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Ambroise Paré: His Contribution to the Future Advancement of Neurosurgery and the Hardships of His Times Affecting His Life and Brilliant Career

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Ambroise Paré was celebrated surgeon of the 16th century whose practical accomplishments, books, and ideas transformed surgery and was a precursor for the later development of neurosurgery. He developed many surgical innovations related to wound management, arterial ligation for the prevention of hemorrhage during limb amputations, and the treatment of war-related head and spine injuries. He maintained that a surgeon should operate gently to reduce pain and improve outcome, and he dedicated his career to the wounded, sick, and poor. He also served 4 consecutive French monarchs—Henri II and his 3 sons François II, Charles IX, and Henri III. As a Huguenot (a Reformed Protestant) by faith, he lived in an environment dominated by Catholicism. Hence, his practice and life were sometimes hindered by political circumstances and religious prejudice. In this historical vignette, we will discuss the professional accomplishments of Ambroise Paré that influenced the future development of neurosurgery, including his descriptions of phantom-limb pain and peripheral nerve injury, his innovations in neurotraumatology, and the saws he invented for use in skull surgery. We will also highlight Paré's broad neurosurgical contributions to the field. Finally, we will discuss his personal life during the difficult and dangerous political circumstances of 16th century France.

INTRODUCTION

Ambroise Paré (c. 1510–1590; Figure 1) was a prominent and celebrated surgeon of the Renaissance, considered by many to be the founder of modern surgery.[1,2] He was a leading innovator who was responsible for the advancement of most surgical techniques and medical education in the 16th century. He also promoted empirical observation and scientific thinking, establishing a methodology for evidence-based medicine that modern anatomy, surgery, and neuroscience uses today.[3] However, Paré's influence on neurological surgery remains far less known than his contributions to surgery.

During the 16th century Renaissance, a wide range of new medical methodologies and education, innovative surgical techniques, and scientific publications became possible.[4] Nevertheless, outmoded Galenic views of anatomy, medical knowledge, and medical education dominated medicine, and this prevented physicians from using treatments based on practical observation and empirical analysis.[5-7] In Galenic medicine, anatomy and surgery were considered less important than other medical disciplines. Practical surgical procedures were, therefore, left to barber-surgeons, who were skilled and well trained but did not have formal academic education.[8]

By this time, the use of guns and other firearms was emerging in European warfare, which dramatically increased the number of soldiers killed and wounded. Firearms were responsible for new types of wounds that had not been previously seen, such as head wounds with retained foreign bodies that can lead to infection and fatal outcomes. As a battlefield doctor, Paré saw these types of wounds frequently himself, which led him to write some of the first texts dedicated to the treatment of gunshot wounds (Figure 2).[9]

France in the 16th century, where Paré spent his life, was also dominated by religious wars and extreme tension between Catholics and Protestant Huguenots. Despite his reputation and incredible professional and scientific accomplishments, his life was sometimes threatened due to the political and social circumstances around him.

This brief historical vignette will discuss chronological facts and the political and religious circumstances influencing Amboise Paré's brilliant career and personal life. We will discuss how he managed to overcome the hardships of his times. This is also a tribute to Paré in which we will honor his work in establishing a distinguished and modern scientific discipline that is a forerunner to contemporary surgery, including neuroscience and neurosurgery.

As a final point, we will try to document his particular contributions to the future advancement of neurosurgery, including his descriptions of phantom-limb pain and peripheral nerve injury, innovations in neurotraumatology, and the invention of saws for use in skull surgery. This vignette will also substantiate Paré's wide-ranging

Figure 1. A portrait of Ambroise Parè, age 72 years ("Portrait of Ambroise Pare [1510–1590], French surgeon"; credit: Wellcome Collection; CC BY).

neurosurgical accomplishments, adding some additional understanding to the field.

POLITICAL CONDITIONS IN 16TH CENTURY FRANCE

The 16th century was a time when the power of Western Europe, including France, grew to new heights. The religious conflicts between Catholics and Protestants dominated the century, initiating the Wars of Religion in France, during which about 3 million people disappeared due to violence, famine, or disease.

In 1515, François I (1494–1547) ascended the French throne as an absolute monarch. He was a patron of the arts who initiated the French Renaissance by attracting Leonardo da Vinci (1452–1519) and other famous artists to France. Da Vinci helped construct the monarch's royal manor houses—designing the central stairs of the Château de Chambord—and brought his famous painting of Mona Lisa to France. During François I's reign, however, continuous wars and political oppression hampered comprehensive reforms. He was succeeded by his son, King Henri II of France (1519–1559).

The Italian War of 1536–1538 between the French King François I and his main rival, Charles V (1500–1558)—the Habsburg King of Spain and the Holy Roman Emperor—was fought over lands in Northern Italy, which resulted in French occupation of Turin. The occupation further provoked the animosity between France and Spain, rival countries vying for European dominance. Charles V also laid unsuccessful siege to the city of Metz, which was defended by French forces of King Henri II in 1552 during the Last Italian War (1551–1559), a conflict that emphasized the importance of gunpowder technology. However, the prolonged wars ultimately destabilized and financially weakened both countries and caused further political fragmentation in Italy. It allowed also the expansion of Protestantism into France, where Protestants were called Huguenots. Political and religious turbulence culminated with the massacre of Huguenots on the night of St. Bartholomew's Day in Paris on 24 August 1572, during the short reign of young King Charles IX (1550–1574).

EXPERIENCED MILITARY MEDICAL PRACTITIONER, EDUCATOR, AND ROYAL SURGEON TO THE VALOIS DYNASTY

Ambroise Paré was born in the French countryside and was initially trained as a barber-surgeon. He became a surgical resident in 1533 at the famous Hôtel Dieu hospital in Paris,[10] a prominent hospital and residence of medical education of the time (Figure 3). Thanks to his academic training, he become an accomplished medical practitioner, military surgeon, and royal surgeon to the French monarchy.[11] As an experienced military practitioner, he tended to wounded battlefield soldiers during the numerous armed conflicts between the French and Spanish forces (Figure 4).

During the military occupation of Turin by French forces in 1536, gunshot wounds were typically treated by boiling an oil solution to seal wounds; the solution was also thought to prevent alleged gunpowder poisoning.[3,9] During the campaign, Paré, working as a military surgeon, ran out of oil while attending to wounded soldiers and improvised a wound-dressing composed of egg yolk, rose oil, and turpentine instead. Soon, he observed that soldiers with wounds dressed with this treatment recuperated better than soldiers treated with boiling-oil cauterization.[12,13] Consequently, he concluded that gunpowder was not toxic and, therefore, each gunshot wound did not require cauterization.[13] This is quite possibly one of the earliest known examples of evidence-based medicine as we know it today applied to surgical practice. Furthermore, his new method of wound treatment was shown to be less damaging; it was far more successful in treating wounds while also being much more comforting to the patient.[3,9] Nevertheless, Paré never entirely gave up the use of hot-oil cauterization and continued to use it in

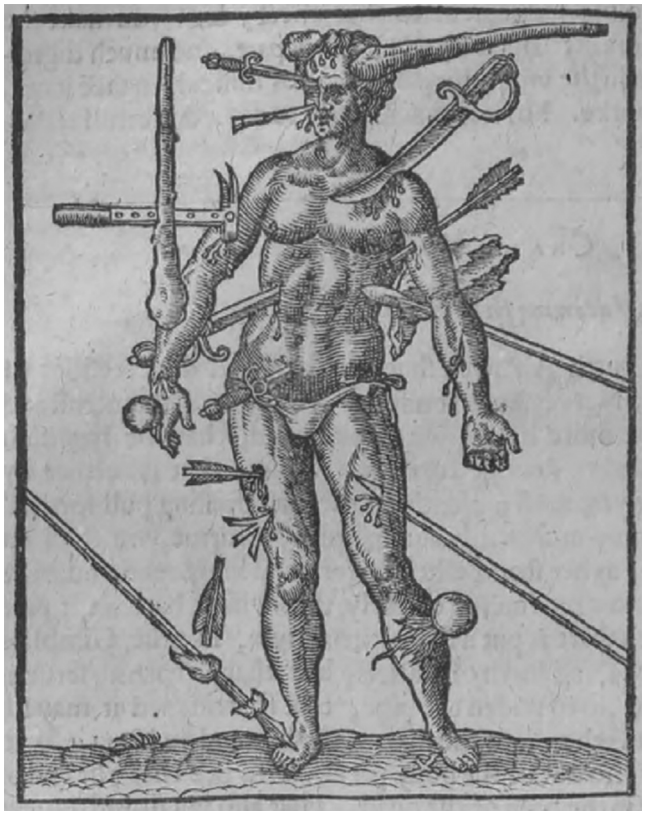

Figure 2. Engraving from a 1634 English translation of Ambroise Paré's writings, specifically from a chapter on gunshot wounds. (Image reproduced from the public domain book, *The workes of that famous chirurgion Ambrose Parey,* (p. 440). Available from the US National Library of Medicine Digital Collections at: http://resource.nlm.nih.gov/2393053R.)

limb amputations for hemostasis from bone. He did abandon it when it came to bleeding vessels, however, and instead introduced arterial ligation to prevent hemorrhaging.[1,13,14]

At the beginning of 16th century, methods for perioperative pain relief were extremely limited. Opium and strong spirits were the only available anesthetics, and many techniques generated unbearable pain—an unfortunate but necessary part of surgical procedures.[15] Paré, on the other hand, came to realize that a surgeon should operate gently and less aggressively to reduce pain and damage to the tissue, which is beneficial in improving patient outcomes.[3] This was a transformative notion that enhanced the capability of a surgeon as well as improving surgical practice from that time on. The idea was also an early precursor that underpins the contemporary notion of minimally invasive surgery.

Ambroise Paré published books on surgery that went beyond mere explanations of procedure. Paré was an anatomist, a founder of modern forensic pathology, and an inventor of surgical instruments.[16] His revolutionary work formed the foundation of surgery as a modern medical discipline[2,15] and laid the groundwork that allowed for the future development of neurosurgery as a distinguished surgical field on its own. While he was involved in treating battle and tournament injuries, he emphasized the importance of understanding anatomical body structure, insisting that surgery must be based on anatomy.

In 1559, the rival rulers of France and Spain, who were both Catholic, reached a peace agreement to contain the spread of Protestantism. The truce was affirmed by the wedding of King Philip II (1527–1598) of Spain to Elisabeth of Valois (1545–1568), the teenage daughter of Catherine de Medici (1519–1589) and King Henri II of France. However, at a jousting tournament to celebrate the marriage, the French King was fatally wounded by a wooden lance fragment that penetrated his brain through the right orbit.[17-20] Paré was asked to give an advice concerning medical treatment of the King, together with the famous anatomist Andreas Vesalius (1514–1564).[17,21,22] He was unable to give direct care to the King, however. Senior royal doctors decided on the King's treatment on their own, inappropriately advocating for a wait-and-see approach to his treatment.[20] The King died 11 days post-injury, probably of meningoencephalitis caused by hematoma of cerebral contusion.[18-20,23] During the autopsy of the King's body, Paré recorded an occipital subdural hematoma with a secondary infection (empyema), but he believed it was a brain contusion on the opposite side to the blow (i.e., a *contre-coup* injury) that mainly resulted in the King's death,[20] which is how this term entered future neurosurgical practice.

Afterwards, Paré successfully treated many other head injuries. He served King François II (1544–1560), the short-lived young successor to the throne, who died suddenly of mastoiditis in 1560.[24] Although Paré was technically skillful enough to perform surgery on the King's post-auricular abscess, he did not attempt it. It is possibly that he was worried of being accused of poisoning or killing the king if surgery was unsuccessful.[24]

Although Paré's professional capability and humanist attitude to his patients made him an ideal practitioner, his theories and writings were often opposed by university authorities who still clung to older incorrect ideas that we would consider backward today. His book *Apologie and Treatise* was written in response to one such attack made by the Dean of the University of Paris School of Medicine, who tried to discredit Paré's scientifically based methods,[25] especially his use of the ligature in amputations.[14]

Paré was a Protestant, specifically a Huguenot, but he seemed to have maintained the appearances of being Catholic

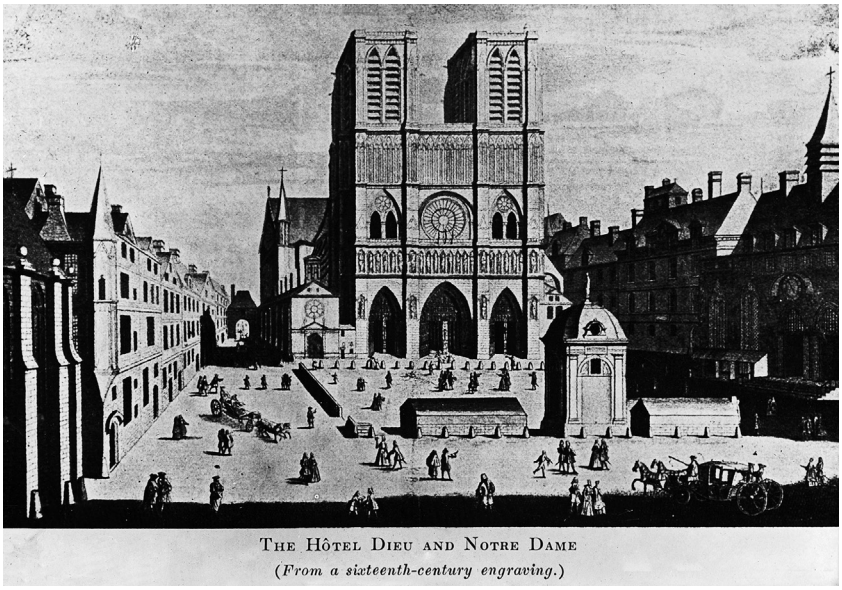

Figure 3. Hôtel Dieu Hospital and Notre Dame Cathedral in Paris at the time of Ambroise Paré ("Paris; The Hôtel-Dieu and Notre Dame"; credit: Wellcome Collection; CC BY).

to avoid danger. He was married twice, his children were baptized, and he was eventually buried in the Catholic faith.[11] During the St. Bartholomew's Massacre of 24 August 1572, anti-Huguenot mob violence was rampant in the streets of Paris. King Charles IX—a Catholic himself—locked Paré in a closet to save his life.[11,13] Although Charles initiated many anti-Protestant purges himself, paradoxically he spared Paré's life. It is likely that Paré would not have survived despite being a well-known, respected, and distinguished professional and scientist.

Figure 4. Paré attending wounded battlefield soldiers. ("Ambroise Paré. Colored line engraving by C. Manigaud after E. J. C. Hamman." by E. J. C. Hamman; credit: Wellcome Collection; CC BY).

A REVIEW OF PARÉ'S INFLUENCES IN NEUROSURGERY

Ambroise Paré introduced many innovations and made various observations that influenced the future development of neurological surgery to a great extent, although these contributions are less well-known than his surgical achievements. In his 1564 book *Treatise on Surgery*, Paré described the pain suffered by amputees when they felt "phantom" amputated limbs, indicating that phantom pain originates in the brain and was not in the remaining part of the limb.[14] This particularly astute observation formed the basis for the development of neuroscience as a distinctive scientific discipline in the future. Paré successfully applied his concept of vessel ligature to the treatment of migraine headache and described ligation of the superficial temporal artery for relieving headache pain.[26] He eventually ligated his own superficial temporal artery to treat self-migraine pain.[11] He also meticulously depicted the brain and nerves of the head and neck in his book *Les Oeuvres d'Ambroise Paré* [The works of Ambroise Paré] in 1575 (Figure 5).

Although altered consciousness after head injury had been recognized since the Edwin Smith papyrus (1700 BC), an ancient Egyptian composite manuscript, the term "brain concussion" was first used in the Renaissance to define the effects of brain damage without a skull fracture. It was described by Jacopo Berengario da Carpi (c.1460–c.1530), a Professor of Anatomy at the University of Bologna, and Ambroise Paré himself, both of whom defined concussion as *commotio cerebri*.[27] Paré further described concussion as a shaking of the brain, and was the first to label contrecoup injury as a consequence of a closed head injury to the brain parenchyma on the opposite side of the blow.[12] A contrecoup injury was noted by Paré in his description of the autopsy of the King Henri II of France.[20]

Paré was particularly concerned with war neurotrauma and described in detail the management of comminuted

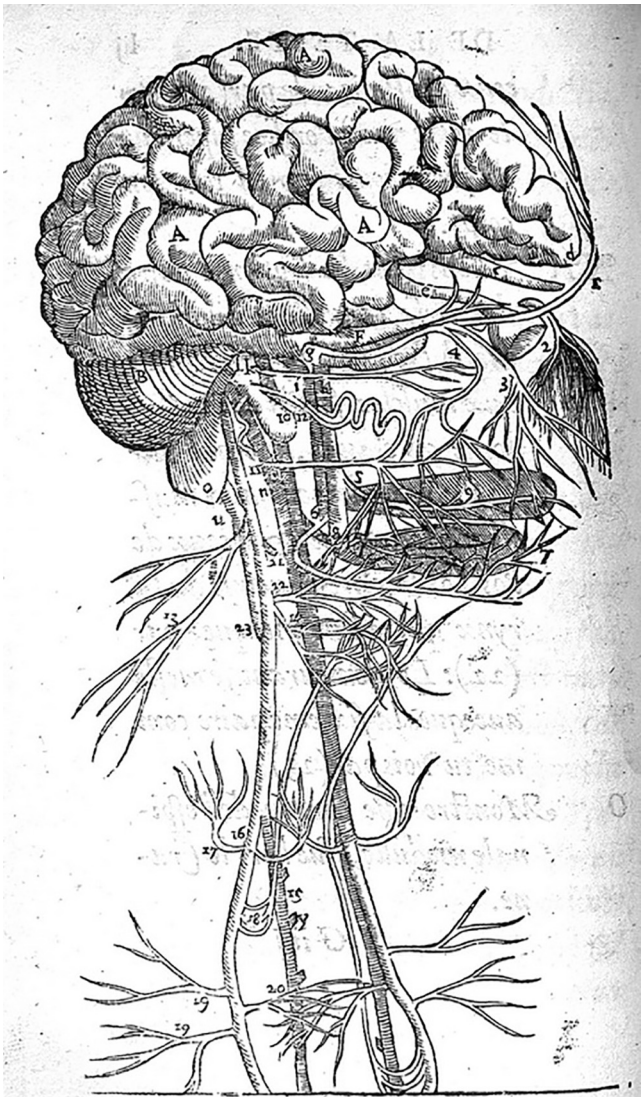

Figure 5. The brain and nerves of the head and neck as depicted by Ambroise Paré in his book *Les Oeuvres* from 1575. (Reprinted from http://www.biusante.parisdescartes.fr/pare/images/gd/029.jpg; reuse granted under the *French Licence Ouverte de type Etalab* [Open License]).

depressed skull fracture by using a cutting forceps and a trepan technique.[10] He considered the dura as a boundary of harmless surgery, however, although he recognized that blood clot might accumulate in the subdural space.[10] Skull trepanation is one of the oldest surgical techniques known and was used for many indications, including head injuries from war. Its use increased with the introduction of firearms and gunpowder. During a siege of the strategic French city of Metz in 1552 by forces of Charles V, Holy Roman Emperor and the King of Spain, Paré treated an unconscious soldier with convulsions who had received a blow to the head from a stone cannonball. He saved the soldier's life by performing a skull trepanation and protected his wounds with a mixture of alum and honey.[10] Afterwards, he successfully performed the same procedure on a series of other soldiers with head wounds.[25]

Instruments for head surgery were largely modernized by Ambroise Paré. He devised a trepan (a round saw for cutting out a circular piece of skull bone), which was used in the same way as a modern-day hand drill (**Figure 6**). He designed the instrument with a protective lid that was less harmful in unskilled hands and improved its safety by moving from a 2-point to a 3-point bearing trepan, which made the drill more stable on the skull.[16] The trepan, however, did not gain popularity among surgeons of his time because it was heavy and clumsy.[16] Paré also applied a skeletal traction to spine injury in a case of spinal dislocation.[10]

In his many writings, Paré contributed to the understanding of peripheral nerve injuries, describing a case of a median nerve injury—a young Charles IX[10] had suffered an injury after a bloodletting for smallpox.[11] Paré provided a detailed explanation of painful median nerve neuroma (causalgia) for the first time, describing persistent pain and contractures of the arm that resemble a complex regional pain syndrome in modern medicine.[11]

Ambroise Parė also described several items of interest to pediatric neurosurgeons, such as cephalohematoma as a consequence of forceful labor, which was incised and evacuated,[10] as well as congenital hydrocephalus, which was clinically distinguished from macrocephaly.[28,29] He also described a simple depressed skull fracture in an infant that was treated by exploration and bone elevation in a manner similar to that done today.[10]

Nonetheless, Paré never rejected Galen's centuries' old ventricular-pneumatic doctrine of cognition whereby mental tasks were contained within the cerebral ventricles, which was the earliest attempt to locate mind functions in separate physical sites of the brain.[30,31]

CONCLUSIONS

The practice, works, and multiple skills of Ambroise Paré put him in the rare category as one of the true giants in the history of medicine. His ideas and methods substantially improved surgery and advanced it beyond religiously dogmatic medieval limitations. He established a solid foundation for modern surgery in general and neurosurgery in particular by paving the way for the development of both

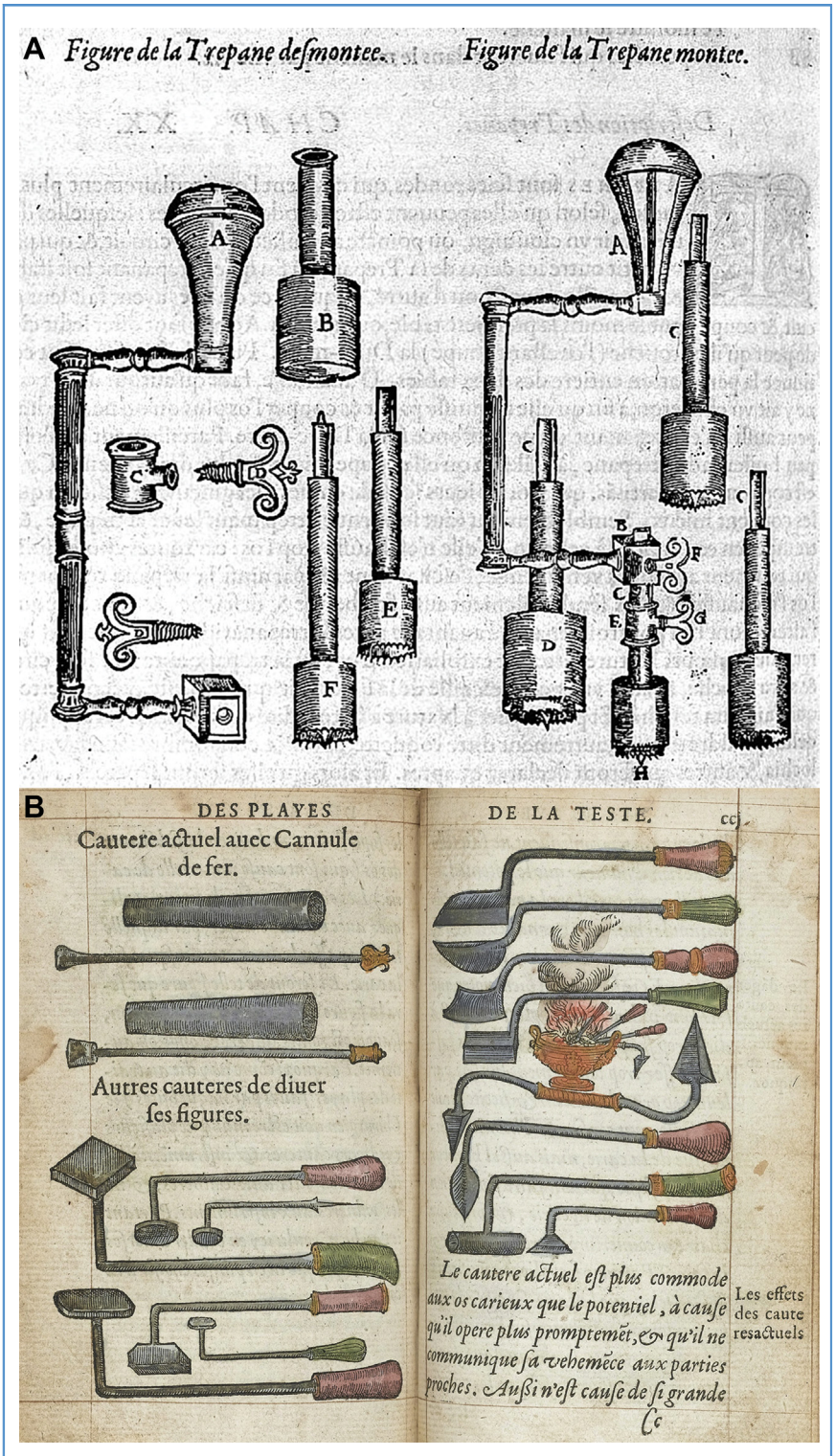

Figure 6. A set of trepanation instruments for head wound management as illustrated in the book *Les Oeuvres* by Ambroise Paré. (**A**) "A. Pare, Les oeuvres d'Ambroise Pare"; credit: Wellcome Collection; CC BY. (**B**) "Hand colored illustration of surgical instruments" by Ambroise Paré; credit: Wellcome Collection; CC BY.

specialties in the centuries to come. Ambroise Paré also developed many inventions and made many contributions that impacted the future development of neurosurgery. He understood the importance of personal experience and expertise, as well as how experience could affect the acquisition of new knowledge. He was also able to exert a powerful influence on future surgical practice by questioning outdated and incorrect academic tradition and dogma. Thus, because of his critical mind, he is seen as a true and an authentic representative of the Renaissance in the field of medicine.

Despite his tremendous professional and scientific achievements, his life's work—as well as his alleged religious beliefs—was burdened by ever-changing political circumstances and social upheaval. In the end, though, it seems that he successfully overcame this by his tolerance and common sense personality.

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