

Please read this bit first

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will **not** issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: **MT-13/00142**.

Each attendee should claim **THREE** CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

CHEMISTRY LEGEND

APRIL 2013

HYPOPHOSPHATAEMIA

Hypophosphataemia is an electrolyte disturbance in which there is an abnormally low level of phosphate in the blood. The condition has many causes, but is most commonly seen when malnourished patients (especially chronic alcoholics) are given large amounts of carbohydrates, which creates a high phosphorus demand by cells removing phosphate from the blood (refeeding syndrome).

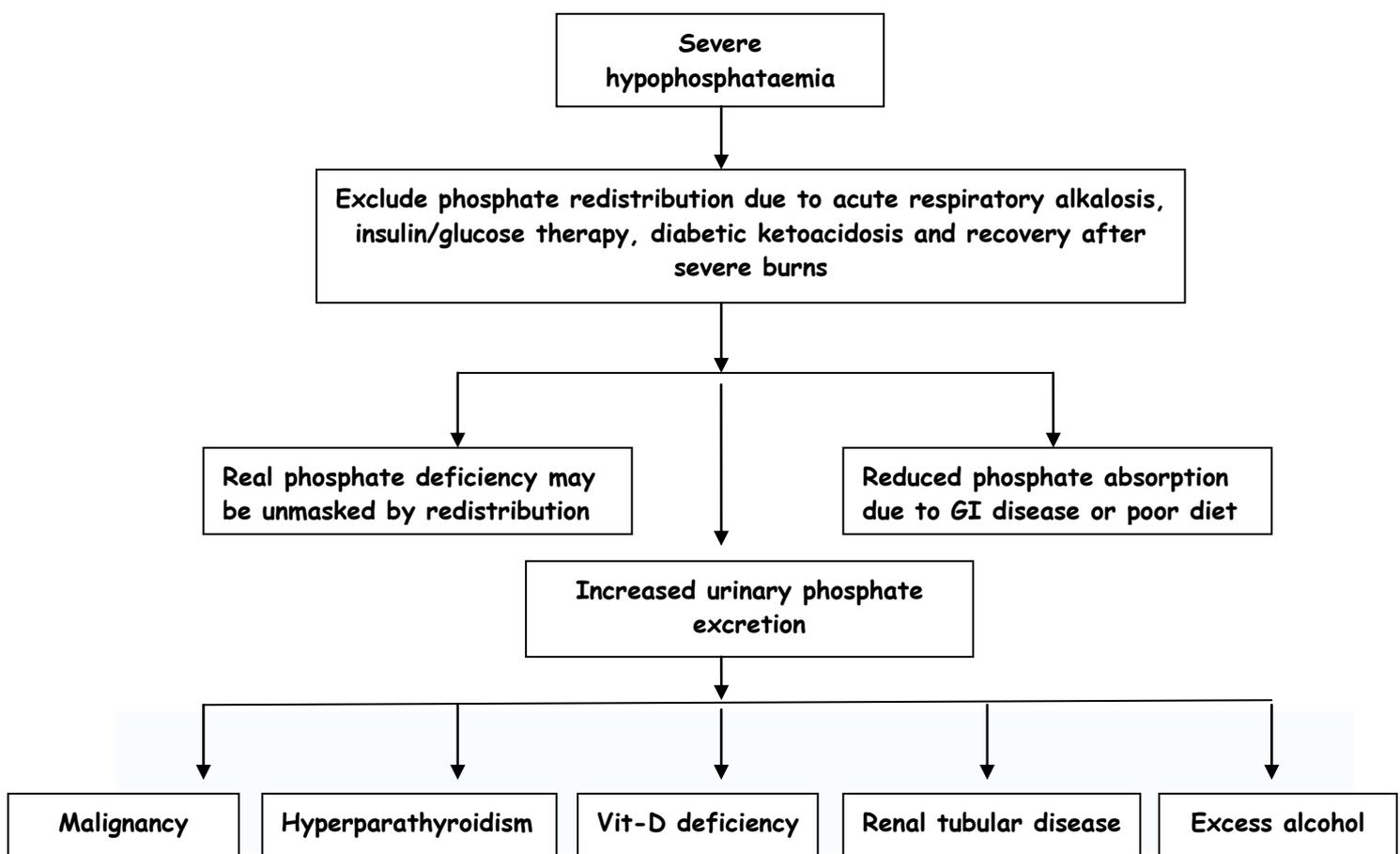
Common causes of hypophosphataemia

- **Refeeding syndrome:** this causes a demand for phosphate in cells due to the action of phosphofructokinase, an enzyme which attaches phosphate to glucose to begin metabolism of this. Also, the production of ATP when cells are fed and recharge their energy requires phosphate.
- **Respiratory alkalosis:** any alkalemic condition moves phosphate out of the blood into cells. This includes respiratory alkalemia (a higher than normal blood pH from low carbon dioxide levels in the blood) which in turn is caused by any hyperventilation (such as may result from sepsis, fever, pain, anxiety, drug withdrawal etc).
- **Alcohol abuse:** alcohol impairs phosphate absorption. Alcoholics are also malnourished with regard to minerals. In addition, alcohol treatment is associated with refeeding. The stress of alcohol withdrawal may create respiratory alkalosis, which exacerbates hypophosphataemia.
- **Malabsorption:** this includes GI damage, and also failure to absorb phosphate due to lack of vitamin D or chronic use of phosphate binders such as sucralfate, aluminum-containing antacids and (more rarely) calcium-containing antacids.
- **Phosphaturia or hyperexcretion of phosphate in the urine:** this condition is divided into primary and secondary types. Primary hypophosphataemia is characterized by direct excess excretion of phosphate by the kidneys, as from primary renal dysfunction, and also the direct action of many classes of diuretics on the kidneys.

- Primary hypophosphataemia is the most common cause of non-nutritional rickets. Laboratory findings include low-normal serum calcium, moderately low serum phosphate, elevated serum alkaline phosphatase, low serum 1,25 dihydroxy-vitamin D levels, hyperphosphaturia, and no evidence of hyperparathyroidism.
- Additionally, secondary causes, including both types of hyperparathyroidism cause hyperexcretion of phosphate in the urine.

Other rarer causes include

- Certain blood cancers such as lymphoma or leukemia
- Hereditary causes
- Hepatic failure



Pathophysiology

Hypophosphataemia is caused by the following three mechanisms:

- Inadequate intake (often unmasked in refeeding after long-term low phosphate intake)
- Increased excretion (e.g. in hyperparathyroidism)
- Shift from extracellular to intracellular space (seen in treatment of diabetic ketoacidosis, refeeding, short-term increases in cellular demand (e.g. hungry bones syndrome) and acute respiratory alkalosis)

Major signs and symptoms

- Muscle dysfunction and weakness. This occurs in major muscles, but also may manifest as: diplopia, low cardiac output, dysphagia, and respiratory depression due to respiratory muscle weakness.
- Mental status changes. This may range from irritability to gross confusion, delirium, and coma.
- Poor white blood cell function causing severe infections.
- Instability of cell membranes due to low ATP levels: this may cause rhabdomyolysis with increased CPK.
- Haemolysis and thrombocytopenia.

Treatment

- Standard intravenous preparations of potassium phosphate are available and are routinely used in malnourished patients and alcoholics. Oral supplementation is also useful where no intravenous treatment is available.
- Hypophosphataemia (<0.7 mmol/L) occurs in as many as 25% of hospital inpatients. However, functional deficiency does not occur until plasma phosphate falls below 0.3 mmol/L. At this concentration, replacement should be considered urgently since hypophosphataemia results in widespread organ dysfunction. If there is insufficient intracellular phosphate, no ATP can be manufactured, which results in widespread organ failure.
- The first diagnostic step is to determine whether hypophosphataemia is due to real deficiency or due to redistribution within the body since the latter is benign. However, in all but short term cases of hypophosphataemia, redistribution is also associated with the conditions that cause renal phosphate loss. Therefore, a pragmatic approach is to consider that individuals with moderately low plasma phosphate (0.48-0.72 mmol/L) do not need replacement unless they have a risk factor for phosphate depletion; whereas if the plasma phosphate is below 0.32 mmol/L, phosphate depletion is likely and replacement should be administered.

References

1. Toy, Girardet, Hormann, Lahoti, McNeese, Sanders, and Yetman. *Case Files: Pediatrics, Second Edition*. 2007. McGraw Hill.
2. Crook M, Swaminathan R. Disorders of plasma phosphate and indications for its measurement. *Ann Clin Biochem* 1996;33:376-96
3. Payne RB. Renal tubular reabsorption of phosphate (TmP/GFR): indications and interpretation. *Ann Clin Biochem* 1998;35:201-206.
4. Weisinger JR, Bellorin-Font E. Magnesium and phosphorus. *Lancet* 1998;352:391-396.

Questions

1. What are the causes of hypophosphataemia?
 2. Discuss the pathophysiology of hypophosphataemia.
 3. Discuss the treatment protocol in patients diagnosed with hypophosphataemia.
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