28 Year-old Male w/Uncontrolled Type 2 Diabetes, Bipolar Disorder Presents with Epigastric Pain

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9/27/12

HPI

- Presented to an OSH with epigastric pain, diarrhea.
- + fevers up to 104.9
- 1 year ago had a similar presentation was found to have pancreatitis from elevated hypertriglyceridemia
- Transferred to UCMC because he had a CT concerning for possible fluid collection

Diabetes history

- Diagnosed 2 years ago
- Was supposed to be taking insulin but stopped this over a year ago, does not remember his regimen
- Never checks blood sugars at home

Bipolar history

- Diagnosed 15 years ago when parents got divorced
- Last major manic episode was in 2009 was when he took a hammer to a car that was not his

PMHx

- Bipolar disorder
- HTN

SHx

- Tobacco- 2 cigs/day
- Marijuana
- EtOH- 1 beer/wk

FHx

- No dyslipidemia
- No heart disease
- No diabetes

Meds

- Depakote 1000mg qAM
- Depakote 1250mg qPM
- Lithium 600mg BID
- Thorazine 100mg qAM
- Thorazine 200mg qPM

Physical Exam

Vitals: 102.2 280lb 146/90, 119, 20, 95%

HEENT: PERRLA, EOMI

Neck: no thyromegaly or nodules

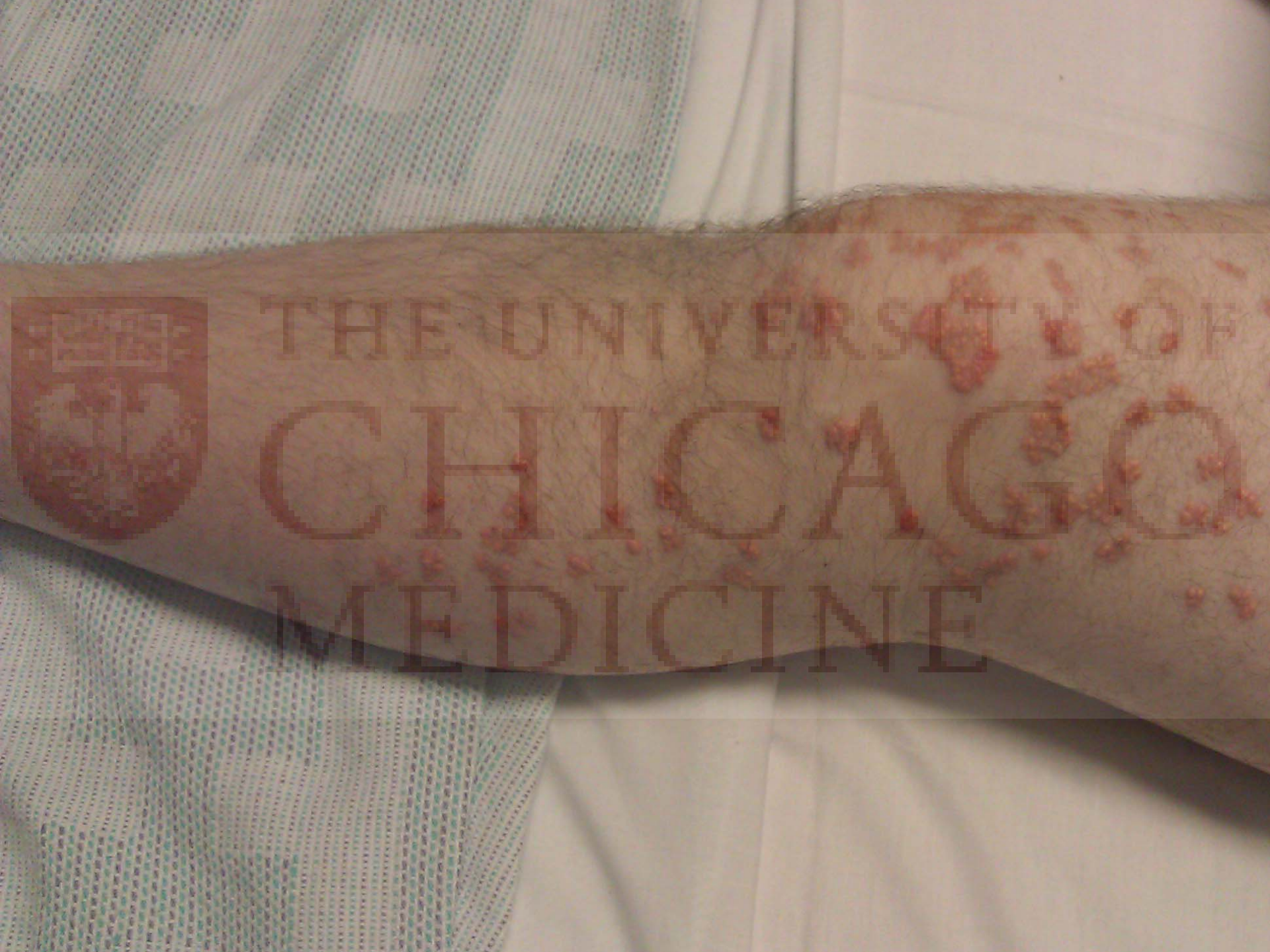
CV: tachycardic, regular rhythm, no murmurs

Resp: no rales or rhonchi

GI: epigastric tenderness, no rebound or guarding

Skin: papular lesions c/w xanthomas

Psych: normal mood, affect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Initial Labs HD #1

129	91	9
3.7	22	0.4

330

9.1
2.0
3.8

14.9
14 222
41

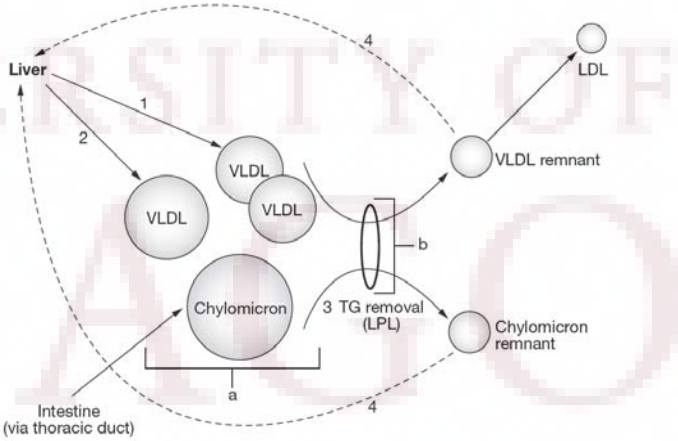
7.2	4.6
0.3	75
13	22

HbA1c 11.2 %
Lipase 988 (13-60)
TG 8590 (0-149)
HDL 72 (40-100)
Non-HDL 1092 (RR 0-159)
TSH 4.0, FT4 1.26 (0.9-1.7)

DDx for Hypertriglyceridemia

TABLE 2. Causes of hypertriglyceridemia

- Primary hypertriglyceridemia
  - FCHL
  - FHTG
  - Familial dysbetalipoproteinemia
  - FHA
  - Familial chylomicronemia and related disorders
- Primary genetic susceptibility
  - Metabolic syndrome
  - Treated type 2 diabetes
- Secondary hypertriglyceridemia
  - Excess alcohol intake
  - Drug-induced (*e.g.* thiazides, β-blockers, estrogens, isotretinoin, corticosteroids, bile acid-binding resins, antiretroviral protease inhibitors, immunosuppressants, antipsychotics)
  - Untreated diabetes mellitus
  - Endocrine diseases
  - Renal disease
  - Liver disease
  - Pregnancy
  - Autoimmune disorders

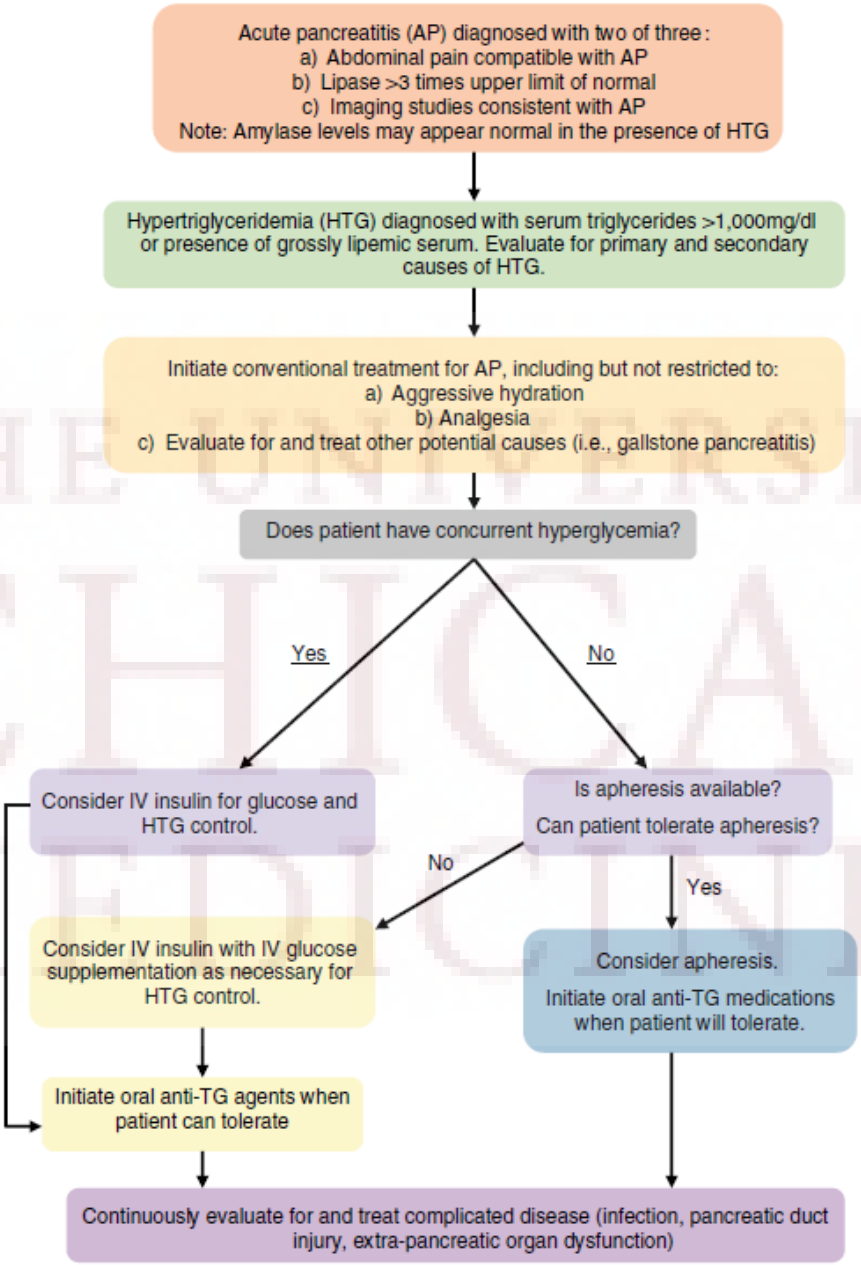


Endocrine Society 2012 Guidelines on Hypertriglyceridemia

CT abdomen/pelvis

Day #1: Acute pancreatitis. Hazy appearance around pancreatic body and tail. Hepatomegaly with fatty infiltration noted.

Day #5: Severe inflammation of the pancreatic tail c/w acute pancreatitis. Fluid collection adjacent to the pancreatic tail measuring 21 x 9 x 12 cm. Consolidation LLL lung, atelectasis vs infiltrate.



American Journal of Gastroenterology 2009; 104:984-991

	9/3	9/4	9/5	9/11
TG	8590	PLASMAPHERESIS	1213	161
Lipase	988		29	29
Amylase			14	

Hypertriglyceridemia Pancreatitis

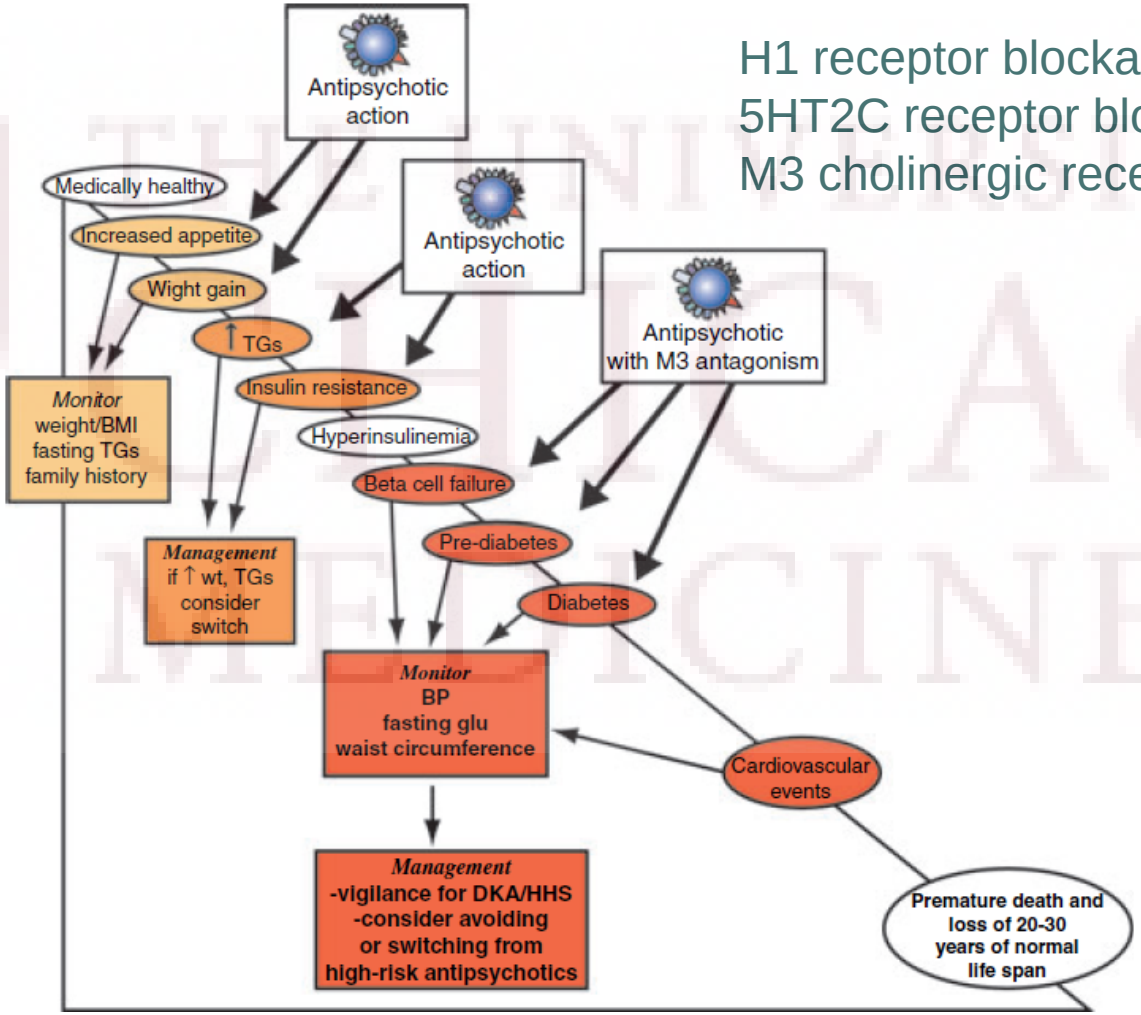
- Hypertriglyceridemia- 1º vs 2º
- 1-4% of cases of acute pancreatitis
- Risk is related to degree of elevation (usually > 1000 mg/dL)
- Pathogenesis
  - TG+Lipase→FFA formation
  - Chylomicrons→pancreatic capillary congestion

Clinical Questions

- Antipsychotics/Bipolar medications causing metabolic syndrome?
- Plasmapheresis in hypertriglyceridemia pancreatitis?
- Combination therapy with fibrates and statins in hypertriglyceridemia and T2DM?

Antipsychotics & Metabolic Disturbances

H1 receptor blockade
5HT2C receptor blockade
M3 cholinergic receptor antagonism



Stahl et al. Acta Psychiatrica Scandinavica 2009.

Antipsychotics & Metabolic Disturbances

Antipsychotic	Risk for weight gain
Clozapine	+++
Olanzapine	+++
Risperidone†	++
Quetiapine	++
Ziprasidone	±
Aripiprazole	±

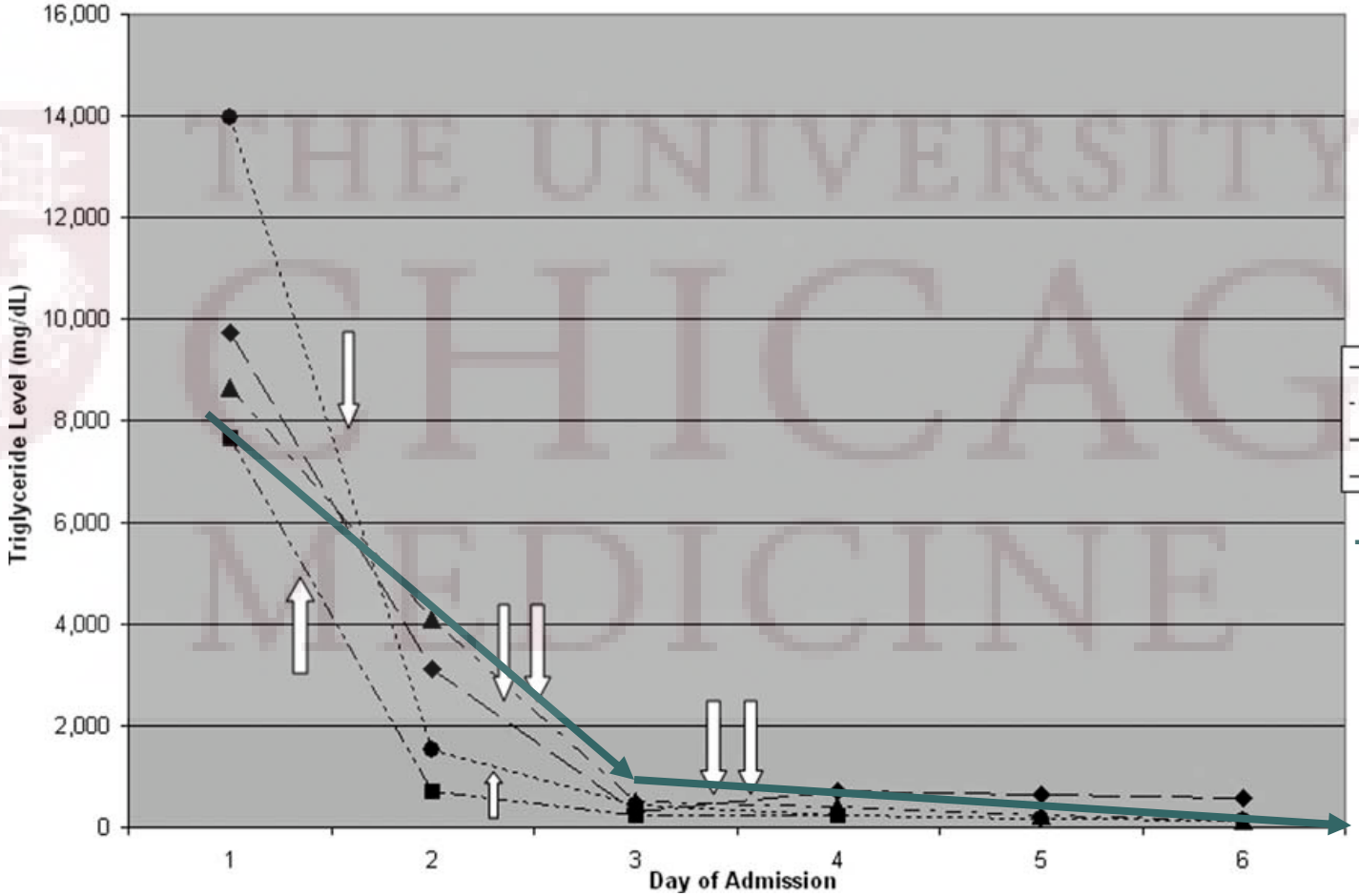
	Cardiometabolic/dyslipidemia/diabetes risk		
Antipsychotic	Expert consensus	CATIE	FDA
Clozapine	Definite risk	ND	Diabetes warning
Olanzapine	Definite risk	Definite risk	Diabetes warning
Risperidone†	Inconclusive	Intermediate	Diabetes warning
Quetiapine	Inconclusive	Definite risk	Diabetes warning
Ziprasidone	±Limited data	Low risk	Diabetes warning
Aripiprazole	±Limited data	ND	Diabetes warning

Stahl et al. Acta Psychiatrica Scandinavica 2009.

Bipolar Disorder & Metabolic Disturbances

- Kemp et al. looked at 2 studies exploring the relationship between lithium and valproic acid to metabolic disorders. Conclusion- BMI was a significant predictor of non-remission
- Biological mechanisms common to bipolar and metabolic syndrome
  - Abnormal glucocorticoid signaling, oxidative stress, altered energy biosynthesis, autonomic nervous system dysfunction
  - Implications for future avenues of treatment

Triglyceride improvement w/plasmapheresis



→Our patient

J Clinical Apheresis 2010; 25:229-234.

Table 1. Apheresis in hypertriglyceridemic pancreatitis (reports with five or more patients)

Study	No. of patients	No. of patients with complete recovery (%)	Mortality (%)
Chen *et al.* (56)	20	0 (100)	0
Yeh *et al.* (64)	17	13 (76.5)	2 (11.8)
Kyriakidis *et al.* (61)	10	9 (90)	1 (10)
Kadikoylu *et al.* (59)	7	7 (100)	0
Lennertz *et al.* (62)	5	5 (100)	0

AJG 2009; 104:984-991.

Fibrate + Statin Combination Therapy

- Endo Society Guidelines 2012
  - Addition of statins in mild-mod hyperTG (150-1000) and high non-HDL cholesterol
- ACCORD-Lipid trial 2010
  - General diabetics: no benefit from combination therapy
  - Sub analysis supports combination therapy in hypertriglyceridemia (TG > 204 mg/dL) and low HDL (HDL < 34 mg/dL)

Fibrate + Statin Combination Therapy

If triglycerides 200-499 mg/dL after LDL goal is reached, consider adding drug if needed to reach non-HDL goal:

- intensify therapy with LDL-lowering drug, or
- add nicotinic acid or fibrate to further lower VLDL.

If triglycerides ≥500 mg/dL, first lower triglycerides to prevent pancreatitis:

- very low-fat diet (≤15% of calories from fat)
- weight management and physical activity
- fibrate or nicotinic acid
- when triglycerides <500 mg/dL, turn to LDL-lowering therapy.

ATP III Guidelines 2001

Hospital Course

- Follow-up appointments
  - Psych: bipolar therapy
  - GI: repeat CT abdomen
  - Endo: hyperTG w/u, DM management
- Discharged home on:
  - Tricor 145 mg daily
  - Lantus 33U qHS, Novolog correction factor

Take Home Points

- Management of hypertriglyceridemic pancreatitis including plasmapheresis for severe cases
- Antipsychotic/Bipolar therapy and metabolic syndrome risk
- Indications for combination statin/fibrate therapy

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