Phosphate: are we squandering a scarce commodity?

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ABSTRACT

Phosphorus is an essential element for life but is a rare element in the universe. On Earth, it occurs mostly in the form of phosphates that are widespread but predominantly at very low concentration. This relative rarity has resulted in a survival advantage, in evolutionary terms, to organisms that conserve phosphate. When phosphate is made available in excess it becomes a cause for disease, perhaps best recognized as a potential cardiovascular and renal risk factor. As a reaction to the emerging public health issue caused by phosphate additives to food items, there have been calls for a public education programme and regulation to bring about a reduction of phosphate additives to food. During the Paleoproterozoic era, an increase in the bioavailability of phosphate is thought to have contributed significantly to the oxygenation of our atmosphere and a dramatic increase in the evolution of new species. Currently, phosphate is used poorly and often wasted with phosphate fertilizers washing this scarce commodity into water bodies causing eutrophication and algal blooms. Ironically, this is leading to the extinction of hundreds of species. The unchecked exploitation of phosphate rock, which is an increasingly rare natural resource, and our dependence on it for agriculture may lead to a strange situation in which phosphate might become a commodity to be fought over whilst at the same time, health and environmental experts are likely to recommend reductions in its use.

Keywords: cardiovascular disease, chronic kidney disease, ecology, phosphate, public health

INTRODUCTION

The element phosphorus is both essential for life on Earth and a troublesome environmental pollutant. Phosphorus is highly reactive and therefore never found as a free element. Nearly all the naturally occurring phosphorus compounds on Earth are phosphates based on the PO₄ group [1, 2]. Phosphate has essential roles in nucleic acid metabolism, glycolysis, bone metabolism, as a regulator of biological processes including enzymes and receptors by phosphorylation, as an essential intracellular buffer and in energy release and storage. Cyclic nucleotide derivatives containing phosphate are essential constituents for hormones, synaptic transmission, mitosis regulation and immune and inflammatory responses. Phospholipids form membranes in all cells and phosphate is involved in active carrier transport through cellular and mitochondrial membranes [3]. Indeed, >2000 chemical reactions in living cells use phosphate [4].

The term phosphorus comes from the Greek phos (light), and phoros (bringing) [5]. Indeed, Greek astronomers gave this name to the morning star—the planet Venus [5]. In this paper we hope to throw new light on the well-rehearsed arguments on reducing phosphate intake, both at a population level and particularly in patients with renal impairment, and to discuss the wider global implications of how to handle the precious world resource of phosphate more wisely.

PHOSPHATE CHEMISTRY

Granted that phosphates are ubiquitous in biochemistry, what do they do? The answer is that they can do almost everything.

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The element phosphorus cannot be synthesized in the solar system. Its synthesis, the fusing of two oxygen atoms together, requires gigantic amounts of energy and temperatures of at least 1000 megakelvins (1 000 000 000 K). These conditions are only present in extremely large stars, at least three times the size of the Sun [3]. In the cosmos, phosphorus is relatively scarce being the 18th commonest element, although it is the 11th commonest element on Earth due to the rocky nature of our planet [3]. This suggests that the cosmic abundance, or indeed the abundance on Earth, of phosphorus was not the decisive factor in determining its important role in living organisms.

The Romans may have discovered, and subsequently lost, phosphorus. They collected and processed large amounts of urine for industrial uses such as tanning and for use by Roman launderers as a source of ammonia to clean and whiten togas. The light emanating from the sepulchers of the early Christians reported by St Augustine might have been the result of self-igniting phosphorus containing gases arising from the decay of bodies [6]. The first isolation of phosphorus is attributed to Hennig Brandt, a German amateur alchemist searching for the philosopher’s stone to turn base metals into gold in the late 1600s. He distilled over 5500 L of urine and obtained just 120 g of a substance that gave off a white light. Antoine Lavoisier (widely regarded as the founder of modern chemistry) was the first to accept phosphorus as an element about 100 years following Brandt’s death [5].

The major elements found in living organisms provide a minimal set of ‘building-blocks’ representing the most common valence states—hydrogen = 1, oxygen, sulphur = 2, nitrogen = 3, carbon = 4 and phosphorus = 5 [3]. Phosphates can form complex, tridimensional networks including rings, cage-like structures and planar arrangements, which may be the key to its biological ubiquity. Phosphoric acid is a key component of nucleic acids because it can simultaneously link two nucleotides and still doubly ionize [7]. Alternative acids, such as esters of silicic, sulphuric and arsenic acids, acid hydrolyse far too rapidly to survive under physiological conditions, so they are an unsuitable substitutes for phosphoric acid in the backbone of nucleic acids [7].

**PHOSPHATE IN EVOLUTION**

The evolution of ecosystems at geological timescales is very tightly linked with the evolving geological processes [8–10]. When life on Earth began, phosphate was present only in rocks [11, 12]. During the Proterozoic period (2.5 billion to 540 million years ago) the amount of oxygen in the atmosphere increased in two phases at the start and end of this period. The initial Great Oxidation Event happened at the start of the Proterozoic period (2.5 to 2 billion years ago) [13]. Oxygen levels in the atmosphere increased from trace amounts to ~2% by volume. Whereas until then, anaerobic microorganisms had been predominant, [14] organisms now acquired mitochondria and the capacity for efficient oxidative metabolism. Between 1 billion and 0.5 billion years ago, oxygen levels rose again to near present levels. The earliest fossils of multicellular organisms as well as a dramatic increase of organism diversity, the ‘Cambrian Explosion’, mark this period [12, 15].

These phases of atmospheric change happened at about the same time as continental rifting and the exposure of extensive glacial deposits. These events would have caused more phosphate to flow into bodies of water [12, 15]. The effect on marine life might have been analogous to that of high-phosphate fertilizers washed into bodies of water today, with massive algal blooms. During the hundreds of millions of years of the Proterozoic period, this dramatic increase in cellular processes led to oxygen production, an oxygenated atmosphere and the rapid evolution of life on Earth [13, 16].

**THE PHOSPHORUS CYCLE**

In Earth’s current biosphere, plants extract phosphate from soil and it is then passed up along the food chain [5]. While most soils and rocks contain phosphates, it is at very low concentration (0.1%) and thus biologically ‘dilute’. In comparison, phosphate-rich rock is rare. It was formed over millions of years from the remains of aquatic life buried on the ocean bed. These remains mineralized and eventually came to the Earth’s surface by tectonic uplift to be subsequently eroded and dissolved back into the soil. Despite the presence of phosphate minerals, most of the phosphorus in the biosphere is unavailable to plants as they can absorb only soluble, inorganic forms [5]. Historically, crop production relied on natural soil levels of phosphate supplemented by that from the addition of organic matter [17] which varied depending on the landscape, climate and culture. These practices included controlled burning, and the use of human and animal excreta as manure. Early peoples lived close to their sites of food production, facilitating the use of their waste to fertilize the fields [5]. The development of an urban population with increasingly large towns and cities, and especially the sanitation facilities that had to be developed, markedly changed the global phosphate cycle [5].

**THE GREEN REVOLUTION**

In 1840, Justus von Liebig (the founder of organic chemistry) discovered that phosphate, nitrogen and potassium salts, and not organic matter per se mediated the fertilizing actions of manure [18, 19]. Liebig’s ‘mineral theory’ had a very significant impact on agriculture. Increasing food shortages and famines in Europe in the 17th and 18th centuries precipitated the importation of fertilizers, such as crushed bones and guano, to boost crop yields. In addition, phosphate rock was thought of as a potentially inexhaustible source of phosphate. The use of mineral phosphate in fertilizers grew rapidly, especially in the post-World War II period—the ‘Green Revolution’. However, phosphate rock is not limitless. Indeed, it is a finite, non-renewable commodity. Today, the people of the world depend upon mineral phosphate to maintain current food production and feed themselves [5].
The human diet has changed markedly since the mid-20th century, especially in terms of meat and calorie consumption. This has been at the expense of a massive increase in the use of phosphates in agriculture. The average per capita phosphate footprint increased by 38% from 1961 to 2007 (Figure 1), although there is huge variation between countries. For example, over this time period the footprint of some countries such as Canada decreased whereas China’s footprint increased by 400%, largely driven by an increase in the consumption of meat [20].

Unfortunately, the Green and Sanitation Revolutions have meant that the once closed-loop and sustainable long-term phosphate cycle (mineral to plant to animal and back to mineral) has been opened. Phosphate now literally flows from mines to oceans at a rate measured in weeks and months. High levels of phosphate in waterways, as a direct consequence of phosphate-rich fertilizer application, lead to algal blooms blocking sunlight and reducing oxygen concentration. In many parts of the world, we are therefore in a situation of simultaneous phosphate excess in our water and mineral phosphate scarcity [21, 22].

There is current active discussion around exactly how much extractable phosphate rock reserves remain. It is becoming increasingly apparent that the remaining rock is of inferior quality compared with traditional sources, being lower in phosphate content and higher in contaminants, as well as being more difficult to access [17]. Many poor farmers (especially in Sub-Saharan Africa) are already struggling to buy phosphate fertilizers and maintain crop yields in phosphate-deficient soils. Further problems may well arise in the future given that only five countries—USA, China, Morocco, Jordan and South Africa—control ~85% of the known global reserves [5, 17].

The relative scarcity of phosphate was highlighted in 2008 when the price of phosphate rock transiently rose by 800% (Figure 2). Estimates of when the demand for phosphate will exceed supply vary widely from 30–40 to 300–400 years [23]. This wide range reflects the uncertainties surrounding the amount of reserves left as well as future demand. No doubt the debate will continue. However, it is clear that at some point the planet will need to achieve a state of phosphate security. This means ensuring enough access to phosphate to produce food in sufficient quantities to feed the world, while simultaneously ensuring ecological integrity [24]. The potential consequences, and a salutary tale, of unconsidered phosphate exploitation can perhaps be best illustrated by the history of the once idyllic island of Nauru, a nation, situated just south of the Equator halfway between Hawaii and Australia. At the start of the 20th century it was discovered that the island consisted almost entirely of rich phosphate deposits from bird excrements. Aggressive mining has now rendered most of Nauru uninhabitable, except for a narrow strip along the shoreline. Despite having built up a considerable capital reserve during the height of phosphate production, Nauru is now impoverished and it may well be that the population will have to be relocated [25].

**MEASURES TO PRESERVE PHOSPHATE**

It is fortunate that phosphate, unlike oil, is not lost to the atmosphere once used. The potential thus exists to recover used phosphate. It is estimated that ~80% of the phosphate mined is applied to the land and that ~50% of this is lost to waterways via soil erosion and leaching [26]. Tragically, only ~8% of the mineral phosphate fertilizer and livestock feed supplements used were consumed as food in 2008. Most of the remaining phosphate accumulated in soil, lost as unused manure, food spoilage and waste as well as loss through processing [27]. Thus, there is a huge loss of phosphate from ‘mine to fork’ [23]. These inefficiencies provide an obvious target for improvement and there are many calls for further research to provide a more integrated approach to phosphate management. There are also moves to maximize the recovery of phosphate from waste, including the recycling of human urine [28].

There has already been a heavy investment in waste treatment globally including ways to prevent phosphate being discharged into waterways. Extending these processes to recover phosphate for reuse should theoretically be possible.

Reduced meat consumption has also been raised as an obvious way of reducing the demand for mined phosphate with a move to vegetarianism seen by some as an essential component of any integrated plan. Biotechnology could also be part of the solution. Like all mammals, pigs cannot digest phosphate in the form of plant derived phytate and thus they have to be fed phosphate supplements for optimal growth. Consequently, pig manure has a very high phosphate content and can contribute considerably to eutrophication of water systems. The Enviropig is a transgenic pig that synthesizes...
phytase in the salivary glands and secretes the active enzyme in the saliva. Thus, these pigs can utilize most of the phosphate in cereal grains and therefore do not require to be fed phosphate supplements. They excrete 60% less phosphate in faeces compared with conventional pigs [29]. There are, however, significant hurdles that need to be overcome regarding both regulatory safety assessments and public acceptance of genetically modified animals in the food chain [29]. Indeed, there are currently no live Enviropigs, although their DNA has been stored for posterity.

**PHOSPHATE IN HEALTH AND DISEASE**

In evolutionary terms, the relative rarity of phosphate has provided a survival advantage to organisms that are best able to preserve it: genetic pressures favouring systems that retain phosphate in times of scarcity. Thus, in a manner analogous to salt, humans are better at facing low phosphate situations than excessive loads [30]. In a situation where dietary phosphate is available in excess, it becomes a cause for disease, perhaps best recognized in its increasing acceptance as a cardiovascular risk factor [31].

The association between elevated serum phosphate and mortality was first observed in haemodialysis patients [32]. Further studies have demonstrated this connection in patients with pre-dialysis chronic kidney disease (CKD) [33, 34], diabetes mellitus [35] and even in patients with normal renal function [36]. Observational studies have also linked serum phosphate, well within the normal range, to an increased risk of mortality [37], cardiovascular events, [36] the development of congestive heart failure and more widespread vascular calcification in the general population [37–40]. Indeed, vascular calcification is a consistent feature in animal models of phosphate toxicity and is a hallmark of patients with CKD [41]. Early stage CKD is by far the commonest condition associated with disordered phosphate homeostasis affecting over 10% of the adult population in developed countries [42]. The damaged kidney initially increases fractional phosphate excretion and is able to excrete the phosphate load with no change in serum phosphate concentration because of the increased synthesis of parathyroid hormone and fibroblast growth factor-23 [43, 44]. However, these phosphatoninins themselves have been demonstrated to be powerful potential mediators of cardiovascular disease [41].

The phosphate content of diets in the developed and developing world is increasing, not only as a consequence of increased meat consumption but also because phosphates are commonly used as additives in food production. Phosphates (e.g. sodium phosphate, E 339; potassium phosphate, E 340; calcium phosphate, E 341; and many others) can legitimately be added to food. They are used widely as preservatives, acidifying agents, acidity buffers, emulsifying agents, stabilizers and taste intensifiers. These agents are especially commonly used in processed foods. Phosphate additives are used to loosen the structure of protein, allowing it to bind more water. Indeed, the phosphate content of processed meat and poultry products, is almost double that of the natural product because of additives [45–47]. Phosphate additives are also found in significant quantities in Cola and other flavoured soft drinks, in powdered milk as well as in powdered coffee [48].

At the same time as phosphate exposure is increased by the food industry, the prevalence of CKD is rising rapidly so that a high proportion of the population are ill equipped to deal with
phosphate exposure. As age increases, nephrons are lost so the increasing numbers of elderly in our populations will automatically increase susceptibility to phosphate exposure; in people over the age of 70 years the prevalence of CKD is almost 50% [41]. The increasing numbers of people with diabetes and hypertension further exacerbate this population vulnerability.

Interventions designed to reduce its intestinal absorption of phosphate have so far been disappointing [49]. Perhaps a more fruitful avenue, as this is becoming a public health issue, would be a public education programme and regulation to bring about legislation to reduce phosphate additives to food [48]. Importantly, food manufacturers are not required to label food with the quantities of phosphate additives in their products [50]. Comprehensive and quantitative labelling of the phosphate content of food would be an essential step in allowing consumers and, indeed, patients to make informed decisions [48]. However, despite the considerable pathophysiological and epidemiological data on the hazards of high phosphate consumption available at a population level there are very limited data on the possible adverse effects of phosphate additives in humans and those that are available are largely derived from animal studies over 40 years old [50]. Thus, food safety authorities may well feel that they do not have enough information on which to base changes to the current regulations [51]. Also, before recommending an increased use of alternative food additives to phosphate, it should be remembered that a significant cause of the increased use of phosphate was as a consequence of demands to decrease the sodium content of food over the years [50]. Thus alternatives to phosphate would need extensive testing before widespread introduction in case their increased use would also have unintended consequences. The importance of phosphates as currently used in the food industry means that such measures would undoubtedly be met with robust opposition from food manufacturers who have developed effective strategies to prevent regulation of their industry [52, 53]. Most of these concerns are, however, also present for food contents such as sodium, calories and saturated fats and all have been overcome by determined regulatory authorities in many countries.

ACKNOWLEDGEMENTS

C.J.F. is the recipient of a National Institute for Health Research Fellowship (PDF-2012-05-205). The views expressed in this publication are those of the authors and not necessarily those of the NHS, the NIHR or the Department of Health.

CONFLICT OF INTEREST STATEMENT

None declared.

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Received for publication: 5.7.2014; Accepted in revised form: 8.8.2014