

HYPERVENTILATION HYPOCAPNIA AS THE LEONARDO DA VINCI'S SYNDROME

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received: 29.8.2018;

revised: 2.10.2018;

accepted: 28.11.2018

SUMMARY

The paper in early history of pulmonary medicine deals with studies of hypocapnia as a result of hyperventilation. Hyperventilation hypocapnia provokes respiratory alkalosis, subsequent ion changes in blood may cause disorders of myocardium conductivity and excitability resulted in arrhythmiae and even heart failure. Besides, hypocapnia limits the cerebral circulation which may be manifested in euphoria and even loss of consciousness. It is dangerous component of high altitude disease. Earliest medical descriptions of hyperventilation hypocapnia and its cardiac consequences are traditionally related with publications by an American physician of XIX age J.M. Da Costa and British doctor A.B.R. Myers. There exists a generally accepted eponym of "Da Costa syndrome". Hereby the authors for the first time coin data that disorders related to hyperventilation were described more than 360 years prior to Da Costa - by an Italian polymath of Renaissance epoch Leonardo da Vinci and suggest new eponym of "Leonardo da Vinci's syndrome". The article also briefly analyzes the medical studies of Leonardo da Vinci and his early contribution into Human Anatomy and Thyroidology.

Key words: hyperventilation hypocapnia - Leonardo da Vinci's syndrome

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Introduction

The unique polymath Leonardo da Vinci (1452-1519) impacted deeply in various fields of knowledge. For instance, his predictions, drawings, and inventions inspired mankind to realize the eternal human dream of flights (Leonardo da Vinci 2017). The aim of this article is to review and partially restore his priority in some areas of Medicine, namely in description of hyperventilation hypocapnia and its consequences.

Medical studies of Leonardo da Vinci

Leonardo (Figure 1) was not a physician, but showed a profound interest in Medicine, in particular, to anatomical research and Biomechanics of the body. Studying the Human Anatomy since 1485 till 1516 in Milan, Florence and later – in Rome, he attended autopsies and even dissected few bodies himself. In Milan he collaborated with a young anatomist from the University of Pavia, Professor Marcantonio della Torre (1481–1511) (Figure 2), and finally created 120 (!) albums of anatomical drawings with 750 pictures (Keele 1983), ahead of the great Andrea Vesàlio aka Andreas van Wesel (1514–1564), who later turned Anatomy into a science. For example, the first anatomically and topographically correct description of human thyroid gland belongs to Leonardo da Vinci. He made it at the Santa Maria Nuova Hospital of Florence around 1505-08 (Figure 3). In the bank of this hospital Leonardo da Vinci, as a member of the local Guild of Artists, Physicians and Pharmacists, kept his savings, which may witness for his continuous relations with medical community.



Figure 1. Leonardo da Vinci. Self portrait (circa 1515, Royal Library, Torino)



Figure 2. Marc Antonio della Torre (Turrianius). Line engraving, 1688. From: Wellcome Library, London. Wellcome Images



Figure 3. Drawings of thyroid gland and notes on it by Leonardo da Vinci. From: Quaderni d'anatomia, I-VI: Royal Windsor Library, publication by C.L. Vangensten, A. Fonahn, H. Hopstock. Christiania: J. Dydward, 1911-1916

Leonardo da Vinci not only depicted the thyroid and neighboring organs but also wrote near the picture his hypothesis: "This gland is created to fill in a space between the trachea and the sternum, where there is no muscle" (Vescia & Basso 1997). Leonardo da Vinci and Marcantonio della Torre planned to publish a textbook and atlas of Human Anatomy together, but the untimely death of the young anatomist from the plague interrupted this promising project able to establish early breakthrough in this science (Keele 1983). Otherwise, perhaps these authors, but not Vesalius, would be considered the founders of Human Anatomy.

Leonardo da Vinci dreamed of a glass model that allowed observing the movement of blood in the heart (Leonardo da Vinci 2017). Despite the obvious relation of Leonardo's creativity with medical items, so far in the world of Medicine, unfortunately, there is not a single eponym that would perpetuate the name of the genius of the Renaissance. This, in our opinion, is unfair. And that's why.

Early contribution of Leonardo da Vinci into Pulmonary Pathophysiology

Getting acquainted with the writings of Leonardo da Vinci, among the collection of his paradoxical riddles, written in the form of parodies of the eschatological clerics of the religious Dominican preacher, Girolamo Savonarola (1452–1498) who one time ruled in Florence – and known as "Prophecies", we accidentally found an interesting text: "C.A. 370 r. *Of extinguishing the light when one goes to bed*".

Any physician will not leave unnoticed the following words: "Many by forcing their breath out too rapidly will lose the power of sight, and in a short time all power of sensation" (Leonardo da Vinci 2018).

Pathogenesis of hypocapnia

Both the humoral activating influence of the increased partial pressure of carbon dioxide (CO_2) on the respiratory center (Guyton & Hall 2006) and antioxidant effect of CO_2 delaying the irreversible stages of hypoxic necrobiosis (Churilov 2015) – are well-proven. Hyperventilation of the lungs leads to the development of hypocapnia – a reduced content of CO_2 in the arterial blood (less than 35 mm Hg), resulting from excessive exhale of carbon dioxide out of the body, which leads to respiratory alkalosis. Hypocapnia can result from an intensive artificial ventilation of the lungs or occur both with involuntary and with arbitrary hyperventilation. It accompanies high altitude disease. Because evolutionary ancestors of humans lived in plains and not in high mountains, hypocapnia could occur in them only as a result of hyperventilation. Hence, natural selection gave for adaptation to it quite a few of mechanisms, including just inhibition of respiratory center and cerebral ischaemia. Teachers

of Internal Medicine are familiar with cases of fainting in patients, which a whole group of diligent students asks for deep and unacceptably long breathing during lung auscultation lessons (Figure 4).



Figure 4. Traditional lesson of auscultation for a group of the cadets of Emperor's Military Medical Academy in Saint Petersburg circa 1880. To the right from the teacher stand the cadets: Vladimir Mikhailovich Bekhterev (with notes in his hands) – in future – outstanding psychoneurologist; Sergei Mikhailovich Lukyanov – in future eminent pathologist and Chief-Procurator of the Holy Synode of Russian Orthodox Church; Ivan Petrovich Pavlov – in future Nobel Prize winner in Physiology and Medicine, all of them were schoolmates of the same class. From Museum of S.M. Kirov Military Medical Academy, courtesy of Assoc. Prof., Leut.-Col. A.E. Korovin

Hypocapnia causes significant changes in the physico-chemical properties of the body, its metabolism and in many physiological functions. The current concept in Pathophysiology of hypocapnia (Kovač et al. 2014a) as well as related clinical cases (Kovač et al. 2014b) are reviewed in details elsewhere by Z. Kovač et al. As the partial pressure of CO_2 in blood decreases, the rhythmic excitation of the respiratory centre gradually weakens; the breathing becomes arrhythmic or completely stops. Pronounced hypocapnia causes a "hyperventilation syndrome" (Guyton & Hall 2006, Churilov 2015, Kovač et al. 2014a, 2014b). At the same time, cerebral circulation suffers with resulting dizziness, darkening and flickering in the eyes; psychomotor activity and fine motor coordination (like handwriting) come to disorder and even panic attacks may occur. Often there is a decrease in mental performance, disruption of orientation, hyper-tonus of skeletal muscles, convulsions and finally loss of consciousness (fainting) may occur (Kovač et al. 2014a, 2014b, Kern & Rosh 2018). Hypocapnia burdens the course of hypoxia and contributes to the pathogenesis of high altitude and mountain diseases and bronchial asthma. Hypocapnic alkalosis may cause severe arrhythmiae (Churilov 2017).



Figure 5. J.M. Da Costa circa 1880 (from the Center for the History of Medicine, USA. URL: <http://www.civilwarmed.org/jacob-mendes-da-costa/>, accessed 27 September 2018)

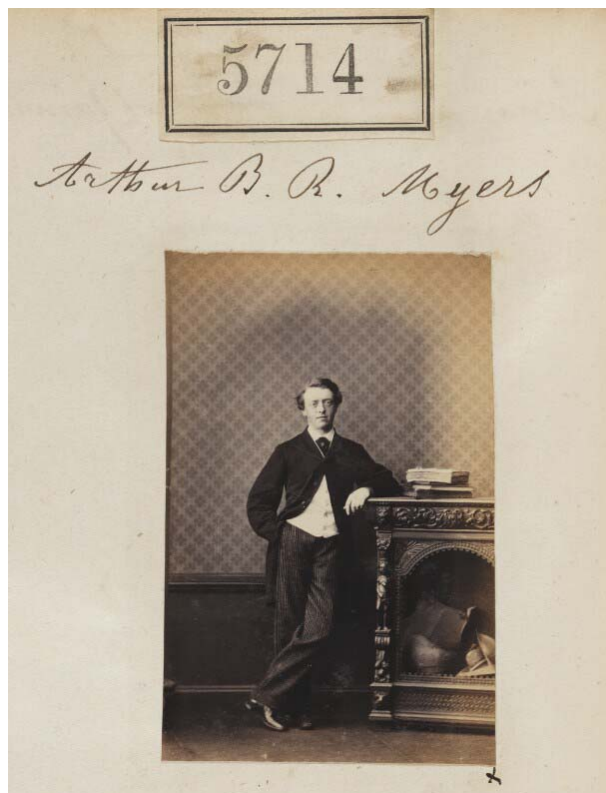


Figure 6. A.B.R. Myers, photo by C. Silvy on 9 September 1861 (National Portrait Gallery, London, UK. URL: <https://www.npg.org.uk/collections/search/portrait/mw193803>, accessed 27 September 2018).

Da Costa syndrome

The term "hyperventilation syndrome" was coined in 1871 to describe disorders associated with shortness of breath in patients with so called "soldier's heart". Both terms were used by a participant in the American Civil War, a Danish-born American physician – Jacob Mendez Da Costa (1833–1900) (Enersen 2018), who is considered the pioneer in description of this syndrome as "irritable heart" (Figure 5). The phenomenon was described by Da Costa as combining effort fatigue, dyspnea, a sighing respiration, palpitation, sweating, tremor, an aching sensation in the left praecordium, utter fatigue, an exaggeration of symptoms upon efforts, and occasionally complete syncope (Da Costa 1871). A year earlier similar hyperventilation disorder was mentioned in soldiers by a British Army surgeon and traveler Arthur Bowen Richards Myers (1838–1921) (Myers 1870) (Figure 6). Now we know that hyperventilation via alkalosis decreases the sensitivity to catecholamines, which may provoke their hypercompensatory excess and result in panic attack when alkalosis is compensated (Sikter et al. 2007).

Legacy of Leonardo da Vinci

However, Leonardo da Vinci noticed and briefly described hypocapnic phenomena more than 360 years prior to Da Costa and Myers. The striking observance of a genius who not only studied Anatomy and Pneumodynamics, but also first described the outcome of hyperventilation of the lungs, makes it possible to consider him a pioneer in this area. Because the science differs from a pseudoscience in that it predicts the future in its field (which first was emphasized by Sir Joseph John Thomson, 1856–1940) (Rayleigh 1942), Leonardo da Vinci convincingly recorded the triumph of the scientific worldview over Savonarola's religious obscurantism in the form of his humorous but surprisingly justified "Prophecies".

We propose the phenomenon of hyperventilation hypocapnia henceforth to be called "*Leonardo da Vinci's syndrome*". Let this eponym be a tribute to the memory of the greatest man of all time – on the part of medical doctors.

Conflict of interest : None to declare.

Contribution of individual authors:

Both authors contributed equally into this article.

Acknowledgements:

Abstract of the short early version of this paper was first published by authors in Russian (*Zhalna patologiya ta patologichna fiziologiya* (Lugan'sk). 2010; 5:55). Authors are grateful to Prof. Carlo Selmi and Prof. Yehuda Shoefeld who inspired them for this article and helped much in its editing.

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