Good surgical practice

Prof. Dr René Remie
René Remie Surgical Skills Centre, the Netherlands

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Many laboratory animals undergo some form of surgery to support the experiment. Unfortunately, during the training of scientists and technicians, the focus is on learning the procedure, and the essential principles of good surgical practice (GSP) often become forgotten.

Nonetheless, GSP remains vital in pre-clinical research. In accordance with the principles of the 3Rs (Replacement, Reduction, and Refinement), we are ethically and legally dedicated to protecting the welfare of laboratory animals. The history of GSP began in the late 1800s when, thanks to the discovery of ether as an anaesthetic, modern surgery was established.

Before 16 October 1846 (Ether Day), surgery emphasised speed. The quicker a surgeon completed the procedure, usually an amputation, the less pain the patient experienced. Once ether was introduced as an anaesthetic, speed became less crucial, and surgeons began to explore the human body.

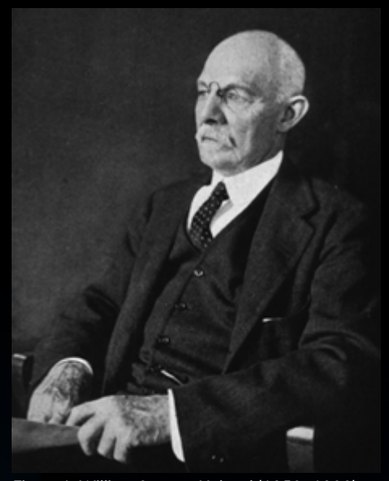

Figure 1: William Stewart Halsted (1852–1922).

One of the most important surgeons of the 19th century was William Stewart Halsted (1852–1922), an American surgeon who followed Joseph Lister's advice for strict aseptic techniques during surgical proce…dures. He was an early supporter of the newly discovered anaesthetic and introduced several new operations, including the radical mastectomy for breast cancer, thyroid surgery, and bile duct surgery (Halsted, 1924; Guitron and Merrill, 2012) Klik of tik om tekst in te voeren..

Like most surgeons in the US, Halsted frequently visited Europe. He studied there for 2 years (in Germany, France, and Austria), mainly in Vienna, under the renowned German surgeon Theodor Billroth, and brought his newly acquired knowledge back to the United States. Along with his colleagues, William Osler (Bliss, 2007), Howard Atwood Kelly, and William H. Welch (Flexner and Flexner, 1993), Halsted was one of the 'Big Four' founding professors at the Johns Hopkins Hospital (Roberts, 2010). They revolutionised the training of surgeons, which is still in use today: 7 years of study and practice to become a surgeon (Slama and Silbergleit, 2016).

Halsted's operating room at Johns Hopkins Hospital in Ward G was described as a small space where medical breakthroughs and miracles occurred. An intern who once worked there noted that Halsted used unique techniques, operated on patients with great confidence, and often achieved perfect results, which amazed the interns. Although Halsted was the least known to the public, he was undoubtedly the most remarkable man. His innovations in surgery were revolutionary. Some of his students are much better known, such as Harvey Cushing, the father of neurosurgery (Bliss, 2005).

However, Halsted had a double life (Imber, 2011; Brumback, 2012). In 1884, at a Heidelberg Congress on ophthalmology, Karl Koller (1857–1944) announced that topical cocaine facilitated eye surgery (Koller, 1928; Liljestrand, 1967; Goerig, Bacon and Van Zundert, 2012). The same year, Halsted began blocking nerves by injecting the drug. Halsted did several experiments on the use of cocaine as an anaesthetic agent. Most of them he performed on himself. In less than 12 months, he became addicted (MacCallum, 1930; Imber, 2011).

In his surgeries, Halsted adopted the Hippocratic approach, progressing from simply avoiding harm to actively preventing tissue damage. It was a set of interconnected principles that remain the foundations of modern surgical practice, not only in human medicine but also in veterinary surgery and pre-clinical research.

Gentle handling of tissue during exposure

Halsted was a master at handling tissue. The key point is not to touch the tissue more than necessary. Remember that cells are killed whenever tissue is handled with instruments. Therefore, a goal-oriented approach is essential. Sharp dissection is generally less traumatic than blunt dissection, but it is more hazardous, especially in small rodents with limited circulating blood. Cooper, McLiver and Bianco (2000) nicely described the importance of good tissue handling.

Preservation of the blood supply

Surgeons must ensure that the blood supply to the tissues is maintained throughout the procedure to prevent tissue damage and promote recovery.

Minimum tension on tissues

Tissues should be closed with minimal or no tension to prevent dehiscence (wound separation) and promote healing. This also entails using proper knot techniques and avoiding over-tying knots, which can lead to weak scars.

Accurate tissue apposition

Tissues should be precisely approximated or accurately aligned to ensure proper alignment.

Obliteration of dead space

Avoid creating dead spaces, which are pockets where fluid can collect, to prevent infection and seromas.

Strict aseptic technique

The fundamental principles of surgery in the laboratory rat are the same as those for surgery on pet animals and humans. Recently, the European Academy for Laboratory Animal Surgery (EALAS) published a paper emphasising the importance of asepsis (Lussier et al., 2024). Asepsis (the method of achieving a close to germ-free condition) is very important in (micro) surgery, and, unfortunately, the opinion amongst researchers that rodents are exceptionally resistant to surgical infections is still widespread (Farris and Griffith, 1942). Many surgeons operate on rats without taking any precautions to minimise the initial contamination of the surgical area. This neglect can lead to infection or even the untimely death of the animal. Another consequence of poor aseptic technique is the reduction in long-term patency rates of inserted catheters (Popp and Brennan, 1981). When using unsterile catheters, cannulas, and instruments, the patency is drastically reduced to 1 or, at most, 2 weeks. Not only is patency affected, but the animal's recovery is delayed, and the time needed to return to the pre-operative weight is extended. On top of that, an inapparent infection will influence the data collected (Bradfield et al., 1992). Leaving behind residual blood, debris, and necrotic tissue can also raise the risk of surgical infections (Mishriki, Law and Jeffery, 1990; Soballe et al., 1998; Cooper, Mciver and Bianco, 2000; Wikström et al., 2019; Bjarnsholt et al., 2022).

Meticulous haemostasis

In rats and mice, the circulating blood volume is approximately 7 ml per 100 g. For a 25-g mouse, this amounts to approximately 1.75 ml of blood. Needless to say, excessive blood loss could easily cause the animal to die prematurely. It is crucial not to panic when bleeding occurs.

Clamping or applying light pressure can stop almost all bleeding. Other options include bipolar coagulation, an electrosurgical haemostasis technique where high-frequency current flows only between the 2 tips of a bipolar forceps, allowing precise coagulation with minimal tissue damage. A more affordable option is the use of a cauteriser. During cauterisation, the temperature of the glowing metal can reach between 700 °C and 1200 °C. It is crucial not to touch the tissue but to allow the heat radiation to do its work. Since more heat penetrates the tissues, greater trauma is caused compared to bipolar coagulation. Ligation can be an effective method for stopping bleeding. Chemical treatment with collagen, ADP, fibrin, and thrombin-containing haemostatics is highly effective. Spongostan®, TachoSil®, and Fibbrilar® are excellent biodegradable haemostatic sponges.

Epilogue

Modern surgery, both pre-clinical and clinical, still relies on the fundamental ideas of William Stewart Halsted, a pioneer in surgical therapy and the father of modern surgery. He should not be forgotten.

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PROJECT SUMMARY

Good surgical practice (GSP) is essential in pre-clinical research. In line with the principles of Replacement, Reduction, and Refinement (3Rs), we are ethically and legally committed to safeguarding the well-being of laboratory animals. This paper will focus on the history of GSP, which began in the late 1800s, when, thanks to the discovery of ether as an anaesthetic, modern surgery was established.

PROJECT LEAD PROFILE

Professor René Remie, Pharm D, DLAS, PhD, author, and editor of the Manual of Microsurgery on the Laboratory Rat, studied Pharmacy at Groningen University. In 1983, he specialised in pharmacology and did his PhD on the presynaptic modulation of noradrenergic neurotransmission in the freely moving rat's portal vein. In 1990, he co-founded Microsurgical Developments and has been its chairman ever since. In 1991, he specialised in Laboratory Animal Science (LAS) and worked as a Welfare Officer at Solvay Pharmaceuticals. He held a chair in Microsurgery and Experimental Techniques in Laboratory Animals at Groningen University (1997–2012). In 2002, he founded 3-R's Education and Consultancy and co-founded the International Microsurgical Training Centre (IMTC), and in 2009, 3-R's Training Centre, known as the RRSSC. He has been training students for almost 50 years.

PROJECT CONTACTS

Prof. Dr R. Remie

r.remie@rrssc.eu

rrssc.eu

/in/rene-remie-57a7731a

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René Remie Surgical Skills Centre
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