

The patient was prescribed fenofibrate 145 mg and niacin was titrated to 2000 mg. During the past week, the patient reported progressive blurriness of vision.

50. Which *one* of the following is the MOST appropriate next step for this patient's condition?
- (A) Neurovascular MRI immediately.
  - (B) Discontinue fenofibrate immediately.
  - (C) Discontinue atorvastatin immediately.
  - (D) Discontinue niacin immediately.
  - (E) Neurosurgical evaluation immediately.

■ Items 51–53

A 22-year-old man is rushed to the emergency room with nausea, vomiting and severe abdominal pain that radiates to the back. CAT scan reveals pancreatic inflammation.

51. Which *one* of the following is the LEAST likely explanation for his condition?
- (A) Excessive alcohol consumption.
  - (B) Apo C-III deficiency.
  - (C) Cholelithiasis.
  - (D) Lipoprotein lipase deficiency.
  - (E) Paramyxovirus (mumps).

Upon further evaluation, the patient has no history of prior hospitalizations. However, when undergoing phlebotomy for routine testing in the past, his plasma resembled the left side of the figure shown below.

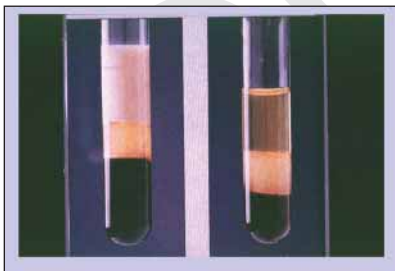


Figure 3.

52. Which *one* of the following represents the MOST likely mechanism for this effect?
- (A) Free fatty acid-induced capillary damage.
  - (B) Cholecystokinin-8-induced NF- $\kappa$ B activation.
  - (C) Endotoxin-mediated apoptosis.
  - (D) Impairment of regeneration following cell injury.
  - (E) Lymphocytic infiltration and immune-mediated destruction.

53. Which *one* of the following medications is LEAST likely to be associated with this disease process?

- (A) Clozapine.
- (B) Trimethoprim-sulfamethoxazole.
- (C) Tesaglitazar.
- (D) Valproate.
- (E) Pentamidine.

■ Items 54–58

A 31-year old woman has the following laboratory values:

|                   |           |
|-------------------|-----------|
| Total Cholesterol | 200 mg/dL |
| Triglycerides     | 150 mg/dL |
| HDL-C             | 50 mg/dL  |
| LDL-C             | 120 mg/dL |
| Lp(a)             | 30 mg/dL  |

She is put on one of the following medications for the next 6 months. For each numbered post-treatment laboratory values in this patient (54–58), select the *one* lettered therapy (A, B, C, D, E) MOST likely associated with it. Each lettered therapy may be selected only once.

- (A) Testosterone (IM).
- (B) Conjugated estrogen and medroxyprogesterone.
- (C) Medroxyprogesterone.
- (D) Tamoxifen.
- (E) Raloxifene.

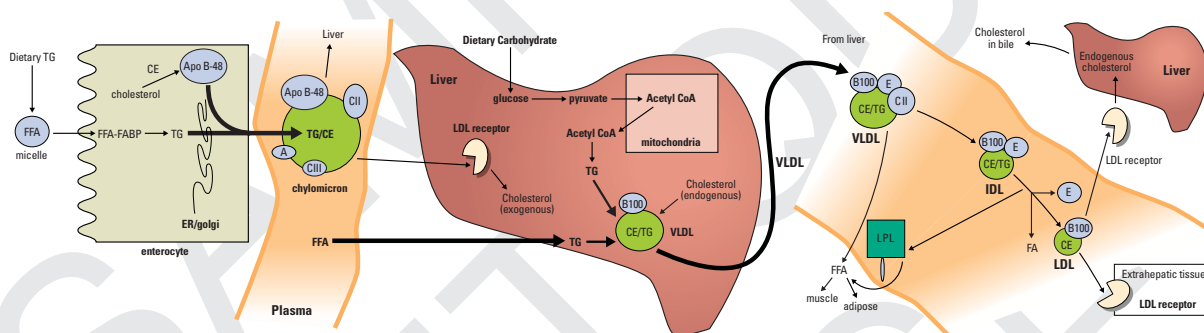
54. Total cholesterol 185 mg/dL  
Triglycerides 150 mg/dL  
HDL-C 50 mg/dL  
LDL-C 105 mg/dL  
Lp(a) 20 mg/dL

55. Total cholesterol 190 mg/dL  
Triglycerides 180 mg/dL  
HDL-C 55 mg/dL  
LDL-C 100 mg/dL  
Lp(a) 20 mg/dL

56. Total cholesterol 190 mg/dL  
Triglycerides 150 mg/dL  
HDL-C 25 mg/dL  
LDL-C 135 mg/dL  
Lp(a) 20 mg/dL

**Items 14–18**      Answers 14 (C); 15 (A); 16 (B); 17 (E); 18 (D)

Fasting triglyceride levels in the plasma are affected by treatments that enhance clearance of triglyceride-rich lipoproteins or decrease VLDL secretion. Glucose is a major substrate for lipogenesis in the hepatocytes and modulates the carbohydrate responsive element-binding protein (ChREBP) which, along with sterol regulating element-binding protein-1c (SREBP-1c), are the two key regulators of glucose metabolism and lipid synthesis in the liver. Carbohydrates are converted into citrate by the Krebs cycle, which serves as the initial building block of triglyceride synthesis. Triglycerides are synthesized from free fatty acids that come from peripheral adipose tissue. Carbohydrate restriction would, therefore, decrease the substrate for triglyceride synthesis and modulate ChREBP, which would also enhance triglyceride production and secretion of VLDL by the liver. Niacin reduces the release of free fatty acids from the periphery and also appears to inhibit the rate-limiting enzyme involved with triglyceride synthesis DGAT-2. Omega-3 fatty acids redistribute fatty acids towards storage or enhance beta-oxidation, thereby reducing the substrate for triglyceride synthesis. Fibrates have multiple mechanisms to decrease triglycerides by both enhancing clearance by decreasing Apo CIII levels (which inhibit lipoprotein lipase) and enhancing beta-oxidation of fatty acids, thereby decreasing VLDL secretion. Statins decrease VLDL secretion and upregulate the Apo B/E receptor which help clear the triglyceride-rich particles that contain ApoB and/or E. (MD)



**Figure 3.** Triglyceride Synthesis

**Bibliography**

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**Item 19**      Answer D

Microalbuminuria has been shown to be an important risk factor in type 2 diabetics for the development of CHD. However, there is a debate regarding the definition of microalbuminuria. In the Third Copenhagen City Heart Study, microalbuminuria defined as >5 microg/min was associated with an 11% incidence of CHD and 28% cumulative mortality rate compared to 5% CHD rate and 13% mortality rate over a 10-year period in hypertensives with urinary albumin excretion <5 microg/min. Also, in the FIELD trial, a subset of 397 type 2 diabetics who underwent carotid ultrasound, intimal medial thickness (IMT) was correlated with even lower levels of microalbuminuria. This patient with type 2 diabetes has not yet achieved his NCEP ATP III goals because his non-HDL-C exceeds 130 mg/dL. Although his HbA1c is below 7.0%, because he does have microalbuminuria, he may benefit from additional glycemic control and improved lipid management. Both pioglitazone, a PPAR-gamma drug, and fenofibrate, a PPAR-alpha, have been demonstrated to reduce microalbuminuria in diabetics while metformin has been shown to have little impact. In the FIELD and DAIS trials, fenofibrate significantly lowered urinary albumin levels. Animal models lacking PPAR-alpha have accelerated diabetic nephropathy and fenofibrate in this model