Introduction
and
History

In order to be able to reach a better understanding of the changes that can be observed at the level of the cerebral vascular structures, both arterial and venous, on the microscopy slides, we shall begin with a short overview of the cerebrovascular development.

The humoral theory of Hippocrates had made possible the beginning of the study of anatomy, and according to it the disease was caused by the disturbances in the balance of the four 4 elemental body humours – the black bile, the yellow bile, the blood and the phlegm.

As an example, epilepsy was believed to be caused by the phlegm which descended from the brain and prevented the pneuma ("the vital air") from entering the blood vessels (Gross, 1987).

In the fourth century B.C. it had been registered a gradual change in the Grecian concepts of death, a new trend which had been heralded by Plato (427 - 347 B.C.) (Danaila, 2016). Crucial to this process had been the dissertations of Socrates which had been described by Plato in the Phaedo dialogue. For Socrates (469 - 399 B.C.), the body merely housed the soul; therefore, the fate of the corpse was of less concern (Kevorkian, 1959).

This school of thought had further evolved through Diogenes (412 - 323 B.C.) and Aristotle (384 – 322 B.C.).

However, Aristotle, who is said to have performed a big number of dissections and vivisections on animals, had observed that in all the animals the brain was located in a position at the front of the head and was surrounded by 2 membranes, the meninges. He dismissed the brain as being bloodless, cold and bipartite, thus advocating and characterizing the cardiocentric theory, which emphasized the heart as the seat of the soul and of the intellect (Gross, 1987; Strkalj and Chron, 2008).

Furthermore, Aristotle is cited as the earliest source which had described the common effect of the compression of both carotid arteries (O'Malley and Saunders, 1983).

Also, Aristotle's seminal observations had suggested that the brain depends on the great vessels in the neck to function.

The contribution of the Greek physician Galen (129 - 199 A.D.) through the animal dissections he had performed had established him as one of the most important figures of the classical medical science. Thus, almost 500 years after Aristotle, Galen had established that the arteries contain blood and not air (Fishman and Richards, 1964)

Much later, during the **Renaissance**, there had been many factors which had led to the medical progress.

The first accurate anatomic illustrations are credited to artists, and especially to Leonardo da Vinci (1452 - 1519) who had produced several detailed anatomic drawings, including depictions of the carotid arteries in the neck, based on the dissections performed on animals and following a rigorous study of a 100-years-old human who had died after he revealed to Leonardo that he felt nothing wrong with his body other than weakness, (O'Malley and Saunders, 1983; Dungan and Heiserman, 1996).

Later, Andreas Vesalius (1514 - 1564) had produced, in his fine work De Humani Corporis Fabrica (1543), more accurate anatomic drawings of the brain, of its ventricles, and of the human vascular system based on dissections he had performed on both animals and human bodies (O'Malley and Saunders, 1983; Feindel, 1995).

These anatomic studies had provided an important roadmap for the vascular network, but the understanding of the blood flow relied on the Galenic theory according to which the blood was delivered to the end organs through both arteries and veins.

According to Roberts and Tomlinson (1992) and to Dungan and Heiserman (1996), it was not until 1628, when William Harvey (1578 - 1657) had published his revolutionary findings in *Exercitatio Anatomic de Motu Cardis et Sanguines in Animalibus* (Anatomical Essay on the Motion of the Heart and Blood in Animals), that our modern understanding of the blood circulation was established.

On the other hand, Johann Vesling (1598 - 1649), in his Syntagma Anatomicum (1641), had only described the parts of the body as they were observed during dissection and had avoided the discussion of the theoretical matters so as not to create confusion.

The illustrations and the text related to the intracranial vasculature had appeared in the subsequent edition published in Padua in 1647 (Lo and Ellis, 2010).

Vesling had been the first to describe the presence of the posterior communicating arteries bilaterally. The basilar artery was divided into 2 posterior communicating arteries, without giving off the posterior cerebral arteries (Lo and Ellis, 2010). Vesling had also described the branches of the middle meningeal arteries as part of the rete arteriosum (Lo and Ellis, 2010).

Thomas Willis (1621 - 1675), who is considered to be one of the greatest neuroanatomists, is best known for his discovery of the circle of Willis and for the characterization of the cerebrovascular anatomy. He was perhaps the first to contribute to a major discovery in the realm of the cerebrovascular physiology and surgery through the characterization of the circle of Willis and of the anastomotic blood flow in ischemic conditions by tying off vessels and then reasoning and noting: "as for example, if the Carotid on one side should be obstructed, then the vessels on the other side might provide for either Province [….]". Further, the both the Carotids should be stopped, the offices of each might be supplied through the Vertebrals." (Willis, 1684 cited in Symonds, 1955) (Willis et al., 1965; O'Conner, 2003; Rengachary et al., 2008).

Thus, the details regarding the outflow of the carotid arteries had been provided by the work *Cerebri Anatome Nervorumque* (1664) of the London physician Thomas Willis, after whom it had been named the anastomotic circle located at the base of the brain (Dungan and Heiserman, 1996).

Interestingly, Willis was not the first to describe this circle of arteries, but he had been the first to do it in such great detail (Mirzadeh and Spetzler, 2015).

Gabriele Falloppius (1523 - 1562), in his *Observationes Anatomicae* (1561), had provided an incomplete, unillustrated and painstaking description of the blood supply at the base of the skull (Meyer and Hierons, 1962).

Giulio Casserio (1552 - 1616), after whom the trigeminal (gasserian) ganglion is named, had been the first to draw the arterial circle. Undoubtedly, Casserio had described the vasculature much more accurately than Fallopius.

After Vesling, it is worth mentioning that the Swiss pathologist Johann Jakob Wepfer (1620 - 1695) had also accurately described this circle of arteries in 1658 in his classic treatise on strokes, *Historieae Appoplecticorum* (Lasjaunias et al., 2006).

Finally, the development of the cerebral angiography by Egas Moniz, as discussed in his classic work *L'Angiographie Cerebrale* (1934), had enabled the radiographic evaluation of the carotid arteries and of the intracranial vasculature in the living patients (Dungan and Heiserman, 1996).