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Dr. Seishu Hanaoka (1760-1835): surgeon, pharmacist, and anesthesiologist.

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Dr. Seishu Hanaoka (1760–1835): Surgeon, Pharmacist, and Anesthesiologist

The notion of decreasing pain in surgery stretches back thousands of years with alcohol noted as one of the first anesthetics. Natural elements including coca and opium have been used by various civilizations in an attempt to mute the searing pain of surgery. By the 16th century, physicians around the world began to experiment with nitrous oxide and ether, providing the groundwork for the future of modern anesthesia. The successful application of general anesthesia in surgery was first documented in 1804 by Dr. Seishu Hanaoka (Fig. 1) in Wakayama, Japan, during a breast lumpectomy. During the case, Dr. Hanaoka served as the surgeon, anesthesiologist, and pharmacist. Although most of his worldwide contemporaries were unaware of his successes, this achievement stands as an emblematic and triumphant landmark in medicine.

Dr. Hanaoka was born on October 23, 1760, in the small village of Hirayama in Wakayama, Japan. He was the son and grandson of physicians and served as his father’s apprentice until the age of 22 years when he left his small hometown to study in the then-capital and epicenter of Japanese medicine, Kyoto. He began his studies under the tutelage of Dr. Nangai Yoshimasu, a prominent practitioner of Chinese medicine. There, he learned about the basic tenets of Chinese herbal medicine and of the multitude of medicines found in nature. This knowledge greatly contributed to Hanaoka’s future creation of a potent anesthetic that he called *tsusensan*. After studying Chinese herbal medicine, his interest in surgery drew him toward the work of Dr. Kenryu Yamato, a Japanese physician who implemented the Dutch surgical techniques that later became paramount to Hanaoka’s career. These techniques were based on the burgeoning fields of surgery

and anatomy in Europe. As an assistant to Dr. Yamato, he honed his craft before returning to his hometown in 1785 to take over his ailing father’s practice. His father was a traditional practitioner, whereas Hanaoka combined his diverse training to create a more radical form of medicine. This mix of Eastern and Western pedagogies, using Dutch surgical methods based on anatomical study, alongside the administration of Chinese anesthetics, ultimately allowed him to make remarkable advances.

Hanaoka’s early observations of traumatically painful operations inspired a decades-long pursuit of an anesthetic strong enough to render a patient unconscious while safe enough to ensure that consciousness and health would soon return. He spent countless hours collecting and combining various herbs in an attempt to find the proper mixture. Dogs served as test subjects until Hanaoka determined that his mixture of seven different herbs and oils, which he coined *tsusensan*, was ready for human trial. The active ingredients of *tsusensan* came principally from three plants: *Datura*



FIG. 1. Portrait of Dr. Seishu Hanaoka in the early 19th century.¹

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stramonium, *Aconitum carmichaelli*, and *Angelica dahurica*.¹ Little did he know, he was mixing a cytochrome P450 inhibitor and several anticholinergics to create a potent narcotic able to temporarily desensitize and paralyze a patient. Dr. Hanaoka's wife, Kae, volunteered as the brave first human subject to test the new drug (Fig. 2). She consequently went blind from repeated experimentation, likely from anticholinergic toxicity, leaving Dr. Hanaoka with the guilt of his wife's misfortune and the disappointment of another failed attempt at creating the anesthetic he was pursuing so relentlessly.²

The pursuit continued until a 60-year-old patient by the name of Kan Aiya presented with a large breast mass in 1804. Dr. Hanaoka counseled her on the gravity of her condition and that a lumpectomy was the only method of treatment. He offered the opportunity of using his still unproven anesthetic to avoid the otherwise excruciating pain she would have to endure, and she consented. Early in the morning of October 13, 1804, Kan Aiya drank 7 g of *tsusensan*, and 3 hours later, she lay unconscious on the operating table. Hanaoka described the procedure in one of his many manuscripts, entitled *Nyugan Bensho*, "The cancerous mass is excised with a curved knife modified by myself, then the wound cavity is washed with ardent spirits [alcohol] to clean and sterilize. Drains of cotton threads are inserted into the cavity, the wound surface is closed by suturing carefully and an ointment made of coconut oil is applied on the suture-line"³ (Fig. 3). Six hours after the surgery began, Kan Aiya groggily awoke as Dr. Hanaoka observed her postsurgical recovery. History had been made, and the incredible news traveled quickly throughout the Japanese medical realm. However, the news did not leave the island. Isolationism reigned supreme, preventing the exchange of most goods and communication with the outside world. In fact, the act of leaving or entering the country of Japan was punishable by death as per the law of *sakoku* ("locked country"). Thus, this tremendous advancement in medicine, the ability to safely perform surgery without pain, went unnoticed in the European and American medical circles.

Dr. Hanaoka performed 156 breast cancer operations in addition to many other procedures such as anovaginal fistula repair, oral and testicular tumor excision, kidney stone removal, and cleft palate repair. He wrote 10 manuscripts describing the operations he performed, all of which were studied extensively by his many students. He also designed several novel surgical instruments that are similar to instruments still in use today. Dr. Hanaoka's legacy continues in several forms. The tragic story of his wife's blindness from *tsusensan* inspired a book and a movie, both



FIG. 2. A young Dr. Hanaoka observes his wife under experimental anesthesia with an assistant.²



FIG. 3. Dr. Hanaoka's lumpectomy procedure performed on the left breast of Kan Aiya in 1804.³

entitled *The Doctor's Wife*. His medical office in Wakayama has also been excavated and rebuilt, now serving as a museum to commemorate his achievements. The Japanese Society of Anesthesiologists (JSA) pays homage through their emblem, with the letters "JSA" overlying a *datura* flower, the main ingredient of *tsusensan*. In addition, The International College of Surgeons inducted Dr. Hanaoka into their Hall of Fame in 1954. Although his work did not permeate the global medical field of his time, his dedication to healing and comfort lives on in modern medicine.

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