Introduction:

Early descriptions of cerebral aneurysms can be found by an Egyptian chancellor, who was glorified and deified to that of the God of medicine healing only to be rewritten in history as an evil mummy. The Old Testament and the writing of Hippocrates in the Greco-Roman period provide further evidence, with the medical observations and writing of a Greek physician becoming the mainstay of medieval medical practice. The 17th century saw the English civil war and a physician whose resilience and dedication in seeking to understand function of the basal arterial circle would have his name immortalised forever.

In the 18th century, autopsy observations and descriptions of the moments proceeding the ictus of aSAH’s provided clear evidence of the mortal nature of aSAH. This included a trio of early and sudden deaths included a Duke, a Prince and the untimely death of the Crown Prince that would change the course of the Swedish Royal family forever. It was not until 1931 that a cerebral aneurysm was first successfully secured using ether anaesthesia and muscle taken from the patient’s leg. Six years later at Johns Hopkins Hospital in America, the first successful surgical clipping of a cerebral aneurysm occurred. Surgical clipping continued to evolve however it was not until the late 20th century that the second major innovative development in intervention post aSAH occurred that would change practice thereafter. Rich in parallels from the early observational studies and describing the journey to current practice, this historical preamble demonstrates the resilience and determination of previous researchers and also the links to the core conceptual frameworks and epidemiological observations that are still applied to this day.

Abstract

The history of aneurysmal subarachnoid haemorrhage (aSAH) is far from modern, spanning close to 5000 years. There are many parallels and references to epidemiological principles that remain current today and are central to modern nursing research techniques. The importance of epidemiology in nursing cannot be overestimated, nursing practice closely aligns with the ultimate goals of epidemiological principle in the promotion of health and reduction of disease related risk factors. Despite nursing holding the conceptual key to enriching epidemiological research, nursing has historically distanced itself from front line epidemiological research, often hesitant about both capability and clinical expertise in leading epidemiological research. The following historical narrative serves as a reminder of how far we have come in the diagnosis, treatment and care of individuals post aSAH as well as serving as inspiration for future nursing research.

Key Words

Circle of Willis, Aneurysm, History, Subarachnoid Haemorrhage, Nursing
Antiquity:

It is impossible to trace the understanding of cerebral aneurysms and subsequent aSAH, with exact certainty. As noted by Thomas Sydenham

‘can no investigator point out the origin of Medicine- mysterious as the source of the Nile. There has never been a time when it was not’(Sydenham, Medical Observations cited in, Sydenham et al., 1848)

Subarachnoid Haemorrhage is a disease of great antiquity with many references in classical literature and ancient writings (Walton, 1955). Whilst the origin medicine is unknown, the Nile is linked to what is perhaps the first description of a cerebral aneurysm that dates back to 3000 years BC. Imhotep, who in life was an Egyptian chancellor is described by some as being the founder of Egyptian medicine. However, it was not until 1,200 years after his death that he was deified to the status of the God of medicine and became the centre of a popular cult (Short, 2009). Despite there being little evidence to support his practice as a physician, he is believed to be the author of section 872, column 108/3-9, found in the Ebers papyrus that describes a globular and firm pulsating swelling of a vessel and the treatment employed using cautery (De Mouliln, 1961). It is perhaps ironic that the image of Imhotep was again rewritten by the motion picture industry to be an evil mummy.

A number of references to neurological function and disorders are contained within the Hippocratic Corpus (Pearce, 2006). Whilst it is impossible to determine the authorship of specific sections with any certainty, as the collection includes around 70 medical treatises (Freed, 2011), Hippocrates is cited as having authored several key neurological observations. The description of people in good health suddenly seized with pains in the head, fatality succumbing to their illness within seven days (Aphorisms of Hippocrates cited in, McHenry & Garrison, 1969), is suggestive of a subarachnoid haemorrhage (Iniesta, 2011), perhaps more significant is the language and tense that is indicative of this being a common observation. Some note this as only suggestive of a subarachnoid haemorrhage (Milinis et al., 2017). However the emphasis in the Hippocratic Corpus on clinical observations, prognostic indicators and epidemiological conclusions are still supported by the literature to this day. In his aphorisms on apoplexy, Hippocrates notes that apoplexy was most common between 40 and 60 years of age, identifying numbness as an impending symptom, and describing sudden and spontaneous headaches and a loss of consciousness as being associated with a poor prognosis (Aphorisms of Hippocrates cited in, Pearce, 2006).

Written around 550 BC during the Babylonian Exile, the Second Book of Kings presents another reference in history to a subarachnoid haemorrhage, with a description typical of the onset of symptoms and rapid demise.

‘And when the child was grown, it fell on a day, that he went out to his father to the reapers. And he said unto his father: “My head! My head!” And he said to a lad, carry him to his mother. And when he had taken him, and brought him to his mother, he sat on her knees till noon, and then died’ (Second Book of Kings 4: 18-20).

This text represents a complex and cryptic script that is contradictory in describing a male child grown, yet sat on his mother’s knees. Applying contemporary knowledge of age and sex characteristics of subarachnoid haemorrhages, this reference is arguably suggestive of a ruptured arteriovenous malformation. However, despite the description being typical of a subarachnoid haemorrhage some dispute it as being unlikely (Milinis, Thapar, O’Neill, & Davies, 2017), while others accept it as a likely reference (Pearce, 2006; Walton, 1955).

Six centuries after the birth of Hippocrates, the writings of Galen of Pergamon would provide another milestone in the evolution of neurosurgery (Caplan, 2015). Galen wrote numerous treatises on human anatomy (Missios, 2007) and whilst many of Galen’s writings were lost in the great fire of 191 AD, samples of his works survived (Ustun,
2004b). Considered an authority on anatomy, Galen wrote of an artery that has become anastomosed and named the affection an aneurysm (Milinis et al., 2017), (Greek aneurysma, a widening; from anu, across; and eurys, broad) and importantly he recognised the two distinct entities of arterial aneurysms (Missios, 2007). Galen advocated for evidenced based practice and the use of proven principles and logical progression in the gain of new medical knowledge (Magnus, 1927). What is valuable to note about both Hippocrates and Galen is that they studied and documented geographic, demographic and epidemiological features (Missios, 2007), many of which remain the focus of modern research. Whilst little was known about the nature and the conditions they described, their writings demonstrate an awareness of preventative and general health measures.

17th Century and a New Era of Understanding:

The 17th century saw medicine in its infancy and the beginning of the establishment of medical specialties. With this new era of modern history of aSAH paralleling that of the history and development of neurosurgery (Swash & Wilden, 2006). It also saw a distinct separation in the practice of medicine, with physicians such as Thomas Sydenhan advocating for clinical descriptions and bedside observation of individual diseases (Bhattacharyya, 2011). At the same time the introduction of autopsies into England was gaining social acceptance (Harley, 1994). One physician who was to utilise this practice to increase the knowledge of others was Thomas Willis. Born in 1621, Willis was educated in Oxford, at Christ Church College (Caplan, 2015), with his studies interrupted by the English Civil War of 1641–1647 and the siege of Oxford (Uston, 2005). It was during this time, and his service as a volunteer with the Royalist army, that he first became exposed to experiential science. The civil war affected medicine profoundly and the study of anatomy benefited from the end of censorship and the retreat of intellectuals to post-war Oxford (Harley, 1994). Willis was practicing autopsies as early as 1650, although his most famous case did not involve an autopsy at all.

Figure 1: Diagram depicting the potential for the vertebrobasilar system to provide collateral circulation when the anterior (internal carotid) system is occluded through ligature from a noose during hanging, as described by Thomas Willis 1664.

(Rigozzi & Nichols, 2019)

‘... there may be a manifold way for the blood to go into diverse regions of the brain that if by chance one or two should be stopped there might easily be found another passage instead of them ...’ (Willis 1664 cited in, Ljunggren et al., 1994).
Hanging remains one of the oldest methods of execution. Unfortunately early hangings were plagued by technical failures, horrific decapitations, survivals and most cases slow, and graphic strangulation and death by asphyxiation (Rayes, Mittal, Rengachary, & Mittal, 2011). In 1650 Willis and his colleagues received the body of Anne Green, which had hung for 30 minutes post execution. Anne Green had been convicted of killing her illegitimate stillborn child. Her execution was a public event taking place in a cattle yard and several attempts were made to ease her agony including jerking her downwards (Hughes, 1982). However when the coffin was opened the young woman remarkably showed signs of life and following resuscitation she survived without complication (Caplan, 2000; Ljunggren, Sharma, & Fodstad, 1994). Given the horrific descriptions of her slow suffocation, it is perhaps a blessing to Anne that she remained amnesic to the hanging event, revival and recovery (Molnár, 2004). Following her recovery she was fully pardoned, eventually marrying and having three more children (Hughes, 1982). It was not until 133 years later in 1783 that judicial hangings were transferred to Newgate prison and the use the ‘New Drop’ gallows was adopted (Rayes et al., 2011).

At the time of Anne Green’s failed execution the basal arterial circle had been described by Gabriele Fallopio almost a century earlier (Mortazavi et al., 2013) and was a well known anatomical feature. However the flow of blood and the importance of the connection between the internal carotid arteries and vertebral arteries was unknown. In the case of Anne Green, where her carotid arteries were occluded through the process of ligation from the noose during her hanging, the blood entering the vertebral arteries was remarkably able to compensate (Figure 1).

Regardless of whether this was the result of a unique anatomical variation or a very incompetent executioner, her story and the chance that it was Thomas Willis who was to receive her body was destined to change the direction of anatomical observation towards the study of function and the mind (Caron, 2015). Willis’ subsequent descriptions of the function and adaptability of the basal arterial circle that now bears his name is one of the greatest contributions to medicine. However, it was his student Richard Lower who actually described this structure for first time in 1660 and named it in honour of Willis (Harrigan & Deveikis, 2012; Scatliff & Johnston, 2014; Wells, 1949).

With the assistance of Lower and the artist Christopher Wren, Willis’ 1664 work entitled Cerebri Anatome went beyond previous unelaborated and detached anatomical descriptions (Caron, 2015) to give the most detailed description and demonstrate the function of the brain including the arterial circle that now bears his name (Ustun, 2004a). Willis describes a number of cases that demonstrate the function of the arterial circle in providing compensatory collateral blood flow (Vrselja, Brkic, Mrdenovic, Radic, & Curic, 2014). One case report noted that the right internal carotid artery was almost totally occluded and that the contralateral vessel was enlarged, thus providing sufficient blood supply (Willis 1664 cited in, Cassels, 1998). Willis described the arteries as communicating with one other reciprocally in various ways (Willis 1664 cited in, Feindel, 1965), an anatomical feature that we now refer to as collateral pathways. Sadly, Willis died at the age of 54 from pleurisy in 1675. While his pioneering work was honoured by burial in Westminster Abbey, following his death there was a relative lull in activity concerning brain anatomy and function (Caplan, 2000).

**18th and 19th Century Royal Links:**

Advancements in anatomy and surgery in 18th century Europe was led by France in part due to the work of Pierre Dionis (Tubbs et al., 2009). France had a long history of royal autopsies as far back as 1536, where autopsies were undertaken often in search of poison (Harley, 1994). In his early 20’s Dionis was already considered a master surgeon and in 1673 was a key member of Louis XIV court, often performing public anatomical demonstrations (Tubbs et al., 2009). Dionis is attributed with elucidating the pathology of subarachnoid haemorrhage (Caplan, 2015) and describing in case reports what may have been ruptured cerebral aneurysms (Longstreth, Koepsell, Yerby, & van Belle,
1985). Dionis’ case reports include two sudden Royal deaths, with the autopsy of the Duke of Aurelia and the Prince of Espinoy both revealing distended cerebral ventricles and a sanguineous extravasation of blood (Ljunggren et al., 1987). However, it is unknown if Dionis made the important link between ruptured cerebral aneurysms and subarachnoid haemorrhage.

Nearly 150 years after the work of Dionis it was English Surgeon, John Blackall, who made the link between the clinical features of a subarachnoid hemorrhage and a ruptured intracranial aneurysm (Engelhardt, 2017). It was Blackall’s observations that led him to note the similarities between the deaths of the Swedish Crown Prince and a local young woman. In May 1810, the 41 year-old Crown Prince, Karl August of Augustenborg was inspecting a regiment when he suddenly experienced an unbearable headache and fell from his horse, dying within the hour (Ask-Upmark & Ingvar, 1950). An autopsy revealed a subarachnoid haemorrhage that extended all the way down the spinal canal, with a clear pronouncement at the base of the brain (Milinis et al., 2017). In the chaos following the Prince’s untimely death a French Marshall was appointed to the throne with the current seventh descendant a direct line of this dynasty and a Royal Patronage linked to the rupture of an intracranial aneurysm some 177 years ago (Ljunggren et al., 1987).

Three years after the death of Prince Karl, Blackall described the clinical presentation and anatomical features of a ruptured basilar artery of a young and healthy woman. The clinical presentation was described as a headache of the most excruciating kind associated with violent vomiting and intolerance to light (Blackall 1813 cited in, Ljunggren et al., 1994). The detailed description of the anatomical features of a subarachnoid haemorrhage were traced to the basilar artery, where at its bifurcation a ruptured aneurysmal sac was noted (Blackall 1813 cited in, Walton, 1956). With the similarities between the two cases noted Blackall attributed a ruptured aneurysm as the cause of sudden death in the Swedish Crown Prince three years previously (Ljunggren et al., 1987).

**20th Century Developments:**

The 20th century saw a number of advancements in the diagnosis and treatment of aSAH, including the use of lumbar puncture and understanding of the chemistry of cerebrospinal fluid and its diagnostic significance (Sakula, 1991). Despite this many believed that the treatment of cerebral aneurysms was unachievable. Harvey Cushing described a cerebral aneurysms as

‘a lesion having such remote surgical bearings … whether there are surgical indications such as ligation of the internal carotid, further experience alone can tell’ (Cushing & Symonds, 1923).

In 1927 Egas Moniz, a professor of neurology at the University of Lisbon, produced the first cerebral angiography images following the injection of a radioactive contrast medium (thorium dioxide) directly into the carotid artery followed by three x-ray images (Doby, 1992; Ljunggren et al., 1994). The risk of stroke initially outweighed the benefits for most physicians, however Norman Dott was fundamental in establishing the practice, through his refinement and use of routine cerebral angiograms to aid surgical planning for cerebral aneurysms (Milinis et al., 2017).

Dott was a neurosurgical surgical pioneer; he was one of Harvey Cushing’s residents and it was during his residency that he was first exposed to the technique of wrapping an aneurysm. This was a distinct difference in approach to attempting to secure ruptured aneurysms using ligation (Louw, Asfora, & Sutherland, 2001) that more often resulted in the intraoperative and fatal rupture of the fragile aneurysm.

In 1931 Colin Black, a 53 year old Edinburgh solicitor and hospital governor, presented to Dott’s care following an episode of sudden and severe pain chiefly affecting the back of his head with associated vomiting. Sixteen days later risking both his career and reputation, using only ether anaesthesia, Dott exposed the brain and was able to wrap the aneurysm with muscle obtained from Black’s leg (Todd, Howie, & Miller, 1990). Black recovered and Dott managed a further 39 sus-
pected aSAH cases, operating on eleven individuals (Ljunggren et al., 1987). Dott never denied fear

‘Sometimes courage is required. Courage implies an appreciation of risk – in fact it implies fear under control. He who knows no fear is not courageous but reckless’ (Dott nd cited in, Rush & Shaw, 1990).

Dott also made a number of key observations about the natural history of ruptured aneurysms including the reasonable possibility of spontaneous fibrosis and cure as the clot around the aneurysm becomes organised, as well as noting that further haemorrhage was often more serious than the initial bleed, with the second haemorrhage often being rapidly fatal (Dott 1926 cited in, Pearce, 2006).

In 1937, six years after Dott first successfully wrapped an aneurysm in Edinburgh, an American surgeon Walter Dandy successfully clipped an aneurysm using a clip originally designed by Harvey Cushing and modified by Kenneth George McKenzie (Pearce, 2006). Dandy’s patient was a contrast to Dott’s in that he was described as a frail, sallow man aged 43, with a stomach that had gone bad from drinking (Ljunggren et al., 1987). He had presented six days earlier with a history of severe frontal headache and third cranial nerve palsy (Milinis et al., 2017). The risk of rebleeding post the initial rupture was well known and in attempts to improve outcomes surgical intervention was routinely delayed (Louw et al., 2001) and Dandy himself noted that one would not dare operate in the immediate period after and aSAH (Ljunggren et al., 1994).

The aneurysm was described as having a narrow neck, which then expanded to the size of a pea (Milinis et al., 2017). This afforded a surgical approach obliterating the aneurysm using a flat clip, ‘where after the aneurysm became much softer and also ceased to pulse’ (Dandy, 1938). The procedure marked the birth of modern neurosurgery and shifted the treatment of subarachnoid haemorrhage to a curable condition. Remarkably it was also undertaken and accomplished without using angiography, despite this having been developed ten years earlier (Louw et al., 2001).

In the following decades substantial modifications to the original flat clips was undertaken including redesigning the clips so they could be opened and repositioned as well as changing the aperture, together with configuration and rounding of the blades (Louw et al., 2001). However, the development and refinement of aneurysm clips was not singularly triumphal but often one of tragedy due to the experimental nature of clip evolution (Dujovny, Dujovny, & Slavin, 1994). With a reported the in-hospital mortality rate of 73% (Rosenorrh et al., 1987), despite the advancements made overall outcomes had not significantly improved in the 50 years since surgery was first attempted. The timing of surgical intervention was also a subject of considerable debate (Phillips, Dowling, Yan, Laidlaw, & Mitchell, 2011).

Whilst delaying surgery was associated with improved surgical outcomes, the incidence of rebleeding was a significant cause of early mortality (Broderick, Brott, Duldner, Tomsick, & Leach, 1994; Ljunggren et al., 1994). With improved surgical approaches the timing of intervention has shifted towards early (within one to three days) if not ultra early (within 24 hours) (Siddiq, Chaudhry, Tummala, Suri, & Qureshi, 2012). This time also saw the introduction of the calcium channel blocker Nimodipine, validated as a pharmaceutical intervention to reduce the risk of cerebral infarction post aSAH (Pickard et al., 1989). Nimodipine has since become acknowledged in international guidelines as evidenced based practice post aSAH (Connolly et al., 2012).

Whilst clip design, surgical approaches, treatment timing and pharmaceuticals evolved, there were no significant changes in the treatment of cerebral aneurysms between 1937 when that first clip was applied until the early 1970’s.

The first CT machine was installed in 1971 and within 10 years there were an estimated 2000 machines in operation around the world (Ljunggren et al., 1994). Whilst this development in technology improved the diagnosis of aSAH, it was re-evaluating angiography and developing an endovascular approach to the treatment of ruptured cerebral aneurysms that revolutionised intervention post aSAH.
Initial attempts in the 1960’s of thrombolysis using injected horse hair and a projection gun developed under the auspices of the Office of Naval Research (Gallagher, 1964), were not unsurprisingly unsuccessful. Serbinenko (1974) published the results of 300 individuals with arteriovenous malformations and cerebral aneurysms treated via an endovascular approach using micro-catheter balloons.

At the same time in Rome, Guido Guglielmi was experimenting with the concept of fine stainless steel wire to coil and occlude aneurysms, although the hurdle of overcoming electrolysis and the erosion of the wires would take years to perfect (Milinis et al., 2017). By attaching electrolysis-resistant platinum coil to the wires, Guglielmi had invented the detachable coil. His first patient was successfully treated in 1990 and the preliminary results were published in 1991, linking the success of his work to the timing of intervention (Guglielmi, Vinuela, Dion, & Duckwiler, 1991). Since its conception, endovascular coiling quickly gained popularity (Milinis et al., 2017) and has become a primary treatment option in the management of ruptured and unruptured cerebral aneurysms (Loewenstein, Gayle, Duffis, Prestigiacomo, & Gandhi, 2012). The use of endovascular coiling has continued to develop and is now used in conjunction with a range of supportive interventions, such as stenting, as well as microsurgical approaches to aneurysm clipping (Prestigiacomo, 2006).

Conclusion:

The history of the observation and treatment of cerebral aneurysms is rich in parallels. From the early observational studies to the fledgling surgical and endovascular approaches, and the growing field of evidenced based practice, the history of cerebral aneurysms has demonstrated the courage, resilience and determination of medical and epidemiological studies. There are many individuals who have played a role in the progression and the philosophy towards treatment of aSAH. This overview provides a brief capture of those most pertinent to the core of our current nursing practice. Nursing practice has been continuously challenged and developed as a consequence of epidemiological research (Jenicek, 1997). From the epidemiological observations of Hippocrates and Galen to the sociodemographic differences in the first patients treated by Dott and Dandy, the history of cerebral aneurysm treatment has not been limited to technological advancements (Prestigiacomo, 2006). Current and future research is in many ways built on both the failures and successes of previous work and it here that nursing holds the key to enriching research and improving patient outcomes. It has been over 350 years since Thomas Willis first described the circle of arteries that now bears his name. Despite the success of treatments and interventions, the overall mortality post aSAH remains high and in a parallel nature of research, a return to epidemiological observations is warranted to gain a better understanding of the incidence, treatment and outcomes post aSAH. In the words of the pioneering neurosurgeon Percival Pott,

‘Many and great are the improvements which the chirurgic art has received within these last fifty years; and much thanks are due to those who have contributed to them; but when we reflect how much still remains to be done, it should rather excite our industry than inflame our vanity’ (Pott, 1790)

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