

# Albert Calmette (1863–1933): Originator of the BCG vaccine

Siang Yong Tan<sup>1</sup>, MD, JD, Erika Kwok<sup>2</sup>

**T**uberculosis has been known by many names – phthisis to classical Greeks, *schachepeth* to ancient Hebrews, consumption to Anglophones and *Mycobacterium tuberculosis* to scientists. It has claimed countless victims throughout the history of man, but it was not until the early 1800s that its aetiology and pathogenesis started to be understood. It remained for a man named Calmette, whose hope and vision helped contain the disease with a vaccine.

## TYPHOID, DYSENTERY AND A VENOMOUS SNAKE BITE

Albert Calmette was born in Nice, France on July 12, 1863, son of the secretary to the prefecture. He moved to Brest at age ten and attended the local lycee with hopes of becoming a sailor. However, at 13, he was struck with a fateful bout of typhoid. Unable to become a mariner in the French navy because of this medical history, he instead enrolled in the Naval Medical School at Brest and became an assistant doctor, shortly thereafter relocating to South-East Asia with the Naval Medical Corps. There, he worked with Dr Patrick Manson at the School of Medicine in Hong Kong, who famously studied the mosquito transmission of the parasitic worm filaria, the cause of elephantiasis.

Upon his return to France in 1885, Calmette completed his medical degree at the University of Paris, with a doctoral thesis on filariasis. It marked the beginning of what was to be a long and successful career in tropical medicine.

Calmette worked abroad in several French colonies, first in Gabon in the French Congo and then in St Pierre and Miquelon in the North Atlantic Ocean. While in St Pierre with his new bride Emilie de la Salle, Calmette, inspired by research from the Pasteur Institute, taught himself techniques of culturing bacteria. With this skill, he managed to isolate a pure culture of a bacillus from freshly salted cod that caused fish discolouration, rendering them unsalable. He solved the problem by inhibiting the growth of the bacillus spores. This work quickly caught the eye of Louis Pasteur, who recommended in 1891 that Calmette be made director of the first satellite Pasteur Institute that was being established in Saigon. There, Calmette displayed his creativity by adapting his methods to the local situation. Smallpox was

prevalent in French Indochina (Vietnam), and vaccine sent from France was usually ineffective by the time it arrived. By cleverly using the omnipresent water buffalo, Calmette was able to harvest enough smallpox vaccine to inoculate half a million people in Indochina. Over the next two years, Calmette began work on an antiserum to snake venom, but his efforts failed. He came down with dysentery and had to return to France, where he joined the laboratory of Emile Roux, the co-founder of the Pasteur Institute and a prolific immunologist. In 1894, after extensive trial-and-error, he finally succeeded in developing an antivenom that provided immunity against snake bites. And just in time too, as Calmette himself was bitten by a snake and his antiserum allowed him to make a full recovery, although he lost the tip of his right index finger.



## AN OBSESSION IN LILLE

In 1895, a new Pasteur Institute was established in Lille, a city in northern France, and Calmette reluctantly moved there as its Director. It was a move that eventually led to the development of an anti-tuberculous vaccine. Calmette quickly recognised tuberculosis as the city's major health problem; 300 out of 100,000 people died each year from

the disease. Over the next 25 years in Lille, Calmette focused on eradicating tuberculosis and wrote of his single-minded determination: *"It is during my stay at Lille that the problem of the scientific and social fight against tuberculosis became for me a veritable obsession. I was better placed than anyone to gauge the extent of the misery and of the ruin caused by this disease in the working class, and I could record each day, the uselessness or inefficiency of the efforts, moreover badly coordinated, of public charities and of private initiatives."*

In his research, Calmette was joined by the able Camille Guerin, a veterinary bacteriologist. Years earlier, Robert Koch, who first identified *Mycobacterium tuberculosis*, attempted but failed to create an effective vaccine. In 1906, while searching for a nonpathogenic strain, Calmette achieved a breakthrough when sterile beef bile added to the culture medium attenuated the virulence of bacterial strains without altering their antigenicity. Unfortunately, his research was interrupted when the

<sup>1</sup>Emeritus Professor of Medicine, University of Hawaii, <sup>2</sup>Research carried out during senior elective, John A Burns School of Medicine, Honolulu, Hawaii

German army occupied Lille in 1915. Public health conditions of the city deteriorated, and Calmette was suspected of being a spy. The German military was suspicious over the pigeons he kept in his laboratory, but he was exonerated after an autopsy proved a bird was infected with avian tuberculosis. Still, Calmette and his wife suffered many indignities at the hands of the German military, the latter being taken hostage for several months in 1918.

**BACILLE CALMETTE-GUERIN (BCG)** After the war, Calmette returned to Paris as assistant director of the Pasteur Institute. He managed to write an important essay on the pathology of tuberculosis, *L'Infection bacillaire et la Tuberculose*, which was published in 1920. In Paris, research on the new non-pathogenic BCG strain continued. In 1921, Calmette, satisfied that the BCG vaccine was safe, administered the first dose to a three-day old infant whose mother had died of pulmonary tuberculosis a day after delivery. The infant's grandmother, who was caring for the baby, was also infected. Repeat doses were given on the 5th and 7th day of life, and at six months, the baby showed no signs of tuberculosis despite continual exposure at home. Because of this initial success, BCG was cautiously given to more children, including Calmette's own family members. By 1928, more than 100,000 doses of BCG had been given and the vaccine gained wide acceptance.

"A rapid thinker, industrious and methodical", Calmette attracted many students who adored this happy man, described as generally cheerful, always unselfish and full of kindness.

Alas, in 1930, a terrible disaster struck Lubeck, Germany, where 251 children were accidentally given virulent cultures of *Mycobacterium tuberculosis*. A quarter of the children died and many others became ill. Calmette was deeply affected by this catastrophe and never recovered his happy disposition. On October 29, 1933, Calmette died after a short illness at the age of 70. Regrettably, he did not live to see BCG given to nearly 14 million people as part of a UNICEF campaign with the Danish Red Cross in 1948. Further research on the BCG vaccine found its greatest efficacy in high-risk infants, capable of preventing 80% of meningeal and miliary tuberculosis. Today, it is still given to those at greatest risk for developing the disease, but its use in the general population is no longer recommended due to a small but real risk of post-vaccination tuberculosis.

**BIBLIOGRAPHY**

- Centers for Disease Control and Prevention. The role of BCG vaccine in the prevention and control of tuberculosis in the United States: a joint statement by the Advisory Council for the Elimination of Tuberculosis and the Advisory Committee on Immunization Practices. *MMWR* 1996; 45(RR-4):1-18.
- CJM. Leon Charles Albert Calmette 1863-1933. *Obituary Notices of Fellows of the Royal Society* 1934; 1:315-25.
- Chung KT, Biggers CJ. Albert Leon Charles Calmette (1863-1933) and the antituberculous BCG vaccination. *Perspect Biol Med* 2001; 44:379-89.
- Daniel TM. Leon Charles Albert Calmette and BCG vaccine. *Int J Tuberc Lung Dis* 2005; 9:944-5.
- Daniel TM. The history of tuberculosis. *Respir Med* 2006; 100:1862-70.
- Hawgood BJ. Albert Calmette (1863-1933) and Camille Guerin (1872-1961): the C and G of BCG vaccine. *J Med Biogr* 2007; 15:139-46.
- Hawgood BJ. Doctor Albert Calmette 1863-1933: founder of antivenomous serotherapy and of antituberculous BCG vaccination. *Toxicon* 1999; 37:1241-58.

# Singapore Medical Journal

## Honour Roll of Editors

Honorary Editor	Term of Service
Dr Gwee Ah Leng	1960 – 1971
Dr Tan Kheng Khoo	1971 – 1975
Prof Lim Pin	1975 – 1978
Prof Feng Pao Hsii	1978 – 1987
Prof Chee Yam Cheng	1988 – 1995
Prof Tan Choon Kim	1995 – 1996
Prof Kua Ee Heok	1996 – 1999
Prof C Rajasoorya	2000 – 2003
Prof Wilfred CG Peh	2004 – 2009
Prof Teo Eng Kiong	From 2010