

Nothing Rhymes With LDH

Dr Leonard Minuk

Presenter Disclosure

- Faculty / Speaker's name:
 - Leonard Minuk
- Relationships with commercial interests:
 - Grants/Research Support: CancerCare Manitoba Foundation, Merck, GSK
 - Speakers Bureau/Honoraria: None
 - Consulting Fees: None
 - Other: I am not a biochemist or an expert in rhyming



Mitigating Potential Bias

- Not Applicable

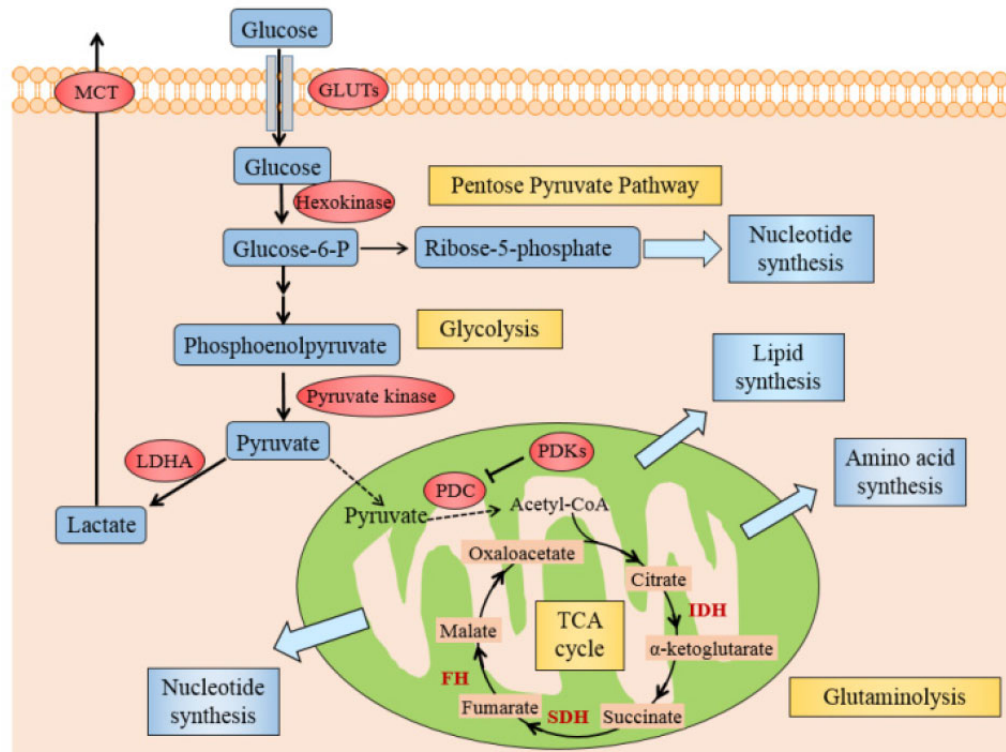
Learning Objectives

- 1) Describe how to work up abnormal LDH values
- 2) Understand the prognostic implications of elevated LDH

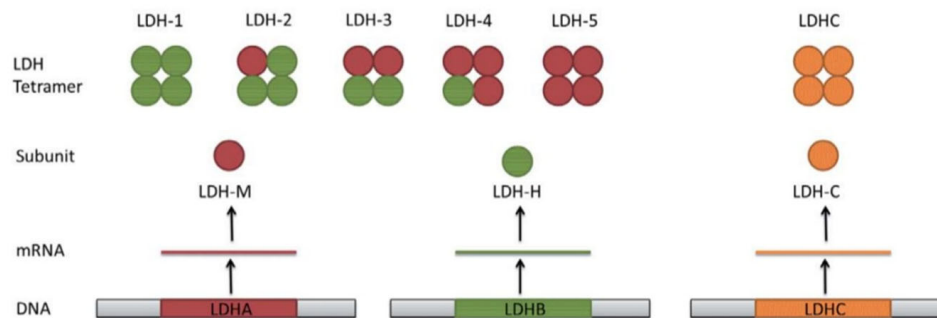
Case Presentation

- 54 male previously healthy presents with 4 months of progressive abdominal distention/bloating and pain
- 20kg weight loss and drenching night sweats, no fever
- Physical exam – abdominal fullness and vague mass; no peritonitis
- CBC
 - WBC 10.5, neutrophils 8.08, hemoglobin 90, platelets 426
- Chemistry
 - Creatinine 76, **Calcium 3.03**, albumin 27, **LDH 4263**, ALT 49, AST 92, GGT 157, alkaline phosphatase 110
- Why is the LDH high?
- How do we investigate?

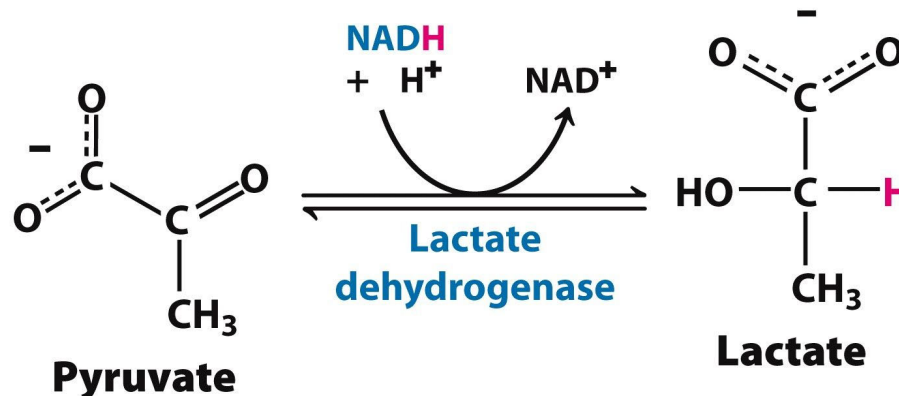
Glucose Metabolism



LDH Isoenzymes



- LDH-1 (4H): Heart, Red Blood Cells, Brain
- LDH-2 (3H1M): Red Blood Cells, Heart
- LDH-3 (2H2M): Lung, Lymphocytes, Spleen
- LDH-4 (1H3M): Liver, Skeletal Muscle
- LDH-5 (4M): Liver, Skeletal Muscle
- LDH-C (4C): Testicles



Unnumbered 16 p468
Biochemistry, Seventh Edition
© 2012 W. H. Freeman and Company

- Sample drawn in a lithium heparin plasma separator tube
- Roche assay used in Winnipeg and Brandon hospitals and Dynacare
 - Measures the conversion of lactate to pyruvate by increase in NADH spectrophotometrically
- Ortho assay used by rural sites
 - Measures the conversion of pyruvate to lactate by decrease in NADH spectrophotometrically
- Reported in units of enzyme activity per litre or U/L



<https://apps.sbgf.mb.ca/labmanual/test/>

Roche Method

Age	Normal Range (U/L)
0-4 wk	290 - 800
5 wk – 12 mo	180 - 450
13 mo – 8 y	190 - 400
9 – 14 y	190 - 325
15 – 16 y	130 - 280
17 – 50 y	63 - 200
≥ 51 y	120 - 230

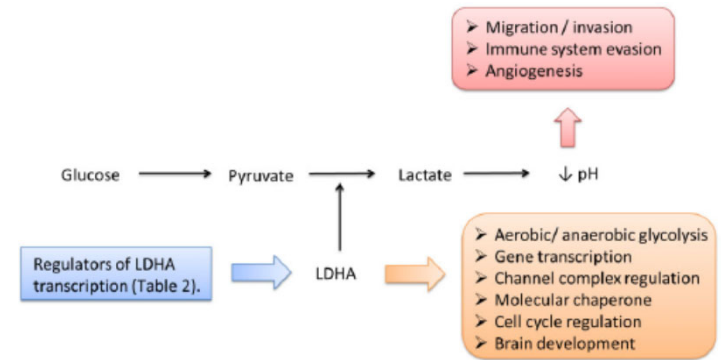
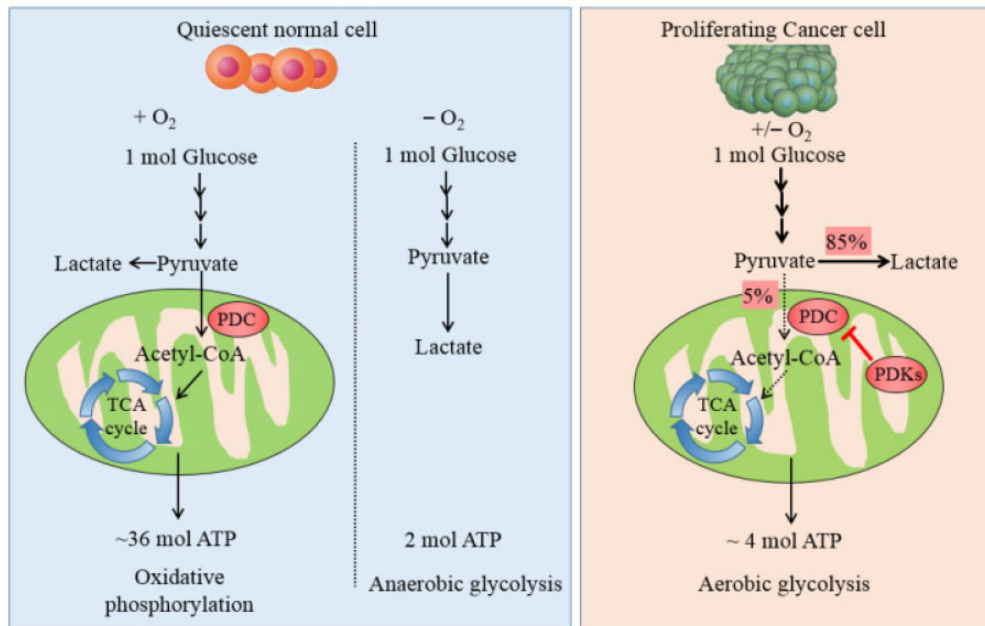
Ortho Method

Age	Normal Range (U/L)
0-4 wk	632 - 1839
5 wk – 12 mo	372 - 1011
13 mo – 8 y	395 - 892
9 – 14 y	395 - 715
15 – 16 y	253 - 608
17 – 50 y	95 – 419
≥ 51 y	230 - 490

Reasons for elevated LDH

- ***Lab Artifact***
- Liver Injury
- Tissue Ischemia (heart/lung/kidney/muscle)
- Hemolysis
- Cancer (esp widespread metastasis and aggressive hematologic malignancies)
- B12 Deficiency
- Infection

Why So High in Cancer?

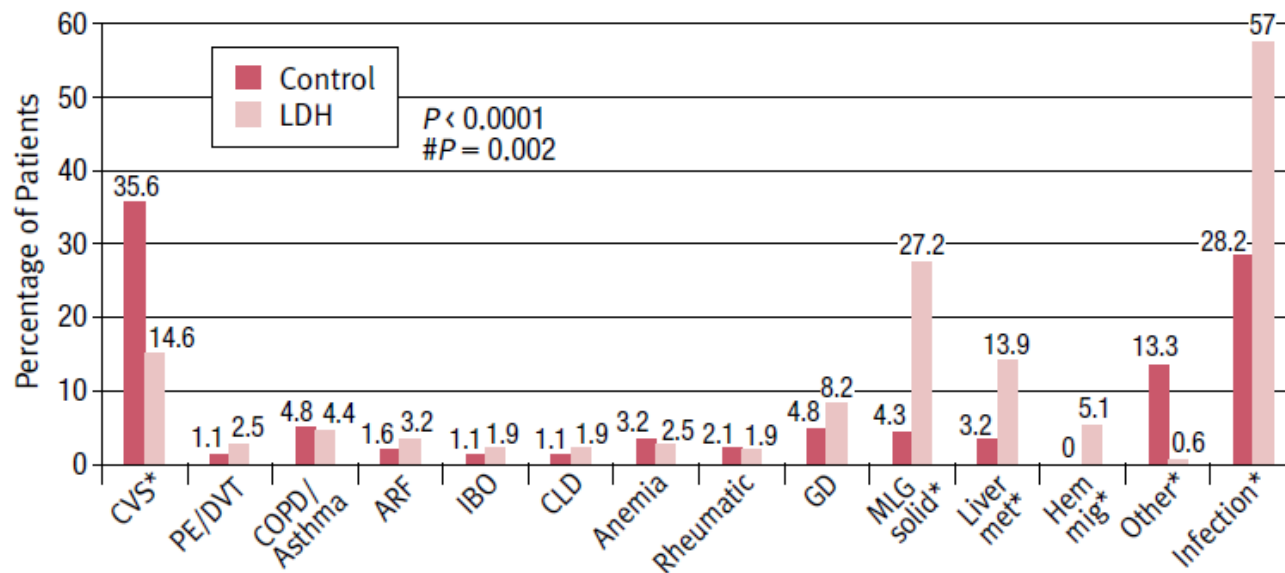


Warburg Effect

What About A REALLY high LDH?

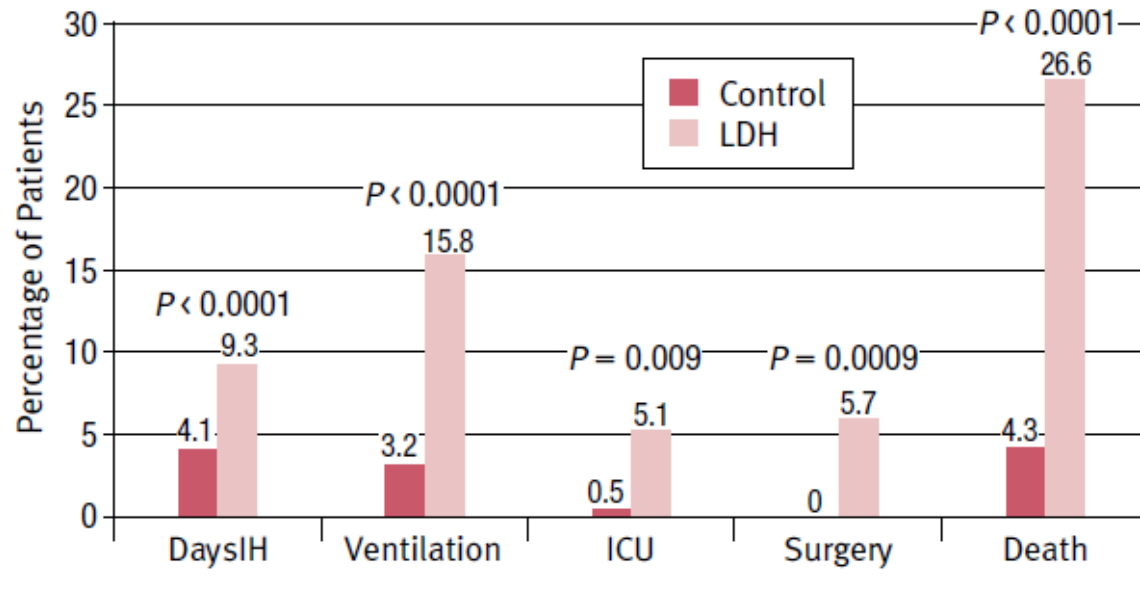


Reasons For Markedly Elevated LDH



Study of 158 inpatients with LDH > 800 compared to 188 consecutive controls with normal LDH

LDH: Marker of Disease Severity

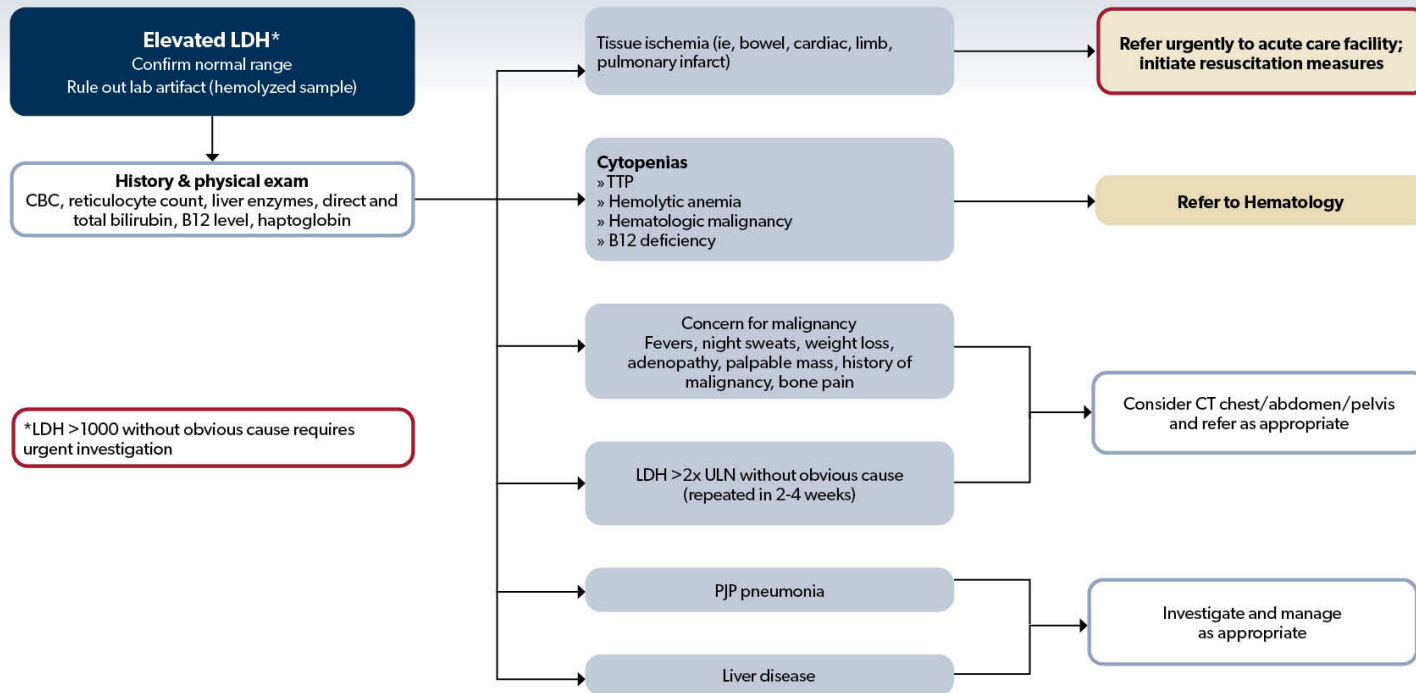


Prognosis in Cancer

- Prognostic Scoring Systems Including LDH
 - Non Hodgkin lymphoma – IPI score, FLIPI score
 - Mantle Cell Lymphoma - MIPI
 - Multiple myeloma – R-ISS
 - Testicular cancer – TNM(S)
- Independent negative prognostic marker in metastatic prostate cancer, renal cell carcinoma, melanoma

Case Presentation

- 54 male previously healthy presents with 4 months of progressive abdominal distention/bloating and pain
- 20kg weight loss and drenching night sweats, no fever
- CBC
 - WBC 10.5, neutrophils 8.08, hemoglobin 90, platelets 426
- Chemistry
 - Creatinine 76, **Calcium 3.03**, albumin 27, **LDH 4263**, ALT 49, AST 92, GGT 157, alkaline phosphatase 110
- Why is the LDH high?
- How do we investigate?



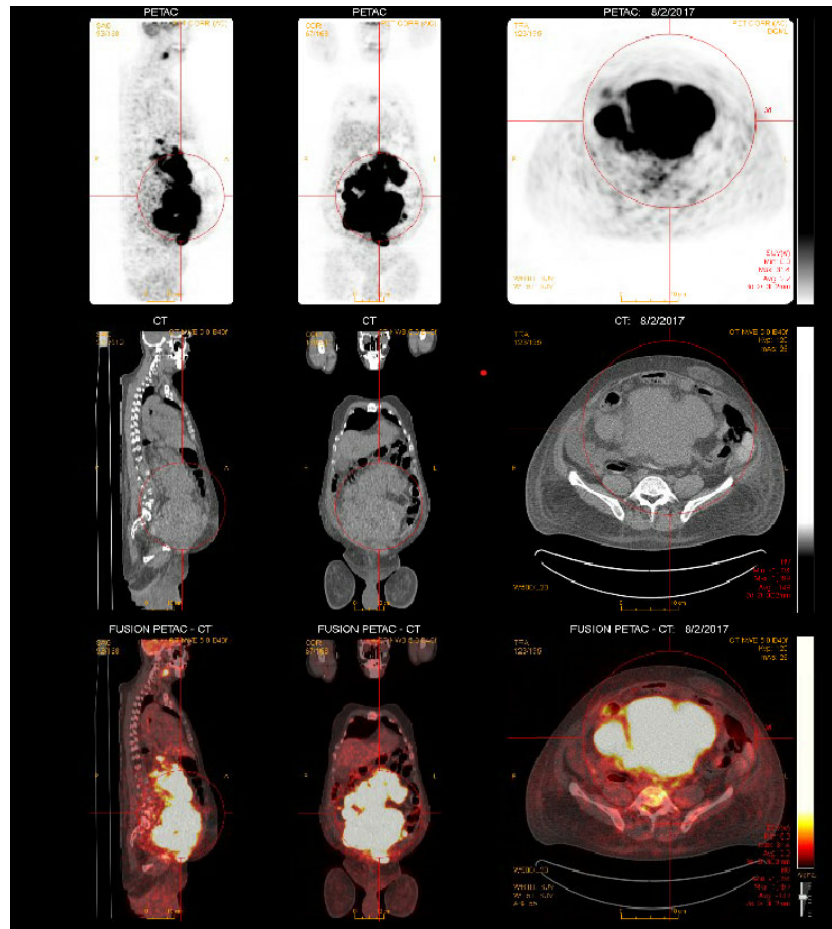
TTP = Thrombotic thrombocytopenic purpura
PJP = Pneumocystis jirovecii pneumonia

LDH = lactate dehydrogenase

© Blood Disorder Day
Pathways are subject to clinical judgement and actual practice patterns may not always follow the proposed steps in this pathway.

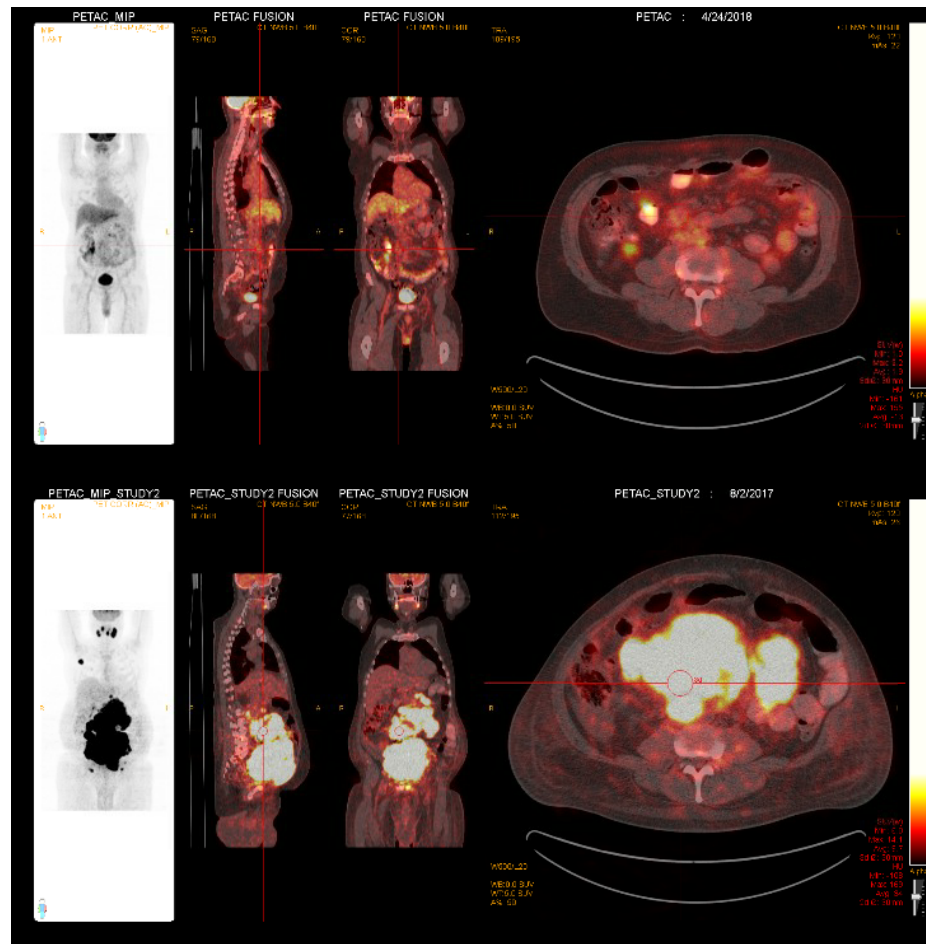


CT abdomen
15.7cm X 13.1cm X 12.9cm intra-abdominal mass



Case Resolution

- CT guided biopsy of abdominal mass
- Diffuse large B cell lymphoma
 - CD20, CD45, BCL2, BCL6, PAX5 and MUM1 positive
- Treated with 6 cycles of R-CHOP chemotherapy with rapid resolution of symptoms and normalization of LDH



Why Order an LDH?

- LDH is a VERY non-specific test so is not appropriate for general screening purposes
 - Use the appropriate specific test (i.e. liver enzymes, troponin, etc)
- Indications:
 - **Investigation of unexplained cytopenias**
 - **Investigation of potential or confirmed hematologic malignancy**

Take Home Messages

- There are multiple causes of elevated LDH
- Know your local normal range and rule out lab artifact (hemolyzed sample)
- Elevated LDH is a **non-specific** sign of tissue injury or rapidly growing cells
- Markedly elevated LDH is **BAD**

An LDH Limerick

By Donald Houston

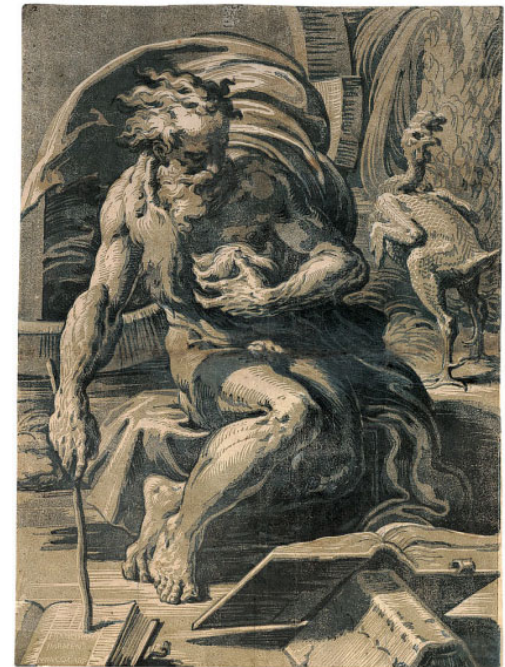
Said the well-known Greek cynic, Diogenes

“Here’s a word I can’t rhyme: ‘dehydrogenase’

Even harder is ‘lactate’

My best efforts are crap-rate!”

(Please excuse me for all improprieties)



References

- Valvona et al. The Regulation and Function of Lactate Dehydrogenase A: Therapeutic Potential in Brain Tumor. *Brain Pathology*, 2015.
- Zhang et al. Targeting Tumor Metabolism For Cancer Treatment: Is Pyruvate Kinase Dehydrogenase a Viable Anticancer Target. *International Journal of Biological Sciences*, 2015
- Erez et al. Diagnostic and Prognostic Value of Very High LDH in Admitted Medical Patients. *Israel Medical Association Journal*, 2014
- Petrelli et al. Prognostic role of lactate dehydrogenase in solid tumors: A systematic review and meta-analysis of 76 studies. *ACTA Oncologica*, 2015

Thank you

Iminuk4@cancercare.mb.ca