oxygen

Review

A Brief History of Oxygen: 250 Years on

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Abstract: Although there has been some controversy surrounding exactly when oxygen was first discovered, it is likely that that accolade should go to Carl Wilhelm Scheele, who isolated oxygen in 1772, or even a year earlier. Others since then have been given the credit for the instrumental work leading to the discovery including Joseph Priestley in 1774 and Antoine-Laurent Lavoisier. Oxygen, a paramagnetic, diradical gaseous (at room temperature) molecule, is instrumental to life as we know it. It is also crucial to some medical therapies, used in multiple industries and has even been found on other planets. The importance of oxygen cannot be overplayed. Now, 250 years since oxygen was discovered, it is timely to revisit some of the history, the controversies and look at how oxygen has evolved during that time. Here, a few of the highlights in oxygen research are discussed.

Keywords: ageing; exoplanets; hypoxia; Lavoisier; medical therapies; mitochondria; oxygen; Priestley; Scheele

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1. Introduction

Oxygen exists primarily as a paramagnetic, diradical which is gaseous at room temperature. However, it was not always known that oxygen existed, with other theories about chemical composition being popular in the 18th century. The scientific thinking, as Neville [1] points out, was dominated by three philosophies:

"(1) the Aristotelian theory of the four 'elements' (viz. air, earth, fire, water); (2) the Paracelsian *tria prima* or 'three principles' (viz. philosophical 'salt,' 'sulfur,' and 'mercury'); and (3) the theory of phlogiston".

Phlogiston was the hypothetical theory of fire and was a constituent of all combustible material. What would now be described as oxidation was thought to be the release of phlogiston and the material left behind, such as ash, would be considered as a dephlogisticated substance. Partington and Mckie [2] discussed the identity of phlogiston and said it was considered to be "negative oxygen", or hydrogen, or "phlogiston must be a very simple body, known only from its effects, since opinions are always more in accord about compound and visible bodies (Leonhardi . . . 1788 . . .)"

Therefore, the time for the isolation of oxygen was ripe, and when it happened, the discovery of oxygen was seen as a scientific revolution, although this has been disputed by some [3].

2. The Discovery of Oxygen

There is no doubt that oxygen was discovered approximately 250 years ago. Having said that, the history probably really starts much earlier. In 1608, Cornelius Drebbel noted that a gas was released on heating saltpetre (potassium nitrate, KNO_3). This was not identified as oxygen. As Neville points out [1], there were several others who were chipping away at the discovery of oxygen, including the French chemist Jean Rey (~1582, after 1645) who was looking at the increase in the weight of lead and tin, published in 1630. Neville also discussed the work of Robert Boyle (1627–1691) and Robert Hooke (1635–1702), who were studying the process of combustion. Boyle described "volatile nitre" in the air in his book *The Sceptical Chymist*, published in London in 1661. There was also John Mayow (1643–1679) who published *Tractatus Quinque Medico-Physici* (Oxford, 1674), and he suggested that air was composed of two components: one of which could support respiration and which he termed “nitro-aerial spirit” [1]. Had any of these philosophers/scientists isolated the gas they were suggesting, then the discovery of oxygen would have probably been assigned to them.

The most significant advances in oxygen’s discovery, however, came in the early 1770s. However, when this was exactly carried out and by whom is somewhat controversial. Many others have written on the topic [4–7], so here, this will be briefly revisited.

Many articles will suggest that oxygen was discovered in 1774 by Joseph Priestley, but they often temper this with the suggestion that oxygen may have been discovered at least two years earlier by Carl Wilhelm Scheele (1742–1786) [4]. Priestley was born in Leeds in 1733 (died 1804), but carried out much of his work at Bowood, Calne, Wiltshire, UK. Interestingly, in a book written by Priestley but published by W.F. Clay in 1894 [8], as in the Harvard College Library (deposited there in December 1898), the Preface states: “It is impossible to overlook the fact that many of Priestley’s experimental results were highly inaccurate, and that his conclusions, often too hastily drawn, were frequently erroneous”. However, it goes on to say: “but at the same time his ingenuity in devising apparatus, and his skill in carrying out experiments, were very remarkable, and placed him amongst the foremost philosophers of the day”. Despite what it says in the Preface, these works establish Priestley as a person who discovered the presence of the element oxygen.

As stated by Severinghaus [4]:

“At Bowood, Priestley set up a laboratory to continue his research on gases. On 1 August 1774, he discovered that by heating the mineral red mercuric oxide with a newly acquired burning glass, a new gas was liberated in which a candle burned furiously and a mouse could live longer than in a similar sealed volume of air”.

Priestley’s work went further and showed that plants could liberate a gas that could sustain the life of mice. However, Priestley called what he discovered “dephlogisticated air”. Others have argued that Priestley’s discovery should be dated to March 1775. Partington, on the other hand, maintains that the earlier date should be accepted [5]. He also suggests three criteria which need to be used to determine whether oxygen has really been isolated, as opposed to other gases that were being worked on at the time such as nitrous oxide. Partington says: “In a modern laboratory a student would be credited with an identification of oxygen if he had shown that: (1) a taper burnt in the gas with a very vigorous flame, (2) a glowing chip inflamed in the gas, and (3) the gas was practically insoluble in water”.

It is clear, therefore, that by 1774/1775, there was a substantial body of evidence that oxygen had been discovered. However, Priestley might not have been the first to do so. As pointed out by the Royal Society Chemistry’s website: “Unknown to Priestly [sic], Carl Wilhelm Scheele had produced oxygen in June 1771” [9]. Although Scheele is usually referred to as a Swedish chemist, he was born in Stralsund, Pomerania, now part of Germany, but at that time under Swedish jurisdiction. Priestley’s work was carried out in 1774, but before then, Scheele had been working in the same field. Scheele published his work in 1777, much later than Priestley, but there have been claims that the work was carried out before this and, therefore, predated that of Priestley. There is some evidence for this. It has been suggested that Scheele wrote to Lavoisier in September 1774, although Lavoisier claims to have never read or received it [4]. Priestley visited Lavoisier in October 1774, and it was probably why Lavoisier became so interested in the subject. What is important to the discussion here is that Scheele published his work entitled “On Air and Fire” in 1777, which would have put Priestley first. However, as pointed out by Partington [5], the Introduction to the book was written by Bergman (Torbern Olof Bergman (1735–1784)) who stated that the work had been carried out by the end of 1775. Publication was delayed whilst Bergman repeated some of the experiments. Furthermore, Bergman, in his memoirs, made a timeline for Scheele’s work clear. Partington [5] suggests that this puts Scheele’s work three months before Priestley’s and that the publication of Scheele’s work was probably first. Partington states:

"Although it is commonly said that Scheele had lost priority of publication by some two years as compared with Priestley, Bergman's publication restores to him a date of announcement of his discovery at least not later than Priestley's".

However, the conclusion of Partington have been thrown into doubt by the work of Cassebaum and Schufle [7], who state: " . . . some other evidence now seems to indicate that Bergman did not learn about Scheele's discovery of oxygen until early in 1776". However, they also say that: " . . . it is shown that Scheele first obtained oxygen in about 1771 by heating MnO_2 with H_2SO_4". Scheele called this "vitriol air" and, accordingly, "With research further performed by him up until about September 1771, Scheele fulfilled all five of our steps for the discovery of oxygen" [7]. In the conclusions of this paper the authors are clearly of the view that by June 1771 Scheele had isolated oxygen and was aware of what he had discovered. However, they also argue that it is very hard to clearly know how communications were established between Scheele, Priestley and Lavoisier but do conclude with this statement:

"It would seem that Scheele has clear priority for the actual discovery of oxygen. As for communication of the discovery to others, the conclusions are not clear, but Scheele and Priestley seem to have nearly equal priority".

However, just to cloud the issue, the authors then say: "But if we consider publication by other than the original discoverers, Lavoisier actually may have priority".

In conclusion, perhaps the statement on the RSC's website [9] sums up the views of many well: "The credit for discovering oxygen is now shared by three chemists: an Englishman, a Swede, and a Frenchman" [9].

Therefore, whether Priestley or Scheele was first, the work also overlapped with that of Lavoisier [10]. It appears that Lavoisier was inspired by the work of Priestley, considering Priestley's: "public announcement of his discovery was not made until 23 March 1775", and Lavoisier: "On 26 April 1775, he read to the Academy his 'Memoir on the nature of the principle which combines with metals during calcination, and which increases their weight'" [11]. Therefore, Lavoisier must have been working in the field already, probably repeating some of Priestley's experiments since August 1774. He subsequently went on to carry out instrumental work on oxygen and respiration. However in 1793 he fell afoul of the revolution and was arrested and imprisoned in the Prison of Port-Libre. His trial was on 8 May 1794, and he was beheaded the same day. A common quote used is: "'Only a moment to cut off his head', said Lagrange, 'and perhaps a hundred years before we see such another'" [11]. Or as Underwood puts it: "The Revolution had accomplished its most criminal act, and the science of respiration had to wait over forty years for its next forward step" [11].

3. Atmospheric Oxygen and Its Evolution

Oxygen at the present time comprises approximately 21% of the Earth's atmosphere. Early atmospheric conditions were devoid of oxygen. Studies of ancient rock samples, for example, can give an indication of oxygen levels over history [12]. It is suggested that oxygen concentration rose in the atmosphere between 2.5 and 2.0 billion years ago. A study in 2000 [13] looked at the oxidation of sulfur and concluded that 2450 million years ago, the atmospheric oxygen was low as were the potential rates of oxidation.

The only source of atmospheric oxygen before photosynthesis was probably the photolysis of water, leading to hydrogen as a second product that would have been rapidly lost into space [14]. Furthermore, the oxygen would probably have been scavenged from the atmosphere by the reductive gases from volcanoes such as hydrogen. Therefore, for the first part of the Earth's history, the build up of oxygen in the atmosphere was not possible and indeed appeared to be depressed. Although it is thought that the generation of oxygen from photosynthesis started approximately 3.8 billion years ago, most of it would have been produced in the oceans and then it would have reacted with the minerals from the weathering and runoff from rocks, partly Fe^{2+} which left the iron deposits seen today. This process may have lasted as long as 2 million years. Eventually, photosynthetic O_2

production would have out-competed the scavenging and atmospheric oxygen would rise [14].

During the Permo–Carboniferous period, the atmospheric oxygen rose to approximately 35%, as opposed to the 21% seen today. This led to the growth of giant insects, and it was thought that wildfires were more common too. The appearance of large plants and the burying of large quantities of organic matter may have been the main cause for this oxygen concentration rise [15]. During the Mesozoic era, it was thought that the oxygen concentration dropped to approximately 15%. However, this has been disputed by some, who say that the record of wildfires indicates that the oxygen concentration was much higher, and they also conclude that no modelling will support the notion of such low atmospheric concentrations [16]. Of course, what we do know is that today the levels are around 21%.

Of course, today, maintenance of Earth's atmospheric oxygen is reliant on photosynthesis [17]. However, how stable is the oxygen concentration in the atmosphere? Looking at the atmospheric oxygen over the last 100 years and then projecting what might happen in the near future, it has been suggested that oxygen levels will drop from 20.946% to 20.825% [18]. This is caused by human activity–fossil fuel consumption, and authors say: "It is time to take actions to promote O_2 production and reduce O_2 consumption". Others agree, and report that the future dissolved oxygen in the oceans over the next 100,000 years is likely to be severely depleted [19]. This is due to the fact of human activity. As the climate changes, the surface 500 m of the oceans will have less oxygen solubility, but there will be effects at greater depths. This is a sobering thought.

It should not be forgotten that molecular oxygen is not the only form that exists or is of interest. Ozone (O_3) has been in the public awareness since it was reported that the atmospheric ozone layer was being depleted, for example see [20]. Ozone was extensively studied by Christian Friedrich Schönbein (1799–1868), but it was Jacques-Louis Soret (1827–1890) who determined its formula in 1865 [21,22].

Other forms of oxygen include singlet oxygen and the superoxide anion, the latter also known historically as hyperoxide. Singlet oxygen is an excited form of molecular oxygen ($O_2(a^1\Delta_g)$) and has been known for approximately ninety years [23]. Much of the work was carried out by Christopher S. Foote and his colleagues in the 1960s, but they were reassessing work already carried out approximately thirty years earlier [24]. Superoxide anions are molecular oxygen with an extra electron, but this has no pair in the outer shell, so that this is a free radical ($O_2{}^{\bullet -}$). Irwin Fridovich and H. Moustafa Hassan wrote about its toxic effects in 1979, and Pauling suggested that it was proposed through the work of quantum mechanics [25]. Lynch and Fridovich were also writing about the effects of superoxide on the membranes of erythrocytes in 1978 [26]. Superoxide readily dismutes to hydrogen peroxide, especially at low pH, and it is a reaction catalysed by superoxide dismutase (SOD), the latter being discovered by J.M. McCord and I. Fridovich in 1968 [27]. Once such oxygen-based compounds are generated, there is the potential for the production of further downstream oxygen-rich compounds collectively known as reactive oxygen species (ROS) and includes the hydroxyl radical ($^{\bullet}OH$). Their importance came to the fore with the realisation of the importance of the respiratory burst in white blood cells and the role of these compounds in host defence. The enzyme responsible was found in 1965 [28], known as the NADPH oxidase. Lack of this enzyme leads to the condition known as chronic granulomatous disease (CGD), where patients have a deficient immune response against pathogens and die young [29].

4. Discovery of Oxygen as Part of Metabolism and Ageing

Oxygen is instrumental for the metabolism of many organisms. Oxygen acts as the terminal electron acceptor in humans, for example, where four electrons are used to create water, which is then lost through the skin or breath. Without the removal of electrons by oxygen at the end of the electron transport chain, the mitochondria would be unable to create an electrochemical potential across the inner mitochondrial membrane. This potential was, of course, mooted by Peter Mitchell [30] (see also [31]). Lack of full reduction of oxygen leads to the production of oxygen-free radicals, notably, the superoxide oxide anion ($O_2^{\bullet-}$) [32]. Such radical production leads to a cascade of oxygen-based compounds, such as hydrogen peroxide (H_2O_2) and the hydroxyl radical ($^{\bullet}OH$). Such ROS led to the idea that their presence, and indeed over accumulation in cells, leads to the ageing process. This was suggested in 1954 [33,34] with papers reporting the presence of free radicals in biological systems [35]. One of the most prolific writers on the subject was Denham Harman (e.g., [36,37]). The idea still has traction today and is widely researched (e.g., [38]).

The idea of oxygen being involved in biological systems, of course, has a much longer history, spanning back to the work of people such as Lavoisier, as discussed above. Mitochondria were first described in the latter part of the 19th century by people such as Rudolf Albrecht von Kölliker (in 1857) and Richard Altmann (in 1898). Fletcher and Hopkins, in 1907, showed that oxygen caused the disappearance of lactate in stimulated muscles. Work by Meyerhof on oxygen and glycogen metabolism was published in 1927 [39], by the 1940s, the cellular location of some of the electron transport chain complexes was being unravelled [40], and by the 1960s the system was quite well characterised. For a good overview of the history of oxygen in metabolism see [41].

The lack of oxygen in biological systems is often referred to as hypoxia. This can be a somewhat misleading term. Atmospheric oxygen is 21%, as stated above, but not many cells in a body will be exposed to this concentration of oxygen. There are many conditions under which the oxygen tension accessible to cells is driven even lower, including during wounding and cancer, which would be true hypoxia. However, today the term hypoxia is widely used to mean an oxygen tension below 21% and not just in the case of true hypoxia. A history of its use was given by Richalet [42], who states:

"Viault and Jolyet used "Hypohématose" in 1894, but this term has not been used since. Hypoxybiosis first appeared in 1909 in Germany, then hypoxemia in 1923 in Austria, and hypoxia in 1938 in Holland. It was then exported to the United States where it appeared in 1940 in cardiology and anesthesiology. The clinical distinction between anoxia and hypoxia was clearly defined by Carl Wiggers in 1941. Hypoxia (decrease in oxygen), by essence variable in time and in localization in the body, in contrast with anoxia (absence of oxygen), . . . "

How cells survive low oxygen, and recover from such conditions, is important to understand. Reperfusion injury, where oxygen is reintroduced to tissues and cells, can lead to damage partly through the generation of ROS [43]. The role of low-oxygen tension in cancer is also important to understand [44].

The use of oxygen in cells is not confined to respiration or causing damage. It has been recognised for many years that ROS and related compounds are instrumental in the control of cellular activities [45]. This was brought to a fore by the publication of the role of nitric oxide (NO) in cell signalling events in 1987 [46]. This opened the door to the idea that other similar molecules could be used for signalling including the superoxide anion, hydrogen peroxide, hydrogen sulfide and even hydrogen gas. It is interesting to note that the generation of NO by the enzyme nitric oxide synthase (NOS) is an oxygen-dependent reaction.

Therefore, the role of oxygen in biological systems has a long history, but is also immensely important to understand. Its role in respiration and cell signalling are vital for the correct functioning of the cell, but the absence of oxygen is also important to consider, especially in tumours. Therefore, this segues into how oxygen can be used in medicine.

5. Oxygen and Its Uses in Medicine

Hyperbaric oxygen therapy (HBOT) [47] was probably first used in 1662 by Henshaw [48]. In 1789 Lavoisier and Seguin reported that high oxygen was detrimental to health, thus dissuading people from using it. This sentiment was probably exacerbated by Bert in 1878, who looked at oxygen toxicity in more detail. By 1887, the concept of HBOT was looked upon more favourably following work by Arntzenius [48]. Many hyperbaric chambers were built including examples in North America in 1860 and 1861. Edwards [48] states that Cunningham built a massive chamber in Cleveland that was "64 feet in diameter, was 5-stories tall and had 12 bedrooms on each floor". In 1937, decompression sickness was successfully ameliorated using HBOT by Behnke and Shaw. According to Biggs et al. in 2022 [49], there were 13 FDA approved uses of HBOT including treating "gas embolism, carbon monoxide poisoning, decompression sickness, and radiation necrosis". They also state that there are some unusual uses too including "cancer, mild traumatic brain injury (mTBI), and Alzheimer's disease".

Oxygen is used too, of course, at normoxic concentration, especially for trauma or if a person has breathing difficulties. However, it has also been suggested that oxygen can be mixed with other gases, which may have a synergistic effect. An example of the this is the suggestion that oxy-hydrogen gas (a mixture of oxygen and hydrogen at a 1:2 ratio) can be used for the treatment of severe COVID-19, the present pandemic caused by the SARS-CoV-2 virus [50].

6. Oxygen and Space

The study of oxygen is not confined to here on Earth. In 2013, the Hubble Space Telescope reported evidence of oxygen at the exoplanet HD 189733b [51]. It is also proposed that the James Webb Space Telescope will be able to detect oxygen on similar planets [52]. Tian suggested [53] that the creation of what is referred to as a massive oxygen atmosphere is not inevitable and that there might be a bimodal distribution of such exoplanets. There is the inevitable excitement that if oxygen can be found on other planets that such places may harbour life [54,55].

7. Oxygen and the Future

The history of oxygen and its influence of on life has been extensively written about, not least by Lane in his book succinctly titled *Oxygen* [56], and others [57]. Two hundred and fifty years since its discovery research on oxygen is still of significance today.

Here, the focus has been mainly on oxygen and biosciences, but of course oxygen is instrumental in many industries too. For example, it is hugely important in the steel industry, in the running of blast furnaces [58]. It is also vital for the papermaking industry, especially in waste management [59] and, in fact, in the treatment of bio-waste in general [60]. There are many other industries not mentioned here. There is a whole research area devoted to anthrogenic activity in megacities and how this impacts the environment, including oxygen in adjacent water bodies [61].

With the world looking for cleaner energy sources of electricity for the future, the development of better batteries is the race that is now taking place [62]. One of the ways forward involves the development of lithium–oxygen ($Li–O_2$) batteries [63,64]. It is thought that air–metal-based batteries are the way to obtain the best energy density and are a step change from conventional lithium batteries. However, it is inevitable that new battery technologies will see massive improvements in the present situation, else the conversion of energy to electricity, especially for transport, may be difficult.

The biomedical field oxygen will always remain important. With the obvious need to give people oxygen when critically, or chronically, in short supply of oxygen, the use of oxygen in medical therapies will remain important. However, the use of hyperbaric oxygen and oxygen mixed with other gases, such as hydrogen, will no doubt increase in the future.

Molecular oxygen, as well as being critical for aerobic respiration, also gives rise to a raft of downstream products including ROS. Originally seen as instrumental in host defence, these molecules are used extensively in cell signalling events [65]. However, the production, accumulation, sub-cellular location, and timing of such control mechanisms is still far from clear as is their role in the process of ageing. Clearly, oxygen atoms are part of a vast range of compounds found in cells, from simple gases, such as NO, to huge proteins. Oxygen is an integral part of life.

Over the last 250 years, regardless of who actually could lay claim to being the discoverer, oxygen research has continued and been part of a range of scientific disciplines, many not even mentioned above. Oxygen research has gone into space, but here on Earth, oxygen will no doubt be part of the future in industries working to create sustainable energy sources, medical therapies and many other uses. In another 250 years, oxygen will no doubt still be at the forefront of human endeavours.

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References

1. Neville, R.G. Steps leading to the discovery of oxygen, 1774: A bicentennial tribute to Joseph Priestley. *J. Chem. Educ.* **1974**, *51*, 428. [CrossRef] [PubMed]
2. Partington, J.R.; McKie, D. Historical studies on the phlogiston theory.—I. The levity of phlogiston. *Ann. Sci.* **1937**, *2*, 361–404. [CrossRef]
3. Allchin, D. Phlogiston after oxygen. *Ambix* **1992**, *39*, 110–116. [CrossRef]
4. Severinghaus, J.W. Priestley, the furious free thinker of the enlightenment, and Scheele, the taciturn apothecary of Uppsala. *Acta Anaesthesiol. Scand.* **2002**, *46*, 2–9. [CrossRef] [PubMed]
5. Partington, J.R. The discovery of oxygen. *J. Chem. Educ.* **1962**, *39*, 123. [CrossRef]
6. Williams, K.R. The discovery of oxygen and other priestley matters. *J. Chem. Educ.* **2003**, *80*, 1129. [CrossRef]
7. Cassebaum, H.; Schufle, J.A. Scheele's priority for the discovery of oxygen. *J. Chem. Educ.* **1975**, *52*, 442. [CrossRef]
8. Priestley, J. *The Discovery of Oxygen*; W.F. Clay: London, UK, 1894; Volume 1.
9. Oxygen. Available online: https://www.rsc.org/periodic-table/element/8/oxygen (accessed on 28 January 2022).
10. Donovan, A. *Antoine Lavoisier: Science, Administration and Revolution*; Cambridge University Press: New York, NY, USA, 1996; Volume 5.
11. Underwood, E.A. Lavoisier and the history of respiration. *Proc. R. Soc. Med.* **1944**, *37*, 247–262. [CrossRef]
12. Kump, L.R. The rise of atmospheric oxygen. *Nature* **2008**, *451*, 277–278. [CrossRef]
13. Farquhar, J.; Bao, H.; Thiemens, M. Atmospheric influence of Earth's earliest sulfur cycle. *Science* **2000**, *289*, 756–758. [CrossRef]
14. Walker, J.C. The early history of oxygen and ozone in the atmosphere. *Pure Appl. Geophys.* **1978**, *117*, 498–512. [CrossRef]
15. Berner, R.A.; Beerling, D.J.; Dudley, R.; Robinson, J.M.; Wildman, R.A., Jr. Phanerozoic atmospheric oxygen. *Annu. Rev. Earth Planet. Sci.* **2003**, *31*, 105–134. [CrossRef]
16. Mills, B.J.; Belcher, C.M.; Lenton, T.M.; Newton, R.J. A modeling case for high atmospheric oxygen concentrations during the Mesozoic and Cenozoic. *Geology* **2016**, *44*, 1023–1026. [CrossRef]
17. Junge, W. Oxygenic photosynthesis: History, status and perspective. *Q. Rev. Biophys.* **2019**, *52*, e1. [CrossRef] [PubMed]
18. Huang, J.; Huang, J.; Liu, X.; Li, C.; Ding, L.; Yu, H. The global oxygen budget and its future projection. *Sci. Bull.* **2018**, *63*, 1180–1186. [CrossRef]
19. Shaffer, G.; Olsen, S.M.; Pedersen, J.O.P. Long-term ocean oxygen depletion in response to carbon dioxide emissions from fossil fuels. *Nat. Geosci.* **2009**, *2*, 105–109. [CrossRef]
20. McKenzie, R.L.; Aucamp, P.J.; Bais, A.F.; Björn, L.O.; Ilyas, M.; Madronich, S. Ozone depletion and climate change: Impacts on UV radiation. *Photochem. Photobiol. Sci.* **2011**, *101*, 182–198. [CrossRef]
21. Rubin, M.B. The history of ozone. The Schönbein period, 1839–1868. *Bull. Hist. Chem.* **2001**, *26*, 40–56.
22. History of Ozone. Available online: https://www.solutionozone.com/ozone/history/ (accessed on 21 February 2022).
23. Ogilby, P.R. Singlet oxygen: There is indeed something new under the sun. *Chem. Soc. Rev.* **2010**, *39*, 3181–3209. [CrossRef]
24. Greer, A. Christopher Foote's discovery of the role of singlet oxygen [$^1O_2$ ($^1\Delta_g$)] in photosensitized oxidation reactions. *Acc. Chem. Res.* **2006**, *39*, 797–804. [CrossRef]
25. Pauling, L. The discovery of the superoxide radical. *Trends Biochem. Sci.* **1979**, *4*, N270–N271. [CrossRef]
26. Lynch, R.E.; Fridovich, I. Effects of superoxide on the erythrocyte membrane. *J. Biol. Chem.* **1978**, *253*, 1838–1845. [CrossRef]
27. Bannister, W.H. From haemocuprein to copper-zinc superoxide dismutase: A history on the fiftieth anniversary of the discovery of haemocuprein and the twentieth anniversary of the discovery of superoxide dismutase. *Free. Radic. Res. Commun.* **1988**, *5*, 35–42. [CrossRef] [PubMed]
28. Berton, G.; Castaldi, M.A.; Cassatella, M.A.; Nauseef, W.M. Editorial: Celebrating the 50th anniversary of the seminal discovery that the phagocyte respiratory burst enzyme is an NADPH oxidase. *J. Leukoc. Biol.* **2015**, *97*, 1–2. [CrossRef]
29. Yu, H.H.; Yang, Y.H.; Chiang, B.L. Chronic granulomatous disease: A comprehensive review. *Clin. Rev. Allergy Immunol.* **2021**, *61*, 101–113. [CrossRef]
30. Mitchell, P. Coupling of phosphorylation to electron and hydrogen transfer by a chemi-osmotic type of mechanism. *Nature* **1961**, *191*, 144–148. [CrossRef]
31. Rich, P.R. A perspective on Peter Mitchell and the chemiosmotic theory. *J. Bioenerg. Biomembr.* **2008**, *40*, 407–410. [CrossRef]

32. Cadenas, E.; Davies, K.J. Mitochondrial free radical generation, oxidative stress, and aging. *Free. Radic. Biol. Med.* **2000**, *29*, 222–230. [CrossRef]
33. Harman, D. Free radical theory of aging: History. *EXS* **1992**, *62*, 1–10.
34. Hensley, K.; Floyd, R.A. Reactive oxygen species and protein oxidation in aging: A look back, a look ahead. *Arch. Biochem. Biophys.* **2002**, *397*, 377–383. [CrossRef]
35. Commoner, B.; Townsend, J.; Pake, G.E. Free radicals in biological materials. *Nature* **1954**, *174*, 689–691. [CrossRef]
36. Harman, D. *Aging: The Theory Based on Free Radical and Radiation Chemistry with Application to Cancer and Athrosclerosis*; Rad. Lab. Calender, University of California: Berkeley, CA, USA, 1956.
37. Harman, D. The free radical theory of aging: The effect of age on serum mercaptan levels. *J. Gerontol.* **1960**, *15*, 38–40. [CrossRef] [PubMed]
38. Polidori, M.C.; Mecocci, P. Modeling the dynamics of energy imbalance: The free radical theory of aging and frailty revisited. *Free. Radic. Biol. Med.* 2022, *in press*. [CrossRef] [PubMed]
39. Meyerhof, O. Recent investigations on the aerobic and an-aerobic metabolism of carbohydrates. *J. Gen. Physiol.* **1927**, *8*, 531–542. [CrossRef] [PubMed]
40. Hogeboom, G.H.; Claude, A.; Hotch-Kiss, R.D. The distribution of cytochrome oxidase and succinoxidase in the cytoplasm of the mammalian liver cell. *J. Biol. Chem.* **1946**, *165*, 615–629. [CrossRef]
41. Glancy, B.; Kane, D.A.; Kavazis, A.N.; Goodwin, M.L.; Willis, W.T.; Gladden, L.B. Mitochondrial lactate metabolism: History and implications for exercise and disease. *J. Physiol.* **2021**, *599*, 863–888. [CrossRef]
42. Richalet, J.P. The invention of hypoxia. *J. Appl. Physiol. 1985* **2021**, *130*, 1573–1582. [CrossRef]
43. Wu, M.Y.; Yiang, G.T.; Liao, W.T.; Tsai, A.P.; Cheng, Y.L.; Cheng, P.W.; Li, C.Y.; Li, C.J. Current mechanistic concepts in ischemia and reperfusion injury. *Cell Physiol. Biochem.* **2018**, *46*, 1650–1667. [CrossRef]
44. Jing, X.; Yang, F.; Shao, C.; Wei, K.; Xie, M.; Shen, H.; Shu, Y. Role of hypoxia in cancer therapy by regulating the tumor microenvironment. *Mol. Cancer* **2019**, *18*, 157. [CrossRef]
45. Mittler, R.; Vanderauwera, S.; Suzuki, N.; Miller, G.; Tognetti, V.B.; Vandepoele, K.; Gollery, M.; Shulaev, V.; Van Breusegem, F. ROS signaling: The new wave? *Trends Plant Sci.* **2011**, *16*, 300–309. [CrossRef]
46. Palmer, R.M.; Ferrige, A.G.; Moncada, S. Nitric oxide release accounts for the biological activity of endothelium-derived relaxing factor. *Nature* **1987**, *327*, 524–526. [CrossRef] [PubMed]
47. Shah, S.A. Healing with oxygen: A history of hyperbaric medicine. *Pharos Alpha Omega Alpha Honor Med. Soc.* **2000**, *63*, 13–19. [PubMed]
48. Edwards, M.L. Hyperbaric oxygen therapy. Part 1: History and principles. *J. Vet. Emerg. Crit. Care (San Antonio)* **2010**, *20*, 284–288. [CrossRef] [PubMed]
49. Biggs, A.T.; Littlejohn, L.F.; Dainer, H.M. Alternative uses of hyperbaric oxygen therapy in military medicine: Current positions and future directions. *Mil. Med.* **2022**, *187*, e40–e46. [CrossRef] [PubMed]
50. Russell, G.; Nenov, A.; Hancock, J. Oxy-hydrogen gas: The rationale behind its use as a novel and sustainable treatment for COVID-19 and other respiratory diseases. *Eur. Med. J.* **2021**. [CrossRef]
51. Ben-Jaffel, L.; Ballester, G.E. Hubble Space Telescope detection of oxygen in the atmosphere of exoplanet HD 189733b. *Astron. Astrophys.* **2013**, *553*, A52. [CrossRef]
52. Fauchez, T.J.; Villanueva, G.L.; Schwieterman, E.W.; Turbet, M.; Arney, G.; Pidhorodetska, D.; Kopparapu, R.K.; Mandell, A.; Domagal-Goldman, S.D. Sensitive probing of exoplanetary oxygen via mid-infrared collisional absorption. *Nat. Astron.* **2020**, *4*, 372–376. [CrossRef]
53. Tian, F. History of water loss and atmospheric O_2 buildup on rocky exoplanets near M dwarfs. *Earth Planet. Sci. Lett.* **2015**, *432*, 126–132. [CrossRef]
54. Léger, A.; Fontecave, M.; Labeyrie, A.; Samuel, B.; Demangeon, O.; Valencia, D. Is the presence of oxygen on an exoplanet a reliable biosignature? *Astrobiology* **2011**, *11*, 335–341. [CrossRef]
55. Meadows, V.S. Reflections on O_2 as a biosignature in exoplanetary atmospheres. *Astrobiology* **2017**, *17*, 1022–1052. [CrossRef]
56. Lane, N. *Oxygen: The Molecule That Made the World*; Oxford University Press: Oxford, UK, 2002.
57. Canfield, D.E. *Oxygen: A Four Billion Year History*; Princeton University Press: Princeton, NJ, USA, 2014; Volume 20.
58. Proctor, D.M.; Fehling, K.A.; Shay, E.C.; Wittenborn, J.L.; Green, J.J.; Avent, C.; Bigham, R.D.; Connolly, M.; Lee, B.; Shepker, T.O.; et al. Physical and chemical characteristics of blast furnace, basic oxygen furnace, and electric arc furnace steel industry slags. *Environ. Sci. Technol.* **2000**, *34*, 1576–1582. [CrossRef]
59. Man, Y.; Shen, W.; Chen, X.; Long, Z.; Corriou, J.P. Dissolved oxygen control strategies for the industrial sequencing batch reactor of the wastewater treatment process in the papermaking industry. *Environ. Sci. Water Res. Technol.* **2018**, *4*, 654–662. [CrossRef]
60. Pásztor, I.; Thury, P.; Pulai, J. Chemical oxygen demand fractions of municipal wastewater for modeling of wastewater treatment. *Int. J. Environ. Sci. Technol.* **2009**, *6*, 51–56. [CrossRef]
61. Von Glasow, R.; Jickells, T.D.; Baklanov, A.; Carmichael, G.R.; Church, T.M.; Gallardo, L.; Hughes, C.; Kanakidou, M.; Liss, P.S.; Mee, L.; et al. Megacities and large urban agglomerations in the coastal zone: Interactions between atmosphere, land, and marine ecosystems. *Ambio* **2013**, *42*, 13–28. [CrossRef]
62. Clayton, M. Worldwide race to make better batteries. *Eureka* **2009**, *1*, 9.

63. Dou, Y.; Lian, R.; Chen, G.; Wei, Y.; Peng, Z. Identification of a better charge redox mediator for lithium–oxygen batteries. *Energy Storage Mater.* **2020**, *25*, 795–800. [CrossRef]
64. Kwak, R.W.J.; Sharon, D.; Xia, C.; Kim, H.; Johnson, L.R.; Bruce, P.G.; Nazar, L.F.; Sun, Y.K.; Frimer, A.A.; Noked, M.; et al. Lithium–oxygen batteries and related systems: Potential, status, and future. *Chem. Rev.* **2020**, *120*, 6626–6683. [CrossRef]
65. Forrester, S.J.; Kikuchi, D.S.; Hernandes, M.S.; Xu, Q.; Griendling, K.K. Reactive oxygen species in metabolic and inflammatory signaling. *Circ. Res.* **2018**, *122*, 877–902. [CrossRef]