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A Career Filled with Viruses

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The different families of viruses can be distinguished morphologically by transmission electron microscopy (EM) and this allows for diagnosis to the level of the family. My career with CDC started in 1983 and I have worked with every family of virus that causes human disease and would like to share my experiences.

The first virus I studied was human immunodeficiency virus (HIV) which is a retrovirus and is roughly spherical with a dense, conical-shaped nucleocapsid [1]. Many other viruses followed, including herpesviruses, which contain a 100 nm icosahedral nucleocapsid enclosed by a tegument layer and surrounded with an envelope [2]. The virus that causes hantavirus pulmonary syndrome is a bunyavirus that is mostly spherical, containing filamentous nucleocapsids surrounded by a rather dense envelope [3]. Ebolavirus is a highly recognized filovirus and in thin sections, viral inclusions are composed of aggregates of filamentous nucleocapsids [4]. Nucleocapsids travel to the plasma membrane where they bud, obtaining a viral envelope. The outbreak of ebolavirus in Zaire in 1995 allowed for the collection of organs in glutaraldehyde, and examples from the liver, skin and lung will be shown. Variola, the causative agent of smallpox, is the most well-known of the poxviruses although there are many others that cause human illness. By negative stain EM, poxviruses appear brick-shaped and in thin sections, spherical nucleocapsids condense down to a dumb-bell shape which buds into the Golgi complex, obtaining a viral envelope. Nipah virus is a deadly paramyxovirus that was first recognized in 1999 [5]. Herringbone-shaped nucleocapsids form intracellular inclusions and bud at the plasma membrane to obtain their envelope. Virions can be large, up to 1900 nm in diameter, and are pleomorphic.

There are several examples where EM was able to identify a viral isolate grown in cell culture and thus change the course of the investigation for an etiologic agent. These include two bunyaviruses (Cache Valley and Heartland viruses) [6, 7], an arenavirus (lymphocytic choriomeningitis virus) [8], an unusual presentation of a flavivirus (West Nile virus) [9] and the initial outbreak of severe acute respiratory syndrome coronavirus (SARS-CoV-1) [10]. SARS-CoV-1 and SARS-CoV-2 have the same morphogenesis where the nucleocapsids bud upon the membrane of the Golgi-complex/rough endoplasmic reticulum region to form roughly spherical particles which stay within a membrane-bound compartment. These migrate to the plasma membrane where they fuse, releasing virus particles which stay attached to the cell surface. In addition, CDC was able to demonstrate virus in the lung and upper airway in autopsy tissues from SARS-CoV-2 patients [11].

These are examples of some of the pathogens I have been fortunate enough to work with over the years, giving me a truly satisfying career collaborating with many especially bright investigators [12].

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[12] The findings and conclusions in this report are those of the author and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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