

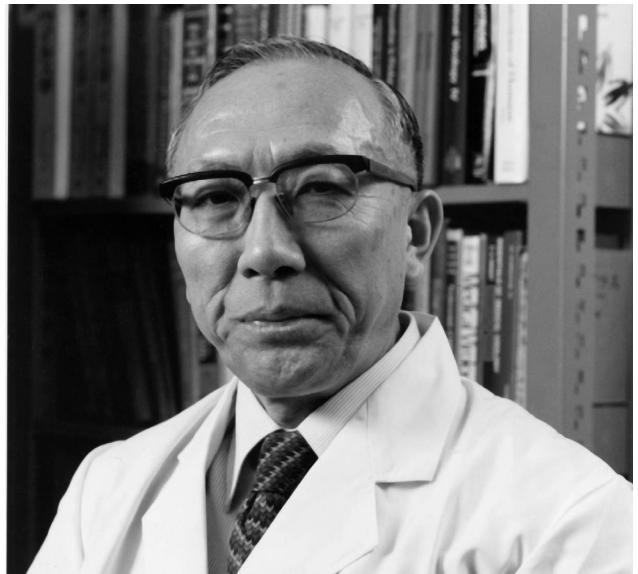
In Memoriam: Susumu Hotta (1918–2011)

Eiji Konishi and Goro Kuno

Susumu Hotta, professor emeritus of Kobe University, Kobe, Japan, passed away on November 17, 2011, at the age of 93. He was one of the early virologists trained broadly in several branches of microbiology, but he was known specifically for his dedicated research on dengue, which spanned nearly 7 decades. During his long career, he left many indelible contributions, including the first isolation of dengue virus and partially successful attempts to attenuate dengue virus for development of a vaccine.

Born in 1918 in Osaka, Japan, he spent much of his youth there. He enrolled in the Faculty of Medicine of Kyoto Imperial University (now Kyoto University), graduating with an MD degree in 1942, after which he joined the staff of the department of microbiology of the same faculty. Although his initial research interest shifted between pediatrics and neurology, he ultimately selected infectious diseases, with Ren Kimura as his advisor. This decision proved to be timely and fortuitous for his career, because in the summer of 1942, dengue outbreaks suddenly emerged in several port cities in Japan. During the next 3 summers, he investigated dengue in Nagasaki, the most severely affected city. In 1943, he succeeded in isolating dengue virus (later identified as serotype 1) from a patient for the first time.

We interrupt the chronology of Dr. Hotta's career to describe the fascinating background of this first isolation of dengue virus because Dr. Hotta rarely revealed it in public, despite its historical significance. The dengue outbreaks in Japan during the summers of 1942–1944, in the midst of World War II, were unprecedented in terms of emergence of a large-scale tropical disease outbreak in a temperate region, involvement of *Aedes albopictus* mosquitoes as the sole vectors, and the large number of patients (estimated to be as many as 2 million). In 1942,



Susumu Hotta. Photograph printed with permission from Hak Hotta.

dengue outbreaks began in several port cities of Japan, where many civilians, seamen, and soldiers returned from the war-ravaged regions of the Pacific and Southeast Asia. Because these outbreaks provided a unique opportunity to study tropical disease outbreaks in a temperate region, several competing research groups, representing academic and military institutions, converged on Nagasaki, the most severely affected city, to investigate dengue.

In the summer of 1943, Dr. Hotta succeeded in isolating a strain of dengue virus (serotype 1) from the blood of a patient named Mochizuki. Dr. Hotta attributed his success to intracerebral inoculation of suckling mice, while his competitors were inoculating chick embryos or other animals. Dr. Hotta continued to visit Nagasaki every summer to pursue his research until 1945, when train service to Nagasaki was suspended because the rail track to the city had been severely damaged by Allied Forces

Author affiliations: Mahidol University, Bangkok, Thailand (E. Konishi); and Fort Collins, Colorado, USA (G. Kuno)

DOI: <http://dx.doi.org/10.3201/eid1905.IM0986>

bombs. Accordingly, Dr. Hotta reluctantly stayed home in Kyoto. This decision saved his life because at the School of Medicine of Nagasaki University, 3 professors who had been investigating dengue and hemorrhagic cases of dengue died instantly when the atomic bomb hit Nagasaki.

At that time in a country at war, preserving isolated virus strains was difficult, because he did not have a freeze dryer, and freezers were useless because of frequent power failures. This difficulty necessitated that he continue passages in mice. Because of shortages of almost everything in his economically devastated country, he had to feed laboratory mice with a portion of his own food ration. At one time when the supply of mice was low, his mother volunteered to keep the Mochizuki strain infectious. After injecting her with the strain, Dr. Hotta published a clinical report of the dengue syndrome in his mother. During the final days of World War II, fearing destruction of his research building and hence loss of his collection of Mochizuki and other isolated dengue virus strains, he put virus vials in a thermos bottle filled with wet ice and carried it at all times, totally unaware that Kyoto had been excluded as an Allied Forces bombing target because of its historical heritage as ancient capital of Japan.

Returning now to Dr. Hotta's career chronology, during 1953–1955, he studied dengue virus replication in cell culture under the guidance of Charles A. Evans of the University of Washington, (Seattle, WA, USA), where he received a PhD degree in 1958. In 1957, he was appointed professor of microbiology at Kobe College of Medicine, which was reorganized in 1964 to become the School of Medicine within Kobe University. He was instrumental in establishing the International Center for Medical Research at Kobe University and contributed to the promotion of international cooperative medical research with other countries, education, and training. Through cooperative international programs, he conducted a series of investigations of dengue hemorrhagic fever in Indonesia.

At Kobe University, he served as chairman of the microbiology department for many years, teaching and

training many graduate students, visiting scientists, and postdoctoral fellows in a variety of subjects such as bacteriology, virology, tissue culture, and immunology. Although dengue was his major interest, he also supervised research on other arboviruses (chikungunya, Japanese encephalitis, vesicular stomatitis, and yellow fever) and on measles, rabies, hepatitis B, smallpox, shope fibroma, myxoma, and polio viruses. After retirement from Kobe University in 1982, he was appointed director of the Institute of Tropical Diseases, Kanazawa University of Medicine, Kanazawa, Japan, and continued his research on dengue until 1989. Even after his second retirement, he continued to write articles, publish books, and even coordinated full-genome sequencing of the dengue strain Mochizuki, which he had isolated in 1943.

Among Dr. Hotta's books, 2 stand out. *Dengue and Related Hemorrhagic Diseases*, published in 1969 by Warren H. Green, St. Louis, MO, USA, was the first book of its kind to focus on hemorrhagic dengue; and *Dengue and Related Arboviruses*, published in 1995 by Yukosha Printing House, Kobe, Japan, was noted for its massive compilation of nearly all Dr. Hotta's early original publications on dengue. This book, for example, reveals his discovery as early as 1949 of the anamnestic protective antibody response in secondary dengue infection. Another of his books, on tissue culture, published in 1976 in collaboration with Ren Kimura and Akio Oyama, was widely used among researchers.

Among many honors and awards that Dr. Hotta received during his life are the prestigious Saburo Kojima Award for contributions to medical science and the Order of the Rising Sun from the Government of Japan. He is survived by 3 sons, including Hak Hotta, a professor of microbiology at the Faculty of Medicine, Kobe University.

Address for correspondence: Eiji Konishi, BIKEN Endowed Department of Dengue Vaccine Development, Faculty of Tropical Medicine, Mahidol University, 420/6 Ratchawithi Rd, Ratchathewi, Bangkok 10400, Thailand; email: ekon@biken.osaka-u.ac.jp



Scan this QR Code with your smartphone and enjoy listening to our podcasts about the latest emerging infectious diseases.

<http://wwwnc.cdc.gov/eid/podcasts.htm>



www.cdc.gov/ncidod/eid/podcast/