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Miscellaneous

A lucky mistake: the splenic glands of Marcello Malpighi☆,☆☆

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Summary Marcello Malpighi (1628-1694) is one of the most important anatomists and physicians in the history of medicine. His contributions to the understanding of human anatomy and physiology span from the first description of capillary circulation to a thorough analysis of the structure and function of body glands. Malpighi believed that most organs consisted of glandular structures, whose distribution and microscopic features determine each organ-specific function. He also applied this view to the study of spleen anatomy, which he recognized as composed of 2 distinct anatomic compartments (ie, the red and the white pulp). Malpighi's observations on the structure and function of the spleen were first published in 1666 in *De Viscerum Structura*. In this paper, we pay tribute to this work, presenting Malpighi's theory of the spleen as a glandular organ. The rationale of Malpighi's view and its value for contemporary pathologists and medical researchers will also be elucidated.

1. Introduction

Marcello Malpighi (1628-1694) is one of the greatest physicians and biologists of the 17th century (Fig. 1). Born into a wealthy family from central Italy, Malpighi studied medicine at the University of Bologna. Here, he became a professor of medicine and devoted himself to the study of microscopic anatomy. This led him to pivotal achievements in the field of anatomy and histology, including the discovery of capillary vessels and pulmonary alveoli and the first description of squamous epithelia and blood cells. These achievements gained him worldwide recognition. He became the personal physician of Pope Innocent XII and was the first Italian to be admitted as an honorary member to the Royal Society [1].

One of Malpighi's most important works is *De Viscerum Structura*, a treatise in 4 essays, discussing the microscopic anatomy of the liver (*De Hepate*), the kidney (*De Renibus*), the cerebral cortex (*De Cortice Cerebri*), and the spleen (*De Liene*) [2]. This work wiped out long-lasting dogmas on human anatomy and physiology, laying the foundations for new, scientifically based medical knowledge.

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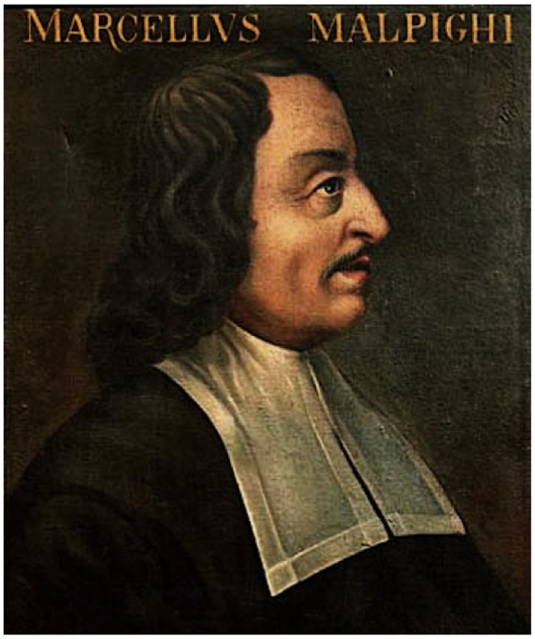

Fig. 1 Marcello Malpighi (1628-1694). This 18th-century portrait of an unknown author is currently located in the Hall of Medicine at Bo Palace, University of Padova (Padova, Italy). It was likely part of a private collection belonging to Giovanni Battista Morgagni, the founder of anatomic pathology and former professor at this university.

Malpighi believed that most tissues consisted of elementary anatomic modules, which he recognized as "glands." The different distribution and microscopic features of these glandular units determined each organ-specific function. In Malpighi's view, glands consisted of minute cavities, equipped with excretory ducts, and surrounded by blood vessels and nerves (Fig. 2A). Their function was essentially to filter blood and to produce different types of secretions [2,3].

Malpighi believed that a huge variety of organs were made up of glands. In *De Viscerum Structura*, he reported experimental evidence that glands are indeed present in the kidney, the liver, the brain, and the spleen. Although Malpighi's achievements on renal and hepatic anatomy are widely acknowledged, legitimate questions remain in regard to the "glands" he observed in the cerebral cortex and the spleen. Recent studies have demonstrated that Malpighi's cerebral glands are artifacts due to inadequate fixation and processing [4]. The history of splenic glands, however, is more complex and intriguing.

In this paper, we pay tribute to Marcello Malpighi's view of spleen anatomy and physiology. To this aim, we will examine selected passages from *De Liene* to investigate the logical and scientific roots that supported Malpighi's theories on splenic structure and function.

2. Malpighi and the red pulp

> *One opinion seems to be shared by all Anatomists: that the spleen originates from some kind of clotted blood, which anchors and fixes vessels that arise from it. As such, the spleen would have some features in common with other organs such as the heart, the liver and the kidneys. Long and laborious research, however, did give me the opportunity to better understand the structure of the spleen, which now seems more clear and precise. The splenic parenchyma is in fact a patchwork of membranes surrounding small chambers and cells.*

Malpighi is rarely remembered as the first anatomist who described the red pulp. In fact, he devoted many efforts to elucidate the intricate network of channels and cavities, which constitute the majority of the splenic tissue. He succeeded by applying macro- and microscopic analyses, which helped him identify fibrous septa originating from the splenic capsule and branching into the red pulp. These fibrous strands ultimately circumscribe blood-containing spaces, referred to as *chambers* or *cells* (Fig. 2B). Such a thorough description constitutes the first modern account of red pulp sinuses and cords. Malpighi's achievement is noteworthy because it challenged long-standing theories, which had considered the spleen to be a mere clot of blood [5].

The method he used to clarify such an anatomic structure deserves special consideration, as it provides invaluable insight into the 17th-century approach to medical and biological issues.

> *To make this structure obvious to all, shall the splenic artery be isolated and knotted up; aftermath, shall air be blown through the splenic vein with a syringe or directly by mouth. The whole spleen will immediately become turgid and of increased volume […]. If, on the other hand, one dries out and cuts such a swollen spleen, he will notice huge numbers of small chambers and cells, similar to a honeycomb.*

For his research activities, Malpighi adopted revolutionary methods and new experimental settings. As a former student of the physicist Giovanni A. Borelli (1608-1679), he systematically applied the scientific method to elucidate the nature of tissues and organs. Spleen inflation and exsiccation are paradigmatic examples of such an approach, as they are specifically aimed to unveil the fine structure of the red pulp: air inflation contributes to the expansion of splenic sinuses to a degree that makes them appreciable even on gross inspection; exsiccation contributes to "fixation" of this anatomic artifact, facilitating spleen sectioning and parenchymal examination. Thanks to Malpighi, this procedure was largely credited throughout Europe and widely applied by several authors, including Herman Boerhaave (1668-1738), Philip Verheyen (1648-1710), and Leopoldo Marco Antonio Caldani (1723-1813) [6-8].

3. Malpighi and the white pulp

> *We have already noticed the extraordinary ingenuity of Nature in organizing the structure of the spleen. In general, it adopts one way to operate and this, as said, is simple: for*