38 yo obese F w/Crohns presents with nausea/vomiting

1/24/13

Jess Hwang

1 week prior to admission

- Seen in ED with fevers, nausea, vomiting, worsening rash
- Hypotensive to 70/40 with lactate of 4.5
- Acute renal failure (GFR 34)
  - 1 month ago it had been >120
- Was given IVF and then discharged in <24h

HPI

- 1 week of nausea/vomiting/diarrhea
- Low grade fevers, chills
- Dizziness, palpitations for 1 day
- Diffuse pruritic rash x 10 days
- Has not been using her U500 insulin pump for 2 days because she was not taking PO and her rash was so itchy, she itched it off

Crohns history

- Followed by IBD clinic
- Prednisone 20-60 mg daily for the past 2 years→currently being tapered.
- Was on Prednisone 20 mg for the last month but has not taken it for 2 days
- 6MP metabolite 49,426 (RR <5700)
  - On admission
  - Toxicities: bone marrow suppression, ?liver
  - Level normalized after stopping drug

Diabetes history

- Diagnosed in 2009
- GAD65 negative at the time
- 2011 HbA1c was 10.5%, GAD65/IA2 neg, c-peptide 3.85 (RR 0.8-3.1)
- Previously was on Lantus 100U BID and Humalog 60U AC + correction factor
- 6/2012 Started on insulin pump with U500

Diabetes History cont.

- Insulin pump settings U500 (U100)
  - Basal 10A 0.8 (4.0), 10P 0.7 (3.5)
  - Insulin:Carb 1:18g (1:3.6)
  - ISF 1:100 (1:20)
  - Target 80-120
- 2012 GAD65 0.08 (RR < 0.02)
- No history of ever having DKA

PMH
- LADA (dx 2012)
- HTN
- Crohns
- Migraines
- Obesity

SHx
- No tobacco/EtOH

Home
- Lives w/husb + 4 kids

Family history
- Father: T2DM, hepatitis
- PGF: T2DM

Meds
- U500 insulin pump
- Asacol
- 6-MP
- Prednisone
- Pepcid
- Gabapentin
- Zocor
- Topamax

Physical exam

Vitals: 37.7, 100, 104/60, 100% RA, BMI 36
Gen: chronically ill-appearing
HEENT: **oral ulcers. Cushingoid.**
Neck: no neck rigidity. No thyromegaly or nodules.
CV: slightly tachycardic, no murmurs
Resp: CTA bilaterally
GI: dry-heaving, no rebound or guarding
GU: **vaginal lesions**
Skin: **+diffuse scabs**
Neuro: oriented but slightly somnolent

Labs

140	94	8
3.2	15	0.7

200

9.3

AG 31

10.4

2.5 392

33

PMN: 50%, ANC 1240
Lymph 49%

6.6	3.6
0.5	84
41	42

Ketones 8.0 (RR < 0.3)
Lactate 2.3 (RR < 2.1)
VBG 7.32/33.7
HbA1c 8.6%

Lipase 46

Labs cont.

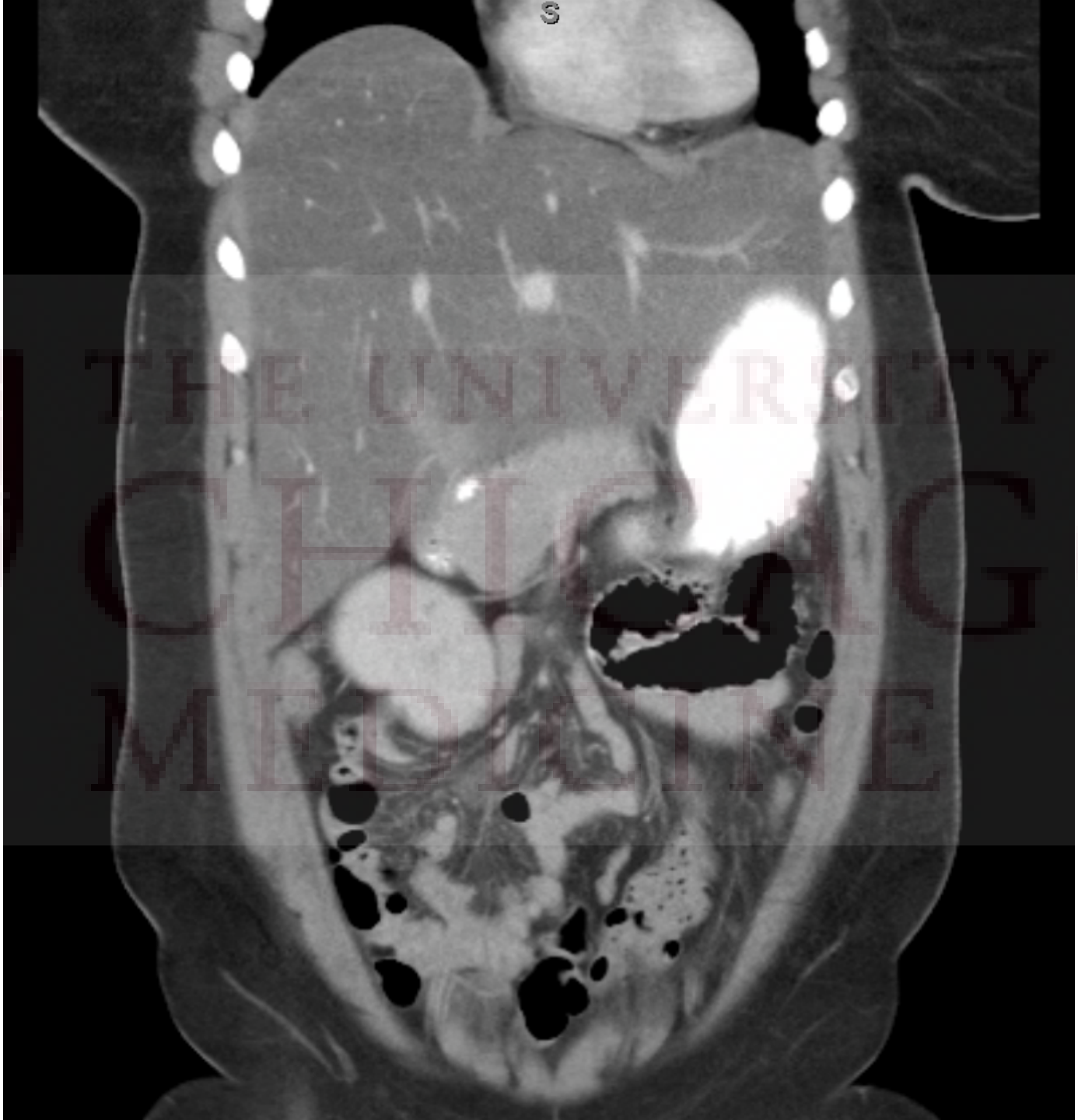
HD#1 TSH 0.09, FT4 1.47, rT3 613, TT3 79
Last HD TSH 1.49, FT4 1.25, TT3 89

Endomysial Ab, TTGAb negative
HDL: 21
25-OH vitamin D: 8
Prealbumin: 22 (RR 21-41)

HSV PCR- positive (vaginal lesions)

CT abdomen/pelvis

IMPRESSION: no free or loculated abdominal fluid collections to suggest abscess. Unremarkable bowel loops without evidence of ischemia, infection or obstruction to explain symptoms. Marked hepatic steatosis.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Gastric emptying study

FINDINGS: Visually there was significant and progressive gastric emptying.

Residual gastric activity at the following postprandial intervals was calculated as follows:

- 30 min: 77% of peak activity (nl > 70%)
- 1h: 41% of peak activity (nl 30-90%)
- 2.5h: 2% of peak activity (nl < 10% by 4h)

IMPRESSION: Gastric emptying within normal limits.

Hospital Course

- ICU for 5 days
  - insulin drip (rate of 20-25 U/h)
  - D10 with 60 mEq KCl drip (100 cc/h)
  - difficult stick so required central line
  - monitoring for re-feeding after transition to TF
- Stress dose steroids
- Developed neutropenic fever
- Oral/genital HSV- acyclovir

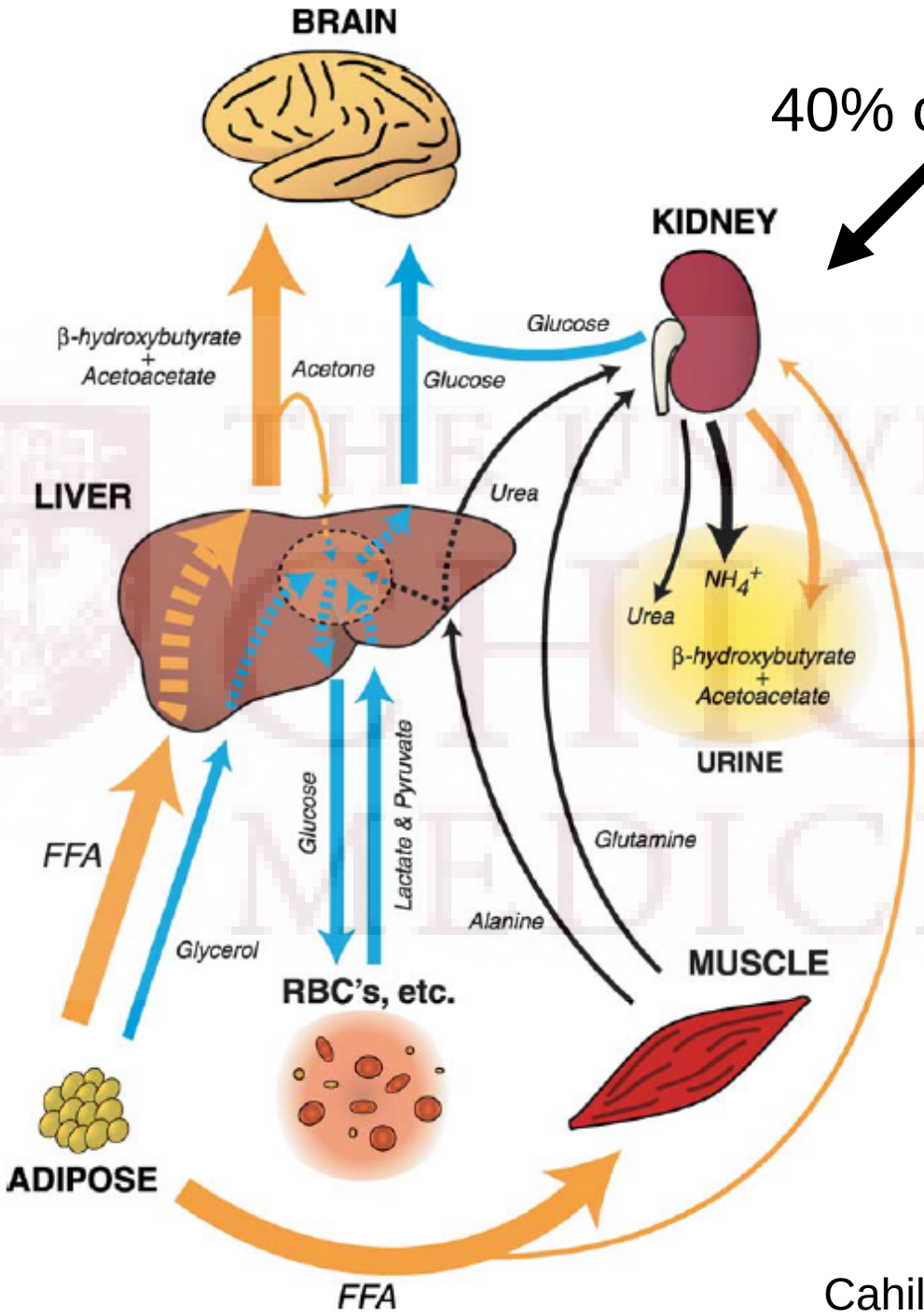
Post-hospital course

- Being tapered off of Prednisone
- Remains off 6MP
- Crohns disease currently quiescent
- Neutropenia resolved
- Still having low-grade fevers 101-102

Clinical Concept/Questions

- Characteristics of LADA
- Pathophysiology of starvation
- Management of euglycemic ketoacidosis
- Glucocorticoid effect on ketoacidosis

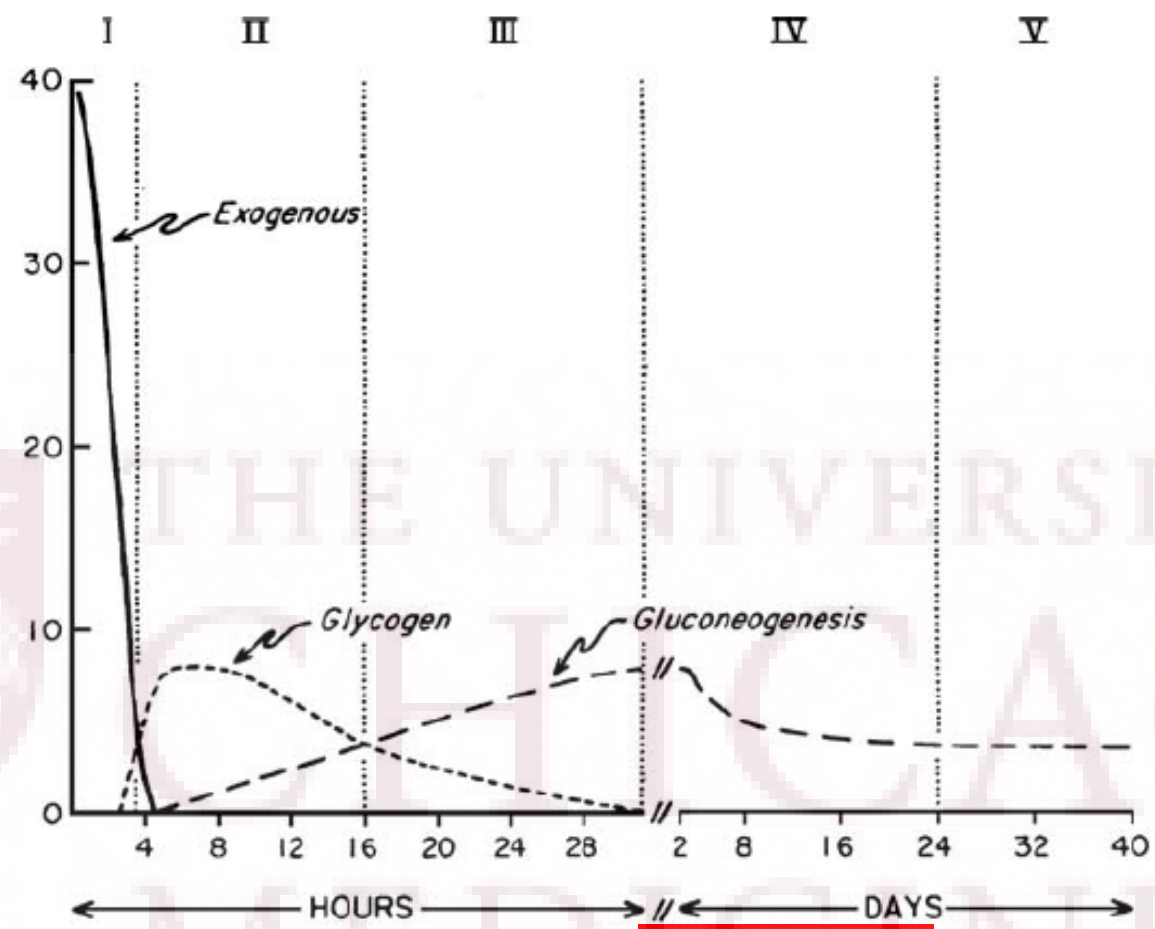
	Type 1	LADA	Type 2
Age of onset	Child/Adult	Adult	Adult/child
Progression to insulin dependence	Rapid (days-weeks)	Delayed (months-years)	Very slow
Presence of Autoantibodies	Yes	Yes	No
Insulin dependence timeframe	At diagnosis	Usually within years	Over time, if at all



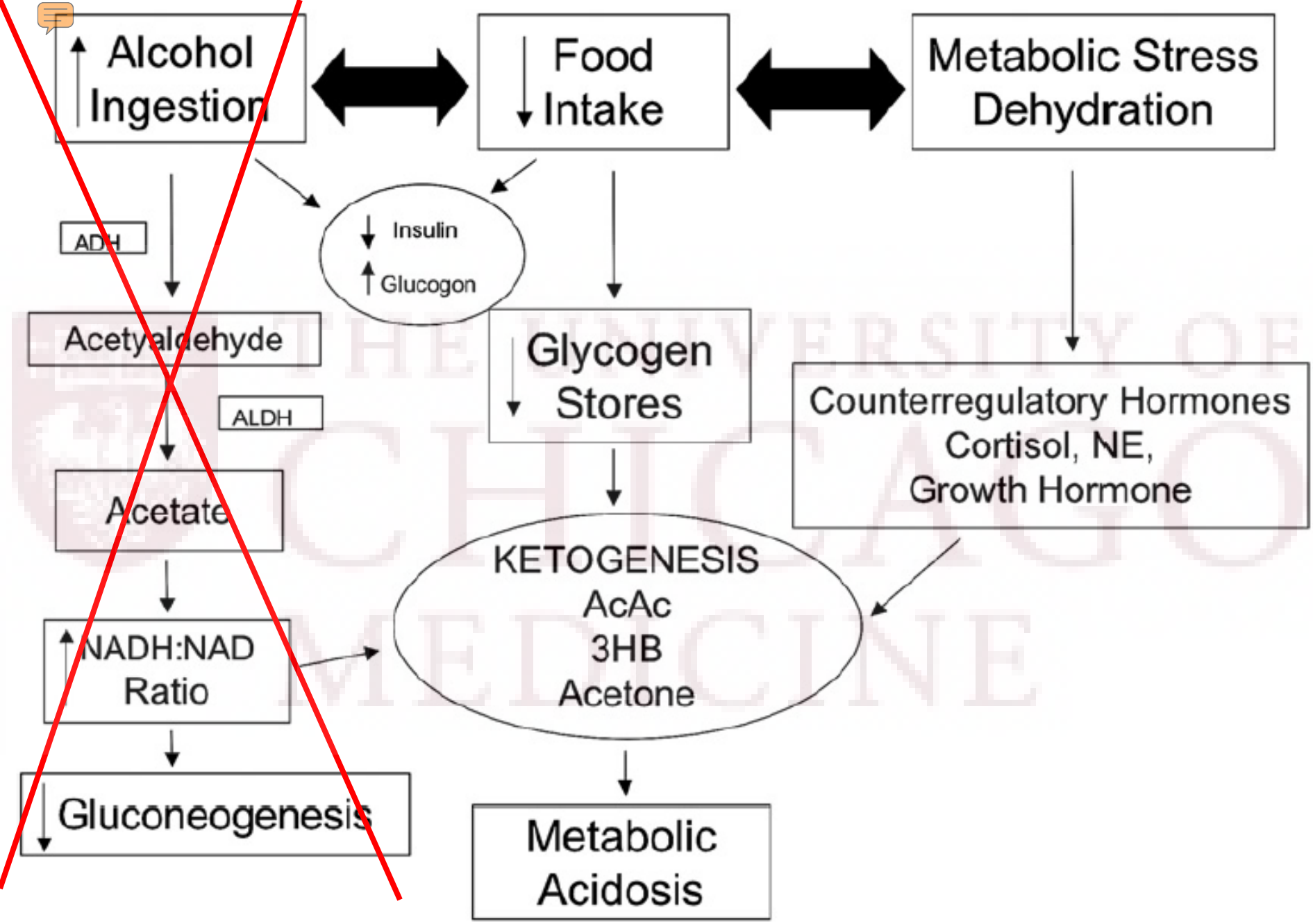
40% of new glucose

Remaining 60% is from
-Liver
-Muscle
-RBC
-Adipose (lipolysis)

Cahill GF. Annu Rev Nutr. 2006;26:1-22.



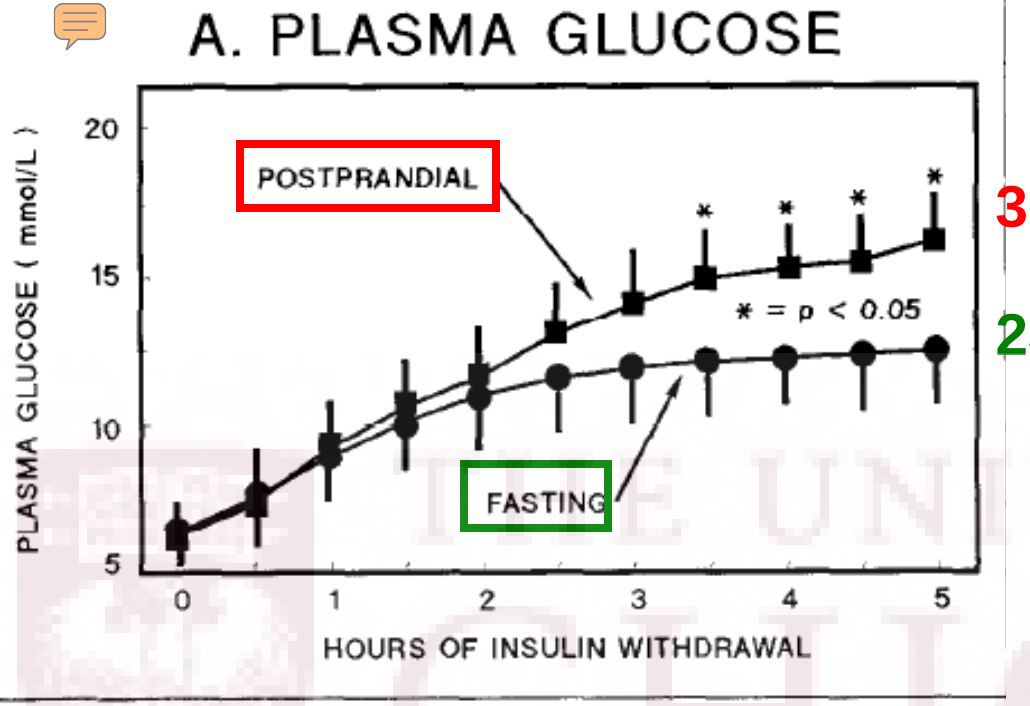
		(I)	(II)	(III)	(IV)	(V)
ORIGIN OF BLOOD GLUCOSE	:	Exogenous	Glycogen Hepatic gluconeogenesis	Hepatic gluconeogenesis Glycogen	Gluconeogenesis, hepatic and renal	Gluconeogenesis, hepatic and renal
TISSUES USING GLUCOSE	:	All	All except liver. Muscle and adipose tissue at diminished rates	All except liver. Muscle and adipose tissue at rates intermediate between II and IV	Brain, rbcs, renal medulla. Small amount by muscle	Brain at a diminished rate, rbcs, renal medulla
MAJOR FUEL OF BRAIN	:	Glucose	Glucose	Glucose	Glucose, ketone bodies	Ketone bodies, glucose



Cartwright MM et al. Crit Care Clin 2012;28:601-631.

Euglycemic Ketoacidosis

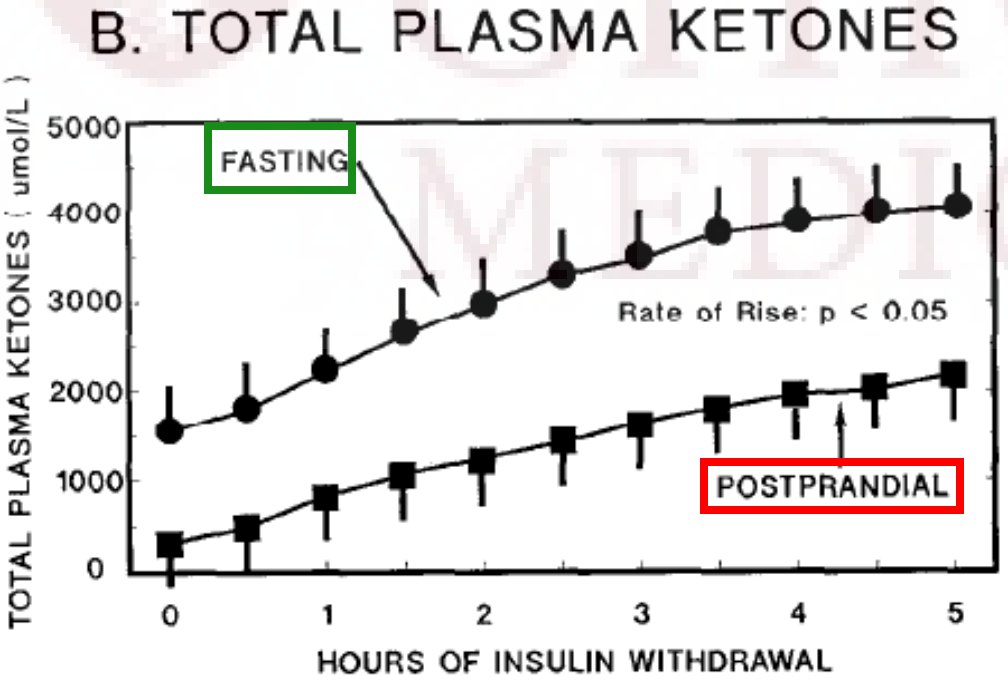
- JCEM 1993
- Hypothesis: fasting predisposes patients with T1DM to euglycemic DKA during insulin deficiency
  - 10 patients with T1DM underwent 5h insulin withdrawal at 8h postprandial and after 32h fast
- Results
  - After 32h fast: lower mean peak plasma glucose, lower rate of glucose production, higher rate of ketone production. Glucagon and Norepinephrine levels were higher.



315 mg/dL

Peak Glucose levels

234 mg/dL



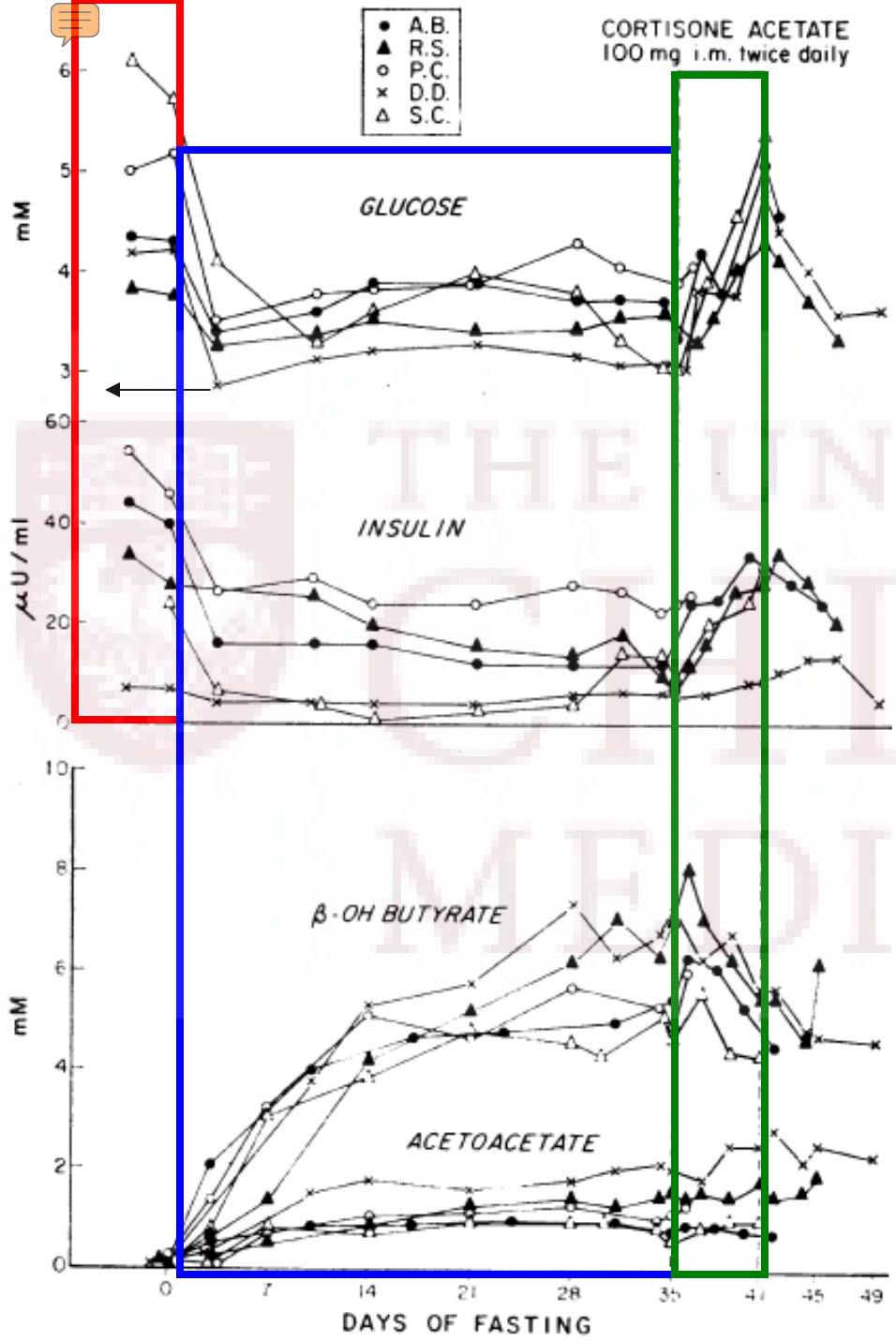
	PP	F	P-value
BL ketones umol/L	314	1532	< 0.01
Rate of rise of ketones umol/L*min	6.23	8.82	< 0.05

Euglycemic Ketoacidosis Treatment

- IVF resuscitation
- IV glucose to replete glycogen stores
  - Causes increased insulin/decreased glucagon
- Insulin repletion
- Thiamine supplementation
- Electrolyte correction

Exogenous GC after Prolonged Fast

- JCI 1973, Owen and Cahill
- 6 obese volunteers
- Objective: examine effect of exogenous GC on glucose/insulin/ketone levels after prolonged starvation
- 35 day fast, followed by 6 days of cortisone 100 mg BID



Pre-starvation period

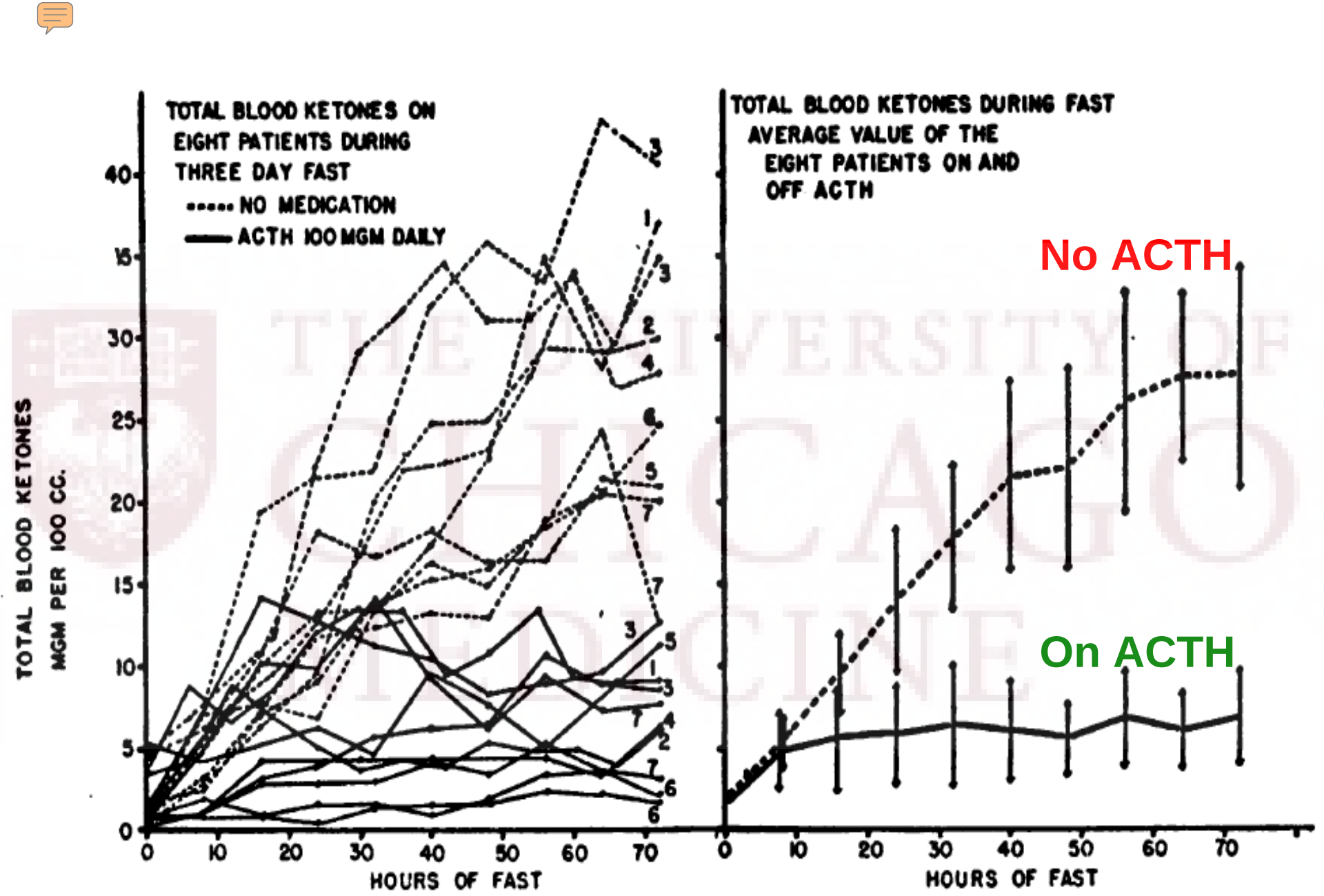
Pre-cortisone starvation

↓ glucose, insulin

↑ FFA, B-OH butyrate and AcAc

6 days of cortisone

↑ glucose and insulin



Kinsell LW, et al. JCI 1951;30;1491-1502.

Effect of ACTH on Fasting-Induced Hyperketonemia in a Diabetic

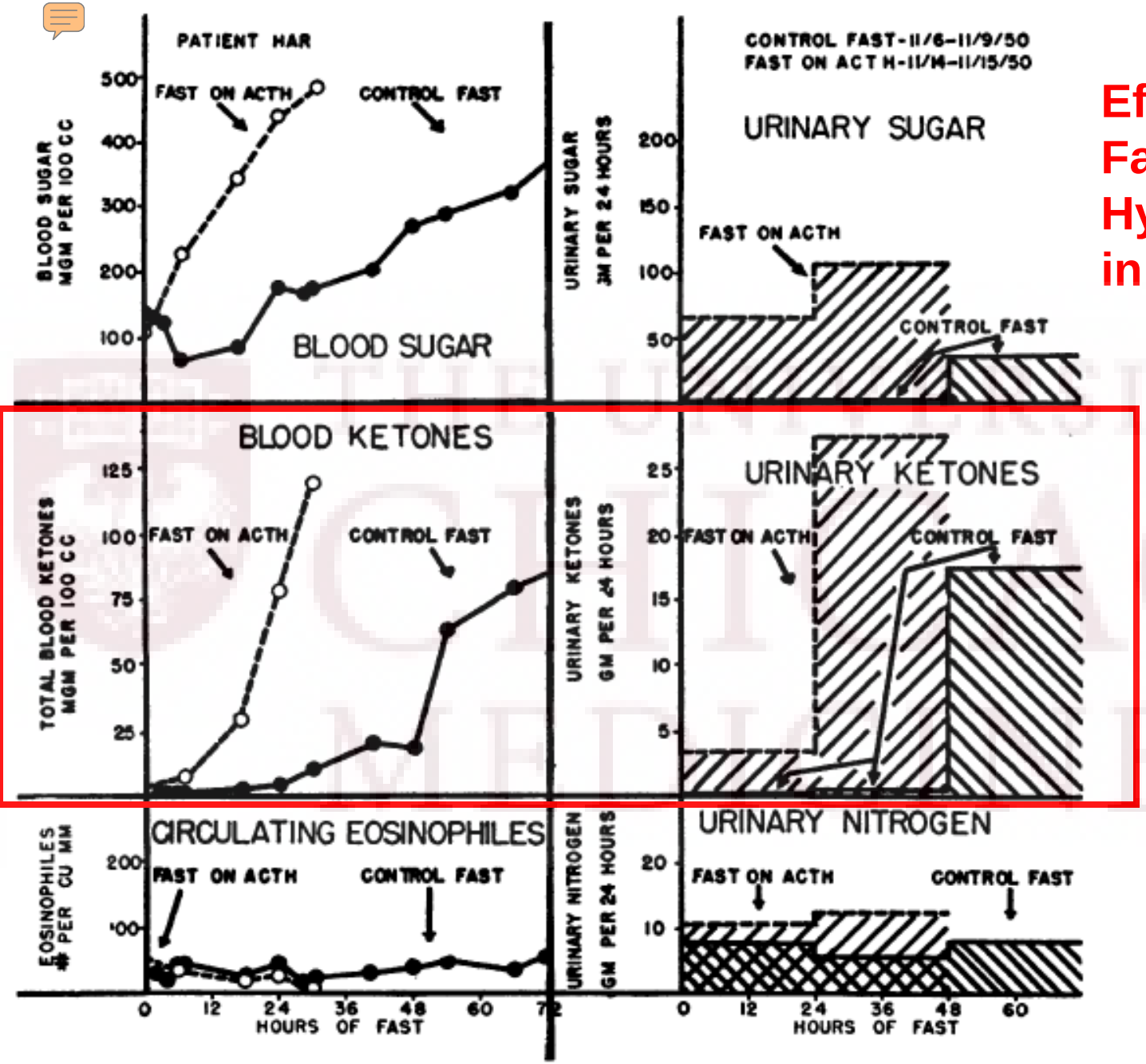


FIG. 12. EFFECT OF ACTH UPON FASTING-INDUCED HYPERKETONEMIA IN A SEVERE DIABETIC

Take Home Points

- Keep LADA in the differential
- Pathophysiology of starvation ketosis
- Identification and management of euglycemic ketoacidosis, precipitated by starvation
- Glucocorticoid effect on hyperketonemia in diabetics vs non-diabetics

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