Hallmarks in the study of respiratory physiology and the crucial role of Antoine-Laurent de Lavoisier (1743–1794)

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Karamanou M, Tsoucalas G, Androutsos G. Hallmarks in the study of respiratory physiology and the crucial role of Antoine-Laurent de Lavoisier (1743–1794). Am J Physiol Lung Cell Mol Physiol 305: L591–L594, 2013. First published September 13, 2013; doi:10.1152/ajplung.00142.2013.—From the early 17th century the advent of physical and chemical sciences developed two important movements toward the explanation of all vital phenomena: the Iatrochemical and Iatromechanical Schools. The important research of their representatives such as Jan Baptist van Helmont, John Mayow, Robert Boyle, Gian Alfonso Borelli, Richard Lower, and Albrecht von Haller, followed by the discovery of the atmospheric gases, provided a fecund soil for the leading work of Lavoisier in respiratory physiology.

history of respiratory physiology; oxygen; phlogiston theory; combustion

IN THE EARLY PART OF the 17th century, a revolution began to be accomplished in the world of medicine. In 1628, William Harvey’s (1578–1657) great discovery on blood circulation was acknowledged to be the foundation for further development, inaugurating a new era in physiology (12). Scientists realized that respiration was a vital function and an interesting subject of investigation. Furthermore, the advances in modern sciences of physics and chemistry contributed in the exploration of respiratory physiology in terms of oxygen consumption and the products of heat in relation to respiration (7).

In that period, the mechanistic tendency in medicine developed an important movement toward a chemical explanation of vital phenomena, the Iatrochemical School. The Flemish chemist and physician Jan Baptist van Helmont (1577–1644) is regarded as the precursor of this school and one of the most distinguished figures of the 17th century, oscillating between science, mysticism, and fierce persecution even to the point of being denounced to the Holy Inquisition by his rivals. He was a pioneer in the chemistry of gases and invented the name “gas” (derived from chaos, the Greek word for confusion or disorder), possibly because its molecules are continually moving in all directions (19, 30). Van Helmont pointed out that air passed through the lungs as if they were a sieve and that the pulmonary cells were endowed with a motor force, although he erroneously sustained that the respiration process was above all accomplished by the muscles of the abdomen (8, 30).

In 1660, the Honorable Robert Boyle (1627–1691) discovered that animal life is not dependent on air in general but rather on one particular component of the air. However, the majority of scientists rejected his theory and continued to believe the erroneous phlogiston theory according to which burning materials release an invisible gas known as phlogiston that is associated with heating. Moreover, Robert Boyle created Boyle’s Law, which states that the volume of a gas varies inversely with pressure (1).

Another important iatrochemist was John Mayow (1645–1679), considered as one of the most important precursors of Lavoisier in the physiology of respiration. He isolated gases emitted from combustion and respiration by using a siphon to capture the gases in a vessel underwater (20, 21). Mayow discovered that only part of a volume of air is utilized during combustion and respiration and called that part “nitro-aerial” particles (nowadays O2). He also confirmed that air was indispensable for respiration and supported that atmospheric air is absorbed into the blood through lungs, carried to the brain, separated into the ventricles, and passed on through the nerve tubules to the muscles. He concluded that increased breathing and muscular work are accompanied by an increase in the nitro-aerial particles from the air (11, 21).

In 1669, the English physician Richard Lower (1631–1691), follower of William Harvey and pioneer in blood transfusion, described in his book Tractatus de corde: item de motu et colore sanguinis one of the most important experiments in respiratory physiology conducted at this time (Fig. 1). Being interested in determining the nature and the color difference between arterial and venous blood, he repeated a series of experiments originally performed by Andrea Vesalius (1514–1564) and Robert Hooke (1635–1703). In that experiment the thorax of a dog was cut open and a bellows was attached to control respiration. Lower noticed that when blood from the vena cava was forced through the lungs and air was passed over it by the bellows, the color of the blood returning to the heart via the pulmonary vein was bright red and concluded: “the purple color of the blood did not occur as a result of weakening by passing through the lungs but because it was mixed with inspired air” (18, 28). However, the fact that this air was oxygen would not be proven until the work of Antoine-Laurent de Lavoisier in 18th century.
Ten years later, in the posthumous edition of *De motu animalium*, the work of the prominent iatromechanist Gian Alfonso Borelli (1608–1679), we may observe the laws of mechanics and statics applied in all physical phenomena, including respiration. Borelli considered that when air particles enter the blood they cause a continuous oscillation that regulates all vital processes and the respiration was due to contraction of the diaphragm, intercostal muscles, and the compressibility of the air (3, 29).

In the early 18th century Albrecht von Haller (1703–1788), author of *De respiratione experimenta anatomica*, perfused frog lungs with dye and demonstrated the effect of respiration on venous return and pulmonary blood flow. He proposed that the enlargement of the thorax during inspiration and the associated reduction of the intrathoracic pressure would cause blood to be drawn from the extrathoracic vessels into the intrathoracic vessels and the heart. Expiration would have the opposite effect, the increased thoracic pressure causing both a reduction in the volume of intrathoracic veins and an increase in their pressure, so that the flow rate into them from the unchanged extrathoracic veins would be reduced. This is what actually happens during quiet breathing (5, 31).

However, the completion of the modern theory of respiration was based on the discovery of the different chemical elements and compounds: carbon dioxide (CO₂) was discovered in 1759 by the Scottish chemist and physician Joseph Black (1728–1799), who mentioned also that CO₂ was produced by animal respiration (4); hydrogen (H) was first recognized by Henry Cavendish (1731–1810) in 1766 (6); nitrogen (N₂) was isolated in 1722 by Daniel Rutherford (1749–1819) (26) and oxygen (O₂) by Joseph Priestley (1733–1804) and Carl-Wilhelm Scheele (1742–1786) in 1771 (25, 27) and 4 years later by Lavoisier, the principal architect of the 18th century great chemical revolution who managed to put the pieces of the respiratory physiology puzzle together correctly (1, 13).
Born in Paris on August 26, 1743 into a wealthy family, Lavoisier received an excellent basic education in the prestigious Collège Mazarin and entered in Law School to satisfy the family’s expectation, as his father, Jean Antoine Lavoisier, was a well-known lawyer, and his mother, Emilie Punctis, the daughter of a judge. Although he received his degree and was admitted in the Order of Barristers, he never practiced law. He was passionate with sciences and at the same time he was studying law he took courses from leading teachers as Guillaume-François Rouelle (1703–1770) in chemistry and Jean-Etienne Guettard (1715–1786) in geology, contributing in 1765 to his first paper in the Royal Academy of Sciences, on gypsum. In 1769, he was elected member of the French Academy of Sciences for his essay on the construction and placement of street lamps in Paris and in recognition of his earlier research (7).

About the same time, Lavoisier became member and invested his fortune in Ferme Générale (tax farm), a private corporation of financiers commissioned by the Crown to collect tolls and taxes. In 1771, Lavoisier married Marie-Anne Pierrette Paulze (1758–1830), daughter of one of his partners in tax farm. Madame Lavoisier became her husband’s valuable assistant by translating for him the works of British chemists like Priestley and by studying art and engraving with the famous painter Jacques-Louis David, to illustrate Lavoisier’s scientific experiments (24).

Among his numerous scientific achievements, Lavoisier was credited for the invention of a systematic chemical nomenclature; gave oxygen its name deriving from the Greek word for acid-former; termed Cavendish’s “inflammable air” hydrogen, from the Greek for water-former; discovered the composition of water; clarified oxygen’s role in combustion and oxidation; and established a new metric system for weights and measures (24).

From the early 1760s the advent of pneumatic chemistry allowed a new start toward understanding respiration. Joseph Black showed that both respiration and combustion produced fixed air (CO₂). Joseph Priestley claimed that respiration produced phlogiston and it remained to Lavoisier to clarify the connection with the theory of combustion (22).

In 1777 in his Mémoire sur la combustion en général Lavoisier states: “pure air (O₂), after having entered the lungs, leaves in part as fixed air, or the acid of chalk (CO₂)” (17). Moreover, he hypothesized that, just as combustion released heat, so did respiration release “animal heat.” In collaboration with his friend, the mathematician Pierre-Simon Laplace (1749–1827), Lavoisier devised in 1782 an ice-calorimeter with which they could measure the quantity of heat released during combustion and respiration (Fig. 2). This apparatus consisted of three concentric compartments. The center compartment held the source of heat, in that case the guinea pig or piece of burning charcoal. The middle compartment held a specific amount of ice for the heat source to melt, and the outside compartment contained packed snow for insulation. They also connected a sleeve in a separate container to collect the “fixed air” that was given off during combustion or respiration. In a set of experiments, Lavoisier and Laplace measured the quantity of carbon dioxide and the quantity of heat produced by confining a live guinea pig in this apparatus or a piece of burning charcoal. Analyzing these data, Lavoisier concluded that respiration was occurring in the lungs and it was in fact a slow combustion process between carbon and hydrogen that used oxygen and resulted in the formation of heat that dispersed throughout the body, enabling the living animal to maintain its body temperature above that of its surroundings (14, 28). It was not until the 19th century that the renowned physiologist Eduard Pfüger (1829–1910) demonstrated that respiration is an intracellular process (23).

But a new challenge came for Lavoisier: to accurately measure the oxygen consumed during respiration. In 1789, he began a new series of experiments on respiration in which he was assisted by a young chemist Armand Séguin (1764–1835). During the experiment, Séguin wore an airtight mask of leather with a tube in its mouthpiece and at the other end of the tube was a pneumatic trough of oxygen. Lavoisier measured the amount of gas Séguin used, the rate of his breathing, and his pulse over the course of an hour. The level of the consumed oxygen varied depending on his activities: he needed three times more oxygen while exercising as when resting, more when eating than fasting, and more when sitting in a cold room than in a warm one. His pulse and breathing rate varied too (2, 15, 28) (Fig. 3).

Lavoisier’s experiment laid the foundations for a new theory that would explain the role of respiration in a broader biological cycle: “The animal machine is governed by three types of regulators: respiration, that consumes hydrogen and carbon and furnishes heat; transpiration, that increases or diminishes, in accordance with the necessity to carry away more or less heat; and finally digestion that restores to the blood that which is lost through respiration and transpiration” (16). For the first time the human metabolic chain was understood as a consequence of physical processes that integrated the traditional physiological function of digestion, respiration, and the dissipation of energy during different kinds of work, paving the way for the modern investigation of the metabolic processes of life.

However, at the height of the French Revolution, Lavoisier’s work ceased. In the prerevolutionary times, he had made a powerful enemy in Jean-Paul Marat (1743–1793), physician, political theorist, and one of the most radical voices of the French Revolution. Marat had applied for membership in the French Academy and had been rejected, with Lavoisier being a major factor in the rejection (9). In 1792 Marat, now a revolutionary leader, demanded Lavoisier’s death. Although Marat was himself assassinated in 1793 (while lying in his bath), Lavoisier was guillotined the following year, in the midst of the Reign of Terror, a period of violence that occurred after the onset of the French Revolution. On 8th May 1794, the revolutionary tribunal sentenced him to death together with 27 other tax farmers as it was believed that they were linked to the Old Regime through the tax farm (24). It is said that Lavoisier asked for the execution to be temporarily suspended for him to complete some of his experiments but the presiding judge replied: “La république n’a pas besoin des savants” (The Republic has no need of scientists) (10).

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