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HISTORICAL PERSPECTIVE

About the glomerulus

Who was Marcello Malpighi? As reported by Belloni [1], Marcello Malpighi was described by Domenico Gagliardi in 1689 in his "*Anatomes Ossium Novis Inventis Illustratae Pars Prima*" as "alter microcosmi Columbus" who "non unum tantum, verum innumeros novos orbes in sola viscerum structura detexit".

A complete biography of the scientist was assembled in 1967 by Luigi Belloni in "*Opere scelte di Marcello Malpighi*" [1]. A summary of that biographical description follows:

Marcello Malpighi was born in 1628 at Crevalcore, a small town close to Bologna. After the completion of high school, he began his studies in 1646 at the University of Bologna under the sponsorship of the philosopher Francesco Natali. It was Natali who advised him to study medicine. Malpighi entered the school of Bartolomeo Massari in 1649, where he became one of the nine pupils of the "chorus anatomicus". In 1653 Malpighi graduated in Medicine and Philosophy. In 1656 he was appointed as a teacher at the University of Bologna; at the end of the same year he was appointed Professor of Medicine at the University of Pisa. It was at Pisa that Malpighi first met Alfonso Borelli (1608–1679) and the anatomist Claudius Auberius (Claude Aubery, Aubry). This meeting was particularly useful to all three scientists in that it allowed them to communicate with each other and discuss the results of their scientific research. This close association led to the discovery of two important structures: the spiral fibers of the heart by Malpighi (according to Belloni [1], Borelli attempted to secure the credit for that observation) and the seminal tubules of the testis by Auberius. Malpighi left Pisa in 1659 after receiving an appointment to the University of Bologna. One year later (1660) he discovered the fine structure of the lung, thus providing a foundation for the discipline of microscopic anatomy. He described his research on the lung in two letters to Borelli entitled "De Pulmonibus", i.e. "about the lung".

In 1662 Malpighi was appointed Professor of Medicine at the University of Messina in Sicily. It was during this appointment that he performed important studies on the nervous system, the lymphatics, and the hematopoietic system. In 1666 he again received an appointment to the University of Bologna. It was in that same year that he discovered the fine structure of the kidney which he described so beautifully in the section "*De Renibus*" of the publication "*De Viscerum Structura*" (a publication which also included sections entitled "*De Hepate*", "*De Cerebri Cortice*" and "*De Liene*") [2].

In subsequent years, Malpighi also published many interesting studies on plants, i.e., "*Anatomes Plantarum Pars Prima*" (1675), and "*Anatomes Plantarum Pars Altera*" (1679). "*De Structura Glandularum Conglobatarum Consimiliumque Partium*" was published in 1689.

In 1691 Malpighi went to Rome as the personal physician to Pope Innocenzo XII; he died in Rome on the 29th of November, 1694, in his home on the Quirinale hill, from a cerebral hemorrhage.

Malpighi and the fine structure of the kidney. The gross anatomy of the urinary system was well recognized prior to 1660, but there was little or no understanding of the mechanism of urine formation since the fine structure of the kidneys was understood so poorly. Earlier attempts of several great anatomists (G. Berengario da Carpi, A. Vesalio, S. Falloppia and B. Eustachi) had been unsuccessful in discovering and demonstrating the fine structure of the kidney. Actually, Bartolomeo Eustachi ("*Libellus De Renibus*", Venezia, 1563–1564) had been able to demonstrate what we now recognize as the arciform arteries and veins, but Nathanael Highmore (1613–1685) in his "*Corporis Humani Disquisitio Anatomica*" (L'Aia, 1651) had incorrectly described these arciform structures as arteriovenous anastomoses which did not exhibit any further ramifications within the renal cortex.

It was in 1662 that Lorenzo Bellini (1643–1704), then only 19 years old, demonstrated that the interlobular vessels were derived from the vasa arcuata ("*Exercitatio Anatomica De Structura Et Usu Renum*", Firenze, 1662). Furthermore, by observing that urine could be obtained by squeezing the papilla, Bellini discovered the tubular structure of the renal medulla and attributed its function to the conveyance of urine from the cortex to the renal pelvis. It was the Master of Bellini, Alfonso Borelli, who suggested that urine formation took place in the "sinuli", i.e., the structures that were described by Bellini as the junctions between the afferent tubule (i.e., the afferent arteriole) and two efferent tubules (i.e., the efferent arteriole and the proximal nephron).

The anatomic observations of Bellini and the interpretation of their significance by Borelli were very impor-

tant; nevertheless, the nature of operation of the "sinuli" was still missing and the recognition of the glomerulus and its function as a "dialyzer" was still lacking.

It was at this time that the genius of Marcello Malpighi became apparent when he described the actual structure of the kidney, first beginning with the discovery of the glomerulus. It was in the Library of the University of Bologna that I recently had the opportunity to read and enjoy Malpighi's description of the fine structure of liver, brain, spleen and kidney in "*De Viscerum Structura*" (1666) [2]. The section entitled "*De Renibus*" was particularly interesting to me as a nephrologist. It provided a complete description of the gross morphology as well as the microscopic structure of the kidney in concise and clear terms as written by Malpighi in his own language, the Latin. Prof. Belloni, Director of the Institute of the History of Medicine at the University of Milan, has recently written a review in Italian of the complete works of Malpighi [1].

I should first like to emphasize and summarize from the introduction as written by Malpighi himself in "*De Renibus*". It can be translated approximately as follows: "In the past the kidneys had so variable a fortune as to be considered useless and unnecessary by some. More recently they have been recognized as a marvelous structure, the function of which provides one of the most important in the human body."

But how could the function of the kidneys be ascertained?

Malpighi stated in "*De Renibus*" that his descriptions were based on utilizing the recent invention (1610) of Galileo Galilei (1564–1642): the microscope. In a very true sense, Malpighi can be regarded as one of the fathers of microscopic anatomy.

Malpighi utilized two different techniques to describe the glomerulus. One consisted of making a section of the organ, spreading India ink on its surface, and then extracting the excess ink from the surface of the section and observing it under the microscope. As stated by Belloni [1], this represented the first attempt to utilize histologic staining techniques. In fact, India ink stained the interstitium while the tubular structures remained unstained. But the tubular structures appeared to be frequently dilated at one end; Malpighi considered these dilatations to be the "little glands", i.e., the actual producers of urine (the glomeruli).

The injection of a black fluid into the renal artery comprised the second technique that was used by Malpighi. The kidney became swollen and darkened and somewhat darker but visible spots could be seen on the decapsulated kidney surface (i.e., the glomeruli, as seen through the "cortex corticis"[1]). Similar "spots" could be seen as well on the surface of cut sections of the organ. In the latter sections, the numerous "little glands" were described by Malpighi as giving the appearance of "apples hanging on their tree", i.e., the origin of the term "vascular tree".

Malpighi's description of the tubular structures is simply wonderful; he described the presence of many convolutions in their cortical portion, i.e., the convoluted tubules, in contrast to their straight pathway in the medullary portion, i.e., the collecting ducts of Bellini. Thus, Malpighi deduced the function of these tubular structures: the "driving" of urine formed by the numerous and scattered cortical "little glands", the glomeruli, to the renal pelvis. In addition, Malpighi recognized that the "little glands" were in continuous connection with the arterial structures

[1] It is now well known that even the most superficial glomeruli do not usually lie on the kidney surface. In fact, they are covered by a thin layer of tubular structures called the "cortex corticis" (i. e., the cortex of the cortex).

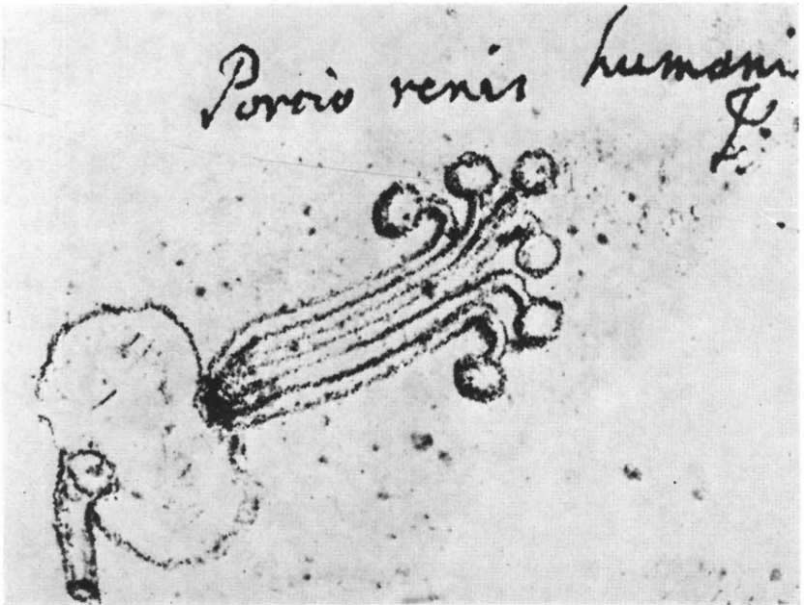

Fig. 1. *Photograph of the original drawing of Marcello Malpighi (1666) from the Library of the University of Bologna (MS 936, II, A, c. 21).* The outline of the kidney gives rise, at one point, to six nephrons. The vascular pole can be recognized in some glomeruli opposite the proximal tubule. "Portio renis humani", i. e., parts of the human kidney, is the autographic description of Malpighi.

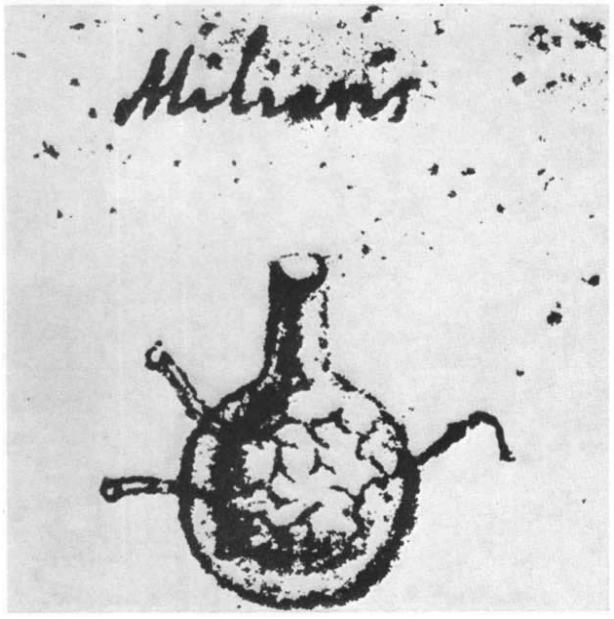

Fig. 2. *Photograph of the original drawing of Marcello Malpighi (1666) from the Library of the University of Bologna (MS 936, II, A, c. 21).* "Miliaris" is the elementary structure of the glandular organs: the follicle or "loculus". The glomerulus is the elementary structure of the kidney.

of the kidney and, presumably, with the venous structures as well. In fact, the injection of black fluid into the renal artery was observed to fill the entire arterial structures as well as the "little glands". On the other hand, the injection of the same fluid into the renal vein was capable of filling only the venous structures but not the "little glands". Malpighi did not recognize what was only to be appreciated by William Bowman almost two centuries later (1842), i.e., that the peritubular capillaries are interposed between the glomeruli and the venous structures, and that their presence provided the reason for his failure to fill the "little glands" by an injection into the renal vein. But Malpighi did state that even if it appeared impossible to demonstrate the continuous connection between the "little glands" and the venous structures, it was reasonable to assume that such a connection existed. According to Malpighi, even the nerves which entered the kidney must reach the "little glands" as well as any other glands.

As he stated clearly in "*De Structura Glandularum Conglobatarum Consimiliumque Partium*" (1688), Malpighi considered that the kidney represented a glandular organ whose elementary structure was provided by the follicle or "loculus", i.e., the "little glands". The latter were thought to possess a round shape with a cavity in which the humour was collected and then conveyed to an excretory duct in continuous connection with the cavity of the "loculus" (Fig. 1). A little artery, a little vein and a nerve went to the follicle and spread on its surface as capillaries and nervous ramifications (Fig. 2). Thus, from this description, it can be noted that Malpighi mistakenly viewed the vascular bed as enfolding the terminal expansion of the tubule (i.e., Bowman's capsule) rather than vice versa as is well recognized today. In spite of this mistake, however, Malpighi assumed and strongly believed in the existence of a direct connection between the urinary lumen of the tubules and the vascular bed. He was unable, as stated in "*De Renibus*", to demonstrate such a connection. Many attempts were made utilizing the injection technique, but colored fluids simply did not appear in the urinary tubules despite the fact that the "little glands" were filled easily. It was not until the fortuitous demonstration of William Bowman in 1842 (176 years later) that the relationship between the glomerular capillary bed and the dilated proximal end of the convoluted tubule was recognized. In actual fact, Bowman's injection of potassium dichromate and lead acetate into the renal artery disrupted the anatomic integrity of the glomerular capillary wall and thus allowed the access of colored fluid into the urinary tubules. Nevertheless, this observation led to the conclusion that the glomerular capillaries are enclosed in an infolding of the proximal end of the tubule (since called Bowman's capsule) rather than surrounding it as was assumed by Malpighi. But such a conclusion was not effected until 1842; how far distant from the anatomic discovery of the "glomerulus" by Malpighi!

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