Surveillance of Yersinia pestis in Los Angeles County

Program Evaluation Research Proposal

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Surveillance of *Yersinia pestis* in Los Angeles County

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Introduction and Background

The Los Angeles County (LAC) Department of Public Health (DPH) Environmental Health under the Vector borne- and Zoonotic Diseases branch adheres to the LAC-DPH mission statement “To prevent and control communicable disease in Los Angeles County utilizing the tools of surveillance, outbreak response, education, and preparedness” (DPH-ACDC, 2012) in order to focus on its vision to keep the Los Angeles County residents free of preventable communicable diseases such as plague. Plague, a disease caused by *Yersinia pestis*, bacteria that has a remarkable place in history (CDC, 2000), is spread by fleas of rodents to humans and continues to cause outbreaks throughout the world attesting to its tenacious nature. Plague is primarily a disease of rats, prairie dogs, chipmunks, squirrels, rabbits, and other similar rodents. Human cases of plague in Los Angeles County are rare, due to the effectiveness of the existent surveillance program in place. Plague is commonly found in ground squirrels around campgrounds in Tehachapi, Lake Isabella, Frazier Park, and in the Angeles National Forest between Los Angeles and Antelope Valley (DPH-ACDC, 2012). Campers, hikers, residents, and domestic animals such as cats, and dogs in those areas are at risk of being bitten by fleas carried by plague infected rodents. Surveillance, rodent control, vector control, case management, chemoprophylaxis, immunoprophylaxis, and infection control are activities in which long term prevention and control of plague is based (WHO, 2009).

Plague is considered as a re-emerging infectious disease with a world incidence of 2,000 to 3,000 reported cases each year and one of the most devastating weapons of bioterrorism; 50kg of *Yersinia pestis* in an aerosol cloud over a 5 million population city might result in 150,000 cases of pneumonic plague (Inglesby, et.al, 2011). The LAC-DPH communicable disease surveillance and control conduct surveillance on plague, investigate disease outbreaks, recommend control measures, conduct special studies and projects on bioterrorism organisms, produce annual reports, and special analysis and procedures. The department also interprets and enforces state and federal laws and regulations on plague surveillance and is interfaced on reporting and communicating findings with local, state, state, national, and federal agencies, and programs in addition to public education (DPH-ACDC, 2012). Due to the current budget reduction, lack of qualified staff, and program reorganization; many environmental programs are either being reduced in their functions and scope of service or completely eliminated, this program evaluation proposal elucidates the importance of the animal plague surveillance program in the LAC.

This evaluation proposal focuses on the plague surveillance program in Los Angeles County that includes rodent and flea surveillance; mainly ground squirrels in campground sites and rats in downtown L.A. Since plague is primarily a disease of rodents, a natural decline in human plague incidence does not indicate that plague has been eradicated from the area (WHO, 2009), but rather reflects the results of a well-run surveillance program working in conjunction with the Bioterrorism Preparedness and Response Unit Laboratory using PCR technology providing a
rapid turnaround in confirmation of plague ensuring that surveillance data and results are available within hours after the samples are received (Engelthaler, et. al., 2010). The objectives of the plague surveillance program are to detect early warning signals of an outbreak, to institute timely response and appropriate control measures, to assess the impact of the needed intervention, to ensure containment of the outbreak, to identify ecological or human activity factors (WHO, 2009), and to detect a bioterrorism attack in the early stages before it can spread and infect population in large numbers. Sudden changes are taking place in the environment which subsequently affects the ecology of LAC which might create a spillover of sylvatic or wild plague into domestic environments (urban plague); therefore, continuous plague surveillance and vigilance should be maintained as part of epidemic preparedness and an early warning system (WHO, 2009).

Literature Review

_Yersinia pestis_ the etiologic agent of plague is a gram negative bacillus that can survive in cool, moist, areas such as the soil of rodent holes. The organism is susceptible to sunlight and dryness so it can be easily destroyed, but if aerosolized it may survive in the air for up to one hour (Bellazini & Myint, 2006). _Yersinia pestis_ was used in ceramic bombs with plague infested fleas in the Second World War II in China by Japanese forces causing outbreaks. It is a Category A organism in the Select Agent Program and CDC Bioterrorism Agent of Disease list, have been previously weaponized, is easy to disseminate in the air, and it has shown resistant to multiple antibiotics.

Inglesby, et.al (2011) enumerates the factors that contribute to the use of _Y. pestis_ as a biological weapon to be the its widespread availability not only in nature in endemic areas, but in microbe banks worldwide, available techniques in the Internet and other sources for mass production and dissemination, high fatality rate if undetected and untreated timely, able to be spread person to person by respiratory route, low infectious dose, and the existence of antibiotic resistance strains in nature.

The LAC-Acute Communicable Disease Manual (2011) indicate that plague can present clinically as bubonic; lymphadenitis of inguinal and axillary nodes that drain the site of fleabite becoming swollen and may suppurate with fever usually present, septicemic; progression of all forms of plague to disseminate by the bloodstream to all parts of the body, and pneumatic; secondary to bubonic plague resulting in pneumonia and pleural effusion being very contagious. The manual also indicated the incubation period of plague to be from 1-7 days and the specific antibiotics used for treatment to be tetracycline or sulfonamides.
A patient with bubonic plague (inguinal bubo)

According to the Centers for Disease Control and Prevention (CDC, 2000) in the United States, plague is endemic in the western states (New Mexico, California, Colorado, and Texas) where in a period of a twenty year study from 1979 to 1998 human cases averaged 13 per year, with a high of 40 cases in 1983. During this study period case fatality rate was 15%. Thirty percent of cases occurred among Native Americans and none was fatal. Pneumonic plague from respiratory droplets occurred in 11% of the cases of which five of seven persons were known to be exposed to infected domestic cats. In the absence of effective surveillance and prevention, the risk of epidemic plague in the U.S. is high in those areas where co-existing of suburban and rural rodents occurs. Plague cycles naturally in its enzootic host (low morbidity, but constantly present in the animal community) circulating between small mammals and fleas with no human involvement for a period of time. A false sense of plague eradication ensues, public health vigilance diminishes, and conditions are set up for panic when plague resurfaces from its natural cycle. The greatest risk of plague is during epizootic cycle when the mortality of rate for rats is high, causing the fleas of infected rats or rodent to seek for another host including humans.

In the plague manual issued by the World Health Organization (WHO, 2007) it is stated that rapid sub-urbanization has increased the number of people living near or in areas of active plague foci and there is an increased role of domestic cats in human plague. It has also been reported in the 2009 publication of Operational Guidelines for Plague (WHO, 2009) that since 2005 it has been observed an upward trend of human plague with an average incidence of 2,083 cases per year in a global scale. Surveillance defined as the continuous collection of data collection is recommended in the rodent population to assess plague activity by collecting and examining dead rodents and trapping rodents for the purpose to collect population data, serum, tissue samples and flea collection for testing serologically and by other laboratory methods for the detection of Y. pestis antigen. The identification of rodents, which includes mainly Norway rat (R. norvegicus) and Roof rat (R. rattus) in downtown area of Los Angeles, the calculation of
the flea index in the rat population, and susceptibility to insecticides is important to determine the potential risk for an outbreak.

Galimand, Carnie, and Corvallis, P. (2006) reported the isolation in Madagascar of a multiple drug resistant strains of *Y. pestis* to all the antimicrobial agents recommended for treatment and prophylaxis of plague. The mortality of plague in the absence of adequate treatment is from 40 to 70%, and the outcome of pneumonic plague would be fatal in less than 3 days. The authors of this article demonstrated the horizontal transfer of genes in the flea’s gut which is a great concern if such strain is used in a biological attack using the flea vector. The importance of surveillance and the study of *Y. pestis* antibiotic resistance are recommended according to the authors to become worldwide.

In another study conducted by Auerbach, et al., (2007) it was found that because *Y. pestis* was first introduced to the Western U.S. just over 100 years, there has been little time for genetic diversity to accumulate. The authors’ study based on single nucleotide polymorphisms have begun to quantify the genetic diversity of *Y. pestis* strains in North America and the sequence of genetic events providing a greater understanding in the evolutionary history of this microbe responsible for three devastating pandemics throughout history of human population. The result of the author’s studies and other recent findings in the *Y. pestis* phylogeny has resulted in the development of new nomenclature based on molecular testing leading to new biovar designations.

Aims and Specific Objectives

The continuation of a comprehensive plague surveillance program in Los Angeles County under the DPH collaborative with the CDC and other local, state, and federal stakeholder’s primary aim is to actively participate in epidemiological and environmental investigations to assess and identify plague risks in the community and follow up with prevention, control, and education. The specific objectives of this plague surveillance evaluation are: demonstrate by December 2012 to DPH’s budget administrators the need of LAC community to continue a collaborative animal-based surveillance program that appropriate preventive measures before an outbreak occur. A second objective is to present to the scientific community and stakeholders by December 31, 2013 the five year compiled laboratory data analysis and results of the case studies examination as evidence that confirms the effectiveness of the program to maintain plague incidence low or almost non-existent. A logic model will be constructed that lay out the goals, objectives, and activities. LAC-DPH animal surveillance program rely on surveillance data generated through serosurvey of rodents and rodents consuming carnivores, analysis of fleas or tissue obtained from routinely trapped, animals or carcasses laboratory testing for the presence of *Yersinia pestis* F1 antigen, and visual monitoring of activity level in colonies of diurnal, plague susceptible rodents (CDC, 2005). The compiled
data in the five year (2008-2012) study will be analyzed and recommendations made to all the parties involved in the plague surveillance program by June 2013. These objectives are specific, measurable, achievable, realistic, and timed (Issel, 2009).

Study Design

The design for the evaluation of the plague animal surveillance program would be one that is free of bias. An ideal design would be one that possesses these three salient characteristics: compares case studies control community or area with similar population and ecology characteristics as LAC where no plague surveillance program exist, measures the outcome variables before and after a period of plague surveillance, and have minimal threats to internal and external validity (Issel, 2009). Such information would not be available or feasible, but alternatively valid data would be provided by examining relevant plague case studies and DPH available laboratory data collected for a period of five years. This retrospective design entails gathering data from 2008 to 2013, case studies analysis, and analyzing the available data from the California plague reports. The sampling method and study population consist of gathering the total number and results of serosurvey samples from different sources such as squirrel’s sera from LAC campgrounds, downtown rats, port of entry to LAC from overseas, and other wild animals such as foxes, raccoons, and other wild animals, human samples suspicious of plague, and culture of animal, human, or environmental samples that the plague surveillance program have submitted to the Public Health Laboratory (PHL) Bioterrorism Response Unit (BTRU) test for the presence of *Yersinia pestis* F1 antigen. This evaluation design would allow for documentation of the effect of the program in terms or reaching the stated outcome and objectives. This design is inexpensive and allows post-test data to be compared to the stated outcome and impact objective targets, implement plague prevention programs (CDC, 2005), and discovery of any existing deficiencies of the LAC-DPH human and animal-based plague surveillance system already in place to be corrected and recommendations to be made for LAC plague surveillance program implementation.

Methods

Qualitative data and quantitative data will be used for this program evaluation.

1. Case studies: to fully understand or depict he effectiveness or lack of plague surveillance programs and conduct comprehensive examination through cross comparison of cases (McNamara, 1999). Two of the various local and national available cases that will be examined for this program evaluation are:
• A Case of Plague in Urban Los Angeles (LAC-ACDP, 2006) in which a human plague case was likely caused by handling the carcass of an infected wild rabbit in a plague epizootic area. Case and contact interviews were used with standardized questionnaires which provided the needed information to reveal the risk factors involved in this case of plague in a non-endemic area. LAC- PHl confirmed the isolate recovered from the patient blood as being indeed \textit{Yersinia pestis} by direct fluorescent antibody (DFA), polymerase chain reaction (PCR), and phage lysis. Sera from wild animals the patient’s family had been associated with in the area such as rabbits and deer mice were also tested using the Hemagglutinin - Hemagglutinin inhibition assay (HA/HI), and the CDC tested the rabbit carcasses. This case analysis would ascertain the importance of a well budgeted, managed, and proper staffed plague surveillance program and the need of public education regarding risk of plague in endemic areas.

• Human Plague--- Four States, 2006 (CDC-MMWR, 2006). In this report the CDC illustrates the increased incidence of plague that occurred in 2006. A total of 13 human plague cases were reported in 2006 from residents of four states: New Mexico (seven cases), Colorado (three cases), California (two cases), and Texas (one case). The reports describes a short summary of six of the cases in different states and highlights the severity and diverse clinical plague presentation as well as the need for animal surveillance and prompt laboratory testing and clinical diagnosis and treatment when plague is suspected. All the six cases discussed in this Morbidity and Mortality Weekly Report (2006) had previous exposure to plague in the peridomestic environment (free roaming pets, cats and dogs bringing infected rodent fleas into the home), had participated in outdoor rabbit hunting recreational activity, or had not conducted yearly rodent control measures such as rodent proofing of structures, eliminating food sources, or removing rodent harborage (piles of wood, debris, or garbage) regularly in the peridomestic environment.

2. Documentation Review: the overall purpose to use this method would be to formulate an accurate impression of how the surveillance program operates (McNamara, 1999) without interrupting the ongoing surveillance program. Review of Environmental Health reports, finances, communication, memos, meetings, agreements, and recommendation discussed with policy development, administration personnel, and other stakeholders such as the California Department of Public Health (CDPH) will provide comprehensive and historical information with few biases (McNamara, 1999). Three example of document
review in this evaluation will be the California Plague Reports on the state surveillance program on humans, domestic pets, and wild animals:

- California Plague Report, Summer 2010 (CDPH, 2010) illustrates the effectiveness of plague surveillance by the Vector Control Program of the LAC-DPH. The report presents the wild animal surveillance positive plague findings at the Los Alamos campground within Los Angeles National Forest detection of a titer1:32 to *Y. pestis* in one of 20 California ground squirrels sampled. In this case, the LAC-DPH closed the campground to conduct flea suppression and initiated rodent control measures. Flea suppression was conducted on two separate consecutive days and two weeks later a post-treatment evaluation showed the flea load decreased from 21 fleas per rodent to 0.16 fleas per rodent indicating effective control. (Please see attachment 1: a power point presentation regarding this case).

- California Plague Report, Winter 2010 (CDPH, 2010) is another example of the importance to conduct plague surveillance in wild animals. It discusses the results of *Y. pestis* F1 antigen-antibody testing conducted on sera collected from various wild animals such as chipmunks, deermice, woodrats, coyotes, and bobcats including positive titers found in chipmunks and ground squirrels surveyed in the same area.

- California Plague Report, Summer 2011(CDPH, 2011) presents the case of a domestic cat with confirmed bubonic plague and discusses the risk of endemic plague exposure to humans and pets. The report explains how temperature and moisture patterns across the state assist in the maintenance of factor for the flea and rodents increase in numbers and the continuation of natural plague reservoirs, foci, and activity.

3. Laboratory data: in program evaluation experimental and quasi-experimental data must meet four requirements: a) the data on the outcome variable exist before the program is delivered; b) outcome information is collected from at least two groups; c) an intervention takes place and is received by one of the groups; and d) after delivery of the intervention, data are collected from one of the groups as were collected pre-program (Issel, 2009). All of the four requirements when applied to the LAC-DPH plague surveillance program qualify laboratory data for quasi-experimental design. The data in Table 1 even though still in the collection process and missing the number of positive samples in each category, and other variables such as individual campgrounds surveyed, type, and size, and number of representative samples etc., will be used for this evaluation. The serological test used for the detection of antibodies to *Y. pestis* F1 antigen is the
Hemagglutination/ Hemagglutination Inhibition test (HA/HI). A single serum/plasma specimen with a titer $\geq 1:10$ is presumptive for $Y. pestis$. A positive serum specimen in conjunction with the recovered isolate that is DFA or bacteriophage lysis positive confirms $Y. pestis$. Agglutination is dependent on the balance of antigen and antibody present in the sample. False negatives and false positives happen when the balance of either component is not optimal (LAC-PHL-BTRU, 2012).

Cumulative *Yersinia pestis* testing LAC-PHL data (Table 1)

<table>
<thead>
<tr>
<th>Year</th>
<th>Animal Surveillance</th>
<th>Serology human</th>
<th>Culture and PCR</th>
<th>Total performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>344</td>
<td>4</td>
<td>3</td>
<td>351</td>
</tr>
<tr>
<td>2009</td>
<td>306</td>
<td>1</td>
<td>5</td>
<td>312</td>
</tr>
<tr>
<td>2010</td>
<td>215</td>
<td>1</td>
<td>5</td>
<td>221</td>
</tr>
<tr>
<td>2011</td>
<td>287</td>
<td>0</td>
<td>5</td>
<td>292</td>
</tr>
<tr>
<td>2012</td>
<td>Data collection in process</td>
<td>Data collection in process</td>
<td>Data collection in process</td>
<td>Data collection in process</td>
</tr>
</tbody>
</table>

Data Analysis

The analysis of both the qualitative or quantitative data will be performed making every effort to achieve scientific rigor as the basis from which claims can be more solidly and confidently made (Issel, 2009). The qualitative data need to be transformed into a format amenable to manipulation and analysis. Comments are organized into similar categories such as concerns, suggestions, strengths, weaknesses, similar findings, program inputs, recommendation, outputs, and outcome indicators (McNamara, 1999). The qualitative data obtained from case studies analysis and document review will be transcribed accurately into codable units of data that can then be classified as categories and subcategories for analysis by qualitative data software such as ATLAS-ti, NUD®IST or the CDC’s AnSWR software system. To assist in determining the codable units and categories to analyze, the Michael Quinn Patton’s Qualitative Evaluation Checklist posted at the Western Michigan University Evaluation Center’s website (http://www.wmich.edu/evalctr/checklist/qec/Index.htm) can be used (Issel, 2009). The quantitative data sets obtained from the evaluation will be placed in spreadsheets and statistically
analyzed by readily available Microsoft Office software packages, or commercially available statistical software programs such as SPSS, Stata, or SAS or the free statistical shareware EpiInfo by CDC. The types of analysis that will be performed include descriptive statistical analysis, frequency distribution, variance, comparison between groups of nominal data by using the chi-square test, association, and prediction statistical analysis (Issel, 2009).

The data in Table 1 was quickly and conveniently analyzed by the Microsoft Office software package as shown below in Table 2:

Yersinia pestis laboratory data (Table 2)

<table>
<thead>
<tr>
<th>Year</th>
<th>Animal Surveillance</th>
<th>Serology human</th>
<th>Humans culture and PCR</th>
<th>Total performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>344</td>
<td>4</td>
<td>3</td>
<td>351</td>
</tr>
<tr>
<td>2009</td>
<td>306</td>
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<td>312</td>
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<tr>
<td>2010</td>
<td>215</td>
<td>0</td>
<td>5</td>
<td>221</td>
</tr>
<tr>
<td>2011</td>
<td>287</td>
<td>0</td>
<td>5</td>
<td>292</td>
</tr>
<tr>
<td>Total</td>
<td>1152</td>
<td>6</td>
<td>18</td>
<td>1176</td>
</tr>
<tr>
<td>Average</td>
<td>288</td>
<td>3.9</td>
<td>3</td>
<td>294</td>
</tr>
</tbody>
</table>

Std. Dev 46.87749993  1.5  0.866025404  47.18580295
Anticipated Implications of the Study for Policy and Practices

The anticipated implication of the evaluation study will be provision of an additional tool to conceptual approach to the use of the data collected for five years from 2008 to 2012 by the LAC-DPH as part of the quality improvement process of the plague surveillance program in keeping the program active and properly staffed to carry the mission and vision of LAC-DPH “To Protect health, prevent disease, and promote health and well-being of the Angelinos” (LAC-DPH, 2012). According to Novick, Morris and Mays, (2008) evaluation is useful to:

- Judge the effectiveness of public health programs.
- Assess how the intervention is being implemented.
- Ensure accountability of contractors and other entities with responsibilities to the public health agency.
- Demonstrate accountability of internal programs to funders or higher authority.

Ethical Considerations

The ethical consideration of the evaluation and the communication of the findings of the LAC-DPH plague surveillance program evaluation helps ensure that the planning and evaluation be carried demonstrating a high degree of responsibility, accuracy, and clarity presenting the data, reporting, maintaining contacts, and the quality of the evaluation (Issel, 2009). The evaluation report must be used to identify the stakeholders interests, goal, and concerns; power and reputation in the community (Novick, Morris and Mays, 2008). An ethical issue would be the need to obtain Institutional Review Board approval and informed consent if using any human plague case studies data and epidemiological findings and serum specimens which must also comply with the Health Insurance Portability and Accountability Act (HIPAA). According to Issel (2009) if the evaluation will be used for internal managerial issues of budget and staff issues in the program implementation, and not to generate knowledge, then the evaluation is not research and informed consent is not required.

Anticipated Constraints

The main constrain in the plague surveillance program evaluation is cost. An economic analysis of the program in the current financial and economic state of the LAC-DPH budgeting of public health programs and reduction of qualified staff may answer questions regarding whether the benefits of conducting this program evaluation are worthwhile to the community.
Plague surveillance is an essential environmental health programs which ensures protection of the community from a plague outbreak, prevent panic by education on how to prevent infected flea biting, and provides effective response and preparedness in the case of a covert bioterrorism attack.

Work Plan and Timetable

The objectives of the evaluation plan pre-determined some of the activities of the work plan and timetable of the evaluation collection of data, evaluation, analysis, and reporting. At the end of 2012; to be exact by December 31, 2012, the data for the five year (2008-2012) study will be available for analysis, and a year later by December 31, 2013 those findings both negative and positive recommendation on the program will be presented to the stakeholders. During the following six month following approval of this proposal and by June 2013 case studies examination, comparisons, and analysis of both qualitative and quantitative will be performed to be a able to obtain the data analysis by the end of August 2013 and begin the recommendation plan to be presented during the rest of the year to the program administrators and other stakeholders.

Conclusions

Even though plague is a disease of rodents it can be transmitted to humans. Those who either reside in areas of higher risk plague incidence in the rodents and wild type animals, or who practice outdoor activities like rabbit hunting are at higher risk of being bitten by an infected flea. Historically plague have devastated entire communities and cities and caused massive mortality and morbidity. Surveillance of domestic and wild animals provides the means to monitor plague activity that could potentially spill over into urban areas of LAC, and may detect a bioterrorism attack in the early stages before it can affect thousand or even millions of Angelinos and neighboring communities. The need for a well-designed, budgeted, and managed wildlife plague surveillance program is critical to both understand better the dynamic of plague in a changing ecological environment and prevent a possible outbreak in the near future.
References


Los Angeles County Public Health Laboratory Bioterrorism Response Unit (2012). Data personally collected by P. Bolivar.


This report contains 15 pages.
SURVEILLANCE OF YERSINIA PESTIS IN LOS ANGELES