We are Ready to Measure New Normal

Overview and Update from Viral and Rickettsial Disease Laboratory

Dongxiang Xia, MD, PhD
VRDL’s Well Recognized Expertise
VRDL first isolated and identified enterovirus D68 in 1960s
National Projects

• CDC-WHO Regional Influenza Lab Network
• CaliciNet
• Vaccine Preventable Disease Reference Center
• Rabies Regional Reference Testing Center
• CDC/NLTN Training Center: Lab Methods for Detecting Rabies
• Laboratory Response Network
• BioWatch
State Projects

• MeaslesNet
• Norovirus Laboratory Network (NLN)
• Unexplained GI Investigation Project
• Respiratory Laboratory Network (RLN)
• Influenza Sentinel Physicians Project
• Neurologic Surveillance & Testing
• WNV Laboratory Surveillance
• Rabies Reference Testing and Surveillance
• Serological Testing Algorism for Recent HIV Seroconversion (STARHS)
Stakeholder Activities

• May: Hosted the CDC/APHL- training on Influenza Detection and Subtyping, attended by 13 County PH Labs
• July: Attended CDC/APHL VPD Reference Center Meeting
• October: Participate in the APHL web-based Informatics Self-Assessment Tool and visualization suite applications
• December: Attend the CDC CaliciNet User Meeting
Medical and Epidemiology Liaison Section – 2014 Update
## Medical and Epidemiology Liaison Section

<table>
<thead>
<tr>
<th>Area</th>
<th>Contact Information</th>
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</table>
| Vaccine Reportable Diseases and General Local Assistance | David Cottam, Ray Sante, Anthony Moore, and Chris Anderson  
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| West Nile Virus and Arbovirus Surveillance and Testing | Maria Salas and Ruth Lopez  
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[Christopher.Anderson@cdph.ca.gov](mailto:Christopher.Anderson@cdph.ca.gov) |
Entering the Digital Age

- MELS Staff can now access CalREDIE database.
- CDC 50.34 PDF “DASH” submittal form
  - Version 1.2 will expire 12/5/14. VRDL will send you a new one with our contact info prepopulated.
  - One downside is that if we receive it as a “hard copy” then we have to retype all the info to update the barcoded information.
- Please check [http://www.cdph.ca.gov/programs/vrdl](http://www.cdph.ca.gov/programs/vrdl) for the periodic updates of the “VRDL Guidelines to Viral Services” and the latest versions of submittal forms.
West Nile Virus and Arbovirus Surveillance

- Epi Team
  - Maria Salas, MPH
  - Ruth Lopez

- Arboviral Testing and Support
  - WNV, Dengue, Chikungunya, and more
  - Provide technical support of WNV testing for PHLs

- Integrated Surveillance
  - WNV human case reporting to CDPH and CDC
  - WNV bird, mosquito, squirrel and equine case reporting to CDC
  - Participate in CDC enhanced arbovirus surveillance activities
The MELS section coordinates VPD testing and support functions for:

- **MeV, MuV, RuV, and VZV**
  - Direct Detection by PCR
  - Serology
- Coordinates specimen shipping between local health jurisdiction and VRDL
- Acts as a liaison between state epidemiologists and laboratory staff

**Highlight:** 61 confirmed measles cases YTD in 2014 - most since 1995 (109 cases)
Middle East Respiratory Syndrome Coronavirus (MERS-CoV)

- On May 2, the first case of MERS-CoV infection detected in the United States was reported by the CDC.
- CDPH has been working with local health jurisdictions (LHJs) to identify suspect cases of MERS. Testing for MERS-CoV and other viral respiratory pathogens is available at VRDL.
- From April 2013 to the present, upwards of 30 suspect cases have been investigated, tested and ruled out for MERS.
Respiratory and Gastroenteric Diseases Section

Section Chief: Deb Wadford
Scientist: Dave Schnurr
PHM Supervisor: Hugo Guevara
PHM Specialist: Chao-Yang Pan
PH Microbiologists: Estela Saguari
Tasha Padilla
Ricardo Berumen
3 Vacancies (2 State PHM II positions)

PH Lab Technician: Brandon Brown
Research Associates: Nohemi (Mimi) Reyes-Martin
Alice Chen – Resp Infections and NLN Coordinator
RGD Section

Testing:
• Influenza rRT-PCR (typing/subtyping/AVR testing/Strain typing (CDC))
• Non-Influenza viral respiratory agents (including MERS)
• Gastroenteric Agents (Noro/Astro/Sapo/Rota/AdV40/41)

What’s New
• CDC sample size goals for influenza virologic testing
• B lineage genotyping reagents available from CDC (see Poster by Rick Berumen et al.)
• Non-Influenza testing will focus on severe/fatal cases and outbreaks: please send to VRDL for testing
CDC Virologic Surveillance
Sample Size Guidelines
2014-15 Season

• Sample size goals for each RLN laboratory (to enhance geographic coverage)
  – Sent to each RLN lab at the pre-season lab call
  – Contact Erin Murray (Erin.Murray@cdph.ca.gov) to receive the sample size goals for your lab/jurisdiction
Influenza Testing Summary
2013-14 Respiratory Season

RLN

- Total samples tested: 11,464
- Total Flu positives: 4,847 (42.3%)

VRDL

<table>
<thead>
<tr>
<th>Type (Total #)</th>
<th>Sub type</th>
<th>Number Characterized</th>
<th>CDC Strain typing Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flu A (112)</td>
<td>2009 A/H1N1</td>
<td>52</td>
<td>A/California/07/2009-like(H1N1)*</td>
</tr>
<tr>
<td></td>
<td>A/H3</td>
<td>60</td>
<td>A/Texas/50/2012-like(H3N2)*</td>
</tr>
<tr>
<td>Flu B (63)</td>
<td>--</td>
<td>52</td>
<td>B/Brisbane/60/2008-Like**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(Victoria lineage)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>11</td>
<td>B/Massachusetts/02/2012-like**</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(Yamagata lineage)</td>
</tr>
</tbody>
</table>

* Matches Northern Hemisphere 2013-14 Influenza vaccine component
** B/Massachusetts/02/2012-like strain was included in the trivalent and quadrivalent 2013–2014 vaccine for the Northern Hemisphere while the B/Brisbane/60/2008-like was included in the quadrivalent vaccine formulation

<table>
<thead>
<tr>
<th>Virus</th>
<th>Resistance to Neuraminidase Inhibitors</th>
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<tbody>
<tr>
<td>Influenza 2009AH1</td>
<td>3/89*</td>
</tr>
<tr>
<td>Influenza AH3</td>
<td>0/60</td>
</tr>
<tr>
<td>Influenza B</td>
<td>0/63</td>
</tr>
</tbody>
</table>

* One additional resistant strain was found as result of enhanced AVR surveillance
Norovirus Laboratory Network (NLN)
26 local health labs and VRDL

VRDL Provides NLN:
• Reagents
• Technical support
• Phylogenetic characterization of Norovirus positive OBs


Number of Outbreaks

Majority of outbreaks continue to come from LTCF (76%)

<table>
<thead>
<tr>
<th>Month</th>
<th>Total Outbreaks</th>
<th>Positive Outbreaks</th>
<th>Total Specimens</th>
<th>Positive Specimens</th>
<th>GI OB</th>
<th>GII OB</th>
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<tbody>
<tr>
<td>October</td>
<td>14</td>
<td>7</td>
<td>63</td>
<td>20</td>
<td>1</td>
<td>6</td>
</tr>
<tr>
<td>November</td>
<td>25</td>
<td>9</td>
<td>114</td>
<td>41</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>December</td>
<td>33</td>
<td>27</td>
<td>165</td>
<td>106</td>
<td>0</td>
<td>27</td>
</tr>
<tr>
<td>January</td>
<td>69</td>
<td>56</td>
<td>309</td>
<td>193</td>
<td>1</td>
<td>55</td>
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<tr>
<td>February</td>
<td>36</td>
<td>28</td>
<td>173</td>
<td>103</td>
<td>2</td>
<td>26</td>
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<tr>
<td>March</td>
<td>20</td>
<td>15</td>
<td>123</td>
<td>52</td>
<td>0</td>
<td>15</td>
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<tr>
<td>April</td>
<td>12</td>
<td>9</td>
<td>87</td>
<td>29</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>May</td>
<td>24</td>
<td>15</td>
<td>111</td>
<td>58</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>233</td>
<td>166</td>
<td>1145</td>
<td>602</td>
<td>9</td>
<td>157</td>
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</table>
# Gastroenteric Diseases Tested at VRDL

<table>
<thead>
<tr>
<th>Agent</th>
<th>Isolation</th>
<th>NAAT^</th>
<th>Genotyping</th>
<th>Serotyping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Norovirus</td>
<td>-</td>
<td>√</td>
<td>√</td>
<td>-</td>
</tr>
<tr>
<td>Rotavirus</td>
<td>-</td>
<td>√</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Astrovirus</td>
<td>-</td>
<td>√</td>
<td>√</td>
<td>-</td>
</tr>
<tr>
<td>Sapovirus</td>
<td>-</td>
<td>√</td>
<td>√</td>
<td>-</td>
</tr>
<tr>
<td>Adenovirus</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Enterovirus</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>-</td>
</tr>
</tbody>
</table>

^ real time PCR
As of October 9, 2014, VRDL has identified enterovirus D68 (EV-D68) infection in a total of 32 patients in the 2014 outbreak. The number is subjected to update.
Vaccine Preventable Diseases and Herpesviruses Section (VPDH)

Section Staff:

- Section Chief: Jill Hacker
- PHM Supervisor: Chris Preas
- Research Scientist: Alex Espinosa
- PHM Specialist: Natasha Espinosa
- Public Health Microbiologists:
  - Regina Chase
  - Giorgio Cosentino
  - Ashraf Fadol
  - Carlos Gonzalez
  - Abiy Tadesse
  - Gordon Shell
- Research Associate: Oliver Oyler
- Senior Lab Assistants:
  - Yao Tsing Chao
  - Denise Dyer

Activities:

- **Molecular: PCR & Sequencing**
  - Measles, Mumps, Rubella, Herpesviruses, *Rickettsia* (Spotted Fever & Typhus)

- **Serology: EIA format**
  - MMR, Herpesviruses, Arboviruses, Adenovirus, Influenza, *Mycoplasma pneumoniae*

- **LRN testing:** Orthopox & Q fever
- **Core Cell Culture**
<table>
<thead>
<tr>
<th>Method</th>
<th>Tests</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PCR</strong></td>
<td>Measles, Mumps, Rubella</td>
</tr>
<tr>
<td></td>
<td>Herpesviruses (HSV, CMV, EBV, HHV6, VZV-vaccine/wt)</td>
</tr>
<tr>
<td></td>
<td>Spotted Fever Group <em>Rickettsia</em></td>
</tr>
<tr>
<td><strong>Genotyping</strong></td>
<td>Measles, Mumps, Rubella, VZV</td>
</tr>
<tr>
<td></td>
<td>Spotted Fever Group <em>Rickettsia</em></td>
</tr>
<tr>
<td><strong>Serology</strong></td>
<td>MMR</td>
</tr>
<tr>
<td></td>
<td>Herpesviruses (HSV, VZV)</td>
</tr>
<tr>
<td></td>
<td>Arboviruses (WNV, Dengue, WEE)</td>
</tr>
<tr>
<td></td>
<td><em>Mycoplasma pneumoniae</em></td>
</tr>
<tr>
<td></td>
<td>Adenovirus</td>
</tr>
</tbody>
</table>

*CDPH Public Health*
Measles, Mumps, Rubella & VZV

• Available Tests
  – Real-time RT-PCR
  – Serology (EIA)
  – Genotyping: Tracking strains and outbreaks, identifying vaccination-related cases

• Viral VPD Reference Center
  – CDPH VRDL and MN, NY, and WI Departments of Health
  – Measles IgM with CDC-approved kits temporarily suspended; VRDL continues to provide in-house EIA and IFA
  – Results reported by HL7 message to CDC
  – APHL-enrolled PHLs provided with free shipping to CDPH
  – Contact VRDL or APHL if interested in enrolling
VPDH: What’s new

• New diagnostic tests on-line:
  – Dengue IgM EIA (InBios) for serum
  – WNV IgM EIA (Focus) now also for CSF

• Surveillance/in development:
  – Real-time PCR for *Rickettsia* for testing humans and ticks/fleas
    • *R. rickettsii*
    • *Rickettsia* species
    • *R. felis/R. typhi*
  – IgM EIAs for 3 historically endemic arboviruses
    • Western equine encephalitis
    • St. Louis encephalitis
    • Jamestown Canyon (California serogroup/Bunyavirus)
MeaslesNet

• Local PHLs performing real-time PCR for measles with CDC protocol
  – Provides local, rapid diagnosis and surge capacity
  – Proved vital during recent measles resurgence
  – Reagents available from VRDL: primers, probes, controls

• Contact Alex Espinosa for reagents and technical help
  – Alex.espinosa@cdph.ca.gov
Zoonotic and Vector-borne Diseases (ZVBD) Section

The dedicated staff of ZVBD:

• Sharon Messenger – Section Chief
• Peter Patiris – PHM Supervisor
• Cindi Cossen – former PHM Supervisor
• Barryett Enge – PHM II
• PJ Gonzales – Lab Tech
• Kristina Hsieh – PHM II
• Maria Liu – PHM II
• Larry Penning – PHM Specialist
• Pat Stoll – PHM II
• Maria Vu – PHM II
• Wanda Wong – PHM II
• Shigeo Yagi – Research Scientist

The focus of the ZVBD Section is:

• Arthropod-borne viral and rickettsial diseases
• Rabies
• Hantavirus
• Poxviruses
• Q Fever
WNV & other Arboviruses

- WNV 2014 – Exceptionally busy season
- Heightened concerns about exotic arboviruses
  - Dengue
  - Chikungunya
  - Zika
  - Others
- Expanded capabilities are being developed through collaborations across VRDL sections (Table next slide)
  - New test development in ZVBD:
    - Dengue RT-PCR – validated
    - Chikungunya IFA – validated
    - Chikungunya RT-PCR – in validation
    - WNV RT-PCR for serum samples – under evaluation
# Arbovirus testing at VRDL

<table>
<thead>
<tr>
<th>Genus</th>
<th>Virus</th>
<th>RT-PCR</th>
<th>Serology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>IgM*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>X</td>
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<td></td>
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<td>X</td>
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<td></td>
<td></td>
<td></td>
<td>IP</td>
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<td>Flavivirus</td>
<td>WNV</td>
<td>X</td>
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<tr>
<td></td>
<td>Dengue</td>
<td>X</td>
<td>X</td>
</tr>
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<td>St Louis Encephalitis</td>
<td>IP</td>
<td>X</td>
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<tr>
<td></td>
<td>Zika</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Japanese Encephalitis</td>
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<td></td>
<td>Yellow Fever</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Western Equine Encephalitis</td>
<td>X</td>
<td>X</td>
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<tr>
<td></td>
<td>Chikungunya</td>
<td>IP</td>
<td>X</td>
</tr>
<tr>
<td>Alphavirus</td>
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<tr>
<td></td>
<td>Jamestown Canyon</td>
<td>IP</td>
<td></td>
</tr>
<tr>
<td></td>
<td>CA encephalitis</td>
<td>IP</td>
<td></td>
</tr>
</tbody>
</table>

* IFA and/or EIA; IP = in progress

VRDL Guidelines to Laboratory Services:
[http://www.cdph.ca.gov/programs/vrdl/Pages/default.aspx](http://www.cdph.ca.gov/programs/vrdl/Pages/default.aspx)
Rickettsial Diseases Diagnostic testing*

• Current testing:
  – IFA panel (IgM & IgG): *Rickettsia rickettsii, R. typhi, Anaplasma phagocytophilum, Ehrlichia chaffeensis, Coxiella burnetti*

• Expanded Testing:
  – *Anaplasma* real-time PCR validation nearly complete
  – *Ehrlichia* real-time PCR to be evaluated
  – Other tick-borne diseases:
    • Colorado tick fever real-time PCR under evaluation
    • Powassan (Deer tick) virus real-time PCR under evaluation

*Additional diagnostic tests developed in Dr. Hacker’s Section*
Rabies

- **Current Capabilities:**
  - **Animal Testing:**
    - DFA (following National Standard Protocol)
    - RT-PCR for strain typing of positive specimens
  - **Ante-mortem human rabies suspect cases:**
    - DFA – nuchal biopsy, corneal impression
    - IFA – serum, CSF
    - RT-PCR – saliva, nuchal biopsy
    - RFFIT – serum, CSF
  - RFFIT to assess response to vaccination (for public health labs)

- Enhanced surveillance efforts:
  - Bat identification
  - Rabies virus strain typing

- CDPH/CDC/NLTN National Lab Training – targeting Spring 2015
How many local Public Health Laboratories have an interest in sending a PHM for rabies training in Spring 2015??
Other Zoonotic Diseases

Hantaviruses

• Current capabilities:
  – EIA (IgM & IgG) to Sin Nombre Virus
    • Can test both humans and rodent species
  – RT-PCR & sequencing under evaluation (i.e., molecular epidemiology)

Poxviruses

• Current capabilities:
  – IFA for parapoxviruses
  – DFA for Vaccinia

• Proposed Enhancements:
  – Parapoxviruses (Orf, BPSV) real-time PCR under evaluation
  – General orthopoxvirus real-time PCR under evaluation
Retrovirus Disease Section

• Dr. Carl Hanson, Section Chief:
  510-307-8540
• Peter Patiris, Acting Supervisor:
  510-307-8927 (lab)

PH microbiologists: Leo Oceguera, Dolapo Afolayan, Theresa Brown, Anna Wong, Mi-Khin Soe

Other scientists: Dr. Mary Kate Morris,
Dr. Dunnie Dixon, Robert Chiles
Retrovirus Disease Section

– HIV-1 & HIV-2 confirmatory serology
– HIV rapid tests & oral fluid tests
– HIV serosurveillance (“STARHS”)
– HTLV confirmatory serology
– Retrovirus & arbovirus assay development

Other:
– Flavivirus confirmatory serology (PRNT, W. blot)
– BioWatch Laboratory
– Encephalitis related diagnostic support
PRNT:
- West Nile virus
- Dengue virus
- St. Louis encephalitis
- Zika virus

- **Alphaviruses:**
  (Chikungunya, Western equine encephalitis)

Western blot (in progress)

→

- need for positive controls and PT samples
BioWatch laboratory

• San Francisco / San Jose jurisdictions
• VRDL: 2003 to present (staff of 5)
• Detect aerosolized agents 365 days/year
• Partner with LRN, CDC, EPA, FBI, LLNL, & city/county P H departments
Acknowledgement

Section Contributors
David Cottam, PHM
Debra Wadford, PhD, PHM
Jill Hacker, MPH, PhD
Sharon Messenger, PhD
Carl Hanson, PhD

All VRDL staff