Marcello Malpighi (1628-1694): Pioneer of microscopic anatomy and exponent of the scientific revolution of the 17th Century

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SUMMARY

Marcello Malpighi (1628-1694) was an Italian anatomist and an eminent scientist who significantly contributed to the advancement of the anatomical sciences in the 17th century. Malpighi was one of the first to use the compound microscope (an instrument designed by Galileo in 1609) and made the most important discovery of his life in 1661 when he identified capillaries as connecting vessels between small arteries and veins in the lungs. Malpighi thus provided the missing link in William Harvey's theory of blood circulation. He made significant contributions in the field of embryology based on his observations on chick embryo, and his efforts provided deep insights into the development of the heart and the nervous system. His communications based on microscopic studies scripted valuable details on the structural organization of organs like the liver, kidney and spleen. He identified the hepatic lobule as the fundamental unit of the liver and noted that bile was being secreted by these lobules and not from the gall bladder (the popular belief then). In the kidney he discovered the glomerulus (Malpighian Corpuscle), and was the first to observe the convoluted tubules in the renal cortex. He was the first to describe the presence of lymphatic bodies (Malpighi's Corpuscle) in the spleen. Although he was exceedingly successful in his scientific activities, his life was fraught with unfortunate events and savage criticism from detractors arising out of professional

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8867502575 7 +91-8017541980; Fax : +91- 11- 4157-1111. Email: drsanjib79@gmail.com jealousy and personal feuds. Nevertheless his exploits were instrumental in understanding the human microscopic anatomy (histology) and his accomplishments have etched his name in the pages of medical science forever.

Key words: Microscope – Capillaries – Circulation – Embryology – Hepatic lobule – Glomerulus

INTRODUCTION

Marcello Malpighi (1628-1694) was an Italian anatomist and an eminent scientist (Fig. 1) who significantly contributed to the advancement of the sciences in the 17th century anatomical (Adelmann, 1966). He successfully ventured into the unexplored domain of microscopic anatomy, and documented observations which revolutionized the understanding of the structural organization of organs in the human body (Clendening, 1960). Malpighi's findings heralded a new era in the progress of medical sciences as such, and set him in a different league altogether as compared to his illustrious predecessors such as Vesalius, Fabricius, Veslingius and Harvey (Ghosh et al., 2014). Although he was exceedingly successful in his scientific activities, his life was affected by unfortunate events and savage criticism from detractors arising out of professional jealousy and personal feuds (Campieri et al., 2004; West, 2013). The following words inscribed in his memorial plate appropriately describes the extraordinary life of this great anatomist in short (Bigoni et al., 2018):

"Summum ingenium/ integerrimam vitam/ fortem strenuamque mentem/ audacem salutaris artis amorem"

[Great genius/ honest life/ strong and tough

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Fig 1. A portrait of Marcello Malpighi from his text *Opera Posthuma (1697)*. Image available online, and is in Public Domain.

mind/ daring love for the medical art]

The present review was undertaken to chronicle a brief outline of the life and achievements of Marcello Malpighi, regarded as the founder of microscopic anatomy. We consider that this review would be relevant to anatomical sciences in the present day, when scientists empowered with technological advances are coming up with radical revelations in relation to the orientation of human anatomy (Benias et al., 2018).

METHODS

An extensive literature search was undertaken for this study and indexed databases such as Medline, PubMed, Scopus, EMBASE, CINAHL, Google Scholar as well as popular search platforms such as Wikipedia and standard Google search engine were referred to for relevant published materials. The following terms were used during literature search: "Marcello Malpighi", "Malpighi", "Biography of Malpighi", "Malpighi and Anatomical Sciences", "Scientific discoveries of Malpighi", "Microscopic Anatomy and Malpighi", "Published texts of Malpighi", "Anatomy in 17th Century", "Malpighi's contributions in Embryology" and "Malpighi as Physician". Published texts of Malpighi and their translations in English were consulted from online libraries while conducting the present study and wherever applicable have been appropriately referenced. The images used in the text were procured from the internet and it was ensured that all the figures included in this study are in public domain, i.e. free from copyright issues.

EARLY LIFE AND CAREER

Marcello Malpighi was born in the town of Crevalcore at the outskirts of Bologna, Italy, on 10 March 1628 (James, 1928). Interestingly in the same year, William Harvey published his groundbreaking findings on the circulation of blood in De Motu Cordis, and years later it was Malpighi that provided the missing link in Harvey's observation through the discovery of capillaries (Lubitz, 2004). Malpighi was born to a family of small landowners and he was raised in the farm that his parents owned. In the early part of his life, he was engaged in grammatical studies mostly under the influence of his father. However by the tryst with destiny, he enrolled at the University of Bologna in 1646 to study medicine and philosophy (Adelmann, 1966). Unfortunately, his academic pursuits were interrupted by the sad demise of both his parents as well as his paternal grandfather when he was just 21 years old. He had to abandon his studies temporarily to take care of his family of eight brothers and sisters. He resumed his studies two years later and obtained doctorates in both medicine and philosophy in 1653 from Bologna (Motta, 1998). He displayed steely resolve as he withstood opposition from University authorities while pursuing his studies because he was not born in Bologna. This aspect of his character later served him well in his defence against aggressive opposition to his academic exploits by his detractors. After completing his graduation in medicine, Malpighi devoted himself to anatomical studies and thus began his extraordinary productive journey in the domain of anatomy. His career was boosted by his appointment as Professor of Medicine at the University of Bologna in 1656 (Nuland, 2008). During this time he became a member of the anatomical society Coro Anatomico which was headed by Bartolomeo Massari, Professor of Anatomy in Bologna and Malpighi's teacher. The society comprised of intellectuals devoted to anatomical studies on cadavers and the group met in Massari's home to conduct dissections and vivisection of animals (Porter 1996). These events were critical in shaping Malpighi's inclination towards rational experimentbased anatomical studies and his refusal to accept Galen's theories, which eventually made him unpopular among his contemporaries. Malpighi later married Francesca Massari (the daughter of his teacher), who however died the following year, bringing an unfortunate twist in his personal life (Malpighi, 1975). Towards the later part of 1656, Malpighi (possibly compelled by the gloomy phase in his personal life) accepted an offer from the Archduke of Tuscany for the Chair of Theoretical Medicine in the newly established University of Pisa, which was specially created for him

ACHIEVEMENTS AND TURBULENCES IN PRO-FESSIONAL LIFE

However, the stay in Pisa proved to be highly productive from a professional point of view for Malpighi. Here he came across Giovanni Alfonso Borelli (1608-1679), an eminent mathematician and naturalist, and this marked the beginning of a long association. Influenced by Borelli, Malpighi became a member of the Academia del Cimento, one of the earliest scientific societies (Giglioni, 1997). As a member of the society, he was exposed to the theory of iatromechanics, whereby the human body is conceived as a set of machines working independently to bring about a combined output. Moreover the members of the society were avid followers of the theories of Galileo Galilei (1564-1642) and to no surprise Malpighi was also motivated by the revelations of Galileo (Duglison, 1868). It was in Pisa that Malpighi was introduced to the microscope, an instrument designed by Galileo in 1609 (Galileo is believed to be the inventor of compound microscope) and a device that would prove instrumental for his scientific studies (Motta, 1998). While in Pisa, he made sincere efforts to counter the Galenic traditions prevalent among scholars in anatomy, and also initiated his experiments on the circulation of blood with the help of his savoured instrument, the microscope. After working for three years in Pisa, in 1659 Malpighi returned to Bologna on account of a tragedy in his family when his brother Bartholomew inflicted a fatal injury on the eldest son of Giovanni Girolamo Sbaraglia (Professor of Anatomy & Medicine in University of Bologna) during an argument. Consequently Malpighi had to grapple with a bitter feud between the families and lifelong severe criticism of his work by Sbaraglia (West, 2013).

In Bologna, Malpighi was relentless in his academic pursuits and his pioneering researches on microscopic anatomy. In 1661, he made the most important discovery of his life, when he identified and successfully described the connections between the small arteries and veins in the lungs, which was previously only referred to by William Harvey. Malpighi christened these structures as "capillaries" due to their hair like appearances (capillus means hair in Latin) (Young, 1929). His remarkable success and increasing popularity was disrupted time and again by the ever increasing controversies and dissent on part of his colleagues, which could be primarily attributed to jealousy and misinformation. In search of tranquillity, Malpighi once more moved out of Bologna (which he always regarded as his home) and accepted the Chair of Medicine at the University of Messina in the island of Sicily and remained there for the next four years (Nuland 2008). During this period, he made remarkable progress in microscopybased studies and made deep inroads into the developmental science through his studies on chick embryo, which he detailed through illustra-

tions (Adelmann, 1966). He was successful in identifying the red blood cells and attributed the colour of blood to them. His communications with his friends and colleagues during his stay in Messina underline the fact that he had to withstand a revolutionary environment of counter-opinion from the followers of Galenic traditions (Piccolino, 1999). Subsequently he returned to Bologna in the later part of 1667 and devoted himself to studies related to the subdivisions of specific organs like the brain, liver, spleen, kidney and the deeper layers of the skin. His extraordinary exploits garnered the attention of the Royal Society of London, and his findings were serially published since 1668 in the "Philosophical transactions", a journal managed by the Royal Society itself (Hall, 2002). Eventually he was inducted as the first member from outside Great Britain by the Society in 1669. The admiration was perpetually mutual and between 1686-1687, the Royal Society published Malpighi's Opera Omnia, which established him as one of the pioneers in anatomical sciences (Malpighi, 1687). In 1684, another unfortunate twist interrupted his scientific endeavour when a disastrous fire at his home destroyed many of his valuable manuscripts and much of his equipment (Giglioni, 1997). 1n 1691, Pope Innocent XII, who was familiar with Malpighi's exploits while in Bologna, persuaded him to join as a Papal physician, whereby he had to move to Rome (Riva et al., 2016). During this time he taught medicine in the Papal Medical School and began work on a long treatise about his studies, which was eventually published in 1697 by the Royal Society as the Opera Posthuma (Malpighi, 1697). Malpighi died of a cerebrovascular accident in 1694 while in Rome, and as per his last wishes his mortal remains were buried in the Church of Santi Gregorio e Siro in Bologna (Duglison, 1868).

DISCOVERY OF CAPILLARIES

Malpighi began his research on the circulation of blood while he was in Pisa and his work got momentum by the use of the compound microscope, which was developed by Galileo in 1609 (Dupont, 1999). Possibly Malpighi was one of the first to use the compound microscope (microscope with both an objective and an evepiece lens), and much of his research was made possible by the introduction of the evolved instrument which as such proved to be a boon for scientific advances. His historic description of the pulmonary capillaries was documented in a letter that was written to his friend Giovanni Borelli in 1661 (Malpighi, 1661). Initially he described the momentous effort he had to undertake to identify the frog as the animal most suitable to his studies. He began with experiments on sheep, dogs and other mammals. However, despite enormous efforts, success eluded him. Eventually his observations proved to be fruitful with frogs, whom he referred to as 'microscope[s] of nature', as even minute features were visible with relatively small magnification. Based on his

experiences he even commented that nature also selects lower/ imperfect animals (frogs) for her experiments to ensure perfection in higher animals (mammals) (Malpighi, 1661). He went on to describe that while the heart was still beating he could observe the movement of blood in opposite direction in the arteries and veins in the frog's lung (circulation was described till this level by William Harvey) (Karamanou and Androutsos, 2010). However, what happens in between is a mystery and the description was beyond the power of the human eye (Cole, 1944). Malpighi admitted that without the compound microscope even he would have hypothesized that between the arteries and veins the blood escaped into an empty space and subsequently gathered up by a gaping vessels and returned to circulation. However, the fact that the evident movement of blood was tortuous, being carried round in sinuous manner, scattered in multiple direction with repeated divisions even gradually losing the red colour and finally getting united, guided him to think otherwise (Malpighi, 1661). His doubts were eventually resolved when he observed the dried lung of a frog under the microscope. He was able to identify some dark spots on the surface of the lungs, which he referred to as 'sagrino'. As it turned out, these were a network of looped vessels which, traced further, were leading

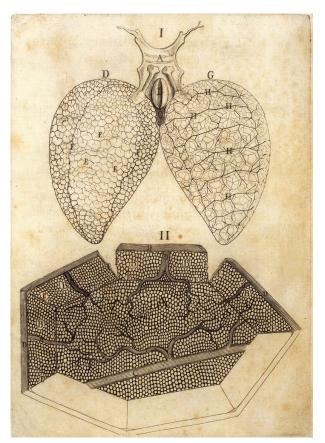


Fig 2. Illustration plate from De Pulmonibus showing lungs with alveoli (above) and pulmonary capillaries in an alveolus that has been opened up (below). Image available in online version of De Pulmonibus (1661), and is in Public Domain.

to a vein on one side and artery on the other (Malpighi, 1697). He was enamoured by the extensive branching of these intermediate vessels, whereby they no longer had a straight orientation (unlike vein and artery), but appeared as a confluence of the two vessels. He further observed that this network occupied the entire floor of the air spaces in the lungs, and also adhered to the outgoing vessel (Fig. 2). Malpighi christened these intermediate vessels as "capillaries" and thus provided the missing link in Harvey's theory of circulation (Malpighi, 1661). Subsequent communications among peers established the value of his discovery, and eventually Malpighi published his findings in the text 'De pulmonibus observationes anatomicae' in the Philosophical Transactions, a journal of the Royal Society of London in 1663 (Young, 1929).

REVELATIONS IN EMBRYOLOGY THROUGH MICROSCOPY

Buoyed by the success of his observations with the microscope, Malpighi embarked on another scientific escapade in the field of embryology while he was in Sicily. He studied the development of chick embryo and detailed his observations through scrupulous illustrations (Ghosh, 2015). His remarkable skills with the microscope enabled him to study much earlier stages of the embryo than had hitherto been possible (Wilson, 1967). His particular interest was in the development of heart and observed the developing heart within 30 hours of incubation. He noted that the organ began to beat before the blood reddened. He meticulously described the development of primitive cardiac tube, its segmentation and the formation of aortic arches (Fig. 3). Malpighi also worked extensively

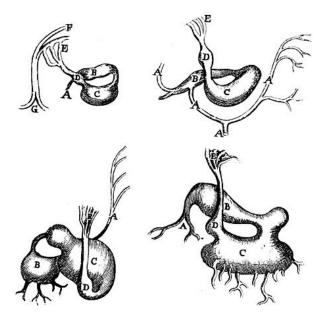


Fig 3. Illustration plate from Dissertation Epistolica de formatione pulli in ovo showing the developing heart in chick embyo. Image available in online version of text (1673), and is in Public Domain.

on the development of the nervous system (Fig. 4) including neural folds, the neural tube, the cerebral vesicles and the optic vesicles (Malpighi, 1673). His results were published by the Royal Society as two memoirs: Dissertatio epistolica de formatione pulli in ovo (Discourse letter on the formation of the chicken in the egg) and Repetitas auctasque incubato observationes continens (Observations on incubated egg) in 1673 and 1675 respectively. The publication of these two elaborate texts complimented with outstanding illustrations essentially established embryological studies on a strong platform based on sound observations (Malpighi, 1673; Malpighi, 1675). Malpighi's understanding of the embryological development as de-

tailed by himself in the text was analogous of an artisan building a functional machine from separate individual parts. Undoubtedly his thought process was in accordance with his inclination towards the theory of iatromechanics which he had imbibed while being a member of Academia del Cimento in Pisa (Felici and Gregorio, 2000).

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TRIUMPHS IN MICROSCOPIC STRUCTURE OF **HUMAN ORGANS**

Malpighi was apparently first to identify the red

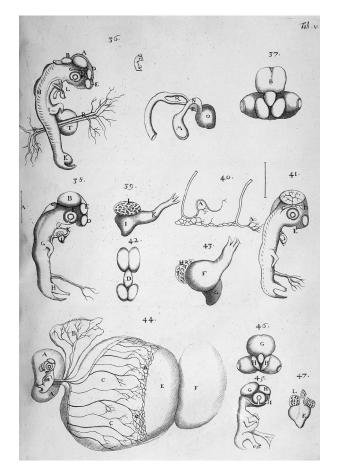


Fig 4. Illustration plate from Dissertation Epistolica de formatione pulli in ovo showing the development of nervous system including neural folds, the neural tube, the cerebral vesicles and optic vesicles. Image available in online version of text (1673), and is in Public Domain

blood cells when he described the presence of 'red globules of fat' in the blood vessels of mesentery in a hedgehog (Porter, 1996). He described the papillae of the tongue and suggested that they may have a role in taste sensation. He also documented the presence of papillae in the epidermis of the skin, and this layer (stratum germinativum) is known as the Malpighian layer after him (Foster, 1901). His description of the brain particularly emphasized on the structural details of the white matter. He noted that the white matter consists of bundles of fibres which connect the brain with the spinal cord (Magner, 2002). Malpighi gave a fairly accurate account of the structure of the liver, spleen and kidney in De viscerum structura exercitatio anatomica (1666), based on observations under the microscope. He identified the hepatic lobule as the fundamental unit of liver, which was connected by central vessels. Malpighi further postulated that hepatic lobules are secretory in function and concluded that the secretion (bile) passes through the bile duct. His findings proved beyond reasonable doubt that gall bladder was not the site of the origin of bile (which was the prevalent concept until then) (Malpighi, 1666). His comprehensive analysis of the blood supply to the spleen made him realize that it was a contractile vascular organ. He was the first to describe the presence of lymphatic bodies (Malpighi's Corpuscles) in the spleen (Malpighi, 1666). His description of the kid-

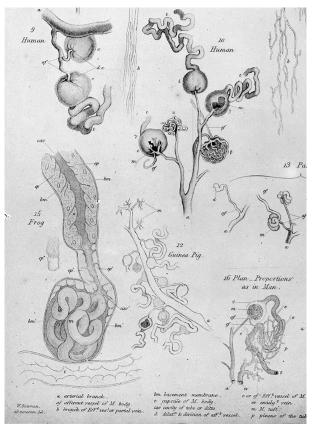


Fig 5. Illustration plate from De viscerum structura exercitatio anatomica showing the microscopic anatomical details of Kidney. Image available in online version of text (1666), and is in Public Domain.

ney literally changed the perception of anatomists about the organ (Fig. 5). He was the first to observe the presence of convoluted tubules (which he described as 'little worm like vessels') in the renal cortex and were referred to as 'canaliculi' (Malpighi, 1697). He gave a detailed description as to how these 'canaliculi' (convoluted tubules) converge on the pelvis and eventually enter the ureter. He was also able to predict the continuity between the convoluted tubules in cortex with the straight tubules in renal medulla. He also discovered the glomeruli (Malpighian Corpuscle) in the renal cortex. Malpighi however described them as 'very small glands' attached like 'apples to blood vessels, swollen with black fluid'. He further noted that the glomeruli at their extreme ends were connected to arteries and veins (Malpighi, 1666). Strangely, Malpighi was not able to ascertain the fact that these glomeruli were actually not glands but networks of capillaries, an architecture he himself had described comprehensively in the lungs (Malpighi, 1661).

COUNTERING HIS DETRACTORS

That Malpighi was a tireless experimenter can be readily assessed from his documented texts. However, his investigations were periodically interrupted as he had to devote himself towards defending his scientific endeavours (Reveron, 2011). Throughout his professional career, Malpighi had to face harsh criticism of much of his scientific work (Campieri et al., 2004). He had to withstand strong opposition from followers of Galen on the one hand, and from supporters of empirical practice of medicine, on the other (Ackerknecht, 1982). His rational approach to modern science was criticised by those who believed that the foundations of medicine had been established by the classical anatomists such as Galen, and hence further research was futile. According to this group, which was very dominant in Messina (Sicily), medicine as a science is similar to mathematics, whereby the principles established by the ancients are absolute truth and hence not open to revision. Malpighi countered this notion through analysis of classical texts, and showed that medical science was far from being a closed book having the last word already documented, and he cited evidence in relation to disagreement between scholars about fundamental aspects of medicine (Malpighi, 1697). His research activities, particularly those with the help of the microscope, were denounced by physicians who were inclined towards the empirical practice of medicine, particularly Giovanni Sbaraglia (Malpighi, 1697). This group were of the opinion that medicine was about recognition of symptoms, assessment of management options and evaluation of outcome. Hence there was no practicality in studying the structural and functional organization of the human body to practice medicine. Malpighi argued that even classical medicine was based on a rational study of the details of human anatomy, and, in the event of emergence of hitherto undocumented and complicated diseases that nobody had encountered, a sound knowledge of anatomical organization of the human body would be more useful to a physician than an empirical approach (Wilson, 1960).

CONCLUSION

Malpighi was a pioneer and luminary in the field of microscopic anatomy, or histology, as it is known today. He showed his flair with the newly introduced device, and his discovery of the capillaries completed the theory of blood circulation, which was initiated by William Harvey. His efforts provided deep insights into the development of the heart and nervous system. His communications scripted valuable details on the structural organization of organs like the liver, kidney and spleen. Through his relentless efforts, Malpighi contributed immensely to the scientific revolution of the 17th century. His exploits were instrumental in understanding the human anatomy in multiple aspects, as evidenced by a number of structures still bearing his name. Malpighi's accomplishments have etched his name in the pages of medical science forever.

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