A middle age Diabetic woman with "DTX 32"

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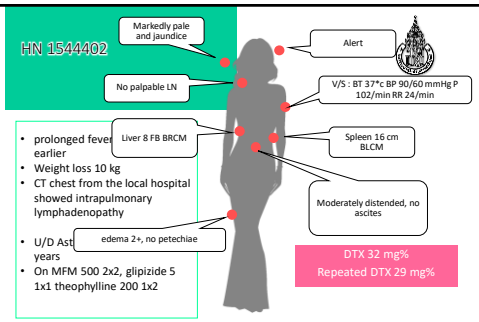


- prolonged fever earlier
- Weight loss 10 kg
- CT chest from the local hospital showed intrapulmonary lymphadenopathy
- U/D Ast years
- On MFM 500 2x2, glipizide 5 1x1 theophylline 200 1x2

Did the patient have hypoglycemia?

- Plasma glucose 39 mg/dl
- Cortisol 16.10 mcg/dl
- Insulin <0.002 uIU/ml
- But she was alert

Journal of Clinical Endocrinology & Metabolism, March 2009, 94(3): 709-728

Hypoglycemia

1.1. We recommend evaluation and management of hypoglycemia only in patients in whom Whipple's triad—symptoms, signs, or both consistent with hypoglycemia, a low plasma glucose concentration, and resolution of those symptoms or signs after the plasma glucose concentration is raised—is documented (1 | ⊕⊕⊕⊕).

Evaluation and Management of Adult Hypoglycemic Disorders:

An Endocrine Society Clinical Practice Guideline

In the absence of Whipple's triad, the patient may be exposed to unnecessary evaluation, costs, and potential harms, without expectation of benefit.

Could her asymptomatic state be "hypoglycemia unawareness"

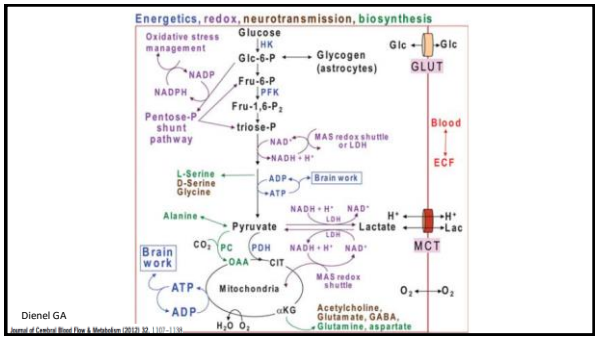
- Frequent hypoglycemia
- Delayed or blunted neurogenic alarm
- May be triggered by exercise or sleep
- Neuroglycopenic symptoms persist

If not "hypoglycemia unawareness"
Why she was alert at that low PG

Not all low plasma glucose are hypoglycemia

	Insulinoma ($n = 7$)	Normal individuals ($n = 5$)
Number of measurements	23	21
Sex (m/f)	2/5	0/5
Age (years)	51 ± 11 (33–69)	48 ± 17 (28–62)
BMI (kg m^{-2})	26 ± 4.4 (19.5–34.2)	22 ± 3.6 (16.4–26)
Test duration (h)	23 ± 10 (8–40)	59 ± 10 (44–72)
Glucose (mmol L^{-1})	2.3 ± 0.2 (1.8–2.5)	2.4 ± 0.1 (2.1–2.5)
Insulin (pmol L^{-1})	197 ± 116 (44–458)	48 ± 24 (15–109)
Insulin to glucose ratio	85 ± 49 (19–183)	20.3 ± 10 (6–47)

Waesli P et al J Intern Med 2002;252:504-9



Initial investigations

WBC 36950
Hct 20.6%
Platelet 20,000

PMN 56
Band 6
Lymph 10
AtypL4
NRBC 3
Blast +
Promono 16

DB 6.02
TB 7.33
SGOT 119
SGPT 12
ALP 153
TP 4.9
Alb2.0

pH 7.4

Lactate 6.2 mmol/L

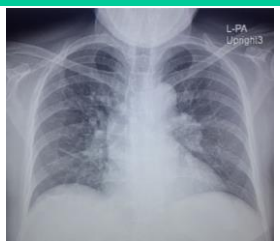
BUN 23.3
Cr 0.41
Na 135.7
K 4.21
Cl 99.8
TCO2 12.7

Corrected Ca 8.7
P 1.5
Uric 4.1

LDH 19666 U/L

PT NR 3.07

Chest X-ray



Problems list

Prolonged fever with

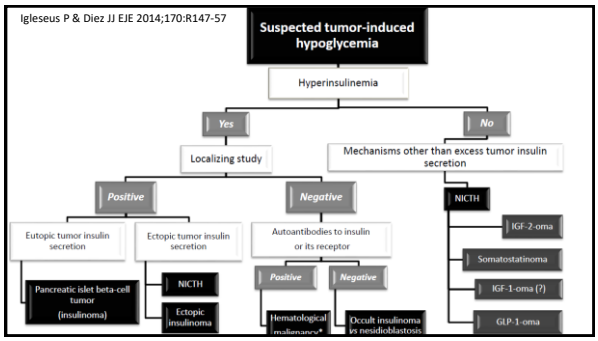
Perihilar lymphadenopathy and hepatosplenomegaly and pancytopenia

Aymptomatic hypoglycemia with suppressed insulin

What is your provisional diagnosis? Please give the most likely diagnosis

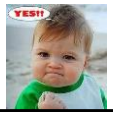
Tumor-induced hypoglycemia

Lymphoma would be the most likely cause of hypoglycemia



What is the next management for her low glucose level?

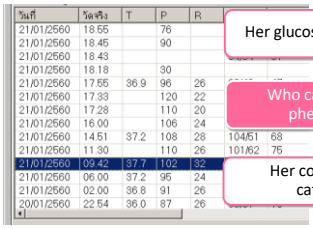
- Wait & See
  - Wait for what
  - If "what" happen, means?
  - Wait for how long
- IV & oral glucose
  - In addition glucose, what else is of special concern



Hypoglycemia management

Time	CPG	IV fluid	Clinical condition
12.00	54	50%dextrose IV push 10%DNS rates 60ml/hr	Alert
13.00	112	10%DNS rates 60ml/hr	Alert
16.00	36	50%dextrose IV push 10%DNS rates 80ml/hr	
17.00	73	10%DNS rate 100ml/hr	Coma Cardiac arrest!

What was happened to her ?



Her glucose level improved

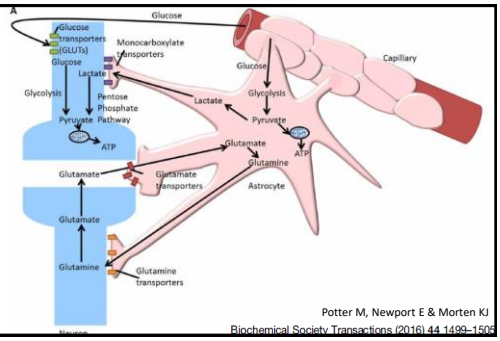
Who can explain this phenomenon?

Her condition went catastrophy

Verdict

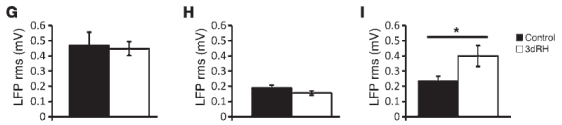
Extensive diffuse large B-cell Lymphoma involved liver, spleen and bone marrow

ABG at 18.00 pH 6.658
Lactate 17 mmol/L



Potter M, Newport E & Morten KJ
Biochemical Society Transactions (2016) 44 1499–1505

Lactate preserves neuronal response in repeated hypoglycemic animals



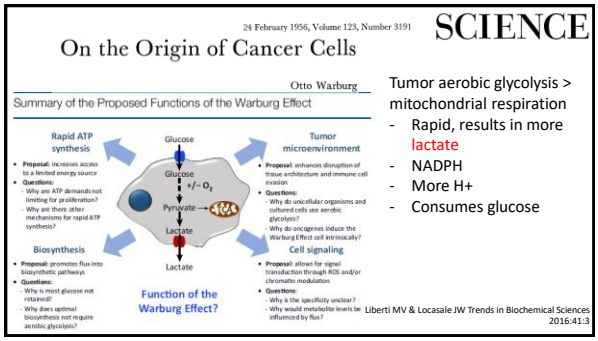
Local field potential response, G = euglycemic clamp, H = hypoglycemic clamp, I = hypoglycemic clamp + lactate infusion

Herzog RI et al JCI 2013;123:1988-98

Brain is amazing

- Glucose is the main fuel
- If prolonged fast, ketone is used
- If wants to preserve glucose, lactate could be used

But why more lactate and hypoglycemia

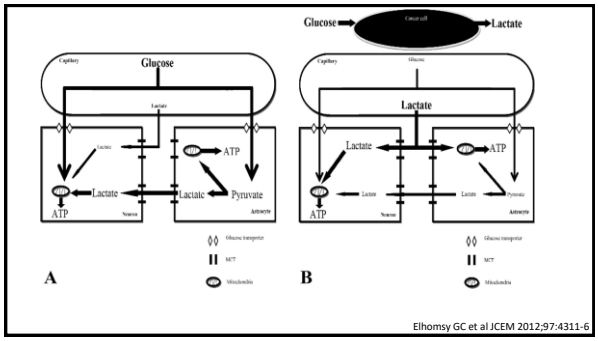


Tumor aerobic glycolysis > mitochondrial respiration

- Rapid, results in more lactate
- NADPH
- More H+
- Consumes glucose

Liberti MV & Locasale JW Trends in Biochemical Sciences 2016:41:3

PET scan

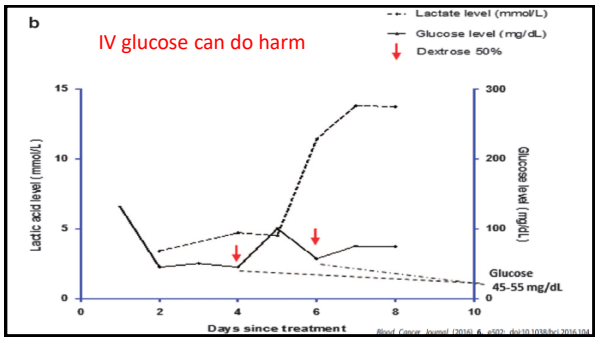


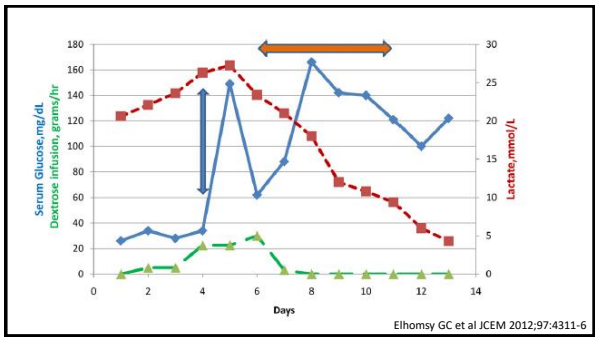
Elhomsy GC et al JCEM 2012;97:4311-6

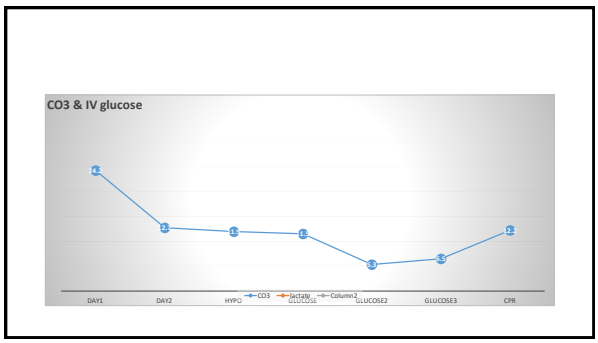
Warburg effect

- Cancers favor glycolysis: hepatoma, ascites, brain, erythroid
- Tissues favor glycolysis: erythrocytes, macrophage, platelet, kidney, endothelium, proliferating thymocytes, coronary smooth muscle
- PET scan uses this concept

X.L. Zu, M. Guppy / Biochemical and Biophysical Research Communications 313 (2004) 459–465







Coarse of her PG and lactate

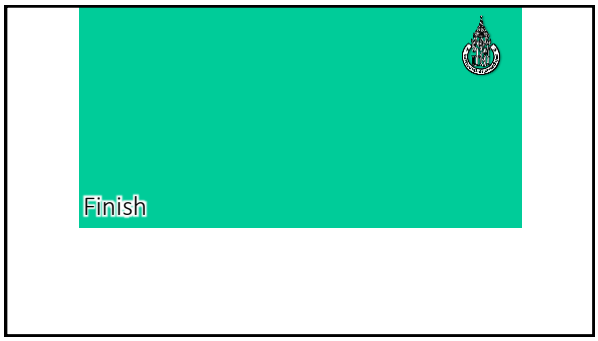
	1	6	7	8	9	12	13	16	17	17.30	18	19
Pg	260	32	65	67	131	54	112	36	72	261	104	67
Lactate	6.2							17			22	25
gluc		/		/		/		/				

Take home messages

- Hypoglycemia not low plasma glucose level, Whipple's triads required
- Brain can use many fuels
- Many tumors consume glucose and produce lactate, when more glucose provided, devastating hyperlactatemia may occur, Warburg effect

"Hyper-Warburgism," a Cause of Asymptomatic Hypoglycemia with Lactic Acidosis in a Patient with Non-Hodgkin's Lymphoma

Georges C. Elhomsy, Vijay Eranki, Stewart G. Albert, Mark J. Fesler, Stacey M. Parker, Amanda G. Michael, and George T. Griffing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