ANCIENT HISTORY OF PITUITARY STALK

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ANCIENT HISTORY OF PITUITARY STALK (Abstract) : Organ of milimetric size, the pituitary stalk has drawn the attention of anatomists since Antiquity. Considered for hundreds of years to be an evacuation path for waste products produced in cerebral ventricles, the pituitary stalk aroused the curiosity of anatomists. In this study, we will be presenting the first contributions of the ancient scholars *Hippocrates of Kos*, *Rufus of Ephesus* and *Galenus of Pergamon* on the anatomy and function of pituitary stalk. **Key words** : PITUITARY STALK, INFUNDIBULUM, HISTORY OF ANATOMY

HIPPOCRATES OF KOS

The father of medicine, the Greek ***Hippocrates of Kos (460-370 BC)*** (Fig. 1) believed that the brain had the role of a cooling organ which secreted *phlegm* (i.e. mucus) through the skull base (1). Hippocrates considered this phlegm to be one of the four bodily humors along with blood, yellow bile, black and that it actually was involved in head diseases. In his view, when excessive heat accumulated in the head, the movement of phlegm was affected and melted phlegm flow in the head was directed to various areas of the body producing symptoms, such as urination, pain, vomiting or impairing hearing (2).

As in Ancient Greece dissections were uncommon and inacceptable due to superstitions related to the violation of human body, Hippocrates could not check his medical theories based mainly on empirical observations (3). Nevertheless, we may consider Hippocrates' theory on the role of phlegm as being the first primitive conception on the physiology of the hypothalamic pituitary axis.

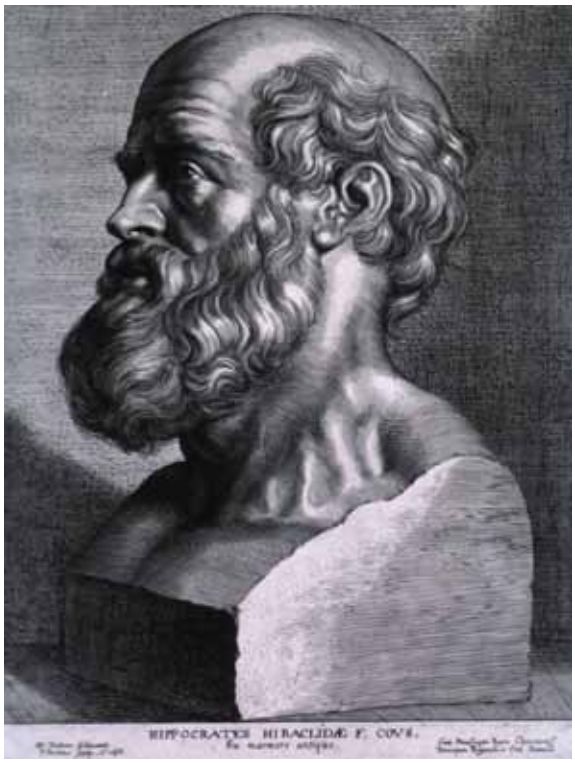

Fig. 1. *Hippocrates* (engraving by Peter Paul Rubens, 1639) (public domain)

Regarding his ideas, the 70 texts of Hippocrates in his paper *Corpus* have been adopted with enthusiasm by the Romanian physician ***Galenus of Pergamon (129-200 A.D.)*** and right after the fall of Alexandria in 642 A.D. the medical knowledge of Hippocrates spread out to the Arab world, where it was been kept by the Arab physicians in the Dark Middle Ages. It was found at the beginning of the 14th century in the curricula of European medical schools.

HEROPHILUS AND ERASISTRATUS

Hippocrates was followed by the anatomists of Alexandria ***Herophilus of Calcedonia (335-28)*** and ***Erasistratus of Kios (304-250)*** who had the chance to dissect human bodies and to contribute with important notions to neuroanatomy (4), but unfortunately most of their works that had been stored at the Royal Library of Alexandria were lost in the fire in 48 BC when Julius Caesar (Fig. 2) wanted to destroy the Egyptian fleet. Then the fire extended from the dockyards to the library and destroyed not only the work of Herophilus and Erasistratus, but also the 500,000 scrolls (5, 6).

RUFUS OF EPHESUS

After the death of Herophilus and Erasistratus, for three centuries nobody had contributed to the development of knowledge in neuroanatomy until ***Rufus of Ephesus (80/90-120/150 AD)*** arrived to Alexandria (7), where he became a personal physician of the Queen Cleopatra (Fig. 2) (8). Rufus started to dissect monkeys and pigs, as the dissection of human bodies from the times of Herophilus and Erasistratus was not allowed in this academic center (9). Compared to his predecessors, Rufus focused more on the anatomy of brain and described cerebral ventricles, the sellar region and the infundibulum. He was the first who introduced the term *infundibulum* to describe this funnel-shaped passage but probably he roughly referred to the hypothalamic part of the third ventricle (10, 11). Rufus compared the funnel shape of the inferior part of the third ventricle with the superior part with a huge leather bag (*infundibulum*) used by Romans to transport wine (12).

GALENUS OF PERGAMON

The last great physician of the Antiquity, ***Galenus of Pergamon (129-200AD)*** was also interested in brain neuroanatomy performing dissections and vivisections on a wide variety

Fig. 2. *Cleopatra and Caesar*
(Jean Leon Gerome, 1866) (public domain)

of animals. Even if human dissection were prohibited during his time, we may suspect that Galenus observed the pituitary gland and the anatomy of the sellar region in gladiators with severe cerebral trauma when he had been their physician in Pergamum. So, Galenus also saw the *infundibulum*, pituitary stalk and the pituitary gland, the function of which he tried to understand (13). Considered to be the first experimental physiologist (14), Galenus took over from Rufus the term i*nfundibulum*, which he suspected to play the role of a funnel to direct waste products made up in the cerebral ventricles by transformation of "energy of the body (the vital spirit) into "sensation and impulse" to the nervous system (animal spirit) and that was transported through spinal cord and then the nerves to the body periphery. This process took place in the vascular network around the pituitary gland that he called "rete mirabilis" (15, 16). Then, through the *infundibulum*, the impurities were transferred to the pituitary gland that filtered them before passing through the perforations of the sphenoid bone and ethmoid towards nose and mouth where they appeared as pituitary or nasal mucous (10, 17, 18). This theory was adopted by Galenus from the Hip-

pocratic Writings written by the author in in Book 9 in his paper *De Usu Partium*, the main physiological work of the Antiquity (15) and had been accepted as the ultimate truth fourteen centuries until Vesalius, who corrected the theory of Galenus (14).

"THE GOLDEN AGE" OF PITUITARY STALK ANATOMY

The interpretations of Galenus regarding the anatomy and physiology of the infundibular-pituitary stalk-pituitary gland complex had been adopted as truth until Renaissance and by the young anatomist ***Andreas Vesalius (1514-1564),*** who at the age of 29 was writing a revolutionary anatomy book "De Humani Corporis Fabrica (1543)". He described the pituitary gland as a separate entity that he named *glandula pituitam cerebri excipiens* and recognized its role attributed that had been given to it by his predecessors in the pituitary secretion to the nose (19, 20). Professor Vesalius also described the infundibulum of Rufus that he named *basinor pelvis* (Fig. 3) and that he stated "is shaped like a funnel […] that receives the cerebral pituita that flows down from the third ventricle […] and […] through which cerebral pituita drips into the gland through foramina next to the gland (17, 21). Moreover, Vesalius

Fig. 3. Vesalius's drawing of the *infunibulum* (adapted from *De humani corporis fabrica*, 1555)

left to us the first diagram of these structures. He proved the funnel function of the infundibulum after filling the third ventricle with coloured liquid (22) and this version of the structure and its functionality had been kept for more than three hundred years.

Through their thirst for knowledge and their studies, the ancient scholars *Hippocrates of Kos, Rufus of Ephesus* and *Galenus of Pergamon* have been viewed as pioneers of anatomy and the function of pituitary stalk (Fig. 4). The anatomical notions on this structure at the basis of the brain had been accepted and perpetuated as an absolute truth until Renaissance when the young anatomist Andreas Vesalius was opening the "Golden Age" of Italian Anatomy.

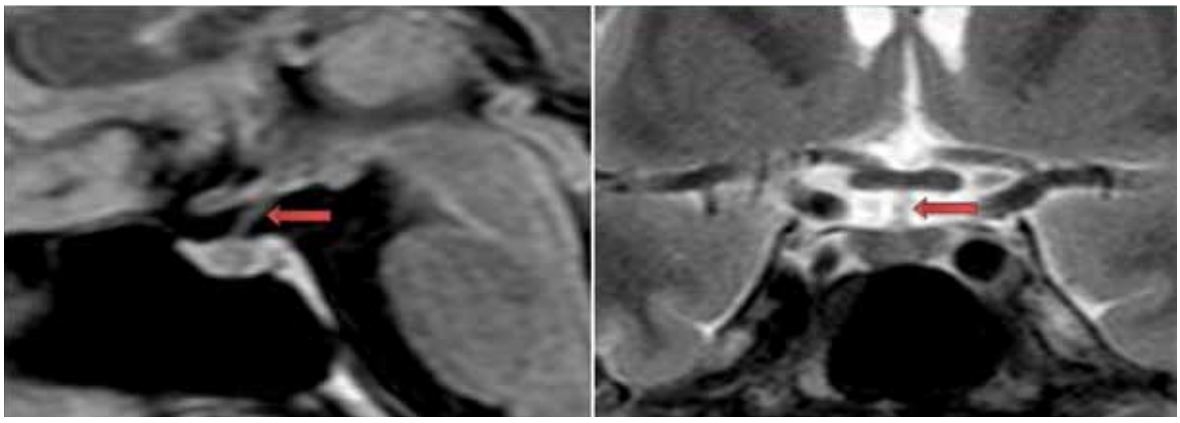

Fig. 4. MRI aspect of pituitary stalk (red arrows) (Dr. A. Cucu's personal collection)

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