

## The Wisconsin Electron Microscopy Diagnostic Proficiency Program

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Negative stain imaging of specimens for virus identification is on the decline in some electron microscopy (EM) diagnostic laboratories. Our laboratory went from over 2000 negatively stained [1] samples to less than 100 per year. This dramatic decrease in samples can have a deleterious effect on keeping one's eye keen for spotting unknown pathogens that do come in for transmission electron microscopy (TEM) examination.

In 2007, the Centers for Disease Control (CDC) and Duke University partnered in a program to improve the use of TEM laboratories in bioterrorism preparedness. Hosts Cynthia Goldsmith from the CDC and Sara Miller from the Department of Pathology at Duke sought to fill a gap in expertise. During this course, it was apparent that a number of laboratories did not have access to a variety of viruses or adequate diagnostic samples to improve identification skills.

The Wisconsin Veterinary Diagnostic Laboratory (WVDL) has a comprehensive virology service and offered to provide additional practice samples. To this end, virologists at WVDL prepare and ship inactivated viruses to the participating laboratories. Each participant then has the opportunity to prepare and evaluate their own grid as well as make the diagnosis. This was the start of the "Wisconsin EM Diagnostic Proficiency Program" and is currently the only one in the United States. The laboratories that have participated show improved expertise in their abilities to prepare and identify unknown viruses grown in tissue culture [Figures 1, 2]. This program has been growing for the last 7 years with 17 laboratories from the mainland US, Hawaii, and Canada currently participating.

PCR has become the standard in many diagnostic tests; however it can miss unsuspected pathogens if the correct primer is not chosen or the sequence is not available. If one simply suspects a viral pathogen, based on symptomatology and runs a PCR test for that pathogen, the "guess" may be incorrect, and the test result would be negative; yet, a virus could, nevertheless, be present. Additionally, some viruses do not grow or are fastidious in culture, making large-scale production of reagents difficult. Thus, commercial diagnostic primers and antibody reagents do not exist for all viral pathogens. In the case of electron microscopy, if a virus is present in sufficient numbers, and if the microscopist is experienced in viral morphology, the pathogen can be recognized and identified. This examination of "whatever is there" has been termed the "Open View" [2] by Hans Gelderblom, one of the giants in the field of virus diagnosis and whose program we have emulated here.

In summary, one should make use of all the tools in their diagnostic arsenal, including EM, when it comes to detecting unknown viruses in samples. We encourage all diagnostic laboratories with EM facilities to participate in this proficiency program.

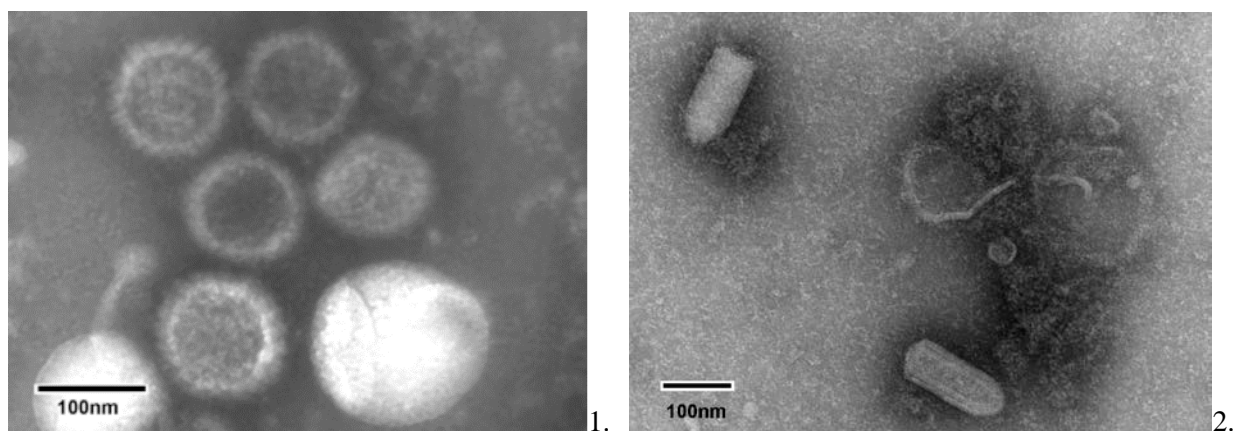


Figure 1. Image of Herpesvirus on grids prepared by participating lab. Image by Sara Miller.

Figure 2. Image of Rhabdovirus on grids prepared by participating lab. Image by Margaret Casey.

*References:*

[1] M.A. Hayat, S. E. Miller. Negative Staining. McGraw-Hill Pub. Co., 1990, 253 pp. .

[2] P. R. Hazelton, HR Gelderblom. Emerg Infect Dis. Mar 2003; 9(3): 294–303.

doi: 10.3201/eid0903.020327. PMID: PMC2958539