MicroDiscoverer Hero: Shibasaburo Kitasato (1853-1931, Japan)

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Portrait of Shibasaburo Kitasato (©The Kitasato Institute The Kitasato Memorial Museum)

Claim to fame: Pure culture of tetanus bacillus and tetanus serotherapy.

Overview. Shibasaburo Kitasato was born on 29th January 1853 in a mountain village in Higo Province (Fig. 1), southwest of Tokyo. He lost two younger brothers and a sister when he was five and six years old, perhaps due to cholera. Although Kitasato did not trust doctors, he chose to become a doctor.

Fig. 1. Kitasato's birthplace (© The Kitasato Institute The Kitasato Memorial Museum)

In 1885, he was sent to Berlin University to study. Under the guidance of Robert Koch (1843-1910, Germany), Kitasato succeeded in 1889 in developing a pure sample of the tetanus bacillus. The tetanus bacillus is a bacterium that makes people sick. The following year, in 1890, he developed a therapy to treat tetanus in animals. He died at his home in Tokyo on 13th June 1931.

Koch's theories (Koch's postulates). Tetanus bacteria infect the deeper parts of a wound and can kill a person within one day. Because a bacterium resembling a drumstick (now called a "drumstick bacillus", Fig. 2) was always found in the victims' bodies, tetanus was thought to be an infection caused by this drumstick bacillus. However, tests suggested that tetanus was not an infectious disease, because this drumstick bacillus did not satisfy the second of Koch's theories (Fig. 2): it did not appear to cause infection. Kitasato decided to prove in the laboratory that tetanus was an infectious disease.

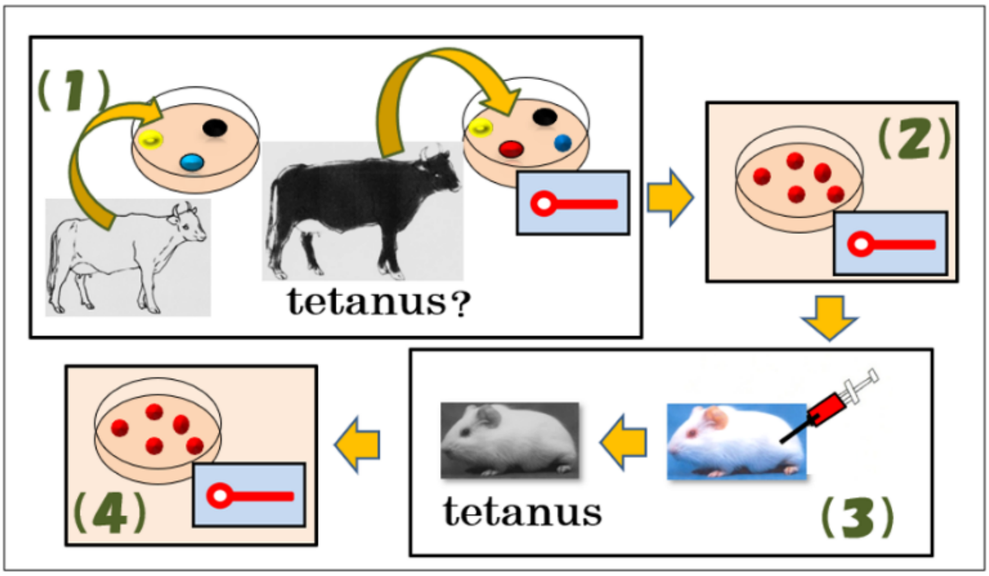

Fig. 2 Koch's theories

(1) the organism is regularly found in the cuts of patients (and animals) with this disease, (2) it can be isolated in a pure culture on artificial media, (3) inoculation of this culture produces a similar disease in experimental animals, (4) the organism can be recovered from the cuts of these animals.

"Drumstick bacillus": Air-hating (anaerobic), heat-resistant (heat-stable) bacterium. Kitasato took pus from tetanus patients and performed tests on it (Fig. 3). He found that most bacteria present in the sample grew on a surface, where much air was available, but the drumstick bacterium grew only where there was little air. He thought that these bacteria might be resistant to heat, so he heated the pus to 80°C. As expected, the heat killed the miscellaneous bacteria, but the drumstick grew. This experiment revealed that the drumstick bacillus withstood heat and didn't need air.

This convinced Kitasato that he could get a pure sample of the drumstick bacterium by first heating pus to kill other germs and then getting the surviving bacteria to grow without air.

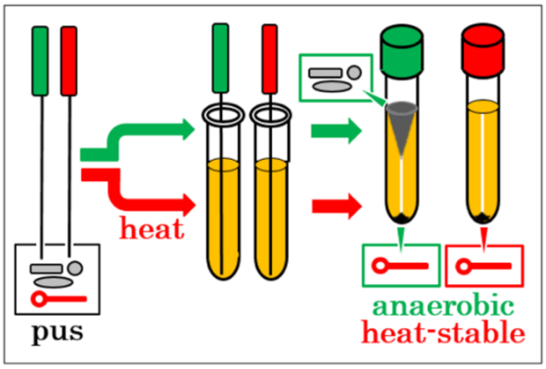

Fig. 3. Tetanus bacillus: anaerobic and heat-stable

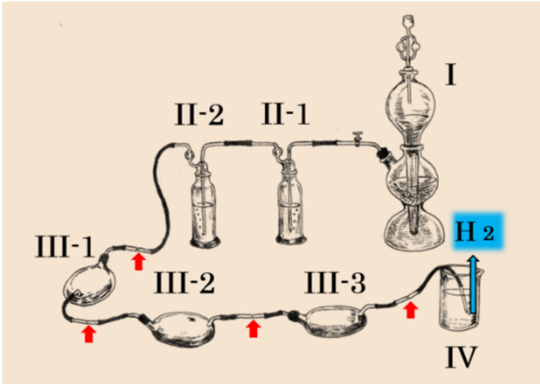

Fig. 4. Kitasato's anaerobic culture system

Pure culture of tetanus bacillus. Fig. 4 shows a pure culture system for tetanus bacteria devised by Kitasato. Ⅲ is a flat culture system, called a "young-turtle shaped dish", which is the heart of this system. In the experiment, heated pus from a tetanus patient is mixed with agar medium, a substance used for testing, and poured into Ⅲ-1, Ⅲ-2 and Ⅲ-3. When the air in the petri dish is replaced by hydrogen gas (H_2), the petri dish is detached by using a Bunsen ↑ burner to melt the part in Fig. 4 . This operation is extremely dangerous and requires caution. In fact, Kitasato has had three hydrogen explosions. Incubating it causes colonies of drumsticks to grow. Experimental animals like guinea pigs and mice, etc., given this pure culture of tetanus bacillus died, and more drumsticks were found in their bodies. Thus, Kitasato satisfied all four of Koch's theories and proved that tetanus was an infectious disease.

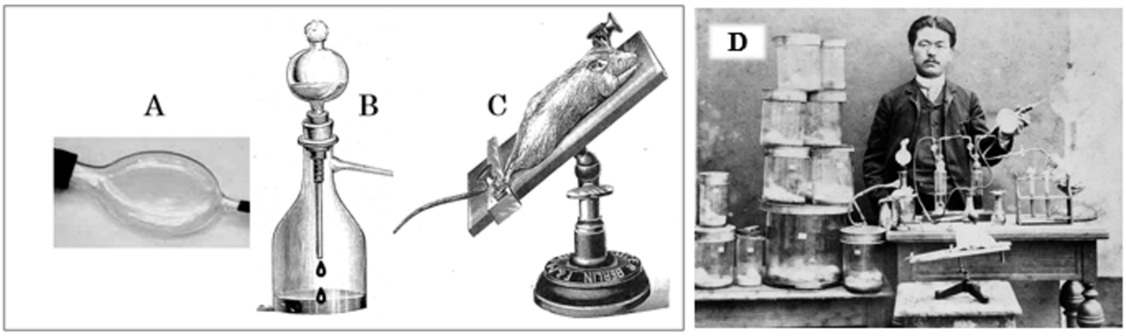

Fig. 5. Kitasato-style innovative devices (© The Kitasato Institute The Kitasato Memorial Museum)

Fig. 5 shows Kitasato's original experimental apparatus: A: "young turtle shaped dish", B: bacterial filter, C: mouse fixation table. Kitasato's research could not have been achieved without any of these three. Fig. 5-D shows Kitasato with the "young turtle-shaped dish" in front of the bacterial filter and the mouse fixation table.

Tetanus serotherapy. Kitasato found that he could make rabbits immune to the tetanus toxin when injected with iodine trichloride. He then used serum (a blood substance) drawn from one of these rabbits and injected it into mice to help them recover from tetanus. Thus, Kitasato perfected a therapy to fight tetanus, called “tetanus serotherapy”.

Dawn of immunology. Tetanus serotherapy was a collaboration with Emil von Behring (1854-1917 Germany). Behring applied this same principle of curing mice of tetanus using a serum from rabbits that were immune to the disease, to the treatment of diphtheria in humans, for which he was awarded the first Nobel Prize in Physiology or Medicine in 1901.

Academic honour. For a time, Kitasato was convinced that the plague bacterium was not the bacterium that he and Alexandre E. J. Yersin (1863-1943, France) had first isolated in 1894. However, when the plague hit Japan in 1899, Kitasato examined the disease again and realized his mistake. He apologized publicly and even dropped his claim of being the discoverer of the plague bacterium. Thus, Kitasato preserved his academic honour and, in 1967, the plague bacterium was named *Yersinia pestis*, after Yersin. However, in 1976, other researchers reported that “most parts of his papers are accurate descriptions of the plague bacterium and Kitasato’s work is eternal” (Bacteriological Reviews, 40,633-651). Nevertheless, the scientific name of the plague bacterium remains *Yersinia pestis*.

Significance of the discoveries of Shibasaburo Kitasato. Tetanus was a common and lethal disease caused by infection of cuts and wounds by a bacterium in soil. Kitasato’s work identified the responsible bacterium and showed that the disease could be prevented by immune serum, thereby laying the ground for the very effective antitoxin vaccine we use today to prevent tetanus, and serotherapy for treatment of tetanus, and other infections like diphtheria. The work of the two heroes, Behring and Kitasato, also opened up the field of immunology, which has continued to produce many Nobel Prize winners in physiology and medicine. The importance of Kitasato’s work was recently recognised by his portrait being selected to appear on the 1000 Yen currency note.