The Weekly Probe

24th March 2017 **Volume 14 Issue 11**

Hand Hygiene- a reminder on hand hygiene. Try to protect yourself and your patients- remember to clean your hands prior to going to see the patient and before you leave that clinical area.

THIS WEEK

LACTATE + LACTIC ACIDOSIS

With increasing use of point of care testing such as blood gas machines, we are becoming exposed to early pathology results, one of which is lactate. Similar to any result we should not treat the lactate alone as it is "just a number", and any pathology result should be put in context: what is the history , what do you find on examination and what have you found on the other examinations? In addition what are the levels doing as a result of our treatment?

What about lactate, a result more commonly reviewed- how is it produced and metabolised – and as a result, what do elevated levels signify?

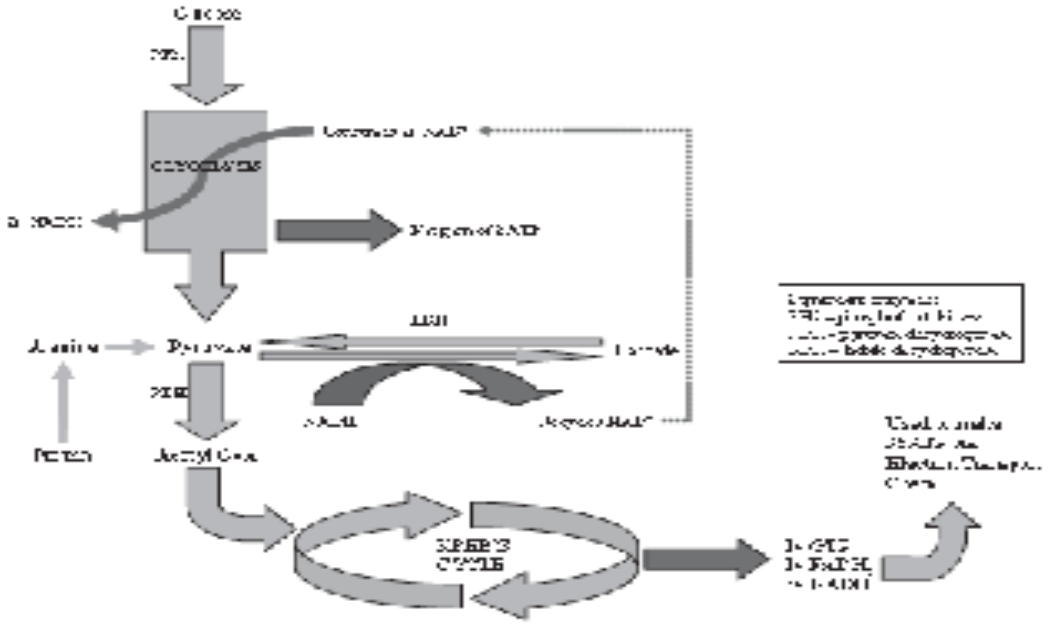
Lactate levels are indicative of the balance between lactate production and metabolism. Apologies for the below diagrams but they are key in understanding lactate.
As they show, lactate is a waste product for one cell yet a useful source of energy for another.

Production – Glucose is metabolised to pyruvate , which in aerobic conditions is further metabolised to acetylCoA which is used in the Krebs cycle. However in anaerobic conditions , the pyruvate is metabolised to lactate by LDH. (lactate and lactic acid are used interchangeably as the lactate dissociates almost completely) .
Tissue sources include RBCs, hepatocytes, myocytes and skin. Basal production is ~ 1300mmol/d.

It was thought that lactate production involved the production of lactic acid which dissociates into lactate and H+. However it has been found that lactate production actually consumes H+ thus mitigating any intracellular acidosis.
As discussed a couple of weeks ago, the alternative thought is based on the Stewart approach in which pH is based on 3 factors- the pCo2, the weak acid concentration (albumin) and the strong ion difference (esp Na and Cl)- the H+ concentration is merely a response the a change in these factors.

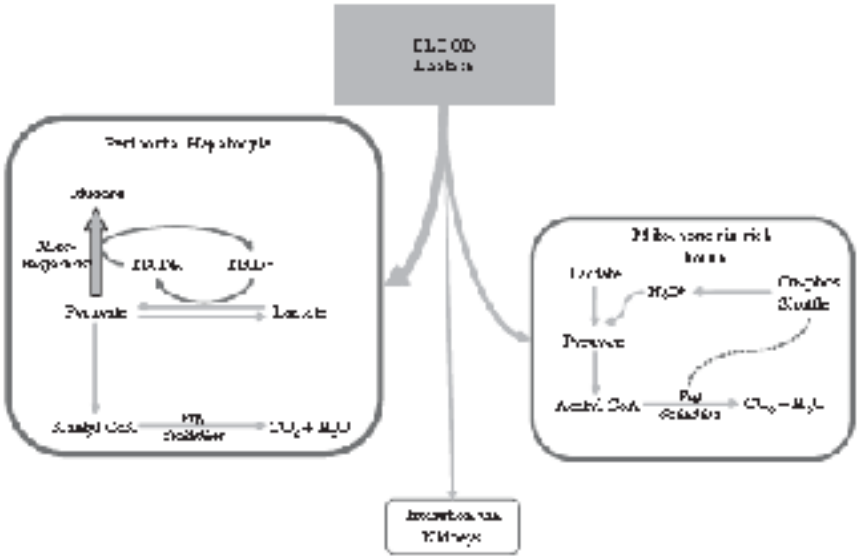
1. If difference shrinks (i.e. relatively more Cl) more acidotic - Principle of electrical neutrality requires more H+ to offset the additional Cl
2. If difference increases (i.e. relatively more Na) more alkalotic - Principle of electrical neutrality requires more bicarb to offset the additional Na

In the case of lactate, this is a strong anion reducing the strong ion difference.(see links below re strong ion difference) leading to acidosis.



Metabolism / excretion- the liver removes ~ 70% of lactate – the metabolism process results in the production of pyruvate then glucose and with oxidation to CO2 and water. The liver receives 25% of cardiac output- portal vv 75% of liver flow and 50-60% of oxygen. When blood flow is reduced to ~ 25% of normal there is a reduction in lactate clearance. When shocked, the liver produces lactate rather than using lactate for glucose production.
Muscle , cardiac myocytes and renal tubules (~30%) metabolise the rest of the lactate . Less than 5% of lactate is renally excreted (only significant when severe hyperlactataemia).

Lactate is transported from areas of production eg muscle to areas of uptake via RBCs and plasma.



NORMAL LEVELS ARE LESS THAN ABOUT 2.0 MMOL/L (The average normal arterial blood lactate level is approximately 0.6 mmol/L and the venous level is slightly higher at 0.9-1.0 mmol/L, but overall, arterial and venous lactate levels correlate well.)

To minimize variations in measurement, ideally blood samples should be drawn without a tourniquet (realistically without a prolonged tourniquet) and processed quickly.

Bloods – as noted a couple of weeks ago when we discussed metabolic acidosis, lactic acidosis is normally associated with a raised anion gap (extra H results in loss of HCO3 with widening of gap). However lactic acidosis may occur with a normal AG or with a normal / elevated pH in the context of a mixed acid-base disturbance. Use the delta gap which compares the change in anion gap in relation to the change in bicarb to help differentiate the causes – USE MEDCALC on CIAP via Firstnet to help with the calculation).

Causes- considering the production and metabolism of lactate, elevated levels occur when production exceeds consumption. We can categorize elevated levels as:

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- Type A - secondary to increased production in conditions of hypoperfusion and hypoxia (type A lactic acidosis), or
- Type B - increased production or decreased clearance not due to hypoperfusion and hypoxia

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Type A lactic acidosis—due to hypoperfusion and hypoxia—occurs when there is a mismatch between oxygen delivery and consumption, with resultant anaerobic glycolysis- increased production of lactate from pyruvate.

- Increased glycolysis
    - Hypoxaemia, anaemia, hypoperfusion, shock , carbon monoxide, cyanide poisoning. (ie systemic shock (all causes) or regional shock (eg limb , mesenteric etc).
    - Endogenous and exogenous administered catecholamines (ie inotropes and Beta agonists that we give patients eg salbutamol) also stimulates glycolysis.
- Decreased liver perfusion (decreased clearance) – shock

Type B - Increased production without tissue hypoxia- Rarer than type A

- Increased glycolysis (Increased production) - Inborn errors of metabolism. Catecholamines as above + phaeo – haematologic malignancies and solid tumours
- Metformin (Decreased clearance) - this reduces hepatic and renal gluconeogenesis which produces NAD , which in turn is required to convert lactate to pyruvate. Alcohol intoxication and type 1 DM can also impair this gluconeogenesis.
- Hartmann' s solution – there is a shift away from the use or normal saline due to the risks of hyperchloraemic metabolic acidosis , chloride load and renal dysfunction. Hartmann's or Ringers lactate is used more often yet this has 29mmol/L (c/w production of 1300mmol/d) and until metabolised this may result in acidosis.
- Thiamine deficiency – reduces pyruvate dehydrogenase activity (PDH on the first diagram)
- Severe liver disease – decreased clearance
- Alanine formation (increased production- see also diagram 1) – malignancy , "critical illness"
- Enzyme defects – increased production – decreased clearance

Note that the two mechanisms can coexist eg septic shock where elevated levels may be related to more to increased pyruvate production than tissue hypoxia.

D-Lactate levels- lactate exists in 2 isomers – L & D-lactate, yet our tests only look for the L isomer. The D-lactate is produced by carbohydrate metabolising organisms in the gut and as a result there are clinical scenarios where the D-lactate may be elevated due to increased carbohydrate delivery to the large bowel eg short gut syndrome. It is also thought to contribute to the acidosis in DKA.

Treatment- Therefore the treatment of a patient with an elevated lactate will differ depending on the underlying mechanism of the lactate elevation: history, examination and other investigations. Similar to many other presentations look at the DDs and consider the worst case scenario and initially with critically ill patients, this is a type A lactic acidosis. The presence of lactate levels > 5mmol/L i association with an acidosis pH< 7.35 carries a mortality of up to 80%. Look for causes of decreased oxygen delivery.

If you are looking at a type A lactic acidosis, aim to improve perfusion and match oxygen consumption with fluids, bloods, and vasopressors or inotropic agents, or both. Also look at the underlying cause and treat – antibiotics, surgical intervention etc.

Treatment of type B involves more specific management, such as discontinuing offending medications or supplementing key cofactors for anaerobic metabolism.

Remember that the higher the lactate level and the slower the rate of normalization (lactate clearance), the higher the risk of death. It has a prognostic role independent of organ failure and BP measures. Treat and reassess the patient and the results.

Refs- Seheult J, Lactic acidosis: an update *Clin Chem Lab Med* 2017; 55(3): 322-333 / Reddy AJ , Lactic acidosis: Clinical implications and management strategies *Cleveland Clinic Journal Medicine* 2015 Sep;82(9):615-624. / Phypers B Lactate physiology in health and disease *Continuing education in anaesthesia, critical care and pain* 2006; 3(6): i28-32
- http://www.anaesthesiamcq.com/AcidBaseBook / http://www.acid-base.com/strongion.php

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LEMIERRE SYNDROME

A 18yo man presents with throat pain with swelling around the angle of the mandible. The best case scenario is tonsillitis with cervical adenopathy, yet there are other “nasties” to be aware of including quinsy , deep neck space infections and Lemierre syndrome.

What is this Lemierres syndrome?

This syndrome refers to thrombophlebitis of the jugular veins with distant metastatic sepsis in the setting of initial oropharyngeal infection such as pharyngitis/tonsillitis with or without peritonsillar or retropharyngeal abscess.

A high degree of suspicion in the appropriate clinical setting is essential for diagnosis.

Clinical presentation
Who? Any age group can be affected yet this is most commonly seen in previously healthy adolescents.

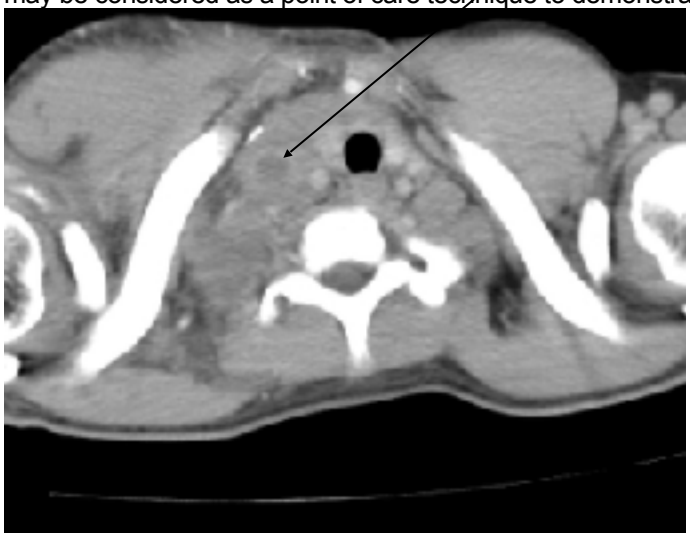
What causes it ? Most commonly this is caused by an anaerobic Gram-negative bacillus, *Fusobacterium necrophorum.* This organism is usually found in the oropharynx, gut or female genital tract, and is difficult to culture. However 1/3 are polymicrobial – including anaerobic streptococci and gram-negative anaerobes. Also reports of MRSA.

How do they present? Patients typically presents with fever, neck pain, sore throat, and painful swelling especially behind the angle of the jaw. They are usually “unwell” with trismus.

As it involves thrombophlebitis, bacteraemia and distal infective thromboembolism is common - lungs are most commonly affected (resulting in septic emboli, empyema etc), however almost any organ may be involved including joints, epidural space, meninges etc.

Diagnosis - characteristic anaerobic bacteria from blood culture may be a key finding

Radiographic features – Aim to demonstrate thrombophlebitis of the jugular veins. Contrast-enhanced CT is considered gold-standard as it will demonstrate the soft tissue changes (source and complications) and can be extended to the chest to assess septic emboli and intrathoracic thrombus extension. Ultrasound may be considered as a point of care technique to demonstrate the thrombosis .



Refs- Lemierre syndrome, Waterman, Paed Emerg care 23 (2), Feb 2007 / https://radiopaedia.org/articles/lemierre-syndrome

NEXT WEEK’S CASE

42yo lady presents with chest pain and SOB. Below is a copy of the ECG. What is going on ?

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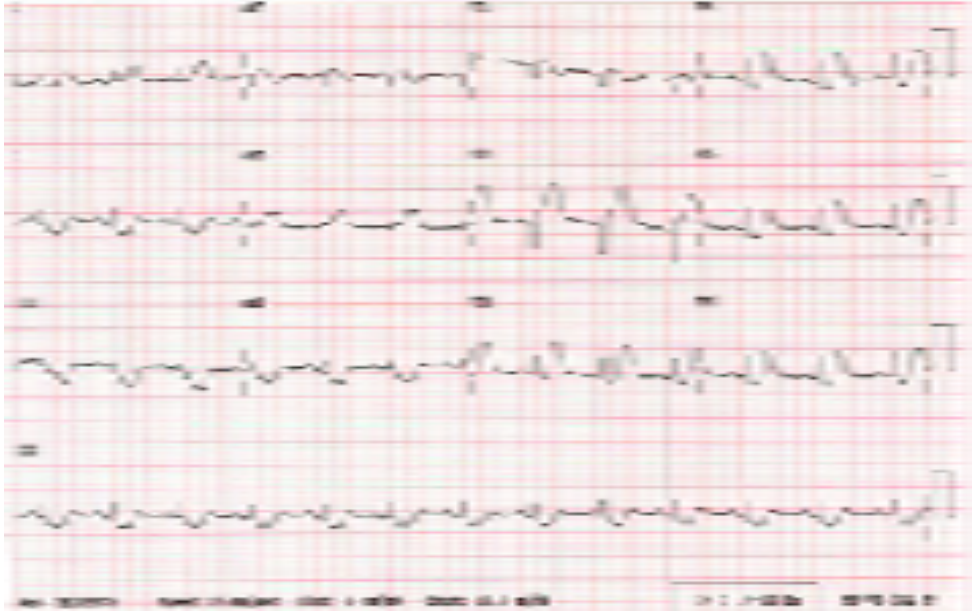
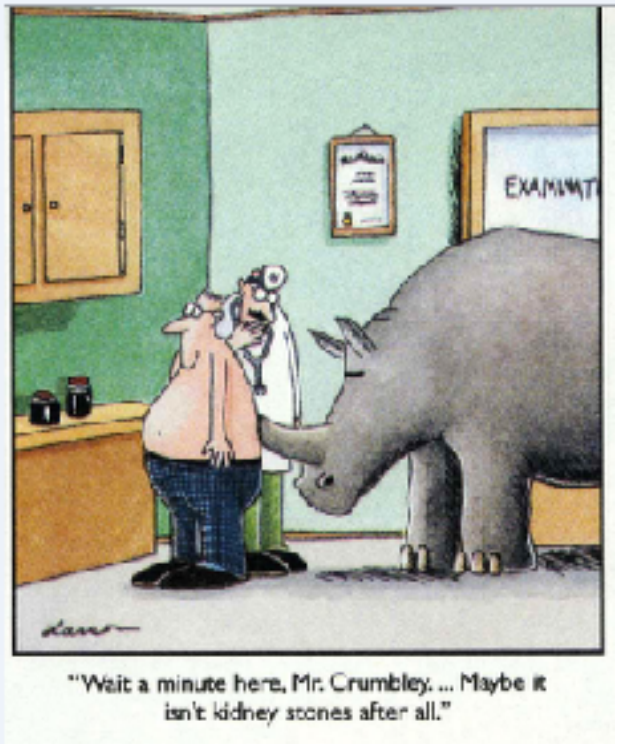


JOKE / QUOTE OF THE WEEK



Please forward any funny and litigious quotes you may hear on the floor (happy to publish names if you want)

THE WEEK AHEAD
Tuesdays - 14:30 – 15:30 Intern & JMO teaching -Thomas & Rachel Moore
Wednesday- 0800-0900 Critical Care Journal Club. ICU Conf Room / 14:30 – 15:30 Intern & JMO teaching -Thomas & Rachel Moore
Thursday 0730-0800 Trauma Audit. Education Centre / 0800-0830 MET Review Education centre / 1300-1400 Medical Grand Rounds. Auditorium.

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