# The Viral and Rickettsial Disease Laboratory Celebrates its 80th Anniversary This Year

The Oldest State Public Health Virology Laboratory in the United States

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The Viral and Rickettsial Disease Laboratory (VRDL) is the oldest state public health virology laboratory in the United States. With support from the Rockefeller Foundation, it was established in 1939 as the Influenza Research Laboratory, the first non-military diagnostic virology laboratory in the US. Under the direction of Dr. Monroe Eaton, the laboratory's first director, the VRDL began offering diagnostic services in 1943.

"The Viral and Rickettsial Disease Laboratory plays a critical role in the diagnosis, surveillance, investigation, and prevention of diseases and outbreaks," says former CDPH Acting Director, Susan Fanelli. "This lab, and its professional staff, scientists, researchers and technicians continues to be a leader in the monitoring and control of epidemics here, and around the world."

The VRDL provides laboratory support, technical assistance, and research required for the diagnosis, investigation, and control of viral and rickettsial diseases in California. The VRDL also provides consultation services for local public health laboratories, State Departments of Public Health, and other state agencies. For counties without public health laboratory services, the VRDL functions as their local and reference public health virology laboratory. For decades, the VRDL staff has conducted an annual virology training course for future public health microbiologists.

## **Pioneering Laboratory for Viral Diagnostics**

In 1947, Dr. Eaton became a professor at Harvard University, and leadership was passed to Dr. Edwin H. Lennette. At that time, the laboratory could test for 14 viral agents or diseases. Dr. Lennette is considered a pioneer, the "father of diagnostic virology."



During his long tenure there, Dr. Lennette developed a major center for the study and diagnosis of viral, rickettsial, and chlamydial diseases, where virologists from all over the world have been trained and extensive studies completed on the nature of many different infectious agents. The quality and accuracy of laboratory diagnoses, methods of isolation of infectious agents, safety procedures, methods of viral preservation and storage, and record keeping established the VRDL as a great research institution.

Under Dr. Lennette's tenure (1947-1978), the "Virus Lab," as it was familiarly known, became one of the foremost centers of viral diagnosis in the world. While at CDPH, Dr. Lennette was an important consultant for the World Health Organization and the Department of Army. His studies on Q fever in the late 1940s and 1950s established Dr. Lennette's reputation as a physician and scientist.

## **Hallmark Achievements**

With a strong commitment to the development and evaluation of new viral assays, led in large part by Dr. Nathalie J. Schmidt, by 1976, the VRDL was able to detect or identify more than 300 different viruses or viral infections. Scientists also performed tests to identify some of the world's deadliest diseases. The laboratory manual Diagnostic Procedures for Viral, Rickettsial, and Chlamydial Infections, edited by Drs. Lennette and Schmidt, is still widely used as a laboratory reference to this day.



Dr. Lennette and other scientists at the VRDL discovered a number of new viruses, including Turlock virus which was identified as a new mosquito-borne virus in 1957, Coxsackievirus A21 was identified as a virus associated with respiratory infections in 1958, enterovirus D68 was described from children with pneumonia in 1962, and enterovirus A71 was discovered in 1974.

The lab was among the very first to utilize fluorescent antibody methods and pioneered the use of this technique for the diagnosis of rabies in animals. Adapting a method first developed in the 1940s by Dr. Albert Coons, VRDL scientist Dr. John Riggs, in 1958, labeled antibodies with a dye he designed, fluorescein isothiocynate (FITC) that revolutionized the use of immunofluorescence for diagnostic virology, essentially allowing virologists to "see" viruses. This tool is widely used today for diagnostic virology and other applications.

With the discovery of HIV in the 1980s, the VRDL played a significant role in diagnostics and research related to HIV/AIDS, from VRDL scientists including Drs. Carl V. Hanson, Michael Ascher, and Haynes ("Chip") Sheppard.

Dr. Carol A. Glaser, VRDL Medical Officer and from 2002 to 2009 the VRDL Director, established the ground-breaking California Encephalitis Project to better understand and describe cases of encephalitis, many of which have no known cause. Dr. Glaser and the VRDL staff worked on several thousand encephalitis cases and were able to

identify infectious and non-infectious causes and establish different categories of this neurologic illness.

Dr. David P. Schnurr was a longtime eminent scientist with the VRDL who worked in many areas of virology including rabies, influenza, enteroviruses, and several others. In 2010, he received the Lifetime Achievement Award for Diagnostic Virology from the Pan American Society for Clinical Virology. In 2009, Dr. Schnurr became the Director for the VRDL until he retired from state service in 2011.

The VRDL's most senior research scientist is Dr. Thelma Dunnebacke Dixon, who still conducts work at the lab, and in 2018, was presented with the Albert Nelson Marquis Lifetime Achievement Award. She was originally a research scientist in the virus laboratory at UC Berkeley from 1954 to 1976, when she began work at the VRDL. One of her greatest achievements was identifying a new species of free-living ameba, which has since been named Naegleria dunnebackei as a tribute to her discovery.



### **Viral and Rickettsial Pathogens**

Viruses cause familiar illnesses such as the common cold, the flu, herpes, and warts. They also cause severe illnesses such as HIV/AIDS, smallpox, Zika, and Ebola. Viruses invade and hijack normal host cells and use those cells to multiply and produce more viruses. This can damage, kill, or change the

cells and make a person sick. Different viruses attack different cells in the body such as the liver, lungs, or nerves.

Rickettsial infections are caused by bacteria that must live within host cells. Most rickettsial organisms are transmitted by ticks, fleas, lice, and mites. Rickettsial diseases are difficult to diagnose, even by health care providers experienced with these diseases. Rickettsial infections such as Rocky Mountain spotted fever, scrub typhus, and epidemic typhus may be fatal if untreated. Antibiotic therapy is available for rickettsial infections, but infections must be recognized. The VRDL provides testing to identify these illnesses.



### **Protecting Lives Yesterday, Today, and Tomorrow**

"VRDL is a prestigious reference lab that connects past with present," says Dr. Dongxiang Xia, the VRDL director from 2012 - 2017. "The lab provides a variety of testing services from plaque reduction neutralization tests to whole genome sequencing for viruses from adenovirus to Zika virus."

Dr. Xia considers the VRDL as an "excellent school, which has great mentors for microbiologists and an environment to foster scientists at any level."

Dr. Debra Wadford has been with VRDL for 17 years and became the director of the VRDL in January 2019. "We never get a lot of advertising," Dr. Wadford says, "but we do a lot to protect the health of Californians."

The Public Health Microbiologists (PHMs) with the VRDL are experts in their field and serve as consultants for local public health laboratories. Every year VRDL PHMs and other scientists train junior microbiologists to become professional PHMs. The VRDL staff collaborate with epidemiologists, clinicians, and other scientists for diagnostics, methods development, and research.

The Viral and Rickettsial Disease Laboratory is synonymous with excellence in the field, says Dr. Paul Kimsey, State Public Health Laboratory Director. "Many developments coming from the VRDL have contributed greatly to diagnostic virology," Dr. Kimsey says. "Diagnostic standards were developed and set in this laboratory for difficult-to-identify viruses, which have become the standard for diagnostic virology labs."

Currently, the VRDL partners with the US Centers for Disease Control and Prevention working on diagnostics and surveillance for several viral diseases of public health significance and serves as a National Reference Center for influenza, measles, mumps, rubella, rabies, West Nile virus and Zika virus. The VRDL also serves as a 'reference laboratory', receiving specimens from hospitals, commercial laboratories and public health labs throughout California that require confirmatory testing or further characterization by advanced tests such as whole genome sequencing which can aid in the investigation of outbreaks and monitor circulating viruses for genetic changes that may enhance their virulence or confer drug resistance.



One of the primary roles of the VRDL is to be prepared for the emergence of new viral diseases that may impact the health of citizens and visitors of California. This includes emerging viruses such as Zika virus, hepatitis A, avian influenza, Middle East Respiratory Syndrome (MERS) coronavirus, Ebola, Sin Nombre (hanta) virus; re-emerging vaccine preventable diseases such as measles and mumps; and rapidly mutating viral pathogens such as influenza and norovirus.

"The 80<sup>th</sup> anniversary of the VRDL is a proud occasion for current and former VRDL staff to reflect on its illustrious history as the first diagnostic virology laboratory in the United States," says Dr. Kimsey. "Since its inception, the staff of the VRDL have been dedicated and committed to their work in identifying the cause of illness in patients and protecting the public's health. We look forward to continuing this legacy into the future."