Laboratory Missions for the MDL High Risk Pathogens Section

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California Department of Public Health
Richmond, CA
• MDL Director: Vishnu Chaturvedi, Ph.D.
• Web Address:  http://www.cdph.ca.gov/programs/mdl
• MDL is the state reference microbiology laboratory. One of the lab tasks is, providing tests on identification and characterization of high-consequence microbial agents and toxins referred by local public health labs and clinical labs throughout state.
• High Risk Pathogens Section includes:
  - Vaccine Preventable Pathogens (VPP) Unit
  - Tier 1 Select Agents and LRN Unit
# Vaccine Preventable Diseases

- Diphtheria
- *Haemophilus influenzae* type b (Hib)
- Hepatitis A
- Hepatitis B
- Herpes zoster (shingles)
- Human papillomavirus (HPV)
- Influenza
- Measles
- Meningococcal disease
- Mumps
- Pertussis
- Pneumococcal disease
- Polio
- Rotavirus
- Rubella
- Tetanus
- Varicella (chickenpox)
VPP Unit Test Program

- Dr. Jennifer Kyle (lead); Microbiologist(s) to be assigned
- Identify isolates of *B. pertussis, C. diptheriae, H. influenzae, N. meningitidis*, and *S. pneumoniae* using culturing and serology agglutination methods
- Identify following bacterial DNA using RT-PCR methods on culture-negative clinical specimens
  - *B. pertussis* (from nasopharyngeal swabs)
  - *N. meningitides, S. pneumoniae, and H. influenzae* (from blood and CSF)
  - *N. meningitides* (capsular genogrouping)
Diseases Caused by *H. influenzae*, *N. meningitidis*, *S. pneumoniae*
VPP Testing Workload Summary (1)
- Bacterial Isolate ID and Serogrouping/typing

![Bar chart showing isolate numbers for B. pertussis, H. influenzae, N. meningitidis, and S. pneumoniae from 2010 to 2014.](chart.jpg)
VPP Testing Workload Summary (2)
- Clinical Specimen PCR Tests

![Graph showing specimen numbers for meningitis and pertussis by year from 2010 to 2014. The x-axis represents the years, and the y-axis represents the specimen number. The graph indicates a significant increase in meningitis cases in 2014, with fewer cases in other years. Pertussis cases are minimal throughout the years.]
Further Typing on California \textit{N. meningitidis} isolates sent to CDC

\textit{Multilocus Sequence Typing (MLST)}

- Sequence differences between strains
- Query MLST database via the internet
- Global Epidemiology Tool – clonal clusters
- >7,000 Sequence Types (ST) in Database
- \textit{porA, nhbA, nadA, and fHbp} (lately on B serogroup)

\textit{Pulse Field Gel Electrophoresis (PFGE)}

- Differences in restriction enzyme digestion patterns
- Gold Standard for outbreak investigations
## Major Cause of Meningitis

<table>
<thead>
<tr>
<th>Bacterial</th>
<th>Viral</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>H. influenzae</em></td>
<td>- Arboviral (mosquito-borne)</td>
</tr>
<tr>
<td><em>N. meningitidis</em></td>
<td>- Influenza</td>
</tr>
<tr>
<td><em>S. pneumoniae</em></td>
<td>- LaCrosse Encephalitis virus</td>
</tr>
<tr>
<td>Listeria</td>
<td>- West Nile Virus</td>
</tr>
<tr>
<td>Group A Streptococcus</td>
<td>- Mumps</td>
</tr>
<tr>
<td>Group B Streptococcus</td>
<td>- others</td>
</tr>
<tr>
<td>others</td>
<td></td>
</tr>
</tbody>
</table>

Future task: developing rapid methods to detect multiple targets on blood and CSF
High Incidence of Pertussis

**MMWR**

**Pertussis Epidemic — California, 2014**

Kathleen Winter, MPH¹, Carol Glaser, MD, DVM¹, James Watt, MD², Kathleen Harriman, PhD¹ (Author affiliations at end of text)

On June 13, 2014, the California Department of Public Health (CDPH) declared that a pertussis epidemic was occurring in the state when reported incidence was more than five times above the expected rate.

<table>
<thead>
<tr>
<th>TABLE 1. Number and rate of pertussis cases among infants aged &lt;12 months, by race/ethnicity — California, 2014*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Race/Ethnicity</td>
</tr>
<tr>
<td>----------------</td>
</tr>
<tr>
<td>Asian</td>
</tr>
<tr>
<td>White</td>
</tr>
<tr>
<td>Black</td>
</tr>
</tbody>
</table>

**Potential Cause**

- Increased Awareness & Detection
- Vaccine Failure
- Waning Immunity
- Unvaccinated Population
- Change In Organism

Isolates with Mutations in the Genes Coding for Pertussis Vaccine Antigens

- Genome sequencing
- *B. pertussis* isolates have been found with mutations on vaccine antigen genes: pertactin, filamentous hemagglutinin and, pertussis toxin (Bouchez et al, 2015: Vaccine 3:751)
- Our future possible project: to genetically characterize California isolates via genome sequencing to understand the nature of this epidemic.
These agents are now designated as Tier-1 biological select agents, and toxins (BSAT), potentially presenting the greatest harm to the public; and are regulated under federal laws 49 CFR Part 73, 7 CFR Part 331, and 9 CFR Part 121.
Tier 1 Select Agents Lab

The new classification established stricter requirements on the personnel with access to those agents with emphasis on risk assessment, training, security, biosafety and incident response.

Majority of the public health labs nationwide are now non-Tier 1 labs. They have still the same capacity to test for select agents and toxins; but are unable to keep the Tier 1 agents for long term storage, and will have to either destroy or transfer their stocks to Tier 1 Lab within a 7 day period.

MDL is now the only Tier 1 select agents lab in California.
Major Tier 1 Lab Regulations

- Suitability Assessments
- Pre-Access Suitability Assessment
- On-going Suitability Assessment
- Designed to reduce the risk of select agents or toxins through “insider” actions/threats
Tier-1 Select Agents Lab

- RO: Paul Kimsey, Ph.D.
- ARO: Mahtab Shahkarami, M.Sc
- PI: Fengfeng Xu, Ph.D.
  (Ph: 5104121470; Cell: 5105174844)
- Back-up PI (application submitted to CDC)
- Select Agents Lab phone: 5106205926
- Microbiologists: Yismashoa Gebremichael and others
- MDL Director and other staff (back-up)
MDL Select Agent Unit Function

1. External BT Training (e.g., first responders)
2. Reference Lab contact database setup
3. Bay area biowatch program
### Select Agent Work Summary (1)
- number of BT isolate rule-out

<table>
<thead>
<tr>
<th>Samples</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>B. anthracis</td>
<td>9</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Brucella sps.</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>B. pseudomallei</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>F. tularensis</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Y. pestis</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>C. botulinum</td>
<td></td>
<td></td>
<td>1</td>
</tr>
</tbody>
</table>
Select Agent Work Summary (2)
- number of BT specimen characterization

<table>
<thead>
<tr>
<th>Samples</th>
<th>2012</th>
<th>2013</th>
<th>2014</th>
</tr>
</thead>
<tbody>
<tr>
<td>Botulinum toxin specimen</td>
<td>144</td>
<td>121</td>
<td>150</td>
</tr>
<tr>
<td>Brucella extract - PCR</td>
<td>20</td>
<td>12</td>
<td>7</td>
</tr>
<tr>
<td>BT specimen (clinical &amp; law enforcement)</td>
<td>12</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>Carcass (Y. pestis &amp; F. tularensis)</td>
<td>14</td>
<td>11</td>
<td>16</td>
</tr>
<tr>
<td>Flea pool (Y. pestis detection)</td>
<td>17</td>
<td>23</td>
<td>0</td>
</tr>
<tr>
<td>CAP-LPX (PT)</td>
<td>6</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>CDC-LRN (PT)</td>
<td>5</td>
<td>10</td>
<td>5</td>
</tr>
</tbody>
</table>
Identification of Vector-borne Agents

- MDL select agent unit provides support for CDPH Vector Borne Diseases Section plague surveillance each year on California parks
- In the past, using in-house prepared fluorescent antibody conjugates to confirm ID of *Y. pestis* and *F. tularensis*
Identification of *Y. pestis* from animal carcasses collected from Yosemite Park in Year 2015

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**Human Plague — United States, 2015**

Natalie Kava, DVM¹,²; Christina Nelson, MD;³ Kirsten Kugeler, PhD⁴; Jeanine Peterson, PhD⁴; Lydia Plaute, MS⁴; Hayley Yaglou, MPH⁵; Vicki Krames, PhD⁶; Benjamin Schwartz, MD;⁷ Jennifer House, DVM⁸; Leah Colton, PhD⁹; Amanda Feldpausch, MPH¹⁰; Cherie Drenick, DVM¹¹; Joan Basambach, MD¹²; Mark DiMenna, PhD¹³; Emily Fisher, MD¹⁴; Emilio Debes, DVM¹⁵; Danielle Burdke, DVM¹⁶; Matthew Weinburke, MPH¹⁷; Christopher Percy, MD¹⁸; Martin Schriefer, PhD¹⁹; Ken Gage, PhD²⁰; Paul Mead, MD²¹

Since April 1, 2015, a total of 11 cases of human plague have been reported in residents of six states: Arizona (two), California (one), Colorado (four), Georgia (one), New Mexico (two), and Oregon (one). The two cases in Georgia and California residents have been linked to exposures at or near Yosemite National Park in the southern Sierra Nevada Mountains of California. Nine of the 11 patients were male; median age was 52 years (range = 14–79 years). Three patients aged 16, 32, and 79 years died.

... of plague patients, results from aerosol exposure to infective droplets and is characterized by a fulminant primary pneumonia. Secondary pneumonic plague can result from the spread of *Y. pestis* to the lungs in patients with untreated bubonic or septicemic infection.

The mortality rate for untreated plague has ranged from 66% to 93%; however, in the antibiotic era, mortality has been reduced to approximately 16% (4). Prompt treatment with antimicrobials such as aminoglycosides, fluoroquinolones, or...
Summery of Laboratory Missions for the MDL
High Risk Pathogens Section

Provides reference, diagnostic and applied research activities for the detection, epidemiologic investigation, control and prevention of high-risk bacterial pathogens and toxins in humans and environmental sources