonate 500 mg BID
  - DEXA scan recommended

Follow up visit

- 2/16/12
  - Ca 9.4
  - PTH 34
  - 25 OH vit D 46
  - TSH 1.17
  - fT4 1.22
- 11/3/11
  - Ca 9.2
  - PTH 173
  - 25 OH vit D 9
  - TSH 3.60
  - fT4 0.87

Follow up visit

- Medication list:
  - Aspirin 325 mg one daily
  - Atenolol 25 mg daily
  - Isosorbide mononitrate 30 mg ER daily
  - Levothyroxine 137 mcg daily
  - Metformin 500 mg daily
  - Lovaza 2 grams BID
  - Ergocalciferol 50,000 IU once weekly
  - Vitamin D 1000 IU daily
  - Ocuvite tablet one daily
  - Tab-a-vite/iron one daily
  - Doc-q-lace 100 mg twice daily
  - Alprazolam 1 mg QHS
  - Saphris 10 mg QHS
  - Proctozone CRE 2.5% cream TID to skin
  - Fluticasone 50 mcg 2 sprays each nostril daily
  - Tylenol PRN
  - APAP/codein PRN
  - Bacitracin PRN
  - Genaton Suspension PRN
  - Guaifenesin Syrup DM PRN
  - Hem-Prep cream PRN
  - Loperamide PRN
  - Prochlorperazine 10mg PRN
  - Sudogest Tab 30 mg PRN
  - Throat Lozenges PRN
- Changes:
  - Addition of isosorbide mononitrate
  - Addition of vitamin D
  - Increase in levothyroxine dose
  - Discontinuation of Naproxen

Follow up visit

- 2/16/12
  - Ca 9.4
  - PTH 34
  - 25 OH vit D 46
  - TSH 1.17
  - fT4 1.22
  - Total chol 577
  - HDL 44
  - Trig 4557
- 11/3/11
  - Ca 9.2
  - PTH 173
  - 25 OH vit D 9
  - TSH 3.60
  - fT4 0.87
  - Total chol 522
  - HDL 44
  - Trig 3610

Hyperchylomicronemia

Table 4. Familial Forms of High Triglycerides

	Inheritance/Population Frequency	Pathogenesis	Typical Lipid/Lipoprotein Profiles	Comments
Rare genetic syndromes presenting as chylomicronemia syndrome				
LPL deficiency (also known as familial type I)	Autosomal recessive; rare (1 in 10^6)	Increased chylomicrons due to very low or undetectable levels of LPL; circulating inhibitor to LPL has been reported	Homozygotes: TG-to-cholesterol ratio 10:1; TG >1000 mg/dL; increased chylomicrons	Homozygous mutations cause lipemia retinalis, hepatosplenomegaly, eruptive xanthomas accompanying very high TG. CAD believed uncommon, but cases reported
Apo CII deficiency	Autosomal recessive; rare	Increased chylomicrons due to absence of needed cofactor, Apo CII	Homozygotes TG-to-cholesterol ratio 10:1; TG >1000 mg/dL; increased chylomicrons Obligate heterozygotes with normal TG despite apo CII levels ≈30% to 50% of normal	Attacks of pancreatitis in homozygotes can be reversed by plasmapheresis; xanthomas and hepatomegaly much less common than in LPL deficiency
Apo AV homozygosity	Rare	Mutations in the *APOA5* gene, which lead to truncated apo AV devoid of lipid-binding domains located in the carboxy-terminal end of the protein	Homozygotes: TG-to-cholesterol ratio 10:1; TG >1000 mg/dL; increased chylomicrons	Apo A5 disorders can form familial hyperchylomicronemia with vertical transmission, late onset, incomplete penetrance, and an unusual resistance to conventional treatment
GPIHBP1	Rare; expressed in childhood	Mutations in *GPIHBP1* may reduce binding to LPL and hydrolysis of chylomicron triglycerides	TG-to-cholesterol ratio 7:1; TG >500 mg/dL; increased chylomicrons partially responsive to low-fat diet	May have lipemia retinalis and pancreatitis; eruptive xanthomas not reported

Circulation. 2011 May 24;123(20):2292-333. Epub 2011 Apr 18.

Dietary Management of Hypertriglyceridemia

Table 11. Effects of Nutrition Practices on Triglyceride Lowering

Nutrition Practice	TG-Lowering Response, %
Weight loss (5% to 10% of body weight)	20
Implement a Mediterranean-style diet vs a low-fat diet	10–15
Add marine-derived PUFA (EPA/DHA) (per gram)	5–1(
Decrease carbohydrates	
1% Energy replacement with MUFA/PUFA	
Eliminate *trans* fats	
1% Energy replacement with MUFA/PUFA	

TG indicates triglyceride; PUFA, polyunsaturated fat taenoic acid; DHA, docosahexaenoic acid; and MUFA acid.

	Apo E2 Response		Apo E3 Response		Apo E4 Response	
Genotype	2/2	2/3	3/3	2/4	3/4	4/4
Population Frequency	1%	10%	62%	2%	20%	5%
Fish Oil[1]	↓↓TG ↓small dense LDL ↑HDL		↓TG ↓small dense LDL ↑HDL		↓TG ↓↓small dense LDL ↓HDL ↑↑LDL	
Low Fat Diet[2,3]	↓LDL ↑small dense LDL		↓↓LDL ↔small dense LDL		↓↓↓LDL ↓small dense LDL	
Moderate Fat Diet[3]	↔LDL ↔small dense LDL		↓LDL ↓small dense LDL		↓LDL ↑↑small dense LDL	
Moderate Alcohol[4]	↑HDL ↓LDL		↑HDL		↓HDL ↑LDL	
Effective Drug Response	Atorvastatin Pravastatin Lovastatin		No distinction		Probucol Simvastatin	

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Berkeley HeartLab. Apolipoprotein E Genotype for Cardiovascular Disease Management.

Sample menu of very low fat diet

- Breakfast:
  - 6 oz tomato juice
  - 4 inch oat bran bagel, 1 tbsp fat-free cream cheese
  - 1.5 oz liquid egg subsitute
  - 8 oz skim milk
- Lunch:
  - Turkey sandwich: 2 oz lean turkey, small whole wheat pita, lettuce, tomato, sprouts, 2 tsps fat-free mayo, 1 tsp mustard
  - 1 cup carrots
  - ½ cup pineapple chunks
  - 8 oz skim milk
- Dinner:
  - 4 oz chicken breast baked in tomato sauce with 1 cup pasta
  - Mixed green salad with carrots, cucumbers, tomatoes
  - 2 slices of french bread, 1 tsp reduced fat margarine
  - Cooked apple with cinnamon and sugar
  - Water, tea, or coffee
- Nutrition: 1,635 calories; protein: 110 g (26% of calories); carbohydrates 262 g (63%); fat: 19 g (11%); cholesterol 140 mg; fiber 25 g

From American Dietetic Association

Pharmacological Management of Hypertriglyceridemia

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Weight loss (5% to 10% of body weight)	20
Implement a Mediterranean-style diet vs a low-fat diet	10–15
Add marine-derived PUFA (EPA/DHA) (per gram)	5–10
Decrease carbohydrates	
1% Energy replacement with MUFA/PUFA	1–2
Eliminate *trans* fats	
1% Energy replacement with MUFA/PUFA	1

TG indicates triglyceride; PUFA, polyunsaturated fatty acid; EPA, eicosa taenoic acid; DHA, docosahexaenoic acid; and MUFA, monounsaturated acid.

Table 12. Effect of Lipid-Lowering Therapies on Triglyceride Reduction[504,480a–480d]

Drug	% Triglyceride Reduction
Fibrates	30–50
Immediate-release niacin	20–50
Omega-3	20–50
Extended-release niacin	10–30
Statins	10–30
Ezetimibe	5–10

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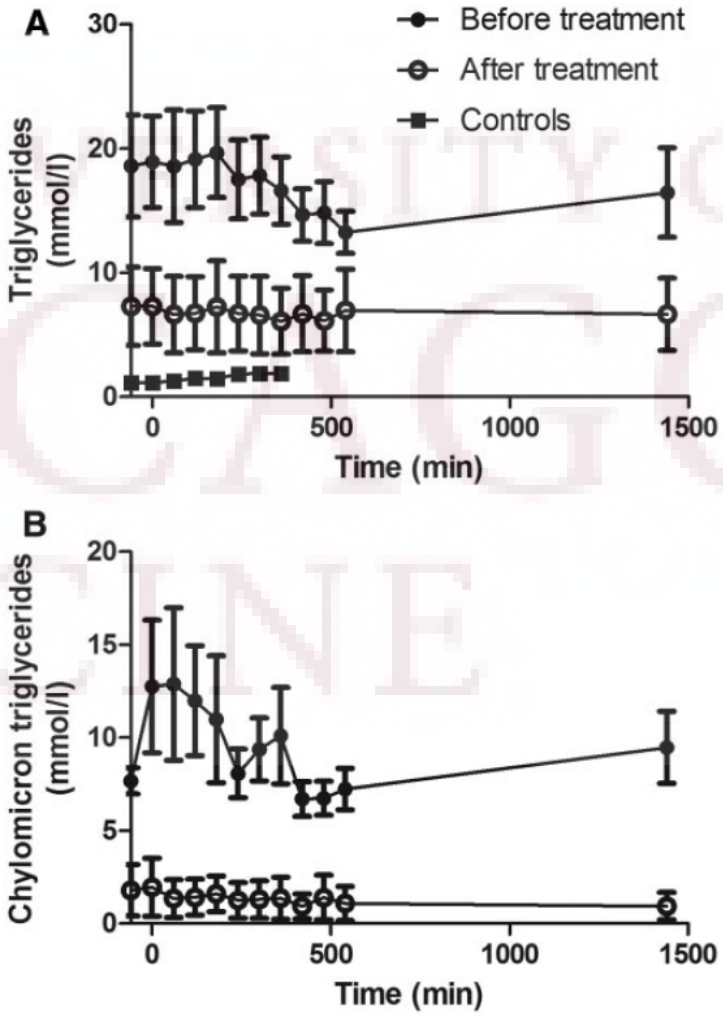
On the Horizon: alipogene tiparvovec

- Alipogene tiparvovec:
  - Contains coding sequence for LPL^{S447X}, a naturally occurring gain of function variant of LPL
- Open label trial for 14 weeks
  - Administered IM x1
- 5 subjects



Carpentier et al. J Clin Endocrinol Metab. 2012 Mar 21. [Epub ahead of print]

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