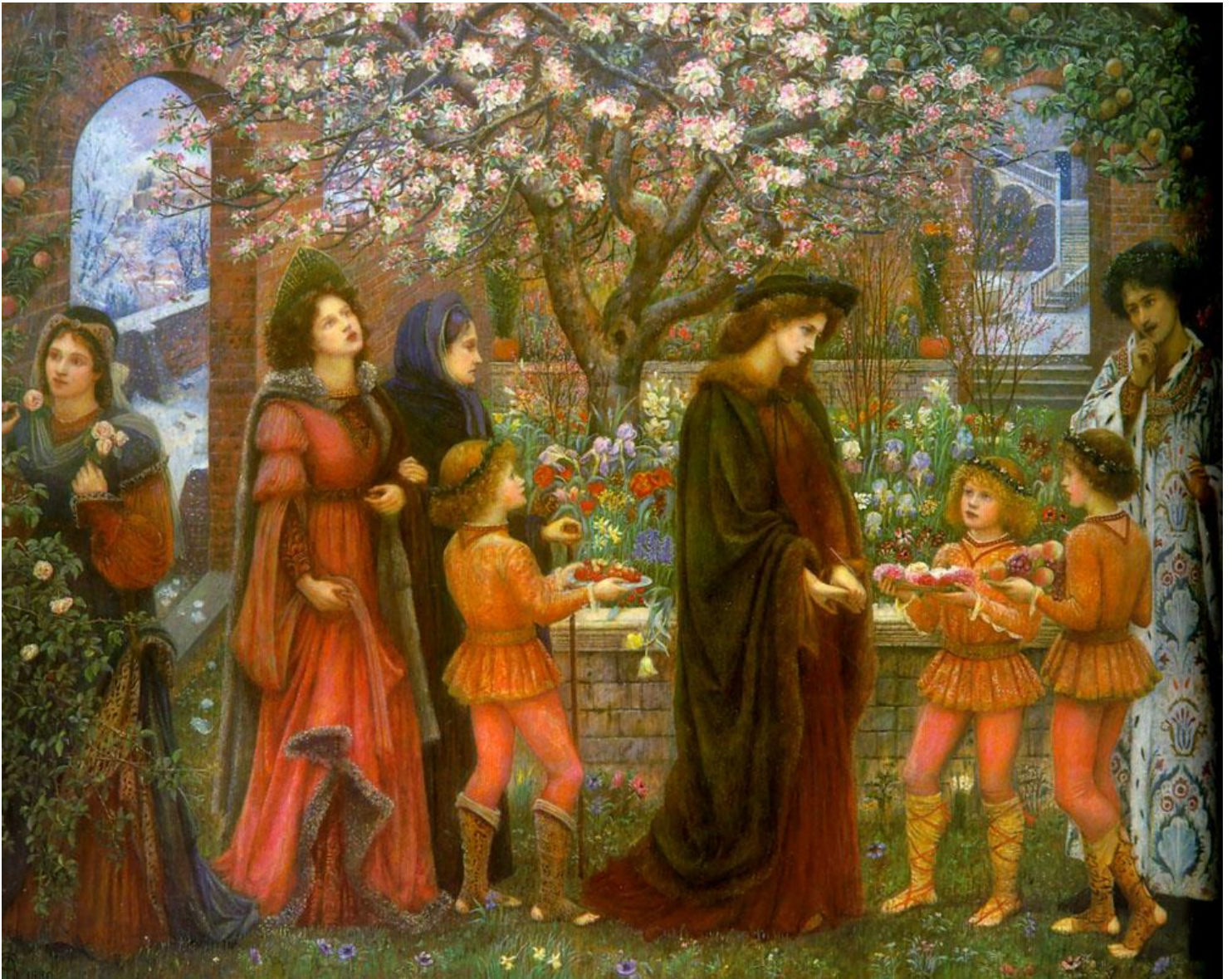


HYPERPHOSPHATAEMIA



“The Enchanted Garden of Messer Ansaldo” - Day Ten, Story Five; “The Decameron”, Giovanni Boccaccio (1350-53); Pre-Raphaelite, oil on canvas, 1889, Marie Spartali Stillman.

*“There are two ways you can live your life. One is as though nothing is a miracle. The other is as though everything is a miracle.” **Albert Einstein***

... “My good woman, you have repeatedly assured me that Messer Ansaldo loves me above all else, and offered me sumptuous gifts on his behalf, all of which I prefer that he

should keep, for they could never induce me to love him or submit to his pleasure. If only I could be certain, however, that he loved me as much as you claim, I should undoubtedly bring myself to love him and do his bidding. So if he will offer me proof of his love by doing what I intend to ask of him, I shall be only too ready to obey his commands”.

“And what is it ma’am,” the good woman asked, “that you want him to do?” “What I want is this”, replied the lady, “In the month of January that is now approaching, I want a garden, somewhere near the town, that is full of green plants, flowers, and leafy tress, exactly as though it were the month of May. And if he fails to provide it, let him take good care never to send you or anyone else to me again. For if he should provoke me any further, I shall no longer keep this matter a secret as I have until now, but I shall seek to rid myself of his attentions by complaining to my husband and kinfolk”.

On hearing about the Lady’s proposition, the gentleman naturally felt that she was asking him to do something very difficult - or rather well-nigh impossible, and realized that here only reason for demanding such a thing was to dash his hopes; but nevertheless he resolved that he would explore every possible means of furnishing her request. He therefore set enquiries afoot in various parts of the world to see whether anyone could be found to advise and assist him in the matter, eventually he found a very powerful magician, who offered to do it by magic, provided he was well enough paid. So Messer Ansaldo agreed to pay him a huge sum of money, and waited contentedly for the time the Lady had appointed. And during the night preceding the calends of January, when the cold was very intense and everything was covered in snow and ice, the magician employed his skills to such good effect that in a beautiful meadow, not far from the town, there appeared next morning, all those who saw it bore witness, one of the fairest gardens that anyone had ever seen, with plants and trees and fruits of every conceivable kind. No sooner did Messer Ansaldo feast his eyes upon this spectacle than he caused a quantity of the finest fruits to be gathered and secretly presented to the Lady, inviting her to come and see the garden she had asked for, so that that she would not only realize how much he loved her, but recall the solemn pledge she had given....

The Lady had been hearing many reports of the wonderful garden, and when she saw the flowers and the fruits, she began to repent of her promise. But for all her repentance, being curious to observe so rare a phenomenon, she went with several other Ladies of the town to see the garden, and after commending it greatly and betraying no little astonishment, she made her way home in the depths of despair, thinking of what it obliged her to do. So profound was her distress, in fact, that she was unable to conceal it, with the inevitable result that her husband, noticing how melancholy she looked, demanded to know the reason....finally he forced her to tell him the whole story from beginning to end. Gilberto was at first extremely angry, but after reflection, he put aside his anger and said...

“Dianora, no wise or virtuous woman should ever pay heed to massages of that sort, nor should she ever barter her chastity with anyone, no matter what terms she may impose. The power of words received by the heart through the ears is greater than many people think, and to those who are in love nearly everything becomes possible. Hence you did wrong, first of all to pay any heed to him and secondly to barter with him...I shall allow you, as to be quit of your promise, to do something which possibly no other man would

permit, being swayed also by my fear of the magician, whom Messer Ansaldo, if you were to play him false, would perhaps encourage to do us a mischief. I therefore want you to go to him, and endeavor in every possible way to have yourself released from this promise without loss of honour, but if this should prove impossible, just for this once, you will have to give him your body, but not your heart”.

Giovanni Boccaccio, Fifth Story, Day Ten, The Decameron, (1350-53).

The medieval mind was a superstitious one. Emilia’s story on the Tenth Day of the group of young Florentines’ self imposed exile in the country to escape the fury of the plague that raged in Florence, may be fiction, but much of the superstitious sentiments expressed in her story were actually very close to the mark for her less educated contemporaries. Many in the Fourteenth century fully believed in witchcraft and magic. In the Twentieth century the evolutionary biologist Richard Dawkins created a sensation in 1976 with his international bestseller, “The Selfish Gene” in which he described, in the eyes of many, the terrifying vision of a godless and uncaring Universe and of a supposedly soulless science that was deeply disturbing. The great Romantic poet, Keats, had lamented Newton’s “unweaving of the rainbow” - the magic of this vision replaced by the cold and calculating laws of prismatic physics. Keats thought the world a poorer place for Newton’s scientific discoveries. But Dawkins strongly disagreed. In 1998 in his book “Unweaving the Rainbow”, he explained to modern audiences the sheer wonder of modern science - a wonder more profoundly “magical” than any medieval Boccaccian mind could have possibly even begun to imagine. In a brilliant answer to Keats (whom he actually greatly admires) he wrote, “Newton’s unweaving of the rainbow led onto spectroscopy, which has proved the key to much of what we know today about the cosmos. And the heart of any poet worthy of the title of Romantic could not fail to leap up if he beheld the Universe of Einstein, Hubble and Hawking. We (now) read its nature through Fraunhofer lines - Barcodes in the Stars - and their shifts along the spectrum”.

Newton did not unweave the rainbow, he enriched it beyond measure! Today we are able to see more magic around us in the real world than ever existed in the most superstitious mind of the Fourteenth century. We see it in the vastness of space when we try to find the very edge of the Universe, or the vastness of time when we look back to the moment of the big bang, but we also see it on the very smallest of scales, in the very cells of our own bodies and those of every living creature on Earth. Each and every living cell is nothing less than a garden of cascading biochemical miracles that makes Messer Ansaldo’s enchanted garden seem like a children’s party trick! All the cells of the body work in perfect unison to maintain the primal environment in which the first cells on Earth evolved. The whole body works in complete harmony through miraculous systems that physiologists call homeostasis. No matter how harsh the conditions of a hostile external environment, these systems work to maintain the primal garden of Eden, evolved over unimaginable eons of geological time. One of the most tightly controlled of these life-giving systems is that of phosphate metabolism in the body. This chemical most essential to life is one of the most important in a vast host of life giving processes maintained in the miracle of each and every enchanted cellular garden of the body. The medieval belief in miracles, may have been lost when Newton unweaved the rainbow - but by so doing, he opened up to us a real world of unimaginable wonders that far surpasses any imagined magic of the past.

HYPERPHOSPHATAEMIA

Introduction

Hyperphosphataemia is an elevated serum phosphate level above normal physiological values, and is generally taken to be greater than **1.4 mmol/L**.

Chronic hyperphosphataemia is much more common than acute hyperphosphataemia

The most common cause of chronic hyperphosphataemia is chronic renal failure.

Oral sodium phosphate laxatives have the potential to cause acute severe hyperphosphataemia, which can be life-threatening.

Physiology

The normal physiologic *blood level* of phosphate is **0.8 mmol/L - 1.4 mmol/L**.

Phosphate is a predominantly *intracellular* anion (with a concentration of approximately 100 mmol/L), where it is predominantly complexed or bound to proteins or lipids

It is one of the major components of the skeleton, providing mineral strength to bone. Indeed the bulk of *total body* phosphate (about 85%) resides in bone as part of the mineralized extracellular matrix. This phosphate bone pool is accessible, but only in a somewhat limited fashion.

Phosphate is critical for a vast number of cellular processes.

It is an integral component of the nucleic acids - DNA and RNA.

Phosphate is also necessary in red blood cells for production of 2,3-diphosphoglycerate (2,3-DPG), which facilitates release of oxygen from hemoglobin.

The phosphate bonds of ATP carry the energy required for all cellular functions.

Phosphate functions as a buffer in bone, serum, and urine. The addition and deletion of phosphate groups to enzymes and proteins are common mechanisms for the regulation of their activity.

In view of its vast physiological importance in the body, phosphate **homeostasis** is very closely regulated in the body, via vitamin D, PTH and the kidneys.

Pathophysiology

Causes:

Hyperphosphataemia can be due to

1. Impaired renal phosphate excretion:

- Renal failure
 - ♥ Chronic renal failure is the most common cause.
- Hypoparathyroidism:
 - ♥ PTH is required for the renal excretion of phosphate

2. Redistribution of phosphate:

Here there is loss of intracellular phosphate resulting in an increased extracellular phosphate):

- Rhabdomyolysis, in general
- Tumour lysis syndrome
- Catabolic states, in general
- Severe haemolysis, (severe)

3. Excess exogenous phosphate:

- Excessively rapid administration by intravenous, oral or rectal route

Acute severe hyperphosphataemia (with electrolyte disturbance and sudden death) has been reported after taking **oral sodium phosphate laxatives** as a bowel preparation, either preoperatively or before a colonoscopy.

This is more of a problem in patients with impaired renal function.

- Vitamin D intoxication:

This can produce hyperphosphatemia as a result of excessive gastrointestinal absorption and increased renal reabsorption.

4. Artefactual:

- This may occur as a result of delayed transport of the blood sample to the laboratory.

Complications:

- Acute and rapid onset hyperphosphataemia:

Rapidity of onset (in contrast to the chronic hyperphosphataemia that is seen with chronic renal failure) can lead to cardiorespiratory collapse and seizures.

- Chronic hyperphosphataemia:

Chronic hyperphosphataemia leads to a reciprocal change (lowering) in serum calcium levels, and complications will then more typically relate to those of the **hypocalcaemia** and wide **ranging ectopic soft tissue calcification**, (high phosphate causes the precipitation of calcium from the serum into the tissues).

Clinical Features

Acute severe hyperphosphataemia:

Hyperphosphataemia of itself is usually asymptomatic, unless very acute and severe.

In these cases, the following may be seen:

1. Seizures
2. Cardiovascular collapse
3. Respiratory depression.

Chronic hyperphosphataemia:

In the far more common chronic situation the most significant clinical manifestations of hyperphosphataemia will usually relate to the *associated serum hypocalcaemia* and muscle tetany.

Investigations

Blood tests:

1. FBE
2. U&Es/ glucose
3. Calcium level
4. Phosphate level
5. PTH/ vitamin D levels

ECG:

Look for associated features of hypocalcaemia

Others tests as clinically indicated, and according to the index of suspicion for any particular causative pathology.

Management

Acute:

Acute severe hyperphosphataemia is an emergency, requiring prompt treatment.

- Volume expansion with saline, (if not due to renal failure)
- Urgent haemodialysis, if no improvement with saline, or renal failure is present.
- Insulin and glucose administration can also lower the serum phosphate level.

Chronic:

For chronic hyperphosphataemia:

- Treat the underlying cause.
- Restriction of dietary phosphate intake, (primarily via protein restriction).
- Phosphate binders, (in the GIT):
 - ♥ Calcium-based phosphate binders (e.g calcium carbonate). This is usually first line treatment.
 - ♥ Aluminium-based phosphate binders are only used in the *short term* (less than four weeks) because of their long-term toxicity.

See latest Endocrine Therapeutic Guidelines for full prescribing details.

- Newer phosphate binding agents (not containing calcium or aluminium) include:
 - ♥ Sevelamer
 - ♥ Lanthanum

See latest Endocrine Therapeutic Guidelines for full prescribing details.

Disposition

Treatment of chronic hyperphosphataemia is complex and drugs must be titrated individually according to calcium and phosphate concentrations and the underlying disease.

For this reason cases should be discussed/ referred to the Endocrinology Unit or Renal Unit as appropriate.

References

1. Endocrine Therapeutic Guidelines, 4th ed 2009.

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