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Idaho Bureau of Laboratories

Clinical Forum

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IDAHO DEPARTMENT OF HEALTH & WELFARE

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Norovirus Genotype Dynamics among Outbreak Associated Strains in Alaska, Idaho, Montana, & Wyoming, 2010-2012

Amanda J. Bruesch M.S. and Christopher L. Ball Ph.D, HCLD (ABB)

Noroviruses (NoVs) are estimated to cause greater than 90% of viral gastroenteritis outbreaks worldwide and over half of all-cause gastroenteritis outbreaks[1]. In the United States, it is estimated that at least 21 million illnesses, 70,000 hospitalizations, and 800 fatalities are attributed to norovirus infections every year[1].

Noroviruses are one of four genera in the viral family *Caliciviridae.* They are categorized into five genogroups, GI – GV, based upon viral capsid protein gene (VP1) phylogenies. Strains from genogroups GI, GII, and GIV are associated with human disease, with GII causing most outbreaks[2]. Norovirus genogroups can be further divided into related genetic clusters or genotypes[3]. For example, NoV GII is subdivided into at least 19 genotypes[2]. Norovirus genotypes are described using a number and the name of the location where the strain was first confirmed (e.g. GII.4_Farmington Hills). Epidemiologic data suggests that over 85% of recent outbreaks have been caused by genotype GII.4 strains[2]. In 2009, the Centers for Disease Control and Prevention (CDC) launched CaliciNet USA, the national norovirus genotyping network, to develop a greater understanding of NoV epidemiology and describe the major strains circulating in the U.S. Interestingly, the inception of CaliciNet coincided with the documentation of a new GII.4 pandemic strain, GII.4_NewOrleans, which replaced the GII.4_Minerva strain that had been the predominant strain in circulation since the 2005-2006 NoV season[2]. Idaho Bureau of Laboratories (IBL) was one of the first state laboratories to join CaliciNet and in 2010 we expanded our role by becoming an outbreak support center (OSC) that provided NoV genotyping for Idaho, Alaska, Montana, and Wyoming outbreaks[4,5]. This regional surveillance has provided new insights into NoV strain circulation patterns and epidemiology in the Northwest.

From October 2010 to May 2012, specimens from 51 outbreaks were submitted to IBL for subtyping. Sixty three percent (32/51) occurred in long term care facili-

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Human Metapneumovirus Outbreak in Long-term Care Facility — Southwestern Idaho, 2012

Contributed by the Office of Epidemiology, Food Protection, and Immunization

On February 8, 2012, Southwest District Health was notified of a cluster of non-influenza pneumonia cases at a long-term care facility with 80 residents and approximately 100 staff; 5 residents were hospitalized. Southwest District Health epidemiologists conducted a public health investigation, with assistance from facility staff and the Idaho Division of Public Health's Office of Epidemiology, Food Protection, and Immunization, to determine the extent and etiology of the outbreak.

Patient records, including prior laboratory results, were reviewed. A case was defined as new cough onset in a facility resident during January 31 to February 29. Nasopharyngeal (NP) specimens from 9 non-hospitalized patients meeting the case definition were collected within 4 days of illness onset for respiratory virus testing at Idaho Bureau of Laboratories (IBL).

Cases were identified in 29 (36%) of 80 residents; 2 (40%) of 5 hospitalized residents died. Median duration of illness among 26 residents was 4.5 (range: 1–14) days. Illness among residents was characterized mainly by lower respiratory tract symptoms; 10 were diag-

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Human Metapneumovirus Outbreak

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nosed with pneumonia by a physician. Eighteen (62%) of 29 resident cases were treated empirically with antibiotics.

Physician-ordered diagnostic tests, including rapid influenza antigen, rapid respiratory syncytial virus (RSV), *Legionella* urinary antigen, *Streptococcus pneumoniae* urinary antigen, and blood, bronchoalveolar lavage (BAL), and sputum bacterial cultures on specimens collected 0–7 days after illness onset were all negative. However, in 2 of 5 patients, blood was collected for bacterial culture 4 days after antibiotic therapy was initiated. Rhinovirus/enterovirus was detected in 1 NP specimen. Human metapneumovirus was detected by qualitative nucleic acid multiplex assay or RT-PCR in 5 (56%) of 9 NP specimens and in a BAL specimen from one patient who died. Eleven clinical cases were identified in facility staff.

First detected in 2001, human metapneumovirus (hMPV) is classified in the family *Paramyxoviridae*, subfamily *Pneumovirinae*, and was classified as the first human member of the *Metapneumovirus* genus. Among the *Pneumovirinae* causing human disease, hMPV is most closely related to RSV and causes an illness that is clinically indistinguishable. Since its discovery, hMPV has been detected worldwide. There are at least two genetic lineages, A and B, which can each be divided into 2 sublineages. Predominant circulating strains can vary by year and might be replaced, on average, every 1–3 years. Infections are seen in all age groups and reinfection occurs often due to incomplete immunity. Very high seroprevalence is observed in children from 5 years of age; all adults are thought to be infected by 25 years of age.[1]

HMPV can cause severe disease including bronchiolitis and pneumonia in both pediatric patients and the elderly. HMPV is second to RSV as an etiology of lower respiratory tract infection in pediatric patients. Although hMPV infection can occur throughout the year, peak hMPV activity is typically observed in late winter to early spring, 1–2 months later than that of RSV.[1] Outbreaks in long-term care facilities have been documented in all seasons and have resulted in attack proportions of up to 72% and case fatality proportions of up to 50%.[2]

In 2012, respiratory virus surveillance by Utah-based Intermountain Healthcare reported on its GermWatch[SM] website a peak in the count of positive test results for hMPV in the week beginning February 19 which coincides with the outbreak reported here.[3] The capability to test for hMPV at IBL allowed us to identify hMPV as an etiologic agent of this outbreak.

References

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Lab Spotlight: Virology Laboratory

Brian Deis M.S.

HIV ELISA Assay: Serum is applied to a plate containing antigen to capture HIV antibodies. A substrate molecule combines with the newly formed antibody/antigen complex and under goes a color change which is used to detect an HIV infection.

From rapid detection of common diseases to providing specialized diagnostic services, the Idaho Bureau of Laboratories' (IBL) Virology Laboratory plays a valuable public health role statewide and nationally. The Virology Lab assists local public health professionals by performing laboratory tests that diagnose and determine immunity status for both common and rare infectious diseases. This lab also participates in statewide and national surveillance testing programs, providing data that detects disease patterns and helps identify and control outbreaks. The Virology Lab strives to stay current with the latest science and technology trends to ensure preparedness for the next emerging disease or public health crisis.

A majority of the Virology Lab's services involve performing tests that can determine immunity to certain vaccine-preventable diseases and detection of common blood borne pathogens. The lab tests for vaccine-preventable diseases such as mumps, measles, rubella, and varicella, allowing healthcare providers to determine the immunization profile of a patient and the effectiveness of recent vaccinations. This is important when evaluating the health and medical needs of Idaho's refugee population who typically don't have well documented medical records. In addition, the lab tests for high consequence viral diseases including HIV and Hepatitis; these diseases can be asymptomatic for years but can be transmitted to others during this stage. Early detection of such diseases allows for early treatment, improved quality of life for individuals and mini-

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Norovirus Genotype Dynamics

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ties and 82% (42/51) of reported transmission was person to person. Over 1,480 ill individuals were associated with these outbreaks. Norovirus outbreaks can occur in all ages and seasons but typically predominate in children, the elderly and immune compromised individuals during cold weather months in temperate climates[6]. In our OSC region, this seasonal increase was observed from October through March. Eighty four percent (43/51) of the subtyped outbreaks were submitted during this time, with an average of 7.2 outbreaks per month. In contrast, the prevalence dropped to 16% (8/51) from April through September, with an average of 1.3 outbreaks per month.

In order to analyze NoV circulation trends in our OSC region, we downloaded national CaliciNet submissions from all states outside of our OSC region during October through May of 2010-2012. This compilation of data was used as a national reference to compare and contrast the strain distribution in our region. In both seasons, there were differences in NoV strain circulation between our OSC and the rest of the nation. Figure 1 is a rank abundance curve that compares the distribution of strains subtyped nationally versus the strains subtyped in our OSC region from October 2010 to March 2011. Four GII genotypes were identified in our region with GII.4_NewOrleans (60%) and GII.4_Minerva (30%) being the most abundant. A similar circulation pattern was seen in all non IBL OSC states (the national reference group). Nationally, 11 GII subtypes were detected with GII.4_NewOrleans (83.5%) and GII.4_Minerva (5.3%) also being the most abundant strains. Interestingly, our region had over 5 times more GII.4_Minerva associated outbreaks than all other states combined. This observation suggests that GII.4_NewOrleans did not penetrate our region and replace GII.4_Minerva as successfully as other parts of the nation.

From October 2011 through May 2012, we saw a substantially different distribution of NoV strains in our region than the rest of the nation. As depicted in Figure 2, NoV GII.1 emerged in our region and rapidly became the most abundant strain in circulation. This strain was attributed to 47.8% of subtyped outbreaks in our region, which was over 3.5 times higher than the rest of the nation. We also continued to see a lower prevalence of GII.4_NewOrleans than the nation. By far, the most surprising trend, however, was the dramatic arrival and penetrance of the GII.1 strain in our Northwest OSC region. As the 2012-2013 NoV season approaches, we will be very interested to see if the genotype dynamics in our region continue to differ from national trends.

"[IBL] was one of the first state laboratories to join CaliciNet and in 2010 [became] an outbreak support center that provided NoV genotyping for Idaho, Alaska, Montana, and Wyoming outbreaks."

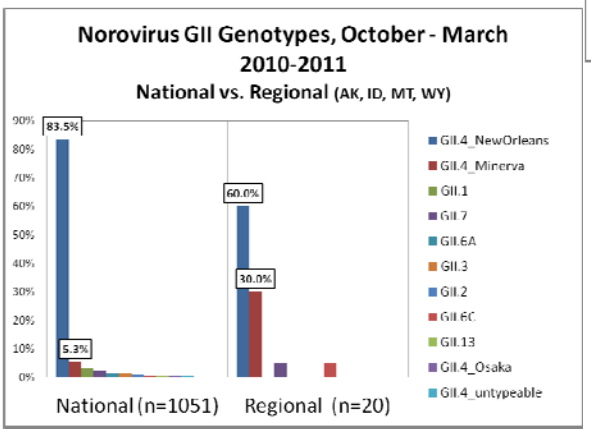

Figure 1 Rank abundance of NoV GII genotypes submitted to CaliciNet nationally (all states but IBL CN-OSC sites) and regionally (AK, ID, MT, WY) from October 2010 through March 2011.

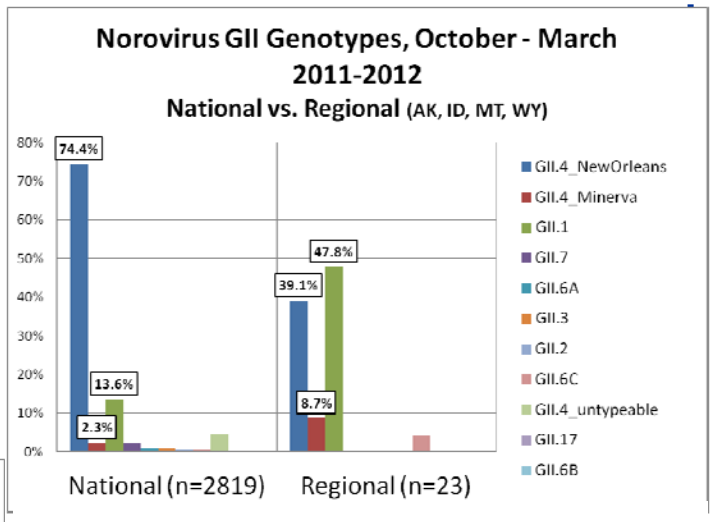

Figure 2 Rank abundance of NoV GII genotypes submitted to CaliciNet nationally (all states but IBL CN-OSC sites) and regionally (AK, ID, MT, WY) from October 2011 through March 2012.

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[1]A. J. Hall, "Noroviruses: The Perfect Human Pathogens?," *Journal of Infectious Diseases*, pp. 1622-1624, 2012.

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Norovirus Genotype Dynamics

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This article was supported by the Association of Public Health Laboratories and by the Cooperative Agreement Number U60HM000803 from the Centers for Disease Control and Prevention and/or the Assistant Secretary for Preparedness Response. Its contents are solely the responsibility of the authors and do not necessarily represent the official view of the Association of Public Health Laboratories, the Centers for Disease Control and Prevention and/or Assistant Secretary for Preparedness and Response. The work described was funded in part by the following federal institutes: National Center for HIV, Viral Hepatitis, STDs and TB Prevention (PS) Coordinating Office for Terrorism Preparedness and Emergency Response (CTPER), Laboratory Science, Policy and Practice Office (LSPPPO) (LS) Coordinating Office of Global Health (GH), Public Health Informatics and Technology Program Office (PHITPO) (HK), National Center for Immunization and Respiratory Diseases (IP), National Center for Environmental Health (NCEH), National Center for Zoonotic, Vector-borne, and Enteric Diseases (CK), and Centers for Disease Control and Prevention (NCBDD).

Virology Laboratory

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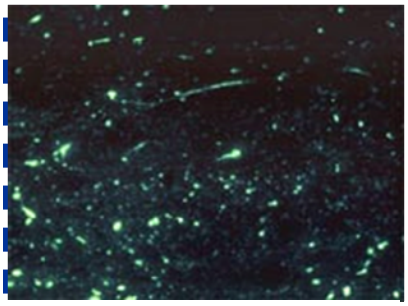


A DFA slide positive for rabies. Fluorescent labeled antibodies attach to rabies antibody from a patient sample and glow under the microscope.

mizes the likelihood of large scale outbreaks.

The Virology Lab also tests for several less prevalent diseases that are not typically offered by other health labs. For example, IBL is the only lab in Idaho that tests for rabies. The Virology Lab may receive six or more rabies test requests a week during the late spring and summer months. Other specialized services include the detection of hantavirus, and norovirus. Although requests for these tests are generally infrequent, IBL staff regularly participate in proficiency programs to maintain competency.

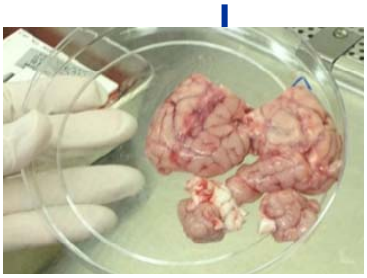
The Virology Lab takes part in proficiency programs for each test method performed. These methods range from traditional microscopy and contemporary immunoassays to the latest genetic sequencing technologies. These competency demonstrations ensure high-quality and accurate work and serve to develop a highly trained staff. IBL's broad expertise allows for quick adoption of the newest test methods to meet ever-changing public health needs.

The Virology Lab uses an electronic reporting system that automatically disseminates disease surveillance data. These data are used to inform epidemiologists and caregivers locally and to populate several national CDC databases. For example, the CDC program, CaliciNet, tracks norovirus outbreaks and their respective genetic signatures. This allows healthcare officials to determine if outbreaks are linked to a common source while monitoring the genetic diversity and the emergence of new norovirus strains. The Virology Lab also reports to the CDC's Influenza Center. This information is used to identify flu outbreaks and the emergence of new influenza strains and to develop the next year's flu vaccine.

The detailed norovirus and influenza analysis reporting would not be feasible without the latest in genetic sequencing technologies. New pyrosequencing methods lead to fast, high-resolution genetic analysis crucial to the evaluation and reporting of this essential genetic information. The Virology Lab constantly evaluates current methodologies and rapidly adopts new technologies. Currently, the Virology Lab is validating a new HIV test matrix that will allow earlier detection of HIV infection while rapidly differentiating HIV 1 from HIV 2.

The IBL Virology Lab is highly knowledgeable and skilled, maintaining a vast array of core competencies and the ability to integrate improved techniques and advanced technologies. These qualities, coupled with local and national partnerships, allow IBL to make major contributions to public health.

"The Virology Lab constantly evaluates current methodologies and rapidly adopts new technologies. Currently, the Virology Lab is validating a new HIV test matrix that will allow earlier detection of HIV infection."



Preparation of brain material for Direct Fluorescence Antibody (DFA) microscopy for rabies detection

Virology Word Find

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ANTIGENIC DRIFT
ANTIVIRAL
BACTERIOPHAGE
CAPSID
ENVELOPE
HEMAGGLUTININ
HIV
INFLUENZA
LATENT
LYSOGENIC
LYTIC
MUTAGENESIS
NEURAMINIDASE
RABIES
RETROVIRUS
RHINOVIRUS
VECTOR
VIROLOGIST
VIRON
WEST NILE

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Idaho Influenza Surveillance 2011/12 Summary

IBL wishes to thank the 35 laboratories and clinics across Idaho who submitted respiratory specimens throughout the 2011/12 influenza season. Idaho's influenza surveillance program succeeds only through the participation, interest, and involvement of our community partners.

IBL confirmed and subtyped its first influenza virus mid-December; however, activity remained very low until mid-March, peaking then in April and May. IBL detected influenza virus in 67% of the 172 specimens received with 38% subtyping as AH3N2, 23% as AH1N1pdm09, and 6% as influenza B. CDC has further characterized 30% of Idaho's isolates thus far, and except for 1 influenza B Victoria-lineage, all have been closely related to the strains in the 2011/12 vaccine formulations.

Although 2011/12 season has officially come to a close, IBL maintains year round surveillance for influenza. Providers are encouraged to submit respiratory specimens from patients demonstrating influenza-like illness throughout the summer.

IBL Updates

Farewell to Phil

April 25th marked the last day for Phil Ciancia as Clinical Laboratory Inspector at the Idaho Bureau of Laboratories, Laboratory Improvement Section. Phil retired after 14 years as the CLIA field inspector of clinical labs in Idaho. Phil usually averaged around 90 onsite inspections a year as he traveled around 13,000 miles each year visiting labs.

Phil came to us after spending 23 years at Holy Rosary Hospital in Ontario Oregon, most of that time as laboratory manager. Prior to that he had earned a BS from Arizona State University in Medical Technology and spent several years with the US Army at Fort Detrick and Hawaii.

Phil will now have more time to work on his El Camino which he races at Firebird Raceway near Emmett. Over the years Phil has restored many "muscle cars", but more recently has concentrated on the El Camino and drag racing. Phil lives in Meridian with his wife Mary. Best wishes to Phil and quick reaction times at the line!

Justin Grant, Scientist 2

Justin Grant joined IBL on May 29, 2012 as a Scientist 2 in the Emergency Preparedness Section. Justin received his Bachelor of Arts and Science dual degree in Chemistry and Biology from The Evergreen State College where he performed research in organic synthesis. His previous jobs include working in a pharmaceutical lab and managing a nutritional supplement lab.

Justin has lived in Idaho for a little over a year with his Rottweiler, Little Bear, and 2 snapping turtles. He spends the majority of his free time outdoors: backpacking, hiking, camping, climbing, exploring hot springs, and hunting.

Lisa Smith, Clinical Microbiology Section Manager

Lisa began her position as Clinical Microbiology Section Manager at IBL in May 2012. She received a Bachelor degree in Microbiology with an Emphasis in Medical Laboratory Technology and an MBA in Technology Management. In addition, she holds certificates as a California Public Health Microbiologist and a Clinical Laboratory Scientist (ASCP). Lisa has many years of experience working in the public health and hospital laboratory settings. She was most recently employed in a California county public health lab which was the site of the initial pandemic influenza outbreak of 2009; this gave her first-hand experience with a major outbreak situation.

In her free time, Lisa practices and competes in barrel racing and enjoys trail riding and spending time outdoors. She also enjoys spending time with her husband, children, cat, and dogs.

A New Road Ahead

After 26 years of service to the State of Idaho, Colleen Greenwalt retired from the Idaho Bureau of Laboratories (IBL) on June 8, 2012. Colleen was a proud graduate of the University of Wyoming. Her career at IBL began as a bench microbiologist working in the Virology/Serology laboratory. In that capacity, she helped implement testing for HIV, norovirus, and influenza and several other important viral diseases. Later she was promoted to the Microbiology/Serology Laboratory Manager position, where she adeptly directed the section and mentored and supervised many talented scientists for IBL.

Colleen's knowledge, talent, and public service were a tremendous asset for the Bureau and the Department. She left an indelible imprint on those who worked with and for her. All of us at IBL extend a big "thank you" to her for many years of dedication to the Bureau. We will miss her and wish her nothing but happiness in her retirement.

Save the Date!

The Sentinel Laboratory Preparedness Workshop is scheduled for Thursday, October 25, 2012.

Flyers and registration forms will be available late summer/early fall.

Please contact Wendy Loumeau at loumeauw@dhw.idaho.gov or 208-334-2235 ext. 258 with any questions.

Solution to Word Find

(Over,Down,Direction)

ANTIGENIC DRIFT(14,4,S)

ANTIVIRAL(28,8,W)

BACTERIOPHAGE(17,29,NW)

CAPSID(3,26,NE)

ENVELOPE(9,10,NW)

HEMAGGLUTININ(14,27,W)

HIV(3,7,NW)

INFLUENZA(10,21,SW)

LATENT(3,29,E)

LYSOGENIC(25,11,S)

LYTIC(24,24,W)

MUTAGENESIS(18,18,N)

NEURAMINIDASE(13,1,SW)

RABIES(18,24,S)

RETROVIRUS(17,14,NE)

RHINOVIRUS(16,20,E)

VECTOR(12,23,SE)

VIROLOGIST(1,17,SE)

VIRON(19,4,SW)

WEST NILE(4,19,N)

Upcoming Teleconferences

September 11, 2012 11:00 Mountain Time

"Bloodborne Pathogens: What, Me Worry?"

September 25, 2012 11:00 am Mountain Time

"2012 Influenza Update"