Animal experimentation in surgery: a comparison between John Hunter's 18th-century surgery and contemporary surgery

"The practical surgeon is a craftsman: Greek and Latin are useful to him [John Hunter] for polish, but think of the natural knowledge a smart boy can collect on a farm [...]." [1].

On the 13th of February 1728, John Hunter was born. The youngest of ten children, raised in a farm just outside Glasgow, he *"disliked school and hated books*", preferring to *"lead an out-of-doors life, looking after nests, insects, and animals"* [1]. After quitting formal education at the age of 13 years old, he devoted his time to exploring the countryside, dissecting small mammals and collecting birds' eggs [2]. Although far from the practical knowledge that is usually associated with a surgeon's expertise, his fascination with the animal world would pave the way for him to become one of the most renowned surgeons of his time. From the anatomy of a popliteal aneurysm and olfactory nerves, to thermogenesis and growth of bones [3], John Hunter would become proficient in comparative anatomy and a pioneer in scientific approach to surgery.

The contribution of animal experimentation to the development of surgery is unquestionable. Drawing on Dr John Hunters' life and work, I will argue that animal experimentation has been crucial in the development of many life-saving surgical procedures, and that animal experimentation provided the basis for the ever-growing number of surgical alternatives being developed today.

Animal experimentation: a brief history

Animal experimentation has had a place in medical history for many centuries. In ancient Greece, dissection of humans was described as taboo, but many reports of animal dissections for anatomical studies are common [4]. Humans had a higher ranking in the "chain of being", and were closer in proximity to the divine than live animals, hence the lack of moral questions asked when the latter were involved in scientific research [4]. In the 3rd century BCE, once the Empiric school of thought replaced the ancient Greek ideals, the use of animals in experiments was rejected [5]. Empiricists believed this was cruel and useless, as pain and death would distort the normal anatomical appearance of an animal and render results inaccurate [5]. Animal

experimentation would only re-emerge in the Renaissance (14th century), as scientists - notably, Vesalius - defied the Catholic Church's ideals and performed human dissections to be able to compare human and animal anatomy [6]. The 17th century was set for many experiments carried out in animals, in what was called the "Age of Enlightenment" [5]. Many renowned philosophers would share their views on animal experimentation, both in favour and against, including Descartes, Locke, and Kant.

In the 18th century, Dr John Hunter came into the picture. During his period as one of the most famous surgeons in the world, he accumulated an impressive collection of over 3,000 animals, both live and preserved specimens [7]. He often developed a hypothesis, tested it on animals, and then proceeded with an attempt at a human operation [7]. He dissected thousands of animals, as well as human cadavers, to study their structures and their organ systems and supplement his findings [8]. He went on to aid in the establishment of a variety of surgical procedures that would soon become commonplace, including mastectomies, amputations, and bone grafts [8]. He is also the author of many books, including *Observations on Certain Parts of the Animal Oeconomy* [9], highlighting his dedication to the animal kingdom.

Animal experimentatiton: its role in surgical developments

Firstly, I argue that animal research has been crucial in the development of many life-saving procedures, once thought impossible [10]. To aid this, I will look at the surgical developments for bicuspid aortic valve replacements, the role Dr Hunter played in its initial discovery and the way animal experimentation has allowed for surgical advancements.

Dr Hunter describes, in 1764, what is thought to be first identification of a bicuspid heart valve: *"a Man who… [...] On examining the valves of the Aorta, I found that there had been two only, instead of three; and that one of them had a kind of fraenum or cross-bar, attaching its middle to the sides of the artery. These valves were very much diseased, became thick and stony, by which means they did not meet entirely, or by even edges."* [11].

After this remark, much research has been made into bicuspid heart valves and we now know that these are a very common malformation, appearing in 1-2% of the population, and can lead to a high incidence of valvular lesions [12]. Many patients who suffer from these will undergo treatment in the form of a transcatheter aortic valve implantation (TAVI) or conventional valve replacement, depending on the patient's risk profile [13]. For these, biological prosthetic valves, mechanical prostheses or reconstructive methods are available. The former, which were first introduced in the 1960s, show the importance of animal research in contemporary surgery [13]. Different mammals' heart valves were studied, and today, there are different types of biological heart valve prostheses, from humans, pigs or cows, and these provide crucial advantages when compared to the alternatives [13]. Firstly, they do not require continuous anticoagulation of the patient. Moreover, they do not produce any sounds, which patients may prefer. However, they have a smaller orifice area and carry a higher risk of valve degeneration, requiring reoperation [13].

A concept that Dr Hunter first introduced in his works, has proved to be immensely important in medicine and surgery. An extremely important procedure has been developed to solve this condition and its symptoms, which relies heavily on animal research to be able to do so.

Secondly, animal research has provided the basis for the increasing number of alternative research methods in contemporary times. In 1790, Dr Hunter completed artificial insemination in a woman, after successfully carrying it out in moths [8]. He advised the woman's husband - who had severe hypospadias - to collect his semen and then used a syringe to implant it in the patient's vaginal canal; the woman conceived soon after [14]. This was an extremely forward-thinking concept, and Dr Hunter is credited for the first ever documented artificial insemination in a human [14]. Today, in the UK alone, over 1.3 million in-vitro fertilisation (IVF) cycles and over 260,000 donor insemination (DI) cycles have been carried out since 1991, which has resulted in the birth of over 390,000 babies [15].

Whilst, traditionally, animal experimentation has been used for scientific testing, methods known as alternatives, replacement, or non-animal methods are becoming more common [16]. Until recently, rodents were used to explore human and

dose-response and comparative toxicity in artificial insemination [17]. However, the rising concern of animal rights and a general public desire to decrease the animal use in medical testing, have served as motivations to find alternatives [17]. This was complemented by evaluations of how well these animal tests are at predicting human safety, which were concluded to be around 50-70% of the time [18]. This suggested that potentially dangerous chemicals are allowed to be developed, and thus called for a more accurate method of screening potential dangerous chemicals.

As of today, the answer for replacement methods to animal testing in artificial insemination lies in the area of cell tissue culture, focused on the potential to avoid the *"inter-species extrapolation problem"* by creating in-vitro models of tissues using human cells [19]. Although technology is being developed, like any method, it will have its shortcomings [17]. In the case of in-vitro models, these are not sustainable and are only valuable in limited duration, as the Sertoli cells are de-differentiating and the germ cells are dying. To further test this, scientists have reverted back to generating primary cultures from animals, allowing for further discoveries to be made, but its unsustainable issue would arise once again [17].

A technique that Dr Hunter pivoted by testing in moths, and then further tested in humans, is now a widely studied and common practice. This is a perfect example of why animal experimentation is key for surgical advancements, as well as the contribution of Dr Hunter to contemporary surgery. It also shows how the progress in surgery or medicine is not linear - today's surgical advancements may be focused on less animal testing and decreasing inter-species discrepancies, but experimentation in animals may re-emerge given the circumstances of a particular case.

Conclusion

In conclusion, using the case-studies of Dr Hunter's depiction of a bicuspid aortic valve and the first human report of artificial insemination, I have argued for the historical relevance of animal experimentation. It has served as the basis for many life-saving procedures, and can be credited as well for the technological advancement of many surgical alternatives today. This is in large part due to scientists such as Dr John Hunter, visionaries and in advance of their time, who devoted their life and work to comparative anatomy between animals and humans.

Whilst he was not praised enough in his lifetime, today he is credited for his many contributions to surgery and every surgeon will feel his impact in their routine, justifying his title of “father of scientific surgery”:

“[About Dr John Hunter:] A man who achieves greatness in any calling inspires others to follow his example. No man retains prominence unless he has impressed others to believe in him and magnify his name.” [1]

Word count: 1550

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