

Thomas Willis, his Life, Legacy, and the Revolutionary Advances Made in Medicine Including in the Field we now know as Neuroscience



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Abstract

November 2025 marks 350 years since the passing of Thomas Willis (b. 1621 – d.1675). Thomas was a pious man who was orthodox in his beliefs and charitable to the end. He lived in an era of political and religious instability, however, despite these turbulent times Thomas along with other colleagues made pioneering medical discoveries and completely changed our thinking and understanding of the human body and disease. He rewrote history and set in place our modern knowledge and understanding of the brain, cerebrovascular system and nervous system. As the English Civil War raged, Thomas' formal medical training was cut short, but he used this to his advantage and undertook a vast range of practical, clinical, experimental and theoretical self-directed learning. Thomas's discoveries and opportunities to understand the brain were influenced by his collaborative and clandestine partnerships, as well as chance meetings, including that with Anne Greene who had hung at the end of a hangman's noose for over half an hour, only to be revived by Thomas and his colleagues. Whilst Thomas studied and wrote on many topics, his cumulating opus was the publication of *Cerebri Anatome*, in which he elicited polarised theories and explanations and changed neurology forever. This manuscript aims to cover Thomas' life, family, the political and religious influences of the time and the impact of these on both his medical career, and work as a medical practitioner, anatomist, scientist and author.

Thomas Willis is undoubtedly the father of neurology and the study of the nervous system. His name is immortalised in the Circle of Willis and whilst every medical and nursing student learns of the Circle of Willis, there is much to learn about the man, his life, his allegiances and devotion to the Church of England, his theories, publications and legacy.

Keywords: Thomas Willis, Circle of Willis, English Civil War, Anatomy,

Thomas Willis was born to simple and humble beginnings and during turbulent times, however his character and ability to grasp opportunities, would direct his career and set him on a path to become one of the most revered neuro-anatomists of all time. As war raged and his home city of Oxford (England) was garrisoned, and then occupied, before finally being restored, Thomas changed from

his first calling (the church) to medicine where he quickly rose from student to doctor, and then Sedleian Professor at the University of Oxford.

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The 17th century was a time of medical and anatomical revolution that saw the beginning of medical specialities as we know them now (Nichols, 2019). Thomas Willis, despite having studied many systems of the body, is recognised as the father of neuroscience. Thomas coined the term neurology (Rengachary et al., 2008) and has had multiple anatomical features named after him, including perhaps the most famous eponym the 'Circle of Willis'. Despite the significant events that occurred during Thomas' life including his fame and rise to be a prominent figure in the intellectual and social landscape of the time he remained grounded, faithful, charitable and pious, spending a significant amount of his time tending to the poor. Thomas was a clinician at heart, and it was his medical observations that he used to support his theories and transform medicine into a rational science.

The impetus to peruse this subject was a desire to write a historical account of Thomas Willis' life that pays attention to the political and religious upheavals of the time. Thomas' work marks an important transition between the medieval and modern understanding of the brain and the central nervous system. Before Willis, the brain was a mystery and although he retained some of the more traditional beliefs regarding one's spirit and soul, he significantly advanced the anatomical and medical understanding at the time. We often take the modern and colourful brain images that we have in our texts for granted, without much thought to the origins of the original and groundbreaking work of anatomical diagrams from whence they came. Thomas was not only an eminent physician in his own time but he is immortalised as one of the greatest neuroanatomists (Uston, 2005 ; A. N. Williams, 2003). His intellectual legacy has been to

provide us with our modern understanding of the brain, the central nervous system and cerebral vascular system (Zimmer, 2004).

This manuscript demonstrates the influences in Willis' life and how he preserved his quest for knowledge. Willis also never lost touch with the fact that the cadavers he met on the anatomy table were humans and individuals. He did justice to their situation in furthering the knowledge of anatomy, health and disease.

Methods:

There are numerous manuscripts on what is probably the most famous eponymous structure in neuroanatomy, the 'Circle of Willis', as well as Thomas' published works, his life and achievements. Undertaking a work such as this requires an awareness of the relevance, authenticity and accuracy of sources, noting that there will always be admirers and critics of historical figures. Thus, consideration of the context in which a work was written was paramount when weighing up the significance of each account.

This manuscript aims to bring both modern and historical works together and present an informative biography, and account of the historical context of life, medicine and academia in 17th century England.

An extensive systematic online search was undertaken utilising the following databases.

PubMed and Medline
CINAHL
Web of Science
Scopus
Google Scholar

The internet was also searched for documentary, biographical, archival and genealogical data including online versions of original documents derived from parish registers.

A number of key themes were identified including

- Thomas Willis' personal life
- Political and religious influences
- Medical beliefs and teaching at the time
- Willis' approach to lifelong learning and his career progression
- Willis' medical practice
- Willis' anatomical and neuro-anatomical work and discoveries
- The story of Anne Greene
- The influence of the Restoration
- Willis' colleagues and collaborators
- The Circle of Willis
- Authorship and works by Thomas Willis
- Willis' discoveries
- Willis' practice in London
- Willis' notes on psychiatry
- Critics and criticism of Willis and his works
- Willis' legacy and his decedents

A hierarchy of evidence was established. Firstly, transcriptions of Thomas' available clinical notations, correspondence and his published works (noting that he elected to write all but one of his works in Latin, and a great number of his early writings were lost in the great fire of London 1666). There also exists the notes taken by students during his lectures. Notations regarding his life, character and works were also located in manuscripts relating to his decedents. Evidence

was also drawn from information relating to Willis' contemporaries, before moving to more recent evidence included in academic contributions.

Personal Life:

Thomas was born on January 27, 1621 (Molnár, 2021; Uston, 2005) in Ivy Cottage, Farm Lane on his parent's farm in the village of Great Bedwyn in Wiltshire, just a few miles northwest of Oxford (Lega, 2006; Molnár, 2021; Symonds, 1960) and 70 miles northwest of London (William Feindel, 1962b). Thomas was baptised at the parish church of St Mary in Greater Bedwyn (Rose, 2012) and was the eldest of three sons and one daughter to Rachel Howell and Thomas Willis senior (see figure 1. for a detailed family tree).

Thomas Willis senior was a staunch Royalist and farmed as a tenet and later a retainer at St. Johns College Oxford, before going on to serve a number of nobles as a steward (Haslam, 1997; Molnár, 2021). The family were of limited means but led an increasingly comfortable life middling on gentry as they became small land owners (Rana, 2005; Wilson, 2012) when Thomas' mother inherited some land a few miles from Oxford at North Hinksey, on an estate now called Ferry Cottage (Choudhari, Sharma, & Leyon, 2008; Alastair Compston, 2021; William Feindel, 1962b; Molnár, 2021). Despite now being landowners, there was not a family history of obtaining university or medical degrees (A. Williams, 2003). This was the opportunity the family needed to ensure a better life for their children, and one of their main priorities was education. Thomas' mother Rachel died when he was 10 years of age and his father remarried a recently widowed family friend, Eliza-

[illegible]

Ordained a Deacon in 1738, spoke of heirs in Willis family

beth (Magdalene/Joane) Ruffin. The two families were joined by their recent bereavements, with Elizabeth's five children joining the Willis household of four children (Çağatay, 2004; Choudhari et al., 2008; Alastair Compston, 2021).

Thomas completed his early studies at the school of Edward Sylvester Academy, walking each day to the school that was located just off High Street in Oxford (Rana, 2005). He became proficient in Classics and showed an aptitude for Latin, an important preparation for future studies (Molnár, 2021). Thomas' college studies took place at Christ Church College (an affiliate of the University of Oxford), where he was admitted, aged 16, (1637) as a servitor or batler (one rank below a commoner) (Çağatay, 2004; Symonds, 1960), a position that provided him with accommodation and free tuition in return for working under the auspice of Dr. Thomas Isles (Cannon of Christ Church) and his family (Arráez Aybar, Navia, Álvarez, Fuentes, Redondo, Bueno & López, 2015; Choudhari et al., 2008; Hawkins, 2011; Hunting, 2022; Rengachary et al., 2008). This opportunity enabled Thomas to receive an education that would otherwise have been beyond his reach. It was during his time with the Isles family that his interest in medicine was sparked, as Mrs. Isles was known and respected for her medical knowledge, serving as an unofficial medical practitioner (Lo & Ellis, 2010). It is believed that Thomas assisted Mrs. Isles in her practice and was at this time exposed to the science of alchemy and her knowledge and treatment of ailments, disease and illnesses (Arráez Aybar et al., 2015). Thomas completed his Bachelor of Arts (Chemistry) at Christ Church, Oxford University around June 1639 (Arráez Aybar et al., 2015; Choudhari et al., 2008; Rana, 2005;

Teive, Coutinho, Camargo, Munhoz, & Walusinski, 2022) and at the age of 21 in 1642 he was awarded a Masters of Arts (Chemistry) (Arráez Aybar et al., 2015; Rengachary et al., 2008; Teive et al., 2022; Wijdicks, 2021).

Thomas' further studies were thwarted by the English Civil War years. Despite being initially interested in theology, with intention to be ordained as an Anglican clergyman (L. R. Caplan & Aggarwal, 2022), the inflexible theological curriculum and his desire to study medicine changed the course of his life (Rengachary et al., 2008). Thomas was among a number of students who changed from their initial religious vocation to medicine during the upheaval of the civil war. (Martensen, 1993). This was also a difficult and challenging time for Thomas, as he would have been aware of the potential political and religious upheaval if the Parliamentarians were to defeat Charles I, and medicine would provide stability regardless of the outcome.

Thomas was also making decisions in consideration of his siblings, as both his father and stepmother died in 1643 at the battle of Gloucester, shortly before the first siege of Oxford (Ethelbert, 1916; William Feindel, 1962b; Hawkins, 2011; Lo & Ellis, 2010). It is likely that they both died of typhus, and it is noted that their deaths occurred within 10 days of each other (Gilboy, 1992) (See appendix 1. for a detailed timeline). Following the death of his father, Thomas returned to the family farm only to find that the parliamentary forces were closing in and plundering everything (Symonds, 1960). With the family farm annexed, Thomas returned to Oxford. While Thomas would change his study to medicine, this would always be closely linked

with his religious beliefs and a desire to understand the body-brain-soul relationship. These resilient religious beliefs were upheld by a number of Oxford staff and students, and this is likely how Thomas would cross paths with Samuel Fell, who was at the time Dean of Christ Church and Vice-Chancellor of the University of Oxford. Unhappy times followed the fall of Oxford to Parliamentary forces, and Samuel Fell would be imprisoned while his family, including Thomas' future wife, would be forcefully removed from their rooms at Christ Church (Caron, 2015). Life during the interregnum was challenging, Oliver Cromwell imposed Puritan restrictions with an aim to limit excesses, the theatre and gambling were banned, and Christmas and Easter were cancelled.

By the 1650's Willis' life was becoming more comfortable, having moved out of university accommodation he was qualified as a doctor and his medical practice had taken off (Molnár, 2004). Thomas occupied Beam Hall from 1657 to 1667 (formally Biham Hall, located at 4 Merton Street Oxford, see Figure 2. Map of Oxford). Beam Hall sits opposite Merton College (see point X on Figure 2.), backing onto the yellow shaded open area. Beam Hall was centrally located, less than half a mile to Christ Church College and only two and a half miles from North Hinksey.

It was an academic hall that was converted into a dwelling in the 16th century. In 1657, the same year he moved into Beam Hall, Willis would marry the Dean of Christ Church Dr.

Samuel Fell's daughter Mary who was 10 years his junior (Hunting, 2022). Mary came from a good religious family that were humble, godly and pillars in the community. Mary's brother John would become Dean of Christ Church and Bishop of Oxford, later writing Thomas' biography.

Mary and Thomas' lives would be marred with tragedy, as they would bear the deaths of all but one of their children and Thomas' siblings would all predecease him (Rana, 2005).

Three of their nine children would die in the first year of life (Samuel (1) only months old, Mary only weeks old and Samuel (2) only weeks old), and two would die as infants (Katherine and Richard) (A Compston, 2023). Mary herself would die in 1670 at the age of 40 of tuberculous (Dewhurst, 1980; A. Williams, 2003). Mary would be remembered as a sweet, pious mother who was loved. Thomas' devotion to her is no more evident than in the text of her tombstone at Westminster Abbey (translated from Latin, Figure 3).

Figure 2. Electronic Copy of John Speed's 1605 Map of Oxford (Google Images)



Figure 3. Translation of the Crypt Stone in Westminster Abbey, Demonstrating Thomas' Love and Devotion of his Wife Mary

Mary, very dear wife of Thomas Willis M.D., daughter of Samuel Fell D.D. and Dean of Christ Church in Oxford, a woman, if ever there was one, distinguished for piety, good sense and sweetness of manners. She died to the great regret and grief of all, especially of her husband, on the eve of All Saints A.D. 1670 and is buried here. And now she lies here, expecting the eternal daybreak of that feast. In the same ground was buried their daughter Katherine, on the day after Michaelmas A.D. 1667. Here also lies the above mentioned Thomas Willis, most famous Doctor of Medicine who died on 11 November 1675 aged 54 years.

Religion at the time was not always theological, there was always the matter of politics, alliances and associates. Willis remarried in 1672 to Elizabeth Calley (nee Nichols), who was at the time a 38-year-old widow. Elizabeth, like Thomas' first wife Mary, had important links to the church as she was the daughter of Mathew Nichols, Dean of St. Paul's Cathedral (Caron, 2015). There are no recorded children from this marriage and Elizabeth survived Thomas by 34 years (Hunting, 2022; Rose, 2012).

In 1675 three of Thomas' four remaining children would die as adolescents (aged 8, 9 and 10 years) (see Figure 1). It would only be Thomas junior that would survive to adulthood. It is unclear if these deaths occurred prior to Thomas' own death in 1675 or following, but it is likely that Thomas did bear the burden of their deaths as he survived to No-

vember 1675. While the cause of the children's deaths is unknown, Thomas' passing was recorded as tuberculosis (J Trevor Hughes, 1991). It is likely that the despair of losing all but one of his children would have impacted his own health.

Disease was prevalent in the 17th century, and Thomas himself wrote a very detailed account on pertussis, that very year, noting that treatment was seldom any use (Still, 1931). It is more likely that Thomas and Mary's children died of tuberculosis having contracted the disease from their parents (J Trevor Hughes, 1991). The death of his children in 1675 could also have been hastened by an influenza outbreak in London at the time (Creighton, 2020). It is difficult to comment with any certainty, as the leading cause of death in England in the 17th century was epidemics and the transmission of disease. Any of prevalent fevers of the time, typhus, smallpox, measles, dysentery, pneumonia, pertussis or diphtheria could have hastened the death of Willis' children if they were already unwell with tuberculosis.

Political and Religious Influences:

The English Civil Wars was a conflict that challenged many allegiances and tore England apart from 1642 to 1651 (Lega, 2006; O'Connor, 2003). There was parliamentary unrest and disquiet in England as early as 1625, with a conscience within parliament that the monarchy was burdensome and unnecessary, and to put it simply, the parliament was weary of Charles I' duplicity. King Charles I also made matters worse by marrying a Roman Catholic (Henrietta Maria) (White, 2003), who can be best described as meddlesome and having a considerable amount of influ-

ence over her submissive and weak husband. Charles I's resolution to this was to simply dismiss parliament in 1629 and not recall it for another eleven years despite significant challenges, such as the national finances that were in crises (May, 1854).

Prior to the Civil War, Oxford was a medieval city with staunchly Royalist support and during the English Civil War, it would find itself a central focus with a series of sieges and skirmishes between the royalist army and the parliamentary forces that were triggered by Charles I's occupation of Oxford in August 1642.

Charles, his court and entourage, including his personal physician William Harvey, laid claim to the city of Oxford as a base, garrisoning the city and occupying many of the College buildings (Molnár, 2004; Neher, 2009; Rengachary et al., 2008). A significant number of the early scientific society as moved to Oxford (Brock, 1966), along with staff and family. The outcome of this was that there was a significant increase in the population in the city, it was overcrowded and cramped (Donagan, 2010; Gilboy, 1992) resulting in shortages, insufficient waste disposal and inevitably there were outbreaks of disease (Dewhurst, 1964). Little did Charles I or anyone realise that they would soon be marooned at Oxford (Arráez Aybar et al., 2015), as the fighting continued as skirmishes, and stagings of strategic towns and strongholds.

As a pious Anglican, Thomas remained loyal to the Royalist cause (Lega, 2006) and there is no evidence to support the claims of Rose (2012) that Thomas remained at the family farm to avoid conscription. Yolton (1991) writes of students, including Thomas, who would leave their studies to man the ramparts and fire cannons at Oliver Cromwell's forces.

Oxford was soon besieged with the university itself becoming a fortress, with the city besieged on three occasions (May 1644, May 1645, and May 1645) (Dow, 1940; Lega, 2006). It was during this time that Thomas was torn between his allegiance and his role of guardian over his younger siblings. It is known that Thomas did make at least one trip (and possibly more) to assist and ensure the safety of his siblings at North Hinkley, with the Parliamentary forces raiding and plundering many homes of Royalist supporters in the area. This was only a distance of around 8km (5 miles) from Oxford, yet still dangerous at the time. It is believed that Thomas, harassed by the Parliamentarians (Symonds, 1955), and with the family farm finally plundered returned to Oxford (Symonds, 1960),.

For the better part of the remaining conflict Thomas, like many others, was marooned in Oxford as it was garrisoned for the King (William Feindel, 1962b). Thomas enlisted in the University legion, serving as a student volunteer in the Royalist Army (Arráez Aybar et al., 2015; Çağatay, 2004; Rengachary et al., 2008). Thomas served from 1643 to 1646 (Rana, 2005), in a regiment raised by the Earl of Dover, though it is not likely that he participated in any battles (Hunting, 2022; Lo & Ellis, 2010; Monteiro, Nardi, & Gomes, 2021). In June 1646, Oxford fell and Charles I was defeated by the Parliamentary forces (C. S. L. Davies, 2008; William Feindel, 1962b; Hawkins, 2011) beginning the period of the interregnum.

The Parliamentarians stormed Oxford and took control of both the town and the university (Hunting, 2022; Lo & Ellis, 2010). The monarchy was extinct, and England was now a Republic, and would remain so for much of

the next decade under the rule of Oliver Cromwell, who assumed the role of Lord Protector of the Commonwealth (Dunn, 2015). It was a joyless and unhappy time. Cromwell set about to destroy all that England's soul and the Royalist cause had stood for, and there would be no peace until the remaining Royalist sympathisers were crushed. A number of individuals who held senior posts were forced to flee the city (Hawkins, 2011). Among many others to be expelled from the city was the Thomas' future father-in-law, Dr. Samuel Fell, and Dr. William Harvey (the personal physician to the king) (Hunting, 2022; Molnár, 2004). Many of the expelled scholars and clergy were first imprisoned, having had all their offices and homes ransacked. Some, like Dr. Fell, never lived to see the restoration in 1651, passing away in a rectory near Abingdon. Thomas escaped persecution by the Parliamentary forces as possibly only because of his medical degree and the fact that he was not yet a Fellow of Christ College (Molnár, 2004). Despite this freedom Willis' life during the interregnum was curtailed by the many terms thrust upon the people of England, including the learned scholars. Many past times were banned, and religious holidays were suppressed.

Cromwell had an apoplectic response to Royalists like Willis, and they were marginalised, had their lands dispossessed, barred from institutions and exiled for declining to acknowledge the Catholic Church and Oaths to Oliver Cromwell. Survival during the interregnum was more that preserving the Royalist cause and the Church of England, it was collaborating with others to ease one's path and the adaption to the political and religious reality of the time (Hawkins, 2011).

Despite Oxford having been a Royalist stronghold there was never a consistent governing presence of the Parliamentarians in the city during the interregnum and a quiet Royalist momentum flourished in Oxford (Hawkins, 2011). At first the Parliamentarians were almost single mindedly focused on finding Charles I and then Charles II, so some of the Royalists were able to undertake activities relatively unnoticed. Thomas retained his strong Anglicanism throughout the interregnum (Rengachary et al., 2008) and offered the oppressed clergy a refuge in his home. This included John Fell (brother of his wife Mary) and Gilbert Sheldon, who would go on to be the Bishop of Oxford and Archbishop of Canterbury, respectively, following the restoration. Despite the Protectorate prohibiting Anglican worship, Anglican services were held there in secret, and it became a clandestine meeting-house for both scholars and Royalists (Arráez Aybar et al., 2015; Descartes, 2010; Dow, 1940; William Feindel, 1962b; Flis, 2012; Hunting, 2022).

When Oxford fell there was some hope for the Royalists, as King Charles I had managed to escape, first in disguise as a servant, and then opting for the cover of a clergyman (Donagan, 2010). However, Oliver Cromwell was the leading advocate for the capture and execution of Charles I. Charles I was captured, tried, convicted and hung for high treason in January of 1649. Charles II was declared king in exile, however when he tried to claim his throne, he was unsuccessful and found himself (like father, like son) on the run and in disguise. Eventually Charles II fled to France and with him went the hopes of the British monarchy (Weber, 1996). Cromwell took control of England as Lord Protector (and king in all but title) until his death in 1658 (Davis, 2015; Harris, 1762).

Thomas' career was understandably shaped and influenced by the English Civil War, a time when England was facing an uncertain future and experienced great political and religious turmoil (O'Connor, 2003). However it was also a time that saw unprecedented growth and understanding in the areas of science and medicine.

Medical Beliefs and Teachings at the Time, Lifelong Learning and Career Progression:

In the 17th century, to gain entrance into Oxford to study medicine, one had to memorise Hippocrates, Aristotle and Galen without much critical thought (Molnár, 2021; Neher, 2009). These fathers of medicine were the respected bearers of medical wisdom; however, the 17th century saw a period where there was increasing knowledge and theories, and the old teachings were to be challenged.

Willis entered to study medicine in 1642 on the background of his undergraduate studies in Chemistry, however his studies were interrupted as the English Civil War began (Hunting, 2022; Uston, 2005). Willis' decision to change to medicine was perhaps driven by the civil unrest at the time, or equally plausible it was driven by the experience and exposure to the sick gained when assisting Mrs. Isles (the Cannons wife). This change meant that Thomas had to begin again to cultivate the social and academic connections required to be successful (Hawkins, 2011). Thomas was set for success in medicine and good standing within the university community due to his mastery of Latin, which was the language of political power, medicine and teaching, in addition to religion (Rengachary et al., 2008).

Willis did not receive a traditional education in medicine. It is believed that his education was perhaps only six months after being granted his qualifications to practice. This probably worked in Willis' favour that he did not receive a traditional education. If he had entered medicine any time prior to the English Civil War, he would have endured fourteen years of erroneous, antiquated, dull, repetitious and theoretical dogma with this experience potentially stagnating his own thought processes and desire to experiment (Arráez Aybar et al., 2015; Lo & Ellis, 2010; Rengachary et al., 2008).

However, during his qualifications, Thomas would have learned of the theories of humours, and that animal spirits were distributed throughout the body, and that disease was the result of internal imbalances (Neher, 2009). He would have also been exposed to the practices at the time including bleeding patients that was based on the ancient belief that certain illnesses were caused by an excess of blood. Mercury and arsenic were commonly prescribed, and the apothecary shop would have been a place of wonders. Records of the time indicate that clinical teaching focused on oral examinations and the assessment and recall of the ancient texts (HEC, 1936).

There are few records surviving of this time, although it was noted that Willis' attendance during his short period of study was exceptional (Choudhari et al., 2008). The class content was significantly improved by the presence of the royal physician Dr. William Harvey, who taught his theory of cerebrovascular circulation (Arráez Aybar et al., 2015; Lega, 2006). Whilst Harvey purported that the heart was the pumping source of blood circulation,

he also focused on the circulation of 'animal spirits' resulting in the generation of the rational soul in the cortex (Flis, 2012) as a justification of the body-brain-soul relationship (Arráez Aybar et al., 2015).

The interruptions of the Civil War, including the besieging of Oxford, turned out to be of benefit and Thomas, with his naturally enquiring mind, was able to apply his time engrossing himself in medical texts, conferring with medical figures in the city and building his reputation as one who was open to new ideas (Arráez Aybar et al., 2015; Dewhurst, 1982; Neher, 2009).

Willis would go on to challenge theological and scholastic teachings that had been held sacred in the field of medicine up until this point. Whilst Willis did not completely discredit the teaching of the time (Rengachary et al., 2008), he did believe that they lacked anatomical detail and were flawed by their Pagen belief systems (Dewhurst, 1972). What marks the turning point of Willis' departure from the teaching at the time is the insight and understating he gained through his own clinical experimentation, his iatrochemistry skills and observational approach to medicine. Due to the turmoil occurring at the time he was a student, Willis was free to read more widely and learn from experimentation and practical learning, building working relationships with the other students stranded at Oxford (Dow, 1940; Rengachary et al., 2008). Willis is perhaps our first modern example of self-directed learning and a lifelong commitment to improving his practice through learning.

Around June 1646, many Royalists were temporarily expelled from Oxford by the Parliamentary forces, with Willis included. However,

like many others he returned by the December (then aged 21) ready for the academic term. He received his Bachelor of medicine (MB) (Arráez Aybar et al., 2015; Çağatay, 2004; Choudhari et al., 2008; Lo & Ellis, 2010; Rana, 2005; Rengachary et al., 2008; Teive et al., 2022), on conferral of the Archbishop of Canterbury for his loyalty to the King, to the royalist cause, his religious observance, and for his commitment during the siege of Oxford (J Trevor Hughes, 2000; Molnár, 2021). It is pertinent to note that these were wartime conditions and the awarding of his degree enabled him to start practicing as a doctor before Parliamentary forces fully took over Oxford (Molnár, 2004).

Willis the Medical Practitioner

Thomas' medical qualification came with the limitations of a meagre education and experience. Despite this he went on to be perhaps one of our earliest generalists in regard to his practice, consulting on a broad and wide range of specialities including dermatology, contagious diseases, mental illnesses, fevers and venereal diseases (Veith, 1982). Thomas also had the advantage of his chemistry background, that he would use as a basis for many of his explanations for illnesses and ails. He received his degree during a time of unrest and uncertainty and only had an informal position at Oxford. What was certain is that he needed an income. The university had basically ceased to function and there was little prospect of a teaching or research position. Although Rose (2012) purports that Willis did not initially seek a position at the university. Jardine (2004) suggests that Willis was one of the Royal Physicians to Charles I in 1646. However this claim, which sits first and foremost in the first paragraph of Wikipedia, does

not align with the known timelines, noting that Willis did not qualify until December of 1646, and Charles had already fled Oxford in April of that year.

Thomas had turned his energy towards being an itinerant or travelling physician, seeking his patients in villages and local markets (Hawkins, 2011). Although Willis had the knowledge and skills he learned from the university and Mrs. Isles, including a basic understanding of alchemy (Arráez Aybar et al., 2015), he needed to draw on all his perceptive skills and experience including his chemistry background to make a living. Willis was a man of deep insight and possessed a remarkable skill set in observation. He was neither overly ambitious nor was he one to seek glorification (Arráez Aybar et al., 2015), but in time he would be sought far and wide by persons of all degrees of faith (Wells, 1949). From some of his own remaining case notes it is evident that Willis followed many of the practices of the time including bleeding patients, herbal remedies, laudanum and opium (Veith, 1982). One of Willis' treatments still survives today and is used by millions of people every morning, is the use of coffee to overcome somnolence (Eadie, 2003).

Earning a living as a medical practitioner was not easy (Choudhary et al., 2008), there was tough competition and Thomas often covered vast distances and initially had difficulty establishing a practice (Robert G Frank, 1990). It has been estimated that while in Oxford Willis travelled a radius of around 57 miles, although most of his clients were within 6 to 16 miles of Oxford. One location that Thomas established a reputable practice was Abingdon, a bustling market town (Symonds, 1960). A weekly market was held there and given its close proximity to North Hinksey, Thomas

would have been also able to check in on his younger siblings. Thomas would make the most of the opportunities available as a travelling practitioner and use this time to gain medical experience (Arráez Aybar et al., 2015), whilst focusing and honing his skills as a logic-based practitioner, setting himself apart from others. Willis' failings were that he was frank and too pessimistic, although this was with the aim to give people time to settle their affairs (Veith, 1982), he is said to have lacked politeness and had a diminutive approach to pleasing others, yet at the same time demonstrated a deep insight.

Willis, whilst being traditionally pious and conservative (even attending services twice daily), fully embraced empirical medical practices (Molnár, 2021). He was described as an industrious man who always searched to find the truth (Symonds, 1955). It was during the interregnum in 1650 that Willis was elected Sedleian Professor and Doctor of Medicine, Oxford (see Table 1). Despite this appointment and a financially secure pathway at the university, Willis continued to tend to those outside the city walls. He was a clinician at heart, but he also wanted answers and following his patients for many years, and in some cases from life to death, provided him the opportunity to test his theories (Molnár, 2004). Thomas' reputation as an anatomist and academic were matched in time by his reputation and growing demand as a practitioner, with his practice becoming most successful (Wragge-Morley, 2018). His income was reported to be £300 a year by 1667 (Hunting, 2022). This can be translated in today's currency to around £45,000 a year; a respectable income but not exorbitant given Thomas was working both as a physician and an academic.

Willis the Anatomist

The dissection of the body and brain has always been a theologically sensitive issue. It was not until the 17th century that it became fashionable, with intellectual and scientific curiosity peaking. It was a time of religious upheaval but despite this, the church neither objected nor obstructed anatomical research (Howse, 2009). Willis' entry to medicine occurred during Oxford's golden era when it was at the centre of experimental anatomy and physiological research and discovery. Much of this was achieved through anatomical dissection that enabled the specifics of human anatomy to be studied. It was also a time where death was much more a common and everyday part of most people's lives (Cavalcanti et al., 2009). Dissection and the study of anatomy was morbid, but there was a desire to understand disease and potentially prevent it. Not unusual for the time, these scientific endeavours occurred not only in the anatomy halls but also in the back room of inns, or the anatomists' own houses and the kitchen was the likely place for this activity (Guerrini, 2016; Molnár, 2021; Uston, 2005). Participating in the dissection of an unfortunate soul who had died is the complete and opposite antithesis of what you would expect of a pious and deeply religious man such as Willis. However, it is his piety that refutes him of the wrong doings in the eyes of the church.

There were two significant events that occurred in 1636 that would shape Willis' medical practice and legacy as an anatomist. The first was the Great Charter of Charles I, granting the Oxford anatomy reader the right to take for anatomical dissections, the body of any individual executed within 21 miles of Oxford (Arráez Aybar et al., 2015; Mitchell et al., 2011; Molnár, 2004). By the 17th century

there were not enough bodies to meet the growing demands of the anatomists (Mitchell et al., 2011). The Charter significantly increased the flow of cadavers as the previous Charter set the limit to within the city itself (Taylor, 2019), with the new Charter hoping to avoid the illegal procurement of bodies. Whilst the bodies of executed felons were the only legally available cadavers to the anatomists for dissection, there is evidence of unclaimed bodies from the workhouses, prisons and hospitals all reaching the anatomists table (Ghosh, 2015; Mitchell et al., 2011; Sinclair & Robb-Smith, 1950). The flow on effect was an increase in available cadavers that resulted in a change to the Oxford medical curriculum, occurring a few months later in 1636. This had a significant effect for Willis as he was exposed to a greater number of dissections as a student; in fact every student was required to participate in at least two dissections (Arráez Aybar et al., 2015; Molnár, 2004).

Thomas soon became firm in his belief that knowledge of anatomy was the key to understanding the body and mind (O'Connor, 2003). Willis who was still practicing as a clinician had direct access to his patients after death and this was potentially critical in understanding the brain, nervous system and cerebral blood flow of patients who had been known to be suffering specific conditions, and it undoubtedly became a key element in advancing knowledge (Molnár, 2021). Willis' postmortem observations on individuals who had died of apoplexy (Çağatay, 2004) (stroke), and those with asymptomatic occluded carotid arteries, enabled Willis and his colleagues to understand how the anastomosis of blood vessels at the base of the brain could prevent apoplexy. Willis was determined to use these opportunities and was instrumental in trending

towards experimental science, a move that at the time was scorned by the authorities (Rengachary et al., 2008). Willis would spend the next decade of his life supplementing his wide-ranging medical knowledge with first-hand experience gained through experimentation, necropsy's, autopsies, dissections and his chemistry background.

Willis believed that anatomy held the key to understanding the soul, citing Anglican theology when referring to the soul, and maintaining both an anatomical and theological perspective (Martensen, 1993). It is perhaps perplexing in today's world as to why Willis would show a seemingly unmedical concern with the soul and its properties (Robert G Frank, 1990). Willis was exceptionally religious and was not immune to the religious preconceptions and superstitions of the time (Dewhurst, 1972). Willis approached anatomy with the belief that individuals were composed of five principles (spirit, sulphur, salt, water and earth) (O'Connor, 2003). Medicine enabled him to understand the soul, and its relation to the workings of the anatomical and physical body (Molnár, 2021). This was radical for the time, where the soul was thought to be singularly responsible for cognition, emotion and the initiation of voluntary activities (Lega, 2006). Thomas was motivated by the goal to identify the relationship between the body and the soul. Willis strongly believed that humans possessed both a rational and an immortal soul (Molnár, 2021). He lectured frequently on the topic, presenting his evolving views of the soul to students and peers (Lega, 2006), with anatomical demonstrations facilitating considerable intellectual and spiritual interest (Tatu, Moulin, & Monnier, 2005).

Those that came before Willis relied on Ga-

lenic descriptions, that proved to be a block to advancing knowledge (Ghosh, 2015). Willis made that important step forward; he was ambitious and not afraid to experiment. Willis provided more than a repetition of the anatomical descriptions of his predecessors. Willis not only provided more accurate descriptions, he was able to correlate function (Barcia Goyanes & Evans, 1995; Dalley, 2002). Willis learnt much of what he knew from the dissection of deceased individuals as well as animal necropsy's, with both involving experimentation (Rengachary et al., 2008). He strived to provide a sufficiently grounded anatomical explanation for his theories.

Anne Greene:

Hanging remains one of the oldest forms of execution (Nichols, 2019), and was the preferred form of execution in England during Willis' time. Anne Greene is linked to Thomas Willis by more than chance, one could say it was fate that brought them together. Anne became a celebrity not for the crime she was convicted of, but for the fact that she survived the hangman's noose. The revival of Anne enhanced Thomas' reputation (Nichols, 2025), in fact making him quite famous in Oxford and in turn aided him in establishing a prosperous career (Choudhari et al., 2008; Dewhurst, 1972).

It was a cold December day in 1650 when Anne, a 22-year-old maid servant, was hanged in the cattle yards of Oxford Castle after being found guilty of murdering her unborn child (Doyle, 2001). There had been testimony and attempts to save her from the hangman's noose, but they were all to no avail. When she was taken down and cut loose from the hangman's noose, she showed

no signs of life. However, when her coffin was subsequently opened, she showed signs of life; perhaps it was lucky that Anne was destined for the anatomy table and not the graveside where she would have been buried alive (Nichols, 2025). The physician conducting the planned dissection was William Petty (Doyle, 2001), with Thomas Willis along with a number of others including Christopher Wren present at the anatomy table and preparing for the dissection (William Feindel, 1962b; Shaw, 2006). In the ensuing historical account, there is a focus on her resuscitation, but who could have foreseen that Anne's revival would forward the understanding of cerebral blood flow and importantly collateral blood flow (Nichols, 2025).

When it was discovered that she was alive, the dissection table became a resuscitation bay with Petty taking the lead in reviving Anne (Robert G Frank, 1990). Interventions to revive her included smoke enemas, poultices, hot bandages, pouring hot and cold spirits into her mouth and bloodletting (C. S. Breathnach & Moynihan, 2009; William Feindel, 1962b; Molnár, 2004; Watkins, 1651; William, 1650). Whilst all the time monitoring her vital signs. Anne's initial recovery was swift and by the following morning she was able to communicate (C. S. Breathnach & Moynihan, 2009), however it would take a month for her to fully recover.

Anne, with the help of Petty and Willis, was pardoned and is said to have lived a happy life bearing three further children. At the time her survival was thought to be divine intervention and there was little attention paid to the undertakings of Petty and Willis to restore her body temperature, tend to her wounds and maintain her hydration during her recovery.

Importantly, for Willis, her survival provided evidence that there could be successful collateral blood flow even when the carotid arteries are blocked (Symonds & Feindel, 1969).

Willis the Neuroanatomist:

In a letter from the time, it is noted that Willis began his brain dissections in the fall of 1660 (J Trevor Hughes, 2000; Scatliff & Johnston, 2014). Willis' work was undertaken primarily with Christopher Wren and Richard Lower, who as a team achieved what no one had before them, the preservation of brain tissue making it amenable to dissection. These individuals were at the forefront of understanding vascular anatomy through pathology. They challenged the medieval thinking and understanding of the brain and nervous system at the time (Wilson, 2012), and made findings that are still recognised today. In regard to the neurovascular system, they developed experimental injection protocols examining the blood supply to the brain, noting that when dye was injected into a carotid, it diffused throughout the vessels of the brain, prefiguring arteriography by several centuries (William Feindel, 2004; Thompson, 1996). It was noted that after injecting the inky substance into one of the carotid arteries the 'vessels got revealed in every secret place of the brain and cerebellum by filling with the same colour' (Arráez Aybar et al., 2015). Further experiments were undertaken focusing on the effect of occluding the opposing carotid or vertebral arteries, thus demonstrating collateral circulation (L. R. Caplan & Aggarwal, 2022; Dumitrescu et al., 2020).

Willis was faced with the same difficulties as others when trying to study the brain. It is perhaps why it was one of the last human organs

to be studied. The brain consists of delicate structures and has a propensity to deteriorate quickly (Flis, 2012; Lo & Ellis, 2010). Prior to Willis' time, anatomists were faced with poorly preserved brains that disintegrated quickly and became a semi-fluid, resulting in a formless, homogenous mass (Descartes, 2010; Lega, 2006; Lo & Ellis, 2010). Christopher Wren developed a method of preservation that afforded Willis and Richard Lower the opportunity to work with anatomically stable brains. Previous dissections of poorly preserved and glutinous brains resulted in the conclusion that the brain held little capacity for thought (Neher, 2009). Willis also approached the dissection of the brain differently. Rather than approach the brain in situ, he removed the brain intact (Arráez Aybar et al., 2015). In 2002 archaeological works being undertaken at Oxford Castle located 62 burials (mostly young males) with evidence of intentional postmortem symmetrical and surgically made (craniotomy) cuts to the skull (Mitchell et al., 2011). Previous findings have also been located on a workhouse site, demonstrating widespread evidence of such postmortem anatomical studies.

Willis' findings were revolutionary, at the time most were working from Galen's teaching that the brain's primary function was to purify the spirit's that were the root cause of most human diseases. (Lega, 2006). It is fair to say that he had an idiosyncratic and creative way in regard to his explanations of the brain (Robert G. Frank, 1996). It was thought at the time that the ventricles were of most importance in the brain, with the anterior ventricles (now lateral) being responsible for the flow of imagination and fantasy (Arráez Aybar et al., 2015); the middle (now third) ventricle responsible for cognition and intellectual activ-

ities; and the posterior (fourth) ventricle being the seat of memory (Lega, 2006). Small locks were thought to pass between the ventricles and could stop all thinking skills (Arráez Aybar et al., 2015). Willis focused on the neurological system hoping it would lead to an understanding of the three (vital, rational and immortal) forms of the soul (Molnár, 2004). This linking to his religious devotion and beliefs.

Willis also undertook a number of neuroanatomical experiments on animals, including the perimortem ligature of the carotid arteries of a spaniel. Willis and colleagues tied a live spaniel's carotid arteries with silk, occluding them and noted that by all accounts the dog was not at all impacted and was of 'pleasant humour' (Lega, 2006). Numerous experiments like this were undertaken, however the results were not always as positive, with some animals experiencing noticeable defects. Whilst this is shocking to think of in the context of our time, these experiments were the basis for understanding collateral circulation and its ability to stabilise blood flow when a principle conduit is occluded (Liebeskind, 2003). In the 17th century Christians believed that animals were created by God to benefit humans, and there were few moral restrictions, and certainly no legal ones, at the time (Guerrini, 2016).

The Restoration:

Following the death of Oliver Cromwell in 1658, there was a disconnect and a political crisis in England. The Royalists that looked to Cromwell's death as an opportunity to revive their fortunes were initially disappointed (Worden, 2010), but they would not have to wait long for their time. Cromwell's son Richard was elected as Lord Protector, but he was

a mere puppet, he was of little learning and was not committed nor fit for the role. It is said that he had not inherited any of his father's political ambition or leadership skills and was ill fitted by character, education and training. Some going as far to note that he was without guile or gall (Burton, 1828). After just eight months he resigned the post of Lord Protector (G. Davies, 1935), and with Scotland's support Charles II returned from nine years in French exile. His ascension saw the return of the Stuart dynasty in 1660, ended the interregnum and two decades of civil war and there was a period of relative stability. As a warning to all that may venture down Cromwell's path his body was exhumed, and he was posthumously executed with his head was stuck on a pole and set up on the roof of Westminster Hall.

Thomas, like many others of his age, had spent nearly a decade of his life enduring the turmoil of war. However Thomas fell into good fortune after the Restoration mainly attributed to his strong Royalist and Anglican connections (William Feindel, 2004). For Thomas opportunities opened, many of his patrons and supporters were reinstated in their positions (Hawkins, 2011). It was the beginning of a liberation from the political and religious influence that had governed their predecessors. Thomas' rise was meteoric, he found royal favour and in 1660 was awarded a Doctor of Medicine and Sedleian Professorship of Natural Philosophy at Oxford University (Çağatay, 2004; William Feindel, 1962b; Hawkins, 2011; Molnár, 2021; Rengachary et al., 2008; Teive et al., 2022) and was appointed to the Oxford Chair of Natural Philosophy (C. S. Breathnach & Moynihan, 2009; J Trevor Hughes, 2000). Willis officially became a member of the learned community of Oxford (Hawkins, 2011).

Willis would use his new roles to his advantage in that he could teach using his own theories as examples (Molnár, 2004). His lectures were a far cry from the erroneous and dull lectures he endured, they were rather stimulating and original. Two students, Robert Boyle and John Loke took notes during Willis' lectures, with these notes surviving to this day (Molnár, 2004; A. Williams, 2003). The surviving documentation provide insight into the cultural and intellectual life in Oxford at the time. Willis disregarded the instructions that he was to teach of the old traditional style of Galen, Hippocrates and Aristotle and rather lectured on his own interests, his theories and observations (Rengachary et al., 2008)

Willis also utilised his new position to embark on a project to understand the brain, map the cerebral nervous system and understand the function of the nervous system (Willis, 1664). It is pertinent to note that this work still required a finite balance between scientific studies and theological discourse (McNabb, 2014). The brain was considered at this time as part of an ordered system, constructed by God (O'Connor, 2003). The restoration brought an assemblance of order and peace and enabled the scientific freedom that Thomas experienced and debate regarding the nature and the soul intensified.

Colleagues and Collaborators:

Willis participated in and was part of the scholarly and intellectual activities that were taking place at Oxford during the mid to late 17th century (McNabb, 2014). He had to work hard, not only at his profession but also at his social standing noting that he was in contrast in his educational and social background with many of his colleagues. This was a period that continued to reap the rewards of the Eliza-

than cultural and intellectual Renaissance (O'Connor, 2003).

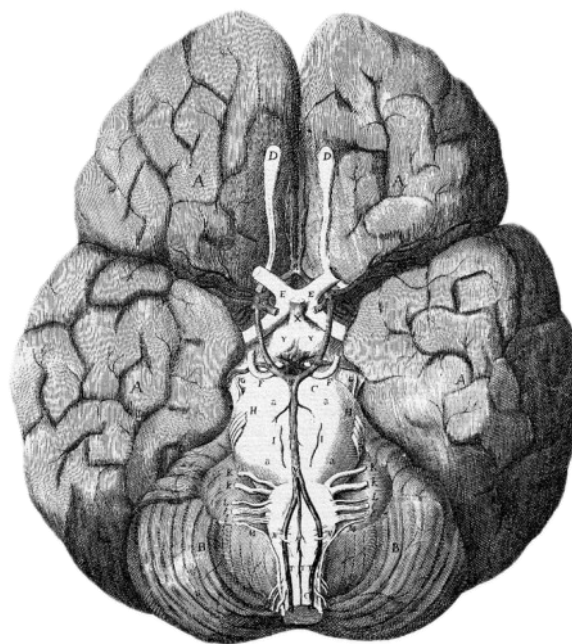
Willis worked closely with a number of colleagues and collaborators that were part of a community of minds that rewrote medicine. They were part of England's early modern scientific movement, shaping new theories and ideas (Mason, 1953). We have mentioned Christopher Wren, who played a fundamental role in the preservation and dissection of brain samples (William Feindel, 2004; McNabb, 2014). He developed the dye techniques used to observe cerebrovascular blood flow and perhaps most well-known for his incredibly detailed illustrations (Gibson, 1970; Zimmer, 2005) including those of the base of the brain and Circle of Willis (see Figure 4.), that would set a precedent for modern scientific illustrations (McNabb, 2014; Meyer & Hierons, 1962; Rengachary et al., 2008). Christopher would soon turn his attention to architecture and the Great Fire of London in 1666 would be his making.

Thomas Millington conferred and participated as a team member and is mentioned in the preface of *Cerebri anatome* (Caron, 2015; Choudhari et al., 2008). Willis describes him as a close friend and a 'most learned man, to whom I from day to day proposed privately my Conjectures and Observations, often confirmed by his Suffrage, being uncertain in mind, and not trusting to my own opinion' (John T Hughes, 2009). Millington would succeed Willis taking the role of Sedleian Professor of Natural Philosophy in 1675 following Willis' death. He would also go on to be a Royal Physician and was knighted in 1679.

Figure 4. Copy of Christopher Wren's Diagram included in the 1664 book *Cerebri*

Anatome of the Base of the Skull Demonstrating the Circle of Willis (yet unnamed)

In equal regard, Richard Lower contributed his meticulous skills in dissection of the corpses and also to the provision of illustrations (Descartes, 2010; McNabb, 2014). He was 10



years younger than Willis, yet one of his closest associates, and had been practicing medicine since circa 1656. He has been described as having a natural curiosity to medicine and as being eager with the knife (Robert G Frank, 1990). Richard was a capable anatomist and played a key role in the experiments of the brain and the study of the Circle of Willis, including the myriad of sequential experiments that included ligation of vessels and observations of collateral circulation using dye experiments (Dalley, 2002; Rengachary et al., 2008). He would go on to do pioneering work with blood transfusions (Donovan, 2004).

There was also a wider group of colleagues that Willis was associated with, and this was the 'Oxford Philosophical Club' also referred to as the 'Oxford Circle'. The club was found-

ed in 1650 following a lecture by Christopher Wren (Rengachary et al., 2008). Members of the club included William Petty, Thomas Millington, Thomas Sydenham, John Locke, Edmond King, Richard Lower and Christopher Wren (Engelhardt¹ & Levy, 2021; Lo & Ellis, 2010; Molnár, 2021). The club was not a formal institution, rather it was an invisible college that practiced in the 1650's with a focus on dissection and experimentation (Flis, 2012). As a group and as individuals the members would go on to achieve remarkable academic, professional and financial success across multiple disciplines (Martensen, 1993).

The club held a collaborative approach to science, they met weekly to perform experiments and debate their meanings, with their motto translating to take nobody's word for it (Arráez Aybar et al., 2015; McNabb, 2014). The Club would become the precursor to the Royal Society that was established in 1660 by Charles II, coinciding with his restoration to the English throne. (Arráez Aybar et al., 2015; Flis, 2012; Rengachary et al., 2008), with Willis a founding member (Rana, 2005), becoming a Fellow in November 1663.

Willis also had a number of high standing patrons, including Archbishop Sheldon who had helped him secure his appointment at the University (Cook, 2019). Willis was a devout and conscientious Anglican and had a number of religious collaborators and allegiances (Descartes, 2010). Each of Willis' medical colleagues and collaborators had distinct interests, roles, skills and expertise. They were a sounding board for his conjectures and observations and an audience to each other's scientific discoveries, experiments and theories. Their work together was of a collaborative nature, and it has only been history that

has credited Willis for the work.

The Circle of Willis:

Following multiple dissections, Willis and his colleagues noted a familiarity in the organisational structure of the anastomosis of arteries at the base of the brain (Dumitrescu et al., 2020), that would in turn be named the 'Circle of Willis'. The Circle was described and named in Willis' honour by Richard Lower (Harrigan & Deveikis, 2012; Scatliff & Johnston, 2014; Wells, 1949). The Circle of Willis is undoubtedly the most famous subject of Thomas Willis' experiments (Neher, 2009). As a team Willis and his colleagues, including Richard Lower and Christopher Wren, undertook a systematic approach to analysing and appreciating the psychological function and significance of the Circle in health and disease (Cavalcanti et al., 2009; Hierons & Meyer, 1962), and through this process they corrected previous descriptions (Zimmer, 2004). Although named the Circle, it is important to note that the anastomosis is actually a heptagon, a seven-sided structure (Meyer & Hierons, 1962).

Thomas was not the first to describe the Circle of Willis. There are references dating back to antiquity (C. Breathnach, 1996; Molnár, 2021; Rengachary et al., 2008). Previously recorded descriptions include those by Falloppio, Colombo, Casserio, Vesling and Wepfer who all made an important contribution to our current understanding of the Circle of Willis (Engelhardt¹ & Levy, 2021; Meyer & Hierons, 1962; Tatu et al., 2005). However, their descriptions were limited to describing the vessels, with those that utilised illustrations generally incomplete (Unknown, 1963) and most failed to grasp the important function of collat-

eral blood flow, thus underestimating the importance of the anastomotic system. Wepfer was perhaps the one to come the closest to discovering the purpose of the arterial anastomosis, publishing his works in 1658, six years prior to Willis (Gowing, 2004; Tatu et al., 2005; Wepfer; Williams & Sunderland, 2001). It is important to stress that Willis never claimed to be the first to describe the Circle (Wolpert, 1997) and acknowledged these earlier works and used them as the basis for his one experiments (A. N. Williams, 2003). Willis' description, along with those that came before him, were challenged by the wide anatomical variations in the calibre of the vessels and at times the absence of key vessels (Rana, 2005).

What made Willis' contribution in the evolution of understanding concerning the Circle of Willis so significant was their experimentation including the injection of a mixture of India Ink, dye, alcohol, mercury and other viscous substances into the brain and cerebral vessels (Cavalcanti et al., 2009; William Feindel, 1962b; Meyer & Hierons, 1962; O'Connor, 2003; Symonds, 1960; Wijdicks, 2021). These experiments allowed critical observations concerning the flow of blood within the Circle, such as dye injected into one carotid artery travelling to another more readily than into the venous system (Rengachary et al., 2008).

Wren developed a method of brain tissue preservation utilising alcohol (Arráez Aybar et al., 2015; Cavalcanti et al., 2009). These techniques of injection and preservation were used by Willis and Lower, who could then inject dye into the carotid arteries and observe and documented the blood distribution throughout the brain (Dewhurst, 1982; William

Feindel, 1962a; Symonds, 1955). Blood was also pumped into the carotid arteries in an attempt to imitate the natural flow of blood (Flis, 2012). It is noted in a letter that all parts of the brain "were imbued with the same colour (of the dye) after the carotids were injected" (J Trevor Hughes, 2000; O'Connor, 2003; A. N. Williams, 2003).

These developments enabled for the first time an almost complete description and demonstration of the anatomical, and physiological function of the Circle of Willis. Specifically, how the cerebrovascular system could provide collateral flow when one or more arteries becomes occluded (Arráez Aybar et al., 2015; King, 1966; Lega, 2006; Rengachary et al., 2008; Symonds, 1960; Uston, 2005; Wijdicks, 2021; A. N. Williams, 2003; Wolpert, 1997). Willis was the first to demonstrate how the anastomoses (continuity of flow) linked the carotid and vertebrobasilar systems, with his descriptions of cerebral circulation centuries before the description of cerebral perfusion pressure (A. N. Williams, 2003). Supporting Willis' work was the first (almost) complete illustration of the Circle of Willis by Christopher Wren (see Figure 4.) (Meyer & Hierons, 1962; Tatu et al., 2005).

As health professionals today we have the technology to look and observe the vessels in the Circle of Willis making note of narrowed or tortured vessels and understanding why an individual may have had reduced blood flow and poor collateral blood flow following a cerebrovascular event. In Willis' day individuals who succumbed to apoplexy simply died or survived; the direction often attributed to religious doctrine or superstitious beliefs with curses, demonic possession, and witchcraft still commonly feared beliefs.

In this statement by Willis about the Circle, he describes their most important discovery.

.... To wit, that there may be a manifold way
..., for the blood about to go into diverse regions of the brain ... so that if by chance one or more should be stopped, there might easily be found another passage ... (Willis, 1664).

Willis Contributions to Psychiatry:

Willis elucidated a number of modern psychiatric conditions, mental illnesses and intellectual disabilities. His careful observations and the conclusions that he made have been celebrated by modern practitioners (Wilson, 2012). Willis incorporated behaviouralism into his practice, and he was one of the first to attribute mental illnesses to the differences in neural function, providing the groundwork for modern psychiatry (Williams & Sunderland, 2001).

Willis brought a number of conditions including hypochondria, headache, lethargy, delirium, foolishness, mania, depression, epilepsy, melancholy, madness and hysteria into the orbit of the nervous system. He offered neurological explanations for presentations that were previously viewed as conditions originating from either bodily organs, heterogeneous particles, bodily fluids, vapours, or organic sources (Williams, 2002; Williams & Sunderland, 2001; Wilson, 2012). As an example prior to Willis, hysteria was believed to be caused by the womb. Willis did challenge this, noting it to be, in his opinion, an explosion of the nerves, but he also considered that animal spirits may be causative.

Willis' theories still focused heavily on the displacement of animal spirits and one's soul

(Tabb, 2014), attributing displacements such as over irritated, excessively in motion, tumultuous, hypermobile, confused, and of being in excess or deficiency to the spirits. Willis, whilst acknowledging the brain as the location of mental illnesses, still presented his postulated abnormalities of the animal spirits were presented as an important part of his explanation. This was during a time when many other physicians were challenging the concept (Tabb, 2014). Willis did not falter in his belief that a corrective approach to the spirits was needed to dampen the symptoms of mental illness.

Willis' enlightenment that he gained in relation to mental illnesses did not always transcribe to logical treatment (Cranefield, 1961). Willis recommended some brutal interventions and therapies, with one case of advocating to hit the patient over the head with sticks noted (Willis, 1681). It is likely that Willis' description of "a folly" relates to schizophrenia, which he describes should be treated with induced fever (Williams, 2002), a practice that continued into the 19th century.

Psychiatry is one area where Willis demonstrated true ambition (Wragge-Morley, 2018) and it is easier to conceptualise and understand Willis' findings with the knowledge that he did not have assessment tools, an understanding of neurophysiological pathways and the imaging technology we have today.

Willis the Author:

Willis used his study of anatomy to advance physiology and pathophysiology, and the timing could not have been better, as it was the golden era of the printing press that enabled the facilitation and exchange of ideas. Willis'

contributions to medicine are presented in fourteen treatises, of these four are illustrated and almost all are written in Latin under six titles between 1659 and 1675, with one posthumously presented in 1692 (A Compston, 2023; O'Connor, 2003).

Whilst writing in Latin brought with it a neatness, elegance, and authority, it also demonstrated that Willis was highly educated, a learned scholar and an authority on the subjects he presented (O'Connor, 2003). However, it limited the general readership of his works significantly. Where it did increase the readership was the church and the crown, with Latin still the language of political power and religious authority (French, 1994). It is estimated that less than 30% of people could read in England at the time, let alone read Latin. In fact, despite Thomas' eagerness to present his working in Latin, the use of Latin was declining in the 17th century.

Thomas' works are riddled with religious sentiment and provide evidence of the significant role religion played in his life and beliefs regarding the human body. It is pertinent to note that Willis' writings were somewhat neglected by his contemporaries (Arráez Aybar et al., 2015). It was an age of discovery, and everyone was wanting to teach and publish their own findings. It has only been through history that Willis' work has been placed in chronological order in relation to contemporaries, sealing his place as having published some of the first great anatomical works of the modern era. His works would begin to be translated from Latin to English starting in 1679, just four years after his death.

Early in his medical career, Willis combined his medical and chemistry knowledge to ex-

plore the theories concerning the fermentation of natural bodies, publishing his work in 1659, which included three treatises (fermentation, fevers and urine) (Caron, 2015).

It would be in 1664, following the restoration of Charles II, that Willis would turn his attention to neuroanatomy and would publish his epoch-making volume *Cerebri anatome: cui accessit nervorum descriptio et usus* (Kramer, 1912). The titles of Willis' subsequent works suggest the progress from anatomy to pathology, and eventually to physiology (Caron, 2015). Although *Cerebri anatome* nearly did not make it to print following the strict censorship and printing restrictions imposed by Charles II (O'Connor, 2003). Amazingly, for how radical his findings were, Willis never really suffered the critical eye of religious censors (Lega, 2006). This was perhaps due to his pious religious views and sensitivity to religion when making scientific statements. For example, he presented the brain as the seat of one's rational soul (Hunting, 2022; Keele, 1967). Secondly, he appeased the 17th century Platonic beliefs held at the time, that the brain was the primary organ of the body (Dumitrescu et al., 2020). Thirdly, he also advertised the support of powerful sponsors, with the dedication of *Cerebri anatome* naming Gilbert Sheldon (the current Archbishop of Canterbury) noting 'it was by your means' (Burns, 2009; Descartes, 2010; Keele, 1967). *Cerebri anatome* is primarily focused on the description of the cranial nerves (Symonds, 1955), however it became perhaps more famous for the dissertation upon what we now identify as the Circle of Willis. In *Cerebri anatome* Willis also described many of the anatomical features that we are familiar with including the internal capsule, cerebellar peduncles, thalamus and many of the nerves

that still bear their original names (Arráez Aybar et al., 2015).

Willis had a skill in providing descriptions of clinical cases with incredible accuracy and insight. In fact, they are still applicable to practitioners today. The descriptions in *Cerebri Anatome* were supported by plates (diagrams) and include both human and animal examples of anatomy (Flis, 2012). The diagram of the base of the skull, (Figure 4) is thought to originate from Wren's and possibly another's hand. However there are a number of anomalies that we would recognise today (Cavalcanti et al., 2009). The first is the omission of the posterior cerebral arteries (William Feindel, 1962b; Hierons & Meyer, 1962; Meyer & Hierons, 1962), followed by the presentation of the posterior communicating arteries as quite large. The image also shows the anterior cerebral arteries as joined with multiple branching (Lo & Ellis, 2010), and not through the anterior communicating arteries, whilst also omitting the crucial branches from the vertebrobasilar artery (Hierons & Meyer, 1962; Wijdicks, 2021). Despite these omissions the image presented by Wren is far superior to any available before it.

Willis' clinical neurological findings as described in *Pathologiae Cerebri* (1667) that translates to 'The Study of Illnesses of the Brain and of the Nerves'. It was largely derived from personal observations and not from traditional and outdated authorities (Eadie, 2003). *Pathologiae Cerebri* is an important work on the pathology of the brain and nervous system looking at a number of conditions including epilepsy, spasms, contusions and scurvy.

De Anima Brutorum (1672), translated to 'of

the Soul of Brutes' is one of the earliest English works on medical psychology (Williams, 2002; Wilson, 2012). It covers a number of topics with an entire chapter on mental impairment (Wilson, 2012). This work marked a move towards empirical findings and away from old beliefs, superstitions and largely inaccurate conclusions related to mental illness. However this work was not widely adopted at the time, and had little impact on the treatment of mental illnesses and disorders in the early modern period (Macalpine & Hunter, 1963; Wilson, 2012).

Diatriba de medicamentorum operationibus in humano corpore (1674) translates to 'Theoretical Pharmacy' or 'a Discussion of Medicines and their Effects on the Human Body' (Scatliff & Johnston, 2014). A second part to this work was published in 1675 and over the two volumes Willis covered a number of topics including heart palpitations, diabetes, vomiting, purgation, opioid medications, asthma, bloodletting, skin diseases (including itching and scabies) and their remedies.

In 1674 Willis published *Pharmaceutiacutice Rationalis*, a series of case histories, postmortem observations and therapies that vied to establish anatomical and chemical experimentation as the basis of pharmacology. This was perhaps his least successful literary endeavour.

One point that is of interest in today's academic context is the fact that despite Willis' works being a collective effort, Willis is recognised as the only author (Gibson, 1970; Symonds, 1960; Zimmer, 2005), with recognition and acknowledgement of his colleagues' contributions given in the preface (Arráez Aybar et al., 2015). Unfortunately, many notations

and artifacts relating to Willis' early works were destroyed in the Great Fire of London in 1666 where many printing houses and booksellers were destroyed. Lost artifacts include Willis' original Latin transcripts and copper plates of Wren's illustrations (Scatliff & Johnston, 2014). Subsequent editions of *Cerebri Anatome* were produced from the two surviving editions that were printed and sold before the fire. Sadly, only one drawing from Wren's collaboration survived, with the others having been lost in the fire (Neher, 2009).

Firsts and Momentous Discoveries

Thomas made a number of discoveries, including the use of the term neurology that was first coined within his works. It is said that he would often be distracted from the dissection table, already framing theories for the observations they were making. Thomas engaged his knowledge of chemistry frequently in his theories; he was a leader of iatrochemistry (the goal of providing chemical solutions to disease and ailments) and strived to explain bodily functions from a chemical standpoint.

Thomas was also the first to distinguish between the functions of the grey and white matter of the cerebral hemispheres (Finger & Finger, 2005). Although Willis believed that the grey matter was important not for the processing of sensation, perception, voluntary movement, learning, speech and cognition, but for the circulation of animal spirits (Pearce, 2000), with the white matter responsible for the distribution of the spirits and this in turn governing sensation and movement (L. Caplan, 2000). Willis observed that the rational soul allowed humans to reason and judge (Tabb, 2014). So not all of his observations and conclusions were entirely correct, but this was a new branch of medicine and a radical

time of learning. It needs to be recognised that up until this time, the hollow spaces in the heart and brain were given spiritual importance (Martensen, 1993). Willis also replaced Nemesius' doctrine, that held the ventricles as the location of cognition, proposing the cortex as the substrate of cognition (Wragge-Morley, 2018).

Thomas also made a number of firsts and discoveries (See Table 1)

This list is perhaps only a fraction of the fallacies that Willis challenged and, in some cases, outright rejected. Importantly his work opened up many new areas of research. These observations and findings were not always so recognised and accepted. At the time there were still the purists that, despite the evidence, were disinclined to accept Willis' theories opting for the traditional Graeco-Roman teachings. Nearly 300 years after the publication of *Cerebri anatome*, Symonds (1955) was one of the first to explore the clinical significance of Willis's work and he began to receive due attention as the 'founder of neurology' (William Feindel, 1962b; Neher, 2009). Willis maintained his interest in diseases of the nervous system throughout his life (Teive et al., 2022), and brought to his practice not aphorisms but a research basis (Arráez Aybar et al., 2015).

Willis' Practice in London:

In 1666, after 20 years of living and practicing in the shadow of the Oxford spires, Willis relocated to St. Martins Lane (now 114), Westminster, London at the request of the Archbishop of Canterbury, Gilbert Sheldon (Dewhurst, 1972; Dow, 1940; Rana, 2005). Sheldon was an important patron and praised

Table 1. Firsts and Momentous Discoveries of Thomas Willis

- He was the first to describe and name optic thalamus, vagus nerve, migraines, corpora striatum, spinal accessory nerve and internal capsule.
- Willis deduced that the medulla oblongata coordinated many of the body's involuntary functions.
- He demonstrated that obstruction to the blood flow to the brain did not always correlate with apoplexy.
- Willis was the first to number the cranial nerves in the order we know them now.
- He described myasthenia gravis as intermittent weakness that worsens with fatigue or activity.
- Epilepsy was redefined as explosive reactions in the brain rather than originating from the muscles, this challenging the assumption of demonic possession. Thomas identified that recurrent seizures could result death.
- Thomas theorised the cerebrum as the centre for memory, cognition, imagination, and volition, rejecting the ventricles theory.
- Dementia was identified as being either congenital or acquired and linked to age, alcohol abuse, or long standing palsy or epilepsy.
- He recognised that hysteria was not a disease of the uterus but was cerebral in origin.
- Willis concluded that a traumatic head injury could result in acquired foolishness and stupidity.
- He described individuals with inflammation of the meninges with concurrent fever (meningitis), noting that the term meningitis would not be coined until the early 1800's.
- Headaches occurred as a result of increased blood flow in the brain.
- Thomas characterised diabetes, noting the sweet flavour of the urine, and adding the word mellitus to the diagnosis.
- He also wrote on a variety of other topics including fevers, urine, fermentation, scurvy and muscular motion.
- Thomas provided a particularly accurate characterisation of epidemics, including detailed descriptions of typhus outbreaks.

(Arráez & Aybar et al., 2015; Çağatay, 2004; Descartes, 2010; Eadie, 2003; William Feindel, 1962b; Finger & Finger, 2005; Martensen, 1993; Molnár, 2004; Rengachary et al., 2008; Symonds, 1955; Wijdicks, 2021; Wragge-Morley, 2018; Zimmer, 2004).

Willis' work after Thomas treated Sheldon following a stroke (Choudhari et al., 2008). The move to London involved leaving his academic career for the most part, although he continued to interact with his academic scholars throughout his time in London. Willis is perhaps best portrayed in the engraving by G. Vertue, 1742, after a portrait completed by D. Loggan, c. 1666 (see Figure 5.).

Willis also continued to publish works up until his death. However, for most of his time in London, Thomas would dedicate himself as a physician. It is unclear if this move to London was planned, as Willis had recently undertaken a forty-year lease of Beam Hall in Oxford (A Compston, 2023). London was a long way from his early days in Oxford where he would have to hustle for patients. Now, he was a man of great material wealth and lived in style. Thomas employed three servants and a coachman, and he held a significant amount in capital including multiple manors (Hunting, 2022). Despite this Thomas always found time to tend to the poor, and donated his Sunday fees (WH Feindel, 1969).

Thomas was immediately successful and the practice was prosperous, despite rumours that he lacked confidence and was not a good physician (Arráez Aybar et al., 2015; Dewhurst, 1962), with some going as far to describe him as a plain man of no carriage, little discourse, complaisance or society (à Wood, 1815). However, for the most Willis was described as a prestigious physician and perhaps the most famous and wealthiest in Europe (Arráez Aybar et al., 2015; Dalley, 2002; William Feindel, 2004; Hunting, 2022; O'Neal, 2017). His success was not only due to the beneficence of Archbishop Sheldon but also due to his skills and breadth of expertise

(Wilson, 2012).

Figure 5. Digitally Coloured and Enhanced Image of the 1742 Engraving of Thomas Willis, after a Portrait Completed in 1666.



Although these references to his celebrity statues do not assess his clinical skills, it is perhaps the notations to his charitability and his attendance to the sick and poor that most describe his character. Thomas would charge his wealthier clients hefty fees to supplement his care of the poor and maintain his status as a generous supporter of the church (Dewhurst, 1972; Dow, 1940). Willis' last years of his life were productive, he was wealthy and respected, working diligently through the upheaval of the English Civil War through to his last posting in London. His London practice was so successful that Willis employed Robert Hook, who would go on to develop the microscope and the first artificial ventilator (Williams & Sunderland, 2001). It is evident from Willis' own notes and correspondence that he was a dedicated physician and clinician at heart, who took great interest in his patient's ailments (William Feindel, 1962b; Molnár, 2004). Willis' approach to patient care was different to his contemporaries, he took time to observe, experiment and col-

lated bedside observations with anatomical fact (Lo & Ellis, 2010; Molnár, 2021). His work and the legacy he left marked the transition between medieval and modern neuroscience, his work was translational and innovative, while his work contributed to the weakening of the Galenian movement (Arráez Aybar et al., 2015).

On more than one occasion Willis was called upon to treat members of the royal family (Williams & Sunderland, 2001), this included consulting Charles II regarding his infertility (A. Williams, 2003). Although Willis' approach or bedside manner did not always win him royal favour, he attributed the deaths of six of the James II children as 'mala stamina vitae' or otherwise derived from diseased, feeble or imperfect parents (Arráez Aybar et al., 2015; J.T. Hughes, 1991). Great offence was taken, and it is perhaps not surprising that he was never knighted, and Willis was never called again to the royal court.

Willis died in November 1675 of pleurisy (possibly secondary to tuberculosis) and was laid to rest in the north transept of Westminster Abbey (Hunting, 2022; Rana, 2005; Symonds, 1955; Symonds & Feindel, 1969; Uston, 2005). Sadly, despite Thomas' early demise at the age of 54 he outlived his beloved wife who died in 1670. Only four of his nine children survived past infancy, with all but his eldest son predeceasing him (A. Williams, 2003). He left to his surviving son a considerable fortune of approximately £1600 (£240,000 in today's money) and three manors (WH Feindel, 1969).

Willis's Legacy and Descendants:

Thomas and Mary's only child that survived to

adulthood was Thomas junior, who was the first born of their nine children at Beam Hall, Oxford. Thomas junior studied at Westminster School, then followed by Christ Church College Oxford. Thomas junior was only around 17 years of age when his father died, going on to marry Alice Browne in 1681 at Westminster Abbey. Thomas junior and Alice had three children (Browne, Thomas and Jane). Their son, again called Thomas, died in 1699 on St. Martins Day, remarkably the same day his grandfather had died. Thomas junior himself died aged 41.

Browne Willis (grandson of Thomas Willis) was an outstanding antiquarian, numismatist, politician, author and Member of Parliament (Symonds, 1955), sitting in the House of Commons from 1705 to 1708. In 1707 he married Katherine Eliot and was said to be still enjoying and living off the good fortune of his grandfather, including an extensive property portfolio. However, within his lifetime Browne managed to significantly depreciate the family fortune. This was not before he had a small church built in 1731 in Buckinghamshire that is dedicated to St. Martin, with Browne himself buried there (Viets, 1917). Browne was described as an eccentric but admiring grandson, but with little skills when it came to managing the wealth he inherited (William Feindel, 1962a).

The lineage of Dr. Francis Willis, noted to be the great nephew of Thomas (John T Hughes, 2009), by Thomas' older brother John (see Figure 1) is difficult to trace. The direct connection indicated by Smith and Peters (2017) through Thomas' brother John, has conflicting data related to Thomas Willis senior's brother John that are both noted to share the same birth and death year. Working through the as-

cendants of Francis Willis the direct connection is still not able to be confirmed with this indicated as // on Figure 1.

Dr. Francis Willis would go on to study medicine and specialise in psychiatry. Speculation as to the genealogical connection persist. Francis would gain national and international celebrity status following his successful treatment of King George III, during his first major episode of insanity (da Mota Gomes, Gonçalves, Cheniaux, & Nardi, 2023; Smith & Peters, 2017). Some of the known interventions included blistering, purging and bloodletting, as well as a strict regime of moral management (Peters & Beveridge, 2010). Francis' treatment was heralded as facilitating King George's recovery. Following this Francis' reputation grew, and he faced increased demand for his services, expanding his clinical practice (da Mota Gomes et al., 2023).

Lessons:

Thomas Willis was an esteemed anatomist and physician whose resilience and dedication have been immortalised forever in the arterial anastomosis that bears his name (Nichols, 2019). There are many lessons that we can learn from Willis and perhaps one that is not often recognised is his approach to research. Willis engaged many of the techniques and approaches that we still use today when addressing a research problem. His observations were careful and proceeded in a logical order, his postmortem findings were carefully documented and fundamentally he worked as part of a team and recognised the significance of differing viewpoints (Molnár, 2021), recognising the skills and attributes of his colleagues. These attributes were coupled with clinical findings as he autopsied many of

his former patients, following them from life to death (Willis, 1684). Willis correlated his anatomical findings with the signs and symptoms of his patients in a quest to understand the mechanism of disease processes (Molnár, 2021; Rengachary et al., 2008).

There are however some aspects of Willis' work that were not revolutionary. For an anatomist, a chemist, physician, and a leading scientist of the time, he still presented some erroneous theories that were metaphysical and theological in nature. For example, the belief that animal spirits were generated in the brain and diffused like rays of light through the brain yet also presented theories that chemical messengers mediated the nervous system (A. N. Williams, 2003; Zimmer, 2004). This a very early prequel to the discovery of neurotransmitter chemicals. Willis also integrated questions about the existence and attributes of the soul into his science of the mind (Wragge-Morley, 2018). Whilst a scientific mind may now regard this as nonsense, however, at the time these were generalised beliefs. Willis was limited by the concepts at the time, instruments available to him and the lack of imaging techniques (A. N. Williams, 2003). Given these barriers, Willis simply made rational conclusions that were swayed by his religious convictions and beliefs. This led him to ultimately view the brain as a harmonious system designed by God (Monteiro et al., 2021). It is important to place this in historical context, as the theory of evolution would not appear until some 200 years after Willis' work.

Willis obtained vast clinical experience during his life, even when faced with the struggles of having to prove himself again and again. He endured many upheavals in his life as well as many personal tragedies, yet he still managed

to revolutionise medicine. It is perhaps due to his unconventional up-bringing, that Willis, throughout his career, always tended to the poor and less fortunate. He donated money to the poor; he supported his less prosperous siblings and gave generously to the church.

Critics and Criticisms:

There is both criticism and admiration for Willis' work. Those less in favour comment that it was Richard Lower who undertook the majority of the anatomical dissections, with Willis merely observing and taking notes, later discounting Lower's participation (William Feindel, 1962b; Robert G Frank, 1990). However Willis neither withheld authorship or recognition that was accepted practice at the time, such as devious act was beyond the very pious and religious Thomas (Robert G Frank, 1990). While Willis did not always take a hands-on approach, it is said that he directed the dissections (Choudhari et al., 2008; Rengachary et al., 2008) and played a leading role (Keele, 1967). This distinction between Willis' directional guidance and Richard Lower's actual hands-on role has led to the suggestion that it is Richard Lower who should be recognised as making many of the anatomical discoveries (Hierons & Meyer, 1962). However, each played their parts, commensurate with their expertise. Christopher Wren was the artist, and Richard Lower held a curiosity for exploring detailed anatomical structures (Robert G Frank, 1990), while Willis was known for his habit of taking detailed notes (Teive et al., 2022). They were a multidisciplinary group each with their own skills sets. Questions regarding his practice are unfounded and rather Willis was one of the most respected and influential anatomist and physicians of his time (Hawkins, 2011).

These claims are likely to have stemmed from malicious gossip by individuals who wished to discredit the work of the more successful members of the Oxford Club (Symonds, 1955). His successors discredited him and hypothesised that he was an inveterate theorist (C. Breathnach, 1996). Willis' success brought upon him the animosity and envy of many, and at times suffered great harassment. His reputation was not as renowned as it is now, and many dubbed his findings as intellectual fantasy (Wragge-Morley, 2018).

The root of many of these unsustained attacks, that in particular regard Thomas' integrity, stem from an Anthony Wood, who harboured a personal dislike of Willis (A. Williams, 2003), possibly over a neighbourly disagreement (Symonds, 1960). In the preface of *Cerebri anatome* Willis is the first to express gratitude for Richard Lower's and Christopher Wren's work as well as identifying a number of others, who together, as a collective, helped and instructed Willis. Additionally, there has been no evidence that Richard Lower nor Christopher Wren ever made any claim that their work had been stolen (Arráez Aybar et al., 2015).

Strengths and Limitations:

There were several limitations of this work regarding the ready identification of original sources and seminal works, given the intervening 400 years. This included seminal genealogical information. To counter this, multiple databases were searched and when a questionable entry was located every effort was made to identify the most likely result, that was supported by multiple sources. When identities and dates were unable to be veri-

fied, a double // was used to indicate a break in the line.

For the conversion of Thomas' income and monies distributed in his will the National Archives Currency Converter were used. Research can also be interpreted in conflicting viewpoints, or simply misunderstood, leading authors to make different conclusions from the same literature source. Many works, although unique and individual, cover the same salient points relating to Thomas' life and works. There was a degree of bias in some published works to meet the consumers' needs and in some instances key points were focused upon with only the brief of mention of related facts. There was in a number of source interpretation challenges and difficulty placing events into the context of the happenings in England at the time. For this manuscript a representation of Thomas Willis' family tree has been included as Figure 1. and a timeline table has been included as an appendix 1. The time and space constraints of printed journals has limited the depth of investigation into facts and in older journals that were published before online services became available. Older articles were also at times poorly copied, with the online versions difficult to read and interpret.

This work aims to avoid anachronism and presentism and worked diligently to ensure that historical facts and events were presented within the historical context of the time and place, thus avoiding judging the past events presented in this work with the distortion of modern values and interpretations. A strength of this work is the extensive search of the literature that was undertaken. Whilst this did result in duplication of authors reference to events and facts it enabled the authors to make evaluated judgements regarding

sources. Multiple sources were referenced where possible to strengthen the fact that seminal works had been accessed at one or multiple points and over the period of multiple generations of historians. This wide source of literature also enabled the authors to understand the history and context of events. This was supported with the inclusion of the two sections regarding the English Civil War and the Restoration. It is hoped that this work contributes to scholarly conversation, regarding not only the literature pertaining to Thomas Willis but also the limitations.

Conclusion:

Willis revolutionised medicine, particularly neuroscience, in a time that was impacted by social, societal and religious upheavals. Willis lived through an incredibly turbulent time; he saw six executive administrations (James I, Charles I, Oliver Cromwell, Richard Cromwell, Charles II and James II), with each came change, restrictions and uncertainty. Despite this it was a dynamic, culturally and intellectually stimulating period of time. Willis challenged authority and history; he was benefited by an unusual medical training. To say that Willis was a pioneer in researching the anatomy of the brain, nervous and cerebrovascular system is an understatement. Although he had many other moments and successes, his neuroanatomical findings are perhaps his finest achievements, with his work culminating in the publication of *Cerebri anatome*.

The stars aligned for Willis, with his work occurring during an era of scientific observation, experimentation and discovery. Willis is an irreproachable example of the medical transitions from medieval notions, beliefs and approaches to our now modern understanding.

He made the connection between anatomy, physiology, and pathophysiology, his many contributions to neuroscience are equally fundamental. Willis was also a pioneer of what we now term translational research, 400 years before it would emerge into our lexicon. Throughout Willis' practicing years his patients remained his abiding interest. He had a simple agenda and that was, he wanted to understand. He learned and acknowledged the antiquated medical theories, but he did not allow them to plague his progress. He experimented and learned through anatomy and bought a new level of medicine to the table.

It is hoped that this work is a true narrative of the time, the people, and the place. It is impossible to make an in-depth reappraisal of Willis' neuroscience achievements let alone his life's achievements. This paper has attempted to demonstrate the influences in Willis' life and how he preserved and never lost his quest for knowledge. Willis also never lost touch with the fact that these were individuals and humans that he met on the anatomy table, he did justice to their situation in furthering his own and other's knowledge relating to anatomy and also to health and disease. It is only fitting that he remains immortalised by the arterial anastomosis at the base of the brain, that we know as the Circle of Willis.

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Appendix 1. Timeline of Thomas Willis' Life, and the events occurring in England at the time, the period of the English Civil War proceeds the green line, the period of the interregnum proceeds the blue line and the restoration proceeds the red line.

Timeline of Events Occurring England	Year	Timeline of Thomas Willis
	1582	Thomas' brothers John and William are born
Court and Parliament temporary move to Oxford due to Bubonic Plague in London, Charles I is born (November)	1600	
James I (born June 1566), and unifies the Scottish and English Thrones	1603	
	1619	Thomas' sister Jane is born
	1621	Thomas Willis born Wiltshire England (January)
	c. 1623	Thomas' mother inherits land in North Hinksey, and the family become landowners
James I and Charles I inherits the throne (March), there is almost instantly Parliamentary unrest and tension with the monarch	1625	
Charles I dismisses parliament and does not recall another for eleven years	1629	
Charles II is born (May)	1630	Thomas' future wife Mary Fell is born
	1631	Thomas' mother Rachael dies
Royal Charter permitting the University of Oxford to claim the body of anyone executed within 21 miles of Oxford	1636	The curriculum at oxford is changed to mandate that all students must participate in at least two dissections.
	1637	Thomas is admitted to Christ Church College, as a servitor to Dr. Thomas Iles
	1639	Thomas is awarded Bachelor of Arts (BA) degree (Chemistry) Christ Church College, Oxford University (June)
Charles I flees north to Oxford and establishes his court at Christ Church College Oxford (August). His physician William Harvey is with him Outbreak of Civil War in England, with first conflict at Edgehill (October)	1642	Thomas is awarded Master of arts (MA) degree (Chemistry) Christ Church College, Oxford University (June)
The city of Oxford becomes headquarters for the king's army First siege of Oxford (May/June)	1644	
Second siege of Oxford (May/June)		
Oliver Cromwell formally accepts the surrender of Oxford	1645	Thomas Enlists in Dover's regiment in the service of Charles I
Charles I flees Oxford in disguise and heads north (April)		
Third siege of Oxford (May)		
End of the Civil War (June), the Royalists have been defeated, Oxford surrenders, and the King is in custody.	1646	Awarded Bachelor of Medicine Oxford by Royal decree and was able to begin medical practice (December) Thomas' father and stepmother die of 'camp fever'
Charles I is being held as a prisoner of Cromwell's at Hampton Court	1647	
Charles I aged 48 is convicted of treason and executed (January)		
Accession of Charles II then aged 19, declared king while in exile in Scotland	1649	
Charles II makes an attempt to get the English crown back but the Scottish army is defeated at Dunbar (September)	1650	Revival of Anne Greene (December)
Founding of the Oxford Circle (Philosophers Club)		
Oliver Cromwell appointed Oxford University Chancellor (January)		
Charles II is crowned with the Scottish regalia (January)		
Charles II and his Scottish forces are annihilated in Woster and Charles II is on the run with a warrant of 1000 pounds on his head (September)	1651	
Charles II flees to France (October)		
Oliver Cromwell forcibly takes control of England and is appointed Lord Protector of England (December)	1653	Thomas publishes De Fermentation and De Febribus
	1657	Thomas moves out of university accommodation and occupies Beam Hall (Just opposite Merton Collage) Thomas marries Mary Fell (April)
Oliver Cromwell dies, naming his son Richard as his successor (September)	1658	Thomas and Mary welcome their first Child Thomas junior
Richard Cromwell steps aside as leader	1659	

Appendix 1. Timeline of Thomas Willis' Life, and the events occurring in England at the time, the period of the English Civil War proceeds the green line, the period of the interregnum proceeds the blue line and the restoration proceeds the red line.

Timeline of Events Occurring England	Year	Timeline of Thomas Willis
Charles II returns to England after living in exile in France on the invitation of parliament. The restoration of the monarchy (May) The Royal Society established (November)	1660	Elected Sedleian Professor of Natural Philosophy at Oxford (by request of Charles II) Thomas begins brain dissections with his colleagues Christopher Wren and Richard Lower Thomas and Mary's second son Samuel is born
Oliver Cromwell's body is exhumed from Westminster Abby and posthumously executed (January) Charles II crowned king of England (April)	1661	Baby Samuel dies
	1660	Thomas is awarded a Doctor of Medicine
The Church of England is restored as the national church of England	1662	Thomas and Mary welcome their first daughter Mary, but unfortunately, she dies not long after birth.
	1663	Thomas and his family move to London Samuel II is born and dies Thomas and Mary's daughter Rachel is born Elected Fellow of the Royal Society (December)
The Restoration	1664	Publication of <i>Cerebri Anatome</i> Thomas and Mary welcome a son Richard
	1664	Elected Fellow of the Royal College of Physicians Thomas is appointed physician in ordinary to the king
A new chapel at Pembroke College is consecrated, marking Christopher Wren's first completed work of Architecture and career change. Charles II and the royal court move to Oxford in September, not leaving until January to avoid the plague in London	1665	Thomas and Mary's daughter Anne is born
Great Fire of London	1666	Thomas and Mary welcome baby Jane
	1667	Mary and Thomas' daughter Rachael is born Both Katherine and Richard die
	1670	Thomas' wife Mary dies of tuberculosis (October)
	1672	Willis publishes the earliest English work on psychiatry Thomas marries his second wife Elizabeth Calley (September)
	1675	Thomas and Mary's two daughters Anne and Rachael die Thomas dies at his home in London aged 54 (November)
Charles II died (February), James II ascends to the throne	1685	
Glorious Revolution	1688	
	1699	Thomas junior dies