ANALYSIS OF THE 2018 LANE COUNTY PERTUSSIS OUTBREAK AND THE SUBSEQUENT PUBLIC HEALTH RESPONSE

By

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This thesis serves as an analysis of the public health response to the 2018 Lane County pertussis outbreak. It considers the magnitude of the outbreak, (a record number of 183 confirmed cases as of October 7, 2018), and explores the links between the impact of the disease on the community and efforts by the Lane County Communicable Disease Department to control it. This thesis combines quantitative statistical analysis with qualitative content analysis to provide a timeline for the disease outbreak in addition to the generation and analysis of epidemiological curves. This thesis will examine the response protocol initiated by the Lane County Communicable Disease Department and discuss the both the strengths and potential limitations of the response. Additionally, the results of the analysis will discuss the preventative methods used by the Lane County Public Health Department, as well other methods employed globally. The significance of this particular research project lies in the cyclical nature of pertussis: outbreaks are recurring and seemingly inevitable. Thus, having a clear understanding of this outbreak and the public health response has the potential to help the Lane County community be more prepared for future pertussis epidemics.

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Introduction

I studied abroad in Peru the summer before my junior year of high school and was fascinated by the public health system. I had always been interested in travel and global issues but found a niche in public health. My junior year of college I had the opportunity to join a global health research group, which was a forum to discuss and learn about interdisciplinary research with topics focusing on infectious disease, global health (with concentrations in Africa), and the history of modern disease. I was then lucky enough to connect with Dr. Patrick Luedtke, the senior health officer at Lane County Public Health, who offered me an internship doing data analysis for the pertussis outbreak that persisted through the spring and summer of 2018. I was interested for a few reasons. Primarily, it was an opportunity to discover firsthand how the public health system works. For years I had been saying that I was interested in public and global health, but in reality, I did not yet know what that field included. Additionally, disease outbreaks do not happen every day, and to track one firsthand would be a unique experience, especially with a disease like pertussis that I did not know much about.

I interned at Lane County Public Health (LCPH) from June through October of 2018. Through the summer, I spent approximately 15 hours a week at LCPH. I was stationed in the communicable disease department and my primary responsibility was to perform data analysis on the case reports that were coming in and look for trends in the outbreak like who seemed to be most vulnerable, or what schools were affected the most. Additionally, I completed side projects that included creating information flyers to be sent home to parents from the schools about pertussis prevention strategies. The communicable disease department was comprised of one supervisor and four public health nurses. The nurses kept track of all reported pertussis cases in an online database called ORPHEUS (Oregon Public Health Epidemiologists User System) which is a system intended for local and state public health epidemiologists and disease investigators to have access to and manage all communicable disease reports. They received reports from a variety of sources and followed up on each reported case through interviews to record necessary information such as classification of symptoms, age, place of contraction, and vaccine status. This was important not just for the wellbeing of the patient, but also helpful in determining who else in the community may have been exposed.

This project did not require the approval of the institutional review board (IRB) given that it did not meet the federal definition of research as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge" (UO IRB). Instead, the primary goal of this project was internal monitoring and evaluation for LCPH. Throughout my internship, I researched the epidemiological nature of pertussis, and its previous effects on Lane County and other areas within the U.S. A lot of that information came from the Centers for Disease Control website, but also from public health articles suggested by Dr. Luedtke. This thesis relies on data like the age, place of school/work, date of symptom onset, vaccination status, and pertussis case classification (presumptive/suspect/confirmed) for each reported case that was compiled in an excel spreadsheet that I had access to. I did not have access to the ORPHEUS database, so all of my data analysis was done based on the data in this excel spreadsheet, which was updated semi-regularly by the communicable disease nurses. I analyzed the data in the excel spreadsheet, looking for trends in relation to where the outbreak began, the most vulnerable populations, how vaccine status affected one's vulnerability pertussis, and the effect of the public health response. All of these questions are significant in understanding pertussis outbreaks in general and understanding them in the context of Lane County can help the community control them more effectively in the future.

There were 183 confirmed cases of pertussis (266 including suspect and presumptive cases) reported between March 29 and October 7 of 2018. There was a clear peak in cases in early May and into early June, with a nearly steady decline after. The age of those affected ranged from 4 weeks to 72 years old, but 96 of the 183 cases (52%) affected people between 11 and 18 years old. Of the confirmed cases, 76% were fully vaccinated, 6% were partially vaccinated, and 18% had no vaccination history for pertussis. There were no fatalities during the outbreak.

These basic numbers highlight a few clear themes defining this epidemic. One of the most interesting pieces of data is that 76% of infected people had been fully vaccinated. This surprising fact is partially explained by the low overall efficacy for this vaccine, which is estimated to be between 80% and 90%, according to the CDC. The unreliability of the vaccine also contributed to significant public hesitancy. If the vaccine is not seeming to prevent kids from getting the disease, parents (especially those who are wary about vaccines in general) are not enthusiastic about it. While DTaP is not completely preventing pertussis, the vaccine does lessen the symptoms and side effects of the disease. Ultimately, the position of the CDC and Lane County Public Health is that vaccines are the best science available and should be highly encouraged for everyone. The outbreak began in a high school, and affected primarily that age group, as the majority of the cases were in youths aged 11-16. The high rates of vaccinated persons affected by pertussis suggests that serious work needs to be done by pharmaceutical companies and the government dedicated to improving the lasting effects of the vaccine, or perhaps federal agencies like the CDC recommending the addition of another of shots to protect people in their later teens. This would have to be combined with public health efforts to convince communities to vaccinate.

Background

Early descriptions of Pertussis, the colloquially known as whooping cough, date back to the Middle Ages (Kuchar, 2016). Described with fits and paroxysms, Pertussis is an extremely contagious respiratory disease that comes from the bacteria *Bordetella pertussis.* The bacteria were first isolated and studied in 1906 in Paris, where it was discovered that the bacteria attach to the cilia in the upper respiratory system and release toxins. These toxins cause coughing fits, and often the infected person cannot get enough oxygen between coughs and therefore exhibits the characterized "whooping" sound because the lungs are unable to fill with enough oxygen between coughs. Because of the uncontrollable coughing fits, cough-induced vomiting (also known as post-tussive vomiting) is a common symptom. Pertussis is only found in humans and is transmitted via person to person contact by respiratory secretions or droplets from a cough or a sneeze (Kuchar, 2016).

Pertussis progresses through three phases. The catarrhal phase occurs during the first 1-2 weeks, and is characterized by mild, upper respiratory tract symptoms gradually developing into a slight cough. The catarrhal phase is also the most infectious period, as it lasts 1-2 weeks after the initial exposure. The paroxysmal stage follows and lasts for another 1-2+ weeks, and infected persons are still contagious, but less so than within the first two weeks. It includes spasms of cough ending with a gasp, whoop, or vomiting. The convalescent stage is the final progression, lasting 2-6+ weeks and is consistent with gradual relief of paroxysmal coughing, patients usually are not contagious during this stage. The incubation period for *Bordetella pertussis* is at max 21 days. Pertussis also often leads to secondary complications, especially in infants and young persons. Secondary bacterial infections are common in young patients, and pneumonia occurs about every 1 in 20 cases (even more frequently in infants and youths). In infants, more severe potential complications include neurological complications like seizures and encephalopathy due to restricted oxygen flow to the brain during coughing fits. Patients of all ages may suffer from fractured ribs, loss of consciousness, hernias, weight loss, and angina (Immunization Action Coalition).

By 1914, a whole-cellular vaccine was invented to combat the disease. The whole cellular inoculation has actual cells from the *Bordetella pertussis* bacteria (Syed, 2017). In the 1940s, the vaccine was combined with diphtheria and tetanus toxoids and became DTP. From the 1940s to the 1980s there was a clear decline in the incidence rates of all three diseases, and it was found that the vaccine had been about 80% effective in preventing serious symptoms or death from pertussis (Kuchar, 2016). Declines in incidence rates are directly proportional to decreased rates of transmission, and therefore lead to a decrease in serious side effects from these diseases. Due to the negative side effects of the whole-cellular vaccination (including swelling, fevers, and febrile seizures), an acellular version without the bacterial cells was developed in the

1990s that gradually replaced the whole-cellular version. The acellular vaccine has fewer side effects, but also offers less protection than the whole cellular. The decreased efficacy of the acellular vaccine in providing disease immunity helps to explain the upward trend in United States incidence rates since the 1980s, as shown in Table 2 below. The data from this table is from the National Center for Immunization and Respiratory Diseases. The first case definition for pertussis was described in 1990, and before that year reports were from passive reporting to the Public Health Service, and each jurisdiction determined what was reported. Testing before 1990 was primarily done by culture, but cases may have also been reported if they were clinically compatible with common pertussis symptoms (CDC).

Year	No. Reported Pertussis Cases
1922	107,473
1932	215,343
1942	191,383
1952	45,030
1962	17,749
1972	3,287
1982	1,895
1992	4,083
2002	9,771
2012	48,277
2016	17,972

Table 2. United States Total Pertussis Cases by Year, reported by The National Center for Immunization and Respiratory Diseases

The recent upward trend in the United States since 1982 has been attributed to many reasons, including but not limited to declines in population immunity combined with wider circulation of the bacteria, improvements in diagnoses and surveillance, and even possibly genetic changes in the bacteria (Kilgore, 2016). In March 2018, Lane County communicable disease department began receiving reports of pertussis from a few of the local public high schools. This was alarming as it is a highly contagious disease, and one that Lane County has dealt with before. While there are cases nearly every academic year, the last particularly large Lane County outbreak was in 2013 with 112 cases reported. Between April and October 2018, more than 250 total cases were reported, though not all were confirmed.

The current vaccination available for Pertussis is called DTaP (vaccination for diphtheria, tetanus, and pertussis), and it is accompanied by a Tdap booster (also a booster for all three diseases). The recommended vaccine regimen includes 5 doses of DTaP administered between 2 months and 6 years: one at 2 months, 4 months, and 6 months, one between 15 and 18 months, and another between 4 and 6 years old. The Tdap booster is recommended at 11 or 12 years old but should be administered to anyone who did not receive it in their youth, especially to pregnant women in their third trimester (CDC Pertussis Guidelines). Pertussis can be fatal to infants if they are unvaccinated, given their smaller and less developed lung capacities. According to the Centers for Disease Control (CDC), since 2010 up to 20 babies a year younger than three months of age die from pertussis in the United States. Contracting the disease while fully vaccinated is possible, but symptoms are usually less severe. The CDC estimates that 9 out of 10 kids are fully protected 1 year following their fifth DTaP, and about 7 out of 10 are still fully protected 5 years following the fifth dose. They estimate that the Tdap booster protects 7 out of 10 people that receive it, with its efficacy decreasing each year. About 4 out of 10 people are fully protected 4 years after the booster shot. There is no long-term immunity to pertussis after exposure.

Years after vaccination	1 Year after final DTaP	5 Years after final DTaP	1 Year after Tdap	4 Years after Tdap
Level of estimated protection (%)	90%	70%	70%	40%

Table 1. Levels of Estimated Protection Based on Years after Inoculation

This data, from the CDC, shows that there is a clear decline in immunity from after the fifth DTaP to time after the Tdap booster, which suggests work needs to be done to improve the longevity of protection from the vaccine. Even if everyone in a community is fully vaccinated, this waning immunity could leave that population vulnerable to the disease in the future.

Pertussis can be treated with antibiotics, which is most effective in the early stages. The CDC recommends administering a course of antibiotics within three weeks of exposure for people over the age of 1, and within 6 weeks for pregnant women and babies below the age of 1. The antibiotics are basically ineffective if not administered within these parameters (CDC Guidelines). The antibiotics will usually only lessen the symptoms, not cure the disease completely. Other helpful treatments may include keeping one's environment free of irritants like smoke or dust, drinking lots of water, and using a vaporizer or humidifier to help loosen mucus and soothe the cough. In serious cases, hospital treatment may include IV fluids and oxygen tanks.

Many infectious diseases, like pertussis, are cyclical in nature and therefore can have recurrent epidemics in a population about every 4-6 years, as there is no long-term immunity to pertussis even after initial exposure. The common pattern of rapid infection and later possible reinfection is characterized by a period of a sharp peak and then decline in incidence as vulnerable hosts become immune following vaccination, which deprives the disease (bacteria, virus, whatever it may be) of the opportunity to continue spreading. Factors such as new births, immigration, or the waning vaccination immunity of humans every 5 years or so due to the weakness of the vaccine can increase the susceptibility of a community, giving rise to another epidemic. Other factors such as environment, host susceptibility, vaccine efficacy, and risk of coinfections may also help drive the spread of infectious disease (Goldstein et.al., 2017). Some researchers are also beginning to study how the more specific behaviors or characteristics of the host, for example age, vaccination history, risk behaviors etc. are associated with the risks of contracting certain diseases. This research is helpful when targeting prevention strategies. If we know which populations are most vulnerable to contracting the disease, prevention measures can be tailored to and targeted at those groups, for example what age group a public health department needs to focus vaccination campaigns.

Pertussis is one of the mandatory reportable infectious diseases in Oregon, and all presumptive or confirmed cases must be reported immediately to the local health department. After a report, a public health nurse calls the patient for an interview and makes sure they are following the proper procedures (i.e. seeing a doctor and getting antibiotics) and enter the case in the LCPH database. The CDC has defined three different stages of case definitions, all of which are included in my data. Confirmed cases are reportable to the Oregon Health Authority and are defined as culture-positive and an acute cough illness of any duration or PCR-positive (a polymerase chain reaction test for viral DNA) and a cough lasting more than two weeks with any of the following; paroxysmal coughs, inspiratory "whoop", post-tussive vomiting, or apnea. Presumptive cases are also reportable to OHA and are defined to include epidemiological links to a case confirmed either by culture or PCR test, and a cough lasting at least two weeks with again any of the following; paroxysmal coughs, inspiratory “whoop”, post-tussive vomiting, or apnea. Finally, suspect cases are not reportable to OHA, and are persons with a compatible illness but neither lab confirmed nor close contact of a confirmed case. A compatible illness is defined as a cough lasting >14 days and at least one of the following; paroxysmal coughs, inspiratory “whoop”, post-tussive vomiting, or apnea. For this analysis, the Oregon Investigative Guidelines offered by the Oregon Health Authority served as the blueprint for descriptions and symptoms, reporting requirements, data collection, laboratory protocols and vaccine recommendations that the communicable disease department used from the beginning of the outbreak, and are outlined in the methods section.

Methods

Laboratory and physician reporting requirements for infectious are very specific and mandated by the Oregon Investigative Guidelines. Physicians are required to report all cases that come into their clinics (including suspect cases) to the Lane County Health Department within one working day. Licensed labs also have one working day after bacteria identification or an initial positive test to report the findings. As previously mentioned, cases can be classified as presumptive, suspect, or confirmed. There are two clinical ways to confirm a positive pertussis case, through a Polymerase Chain Reaction test (PCR), and by testing a live culture. The PCR test does not require a live culture and instead tests DNA sequences for the *Bordetella pertussis* bacteria, but often gives false positives – especially after the fourth week of coughing. Only people presenting with signs and symptoms of pertussis should be tested using the PCR method, and it is most effective within the first three weeks of coughing when the bacterial DNA is in the nasopharynx (Centers for Disease Control). The live cultures are obtained from a nasopharynx swab within the first two weeks of coughing. Lab culture is are the most accurate and preferred way of testing. It is likely that there was an overrepresentation of confirmed pertussis cases in the data due to false positives from PCR testing.

There were a few different ways the Lane County Public Health Department (LCPH) was alerted to pertussis cases over the course of the outbreak. Once one case has been reported in a school, all the staff is put on alert to look out for signs and symptoms. All healthcare providers report to LCPH, who dictates that coughing, PCR positive cases should be recorded as "confirmed" cases, and control measures including treatment, prophylaxis of contacts, and exclusion from school/health-care work or attendance are necessary. Cases should be called back to determine the duration of cough and to elicit any additional symptoms (whoop, paroxysms, post-tussive vomiting). Cases whose coughing resolves after a total of less than 14 days should be downgraded to "suspect." In my experience, all reported cases were followed up on by phone call, but I do not know how regularly case statuses were updated in the excel spreadsheet, so it is possible that when I was analyzing the data not all the cases were accurately reflective of their final case definitions.

The communicable disease department at Lane County Public Health stored all case information in an excel spreadsheet, including reported date of symptom onset according to the patient, name, age, pertussis status (confirmed, presumptive, suspect), school/work, any defining classes/sports teams, vaccine status, and treatment. The data was collected through primary and follow up interviews done by the nurses in the

Communicable Disease Department with every case reported in Lane County. All supposed, presumptive, and confirmed cases were included in the data spreadsheet. I relied on this collected data for all analysis of current cases.

For my analysis, I calculated percentages of fully vaccinated, partially vaccinated, and unvaccinated cases from the reported list of confirmed cases. I also calculated what age range the majority of the cases occurred within. To display the entirety of the outbreak, I created an epi curve which scaled number of single cases against date of illness onset to show the transmission progression of the disease. I researched the incidence rates of surrounding counties to contextualize the Lane County data and compared those rates to the national averages to determine how severe the outbreak was.

It must be noted that the data had some limitations. Primarily, the date of symptom onset was most often an estimated date, as people don't usually remember the first day they began coughing and often do not report accurately. This means that the pattern of disease spread based on illness onset is probably slightly skewed, though without ever knowing the true date of illness onset it is impossible to tell how far off the reported data was. If this isn't done properly, then graphs like epidemiology curves that are scaled by date of illness onset will not be truly demonstrative of the outbreak, and therefore potentially misleading data. Misreported date of illness onset, for example, could influence when the true peak of the cases occurred, and the waves of infection that are characteristic of a propagated epidemiological curve could be misrepresented. Additionally, only one column was created for vaccine status, and patients were recorded as "up to date," "partial," or "none." The "partial" category unfortunately is vague, as it does not provide information on how many rounds of DTaP a patient received, or if they only got the booster shot etc.

Literature Review

Vaccines and immunizations have been a contentious issue practically since their conception. One of the most common recent threads in this debate is the alleged link between vaccines and autism. In 1998, former physician Andrew Wakefield and his colleagues published a (now retracted) article in the *Lancet*, peer reviewed medical journal, claiming that the MMR (measles, mumps, and rubella) vaccine caused autism (Rao, 2011). This article was widely criticized immediately after publication and it was determined that there was no causal link between the vaccine and autism, the Wakefield data had been blatantly falsified for financial and political gains. Despite the completely false data, the seed was planted, and MMR vaccination rates began to drop rapidly. This sparked a wave of anti-vaccination movements leading to disease outbreaks that may have otherwise been easily vaccine preventable. Recently, for example, a 2008 measles outbreak was believed to have originated at Disneyland in Anaheim California. 125 people were infected, and it was estimated that MMR vaccination rates among the exposed population was as low as 50% and likely no higher than 86% (Hussain, 2018). Prior to Wakefield's publication, measles was nearly extinct and had been declared eliminated in the United States, meaning that national immunization levels in the western world were high enough to provide the herd immunity to avoid outbreaks, which for a highly contagious disease like measles is between 96% and 99% (Hussain, 2018). Herd immunity refers to when a high enough percentage of a population is vaccinated against a disease that even the unvaccinated people are protected, because the germ or bacteria doesn't infiltrate the community. Outbreaks like the one at Disneyland do not happen if there is herd immunity. The problem of low vaccination rates was not just restricted to America either, in the UK the MMR vaccine dropped from 92% in 1992 to 84% in 2002 (Murch, 2003). This early article contributed significantly to vaccine hesitancy, which has only been exacerbated by the less than stellar efficacy of the acellular pertussis vaccine.

All states in the U.S. have some vaccines that are required before children start preschool, but there is a nonmedical exemption loophole that has put many communities at a very high risk for widespread disease outbreaks. Nonmedical exemptions allow parents to refuse vaccinations due to religious, secular, or other personal beliefs, and have added to vaccine resistance. A 2012 study published in *Pediatrics* found that in schools within New York state, religious exemptions increased from 23% to 45% from 2000 to 2011 (Imdad, 2012). It was also shown that states with easily obtained exemptions have higher rates of exempted students. Researchers found that the exemptions tended to be clustered in certain communities throughout the state, and areas with exemption rates higher than 1% had significantly higher rates of pertussis cases than areas whose exemption rates were lower than 1% (Imdad, 2012). Research has also shown that individual attitudes toward vaccines are significantly affected by the general attitude of the local community. A Seattle, Washington survey collected information about vaccine attitudes. Of the 196 people who participated, 126 were parents of children who had received their recommended vaccinations and 70 were parents who did not follow the recommended schedule in some way. It was found that 72% of the non-vaccinator's friends and family recommended non-conformity with the state recommended vaccine schedule, and only 13% of their social contacts did (Brunson, 2012).

A 2000 study published by the *American Journal of Medicine* was designed to determine "whether personal exemption from immunization is associated with risk of measles and pertussis at individual and community levels," and measured the relative risk of pertussis for unvaccinated children and the associations between exemptions and incidence rates (Feikin, 2000). Contextually, this is important given the low rates of children that have been administered the full course of the pertussis vaccinations. Often the lack of vaccination is a choice parents have made for their school aged children, but the effect of lost herd immunity can pose a grave threat to children who may have obstacles such as autoimmune diseases that prevent them from getting vaccinated. The researchers in this study designed a retrospective cohort study using all reported cases of both pertussis and measles from 1987-1998 from children ages 3 to 18 in Colorado. The goal was to measure the "association between incidence rates among vaccinated children and frequency of exemptors in Colorado counties; association between school outbreaks and frequency of exemptors in schools; and risk associated with exposure to an exemptor in measles outbreaks." They found that exemptors were 22.2 times more likely to contract the measles and 5.9 times more likely to get pertussis than vaccinated children. Schools with pertussis outbreaks were also proven to have more exemptors than schools that did not experience a pertussis outbreak. This study concluded that the risk of becoming infected with the measles or pertussis is higher in vaccine exemptors (Feikin, 2000). This data is relevant in the exploration of the Lane County report, in recognizing that the level of risk is higher in the unvaccinated/exemptors, and public health officials must adjust to compensate for that risk.

Many studies have attempted to link vaccine exemptions to pertussis outbreaks. A meta-analysis of some of these studies found that in the top 5 largest statewide pertussis epidemics, unvaccinated and undervaccinated people were largely affected across all age groups. For example, in 2010 California had 4,415 cases reported in children ages 6 months to 10 years. 45% had not received the recommended vaccinations. In Washington in 2012, 28% of the infected children were not up to date on their vaccinations. Oregon also experienced an outbreak in 2012, and among pertussis cases in children ages 2 months to 6 years, 31% were completely unvaccinated and 24% were undervaccinated (Phadke, 2016). These are large portions and while not the majority of the population, it is important to question if these outbreaks would even occur if there wasn't a large population of unvaccinated people to get exposed and further risk the health of the vaccinated population. The still substantial number of vaccinated people who contracted pertussis in these outbreaks also highlights the effect that waning immunity has on the prevalence of the disease. It is suggested that vaccinated people with waning immunity contract pertussis from the unvaccinated populations but tracking case progression accurately is quite difficult. It has been documented that schools and communities with high rates of vaccine exemption also had high rates of pertussis, and the risk of contracting the disease was higher for everyone – including fully vaccinated persons (Phadke, 2016).

Human behavior plays a significant role in the spread of infectious disease, not only on transmission, but also in regard to what people do when they are afraid of contracting disease. The tendency to wear face masks, self-quarantine, or changes to attendance at school or work for example, are all common changes in behavior that public health needs to keep in mind when devising a plan to control the disease spread. If a predicted behavior was leaving town to avoid exposure, that could risk a whole new infected population and must be dealt with appropriately (Funk, 2010). Traditional responses to disease outbreaks can be categorized into two main categories: 1. Decreasing contact between infectious and susceptible people through quarantines, travel bans, increased social distancing, and 2. Decreasing effective contact (i.e. the likelihood of transmission if contact is made between and infectious and susceptible person) through handwashing, mask wearing, or other hygienic practices (Smith, 2006). Of course, it is true that the efficacy of these measures is dependent on the disease specifics like primary mode of transmission, incubation period, most vulnerable populations, and degree of infectiousness, all of which tend to be unclear at the beginning of an outbreak.

Epidemiology is, technically, the study of what comes upon groups of people, with the etymology translating as *epi,* upon; *demos*, people; *logos,* study (Omran, 2005). More specifically, epidemiology deals with the distribution of death and disease, and the relation to health, as well as the economic and social determinants of the population. Health and disease determinants and patterns are the backbone of epidemiology, and the basis of nearly everything we have learned about population health – including how to track and prevent disease. Pertussis has an interesting epidemiology, as epidemics tend to follow a cyclical pattern peaking every 2-5 years (Cherry, 2005). While rates have declined since the development of the DTaP vaccine, the cyclic pattern continues. This pattern is different from many other diseases, the introduction of the measles vaccine for example, resulted in a lengthening of time periods between outbreaks (Cherry, 2004). For pertussis, immunity after infectious varies, but is generally not longer than a couple years.

Late spring and summer months are typical months for increases in pertussis incidence. The reasons behind the seasonality trends are largely unknown, and most studies simply acknowledge a lack of explanation. One theory behind the decrease in cases in winter months is that the cooling of nasal passages may not be a suitable environment for the *Bordetella pertussis* bacteria (Eccles, 2002). Most researchers agree that seasonality most likely affects the mechanism of transmission and survival of the infectious agent and affects the relationship between the environment and the host. A study in Iran comparing seasonal patterns of laboratory confirmed cases and clinically suspected cases of pertussis showed that between 2011 and 2013, the maximum incidence of clinically suspected cases was in May ($p = 0.6$), and the maximal seasonal incidences of confirmed pertussis cases were reported within summer months ($p=0.004$) (Ghorbani, 2016). This trend was supported by another study done in Queensland, Australia that also showed pertussis incidence peaking in summer months, though they offered no explanation as to why (Kaczmarek, 2016). A linear regression done on the incidence of United States pertussis cases from records from Center for Disease Control from 1990 to 2003 showed an increasing trend in incidence over that particular time period, with most significant peaks in August (Shah, 2006). While the reasons behind seasonal variations in infectious diseases are not a well understood phenomenon, suggestions for pertussis being most common in the summer months include changes in the environment that favor pathogen transmission (perhaps Oregon experienced more humidity), or changes in host behavior (more close contact, outdoor play for children) (Bhatti, 2017). This information is most useful in thinking about effective vaccination strategies.

Chapter 1: Vaccinations

The CDC publishes a summary of all the protocols for states to follow in the event of an outbreak. The summary also offers a comprehensive explanation of all pertussis related matters, including an evaluation of vaccine efficacy. With "measured vaccine effectiveness ranging from 47% among adolescents 13-16 years of age to 95% among children 15-47 months old," the CDC is confident in their recommended vaccine regime for pertussis. While the vaccine may not be 100% effective in providing complete immunity, cases contracted in people with the vaccine have been shown to have less severe symptoms and result in fewer serious complications and side effects (Rapaport, 2017). Vaccination rates in Oregon are not what health officials would like to see. In the summary the CDC notes that in the 2012 outbreak and of the cases in the 2 months to 6 years age range, 31% of the people who were infected were completely unvaccinated and 24% were only partially vaccinated. From the 2015 data, the same issue persisted. Among the 269 cases in 2 months, only 46% had up to date pertussis vaccinations (CDC Summary, 2016). As discussed earlier, the pertussis vaccine series is particularly involved. There are 5 doses plus a booster dose, and it is not uncommon for people to not have finished the whole series. Out of the 183 confirmed cases in 2018, (i.e. excluding presumptive and suspect cases), about 18% had no vaccination for pertussis whatsoever, and 6% had partially completed the vaccine regimen, leaving 76% with up to date vaccinations – not nearly enough to provide herd immunity.

A significant percentage of the non-vaccinators is due to parents or individuals petitioning and receiving non-medical exemptions. In 2018, 7.5% of Oregon kindergarteners turned in nonmedical exemption forms (Harbarger, 2018). A non-medical exemption is available two ways. One is watching an online education model and signing a form that dictates that the parent "understands that [his or her] child may be excluded from school or child care attendance if there is a case of disease that could be prevented by vaccine." Alternatively, one can also talk to a health care provider and have the practitioner sign a vaccine education certificate. Non-medical exemptions can be attained for personal or religious beliefs. Medical exemptions exist for students or community members who cannot get immunized for health reasons, for example if they are immunocompromised and the vaccine would be physically harmful to them.

As with nearly every vaccine, DTaP and Tdap have been met with public resistance. In Eugene, a vocal parents group called "Parents for Inclusion not Exclusion" were very adamant about their resistance to forced immunizations, and diligently fought against the public health department, especially in the face of school exclusion day. The group attended open forum public health advisory meetings held at LCPH to protest school exclusions, as well as circulated petitions to abolish the exclusions. Ultimately, 160 children were excluded. If a child was diagnosed with pertussis, children could either wait the 21-day incubation period and then get the DTaP vaccine or take 5 days of an antibiotic prophylaxis. Unvaccinated elementary school children were required to either get all 5 rounds of the DTaP vaccine series (for high school only the booster was required) or complete the 5-day antibiotic treatment without being infected. Exclusions are also to protect children and staff who medically cannot get vaccinated, perhaps due to an autoimmune disease.

Compulsory vaccinations are both a political and legal issue, with tensions between those who believe it is the healthiest choice (and one's civic responsibility) to vaccinate, and those who are hesitant about vaccinations and do not feel that they should be forced to do so. In September of 2010, Senate Bill 354 was signed into law by the state of California, requiring students entering or advancing to grades seven through twelve in the 2011-2012 school year to have proof of receiving the Tdap booster shot (Yang, 2015). As of March 2019, Washington state house passed a bill banning personal or philosophical exemptions to the MMR vaccine for measles, mumps, and rubella for school-aged children (Seattle Times Board, 2019). The bill is now in the hands of the state senate. This bill was pushed primarily as a response to the very recent measles outbreak that spread quickly through Washington state, though a similar bill was soundly struck down in 2015.

Prompted by the 2014 measles outbreak at Disneyland, California passed Senate Bill 277 in 2015 that removed all personal belief exemptions from vaccinations for all public and private schools and daycares. Oregon currently has the highest rate of legal exemptions from school vaccinations in the country, and state representative Mitch Greenlick has proposed a bill that would eliminate personal, religious, and philosophical exemptions throughout the state, leaving only medical exemptions. Greenlick argues that this bill is about protecting vulnerable populations, in particular infants who are too young to be vaccinated. In response to critiques that his proposal infringes on human rights to choose, Greenlick said “you want to homeschool your kids and you want to keep them out of reach of other kids? Go for it. I’m not affecting their rights with this bill, I’m affecting the right for them to endanger other kids in the schools if they’re not protected” (Douglass, 2019). Yet another piece of Oregon legislation that complicates the vaccination conversation is statute 433.416 that states “a worker shall not be required as a condition of work to be immunized under this section, unless such immunization is otherwise required by federal or state law, rule, or regulation” (oregonlaws.org). This statute means that the Lane County public health department cannot require teachers or other school staff to immunize, a gap that parents rightfully find unfair, and could be a potential hazard to classroom health.

Chapter 2: Epidemiological Trends

One CDC summary tracks incidence rates in Oregon from 1995 to 2016 and breaks down the confirmed cases by age group and vaccine status to provide an exceptionally comprehensive view of the prevalence of pertussis in Oregon in a 10-year period. Not including the 2018 outbreak, the last pertussis epidemic to significantly affect the state of Oregon was in 2012, with 910 cases being reported across the state. The incidence rates of pertussis in Oregon tend to be higher than the national average, probably due to low vaccination rates and high rates of nonmedical exemptions. Figure 1 below offers a graphical display of the comparison between rates in Oregon and the national average from 2002 to 2016.

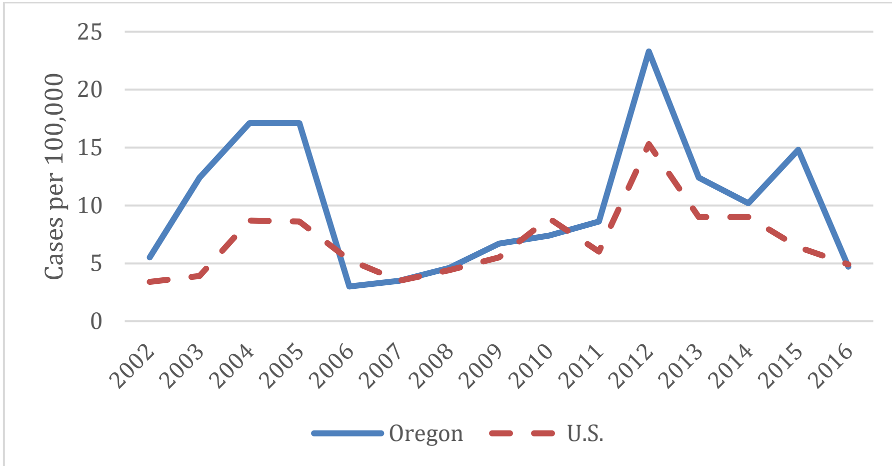

Figure 1: Pertussis Incidence Rates in Oregon Compared to National Average

As shown in the graph, in 2015 the reported incidence rate for pertussis in Oregon was 15/100,000, which was well above the national average of 6/100,000. In 2016 the incidence rate was 4.7/100,000, slightly lower than the previous year. Provisional reports for 2018 have an incidence rate of 11.47 cases per 100,000, or 475 cases statewide, and an increase from two years before. With the exception of 2006 and 2010, Oregon had a higher incidence rate than the national average. Oregon's generally higher incidence rates can most likely be attributed to low vaccination rates for pertussis within the state. Figure 2 below displays incidence rates for Lane County and its 6 neighboring counties. In Lane County specifically, the incidence rate from 2007 to 2016 was averaged to be between 9.3 and 11.6 cases per 100,000. As for the surrounding counties, Linn County had the same incidence rate, Deschutes and Klamath counties were lower with 6.7 – 9.2 per 100,000, Douglas and Lincoln counties were even less with 2.2 – 6.6 per 100,000. Benton county had the highest rates of all neighboring counties, with 11.7 – 15.8 cases per 100,000.

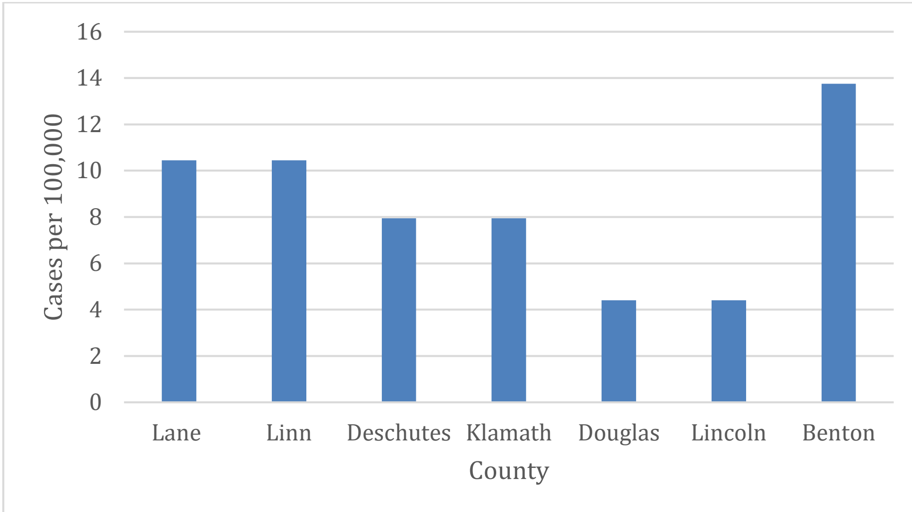

Figure 2: Average Incidence Rates in Oregon Counties from 2007-2016

With disease outbreaks, public health officials try to locate a patient zero, or a specific source. In many cases this is impossible, but when the initial source can be located it is extremely helpful with tracking the course of the disease and in the best-case scenario, preventing it from spreading further. Unfortunately, with pertussis outbreaks it is usually hard to pinpoint the source of the outbreak because the incubation period for pertussis ranges from 4 to 21 days, and in this time frame is also when they are most infectious so it is possible to have a child attending school while they are infectious but not yet symptomatic for pertussis. Additionally, initial symptoms present as just a common cold, so children can pass it around classrooms without anyone necessarily suspecting how infectious their cough may be. In this particular outbreak, the timing of the initial cases here in Lane County further complicated the search for a patient zero. Spring break for the Eugene public schools was March 26-30, 2018. The first confirmed case reported to Lane County was April 5(the first case technically reported was on March 1, but because it was a full month until the next reported case it will be treated as an outlier and not considered in the data analysis), with two more 5 days later. With families travelling for spring break and everyone out of school, it was impossible to determine if the disease outbreak had been started in Lane County or picked up somewhere on vacation. Figure 2 below illustrates the timeline of the outbreak, with peak number of cases occurring in May.

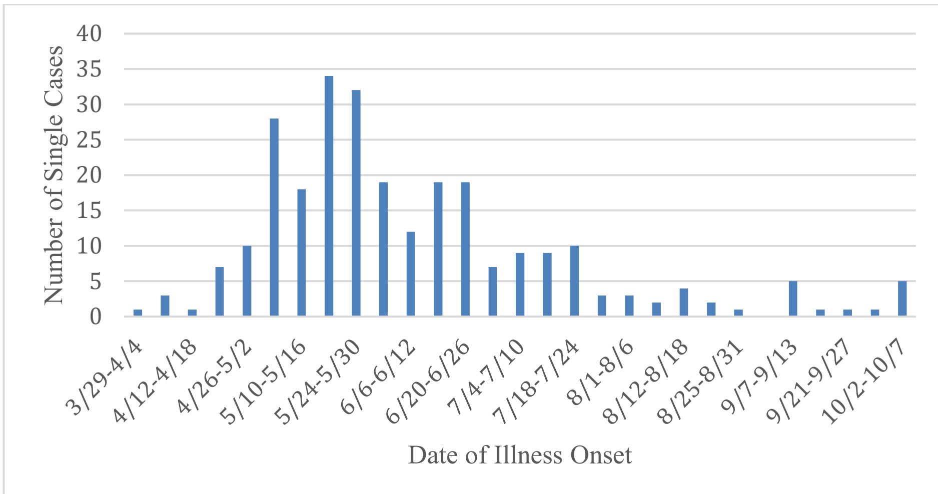

Figure 3: Lane County Pertussis Cases from March – October 2018

Epidemiology curves such as this one serves as a visual representation of the number of new cases over a period of time, based on the estimated date of disease onset in the population. This particular epidemiology curve is known as a propagated, or progressive, source. Propagated epidemics begin with a single index case who infects other people through person to person transmission, in comparison to outbreaks that begin with a common contaminated source. The timing of the outbreak is consistent with the research discussed earlier that highlights late spring and summer months being most conducive to pertussis epidemics.

Between March 29th and October 7th of 2018 (the data collection stopped after my internship ended on October 7th, but the outbreak was officially declared over on October 15th, 2018), there were 183 confirmed cases of pertussis, 41 presumptive, and

42 suspect cases in Lane County. The age group affected ranged from 2 months to 72 years old. Most exposures happened within the schools, and the majority of cases were in youths ages 11 to 16. 76% of people who contracted the disease had up to date vaccinations. The outbreak peaked in May of 2018 and there were no reported deaths. For clarity and given the very large age range of people affected by this outbreak, I have separated infant cases from the youth, young adult, and adult cases. In Figure 4, infants are defined as between 1 and 23 months, a demographic that unfortunately is most likely to have the worst responses to pertussis and experience the most severe side effects (including death), and hospitalizations.

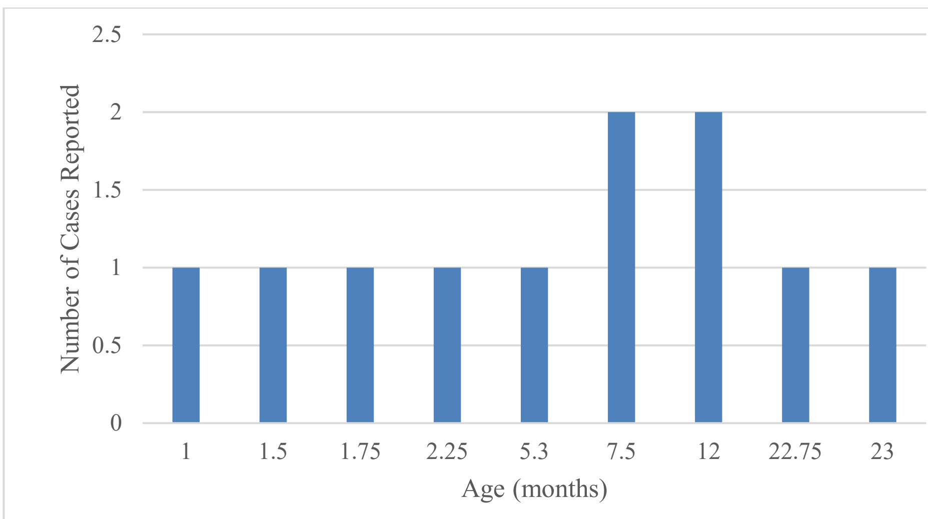

Figure 4: Confirmed Infant Pertussis Cases

There were 11 total cases within this age range, with 1 hospitalization due to critically severe symptoms but thankfully no fatalities. 54% of the infants were not up to date on their vaccinations, which may have meant that the mom declined the booster shot in her third trimester as her doctor suggested, or they had not yet gotten their first round of DTaP since their birth (recommended at 2 months of age), either due to age (if they were less than two months of age and not yet old enough for the first shot) or parental preferences. Unfortunately, data was not collected on the mother's vaccination status if she did not contract pertussis herself. It would be interesting to determine how many of the babies who contracted pertussis were from mothers who had gotten the Tdap booster in their third trimester, to determine how much the booster affects the fetus in utero. Studies have shown that infants were 43% less likely to contract pertussis if their mothers received Tdap in their third trimester, but future data analysis could show how the Lane County data compares to that statistic (Becker-Dreps, 2018).

In the California outbreak of 2010, out of the total 5,482 confirmed cases, a total of 808 patients were hospitalized, and of that number 72% (584 cases) were in babies younger than 6 months. 55% (446 cases) were younger than three months. Among all hospitalized cases, the average age was 2.6 months (the total range was less than 1 month to 92 years). Ten fatalities were reported from this outbreak, all infants. Nine were previously healthy newborns younger than 2 months old who had not yet been immunized, seven of them were younger than 6 weeks. The other baby was 2 months old and had received the first DTaP 15 days before contracting the disease (Winter, 2012). The most common source of infant pertussis infection is contraction from family members, especially older siblings who are in school or day care. Secondary attack rates (infection of vulnerable persons after known contact with an infectious source, i.e. a sick sibling) are 25- 60% among household contacts in the developed world and reach 80% among fully susceptible persons (i.e., neither immunized nor previously infected), according to the Oregon Health Authority. This is important information for public health departments and highlights the need to push vaccinating older siblings in order to protect the vulnerable younger populations.

The remaining 172 cases were in the 2 to 72-year-old age range. Out of the 172 confirmed cases within this demographic, 18% had no vaccinations and 6% had only partial vaccinations. Unfortunately, it was not specified in the data what “partial” meant and may have varied from case to case. Figure 5 below clearly demonstrates that the majority of the cases were in youths, ages 11 to 16. Within this age range, 85% were up to date on their pertussis vaccinations. This outbreak began in the public high schools in Eugene and spread rapidly amongst the student body population, so that age range makes sense, and we again see a propagated curve. Figures 5 and 6 below show the rest of the confirmed cases, separated to more clearly show the age distributions.

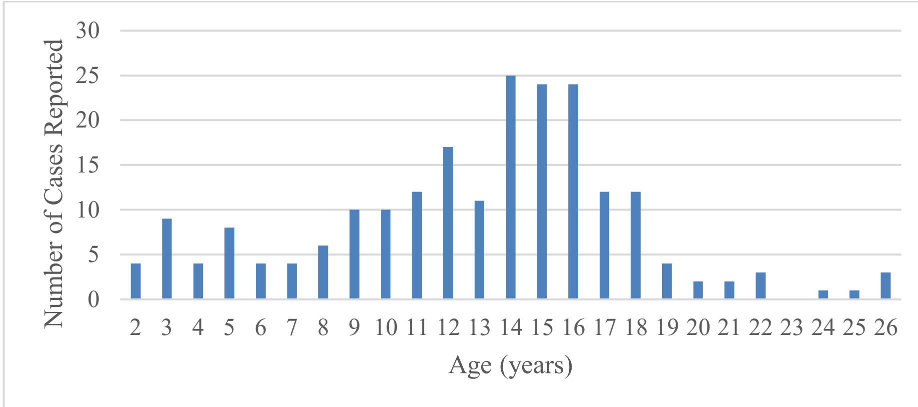

Figure 5: Confirmed Pertussis Cases, Ages 2-26

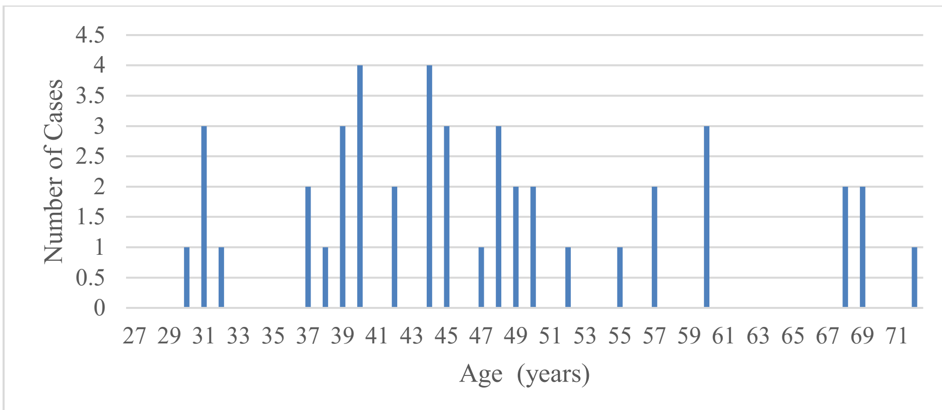

Figure 6: Confirmed Pertussis Cases, Ages 27-72

Interestingly, cases in older demographics have been increasing. According to the Oregon Health Authority, 51% of pertussis cases reported in Oregon since 2003 have been from children older than 10 years of age. This trend should most likely be attributed to the gradual waning immunity of the DTaP vaccine, the last round of which should be administered around age 6. The booster is recommended around 11 years old. Looking specifically at the 11-year-old group, 40% had not yet received the Tdap booster, nor had 31% of 12-year old's who contracted pertussis. It is a common trend for people to stop going to the doctor as frequently as they age, which could help explain the decrease in high school immunity, kids in high school and through college tend to stop going to the doctor as regularly. The lack of booster immunity in at-risk populations may help to explain the high number of cases throughout the Eugene high schools.

Chapter 3: The Public Health Response

The communicable disease department of Lane County Public Health consists of four public health nurses and a supervisor who collect all the data from the outbreak and compile it into databases. They are also responsible for tracking all other communicable and infectious diseases within the county. There are 8 key steps the Lane County Public Health Department follows in the event of an outbreak, which will be outlined in this section.

Initially, the outbreak must be confirmed. In this case, that meant two cases that had a distinctive link. Two cases in one school would not constitute the beginning of an outbreak, unless those two students shared a class, or played on the same lacrosse team. The outbreak was first confirmed at Sheldon High School in April of 2018, with the first laboratory confirmed cases of pertussis. Early disease detection is highly important. The two primary goals of early disease detection are 1. Identifying the duration, locations, and sizes of potential disease clusters, and 2. Determining whether each of these potential clusters is due to an outbreak or to chance fluctuations in case counts (Liao et.al., 2017). It is extremely important that infectious diseases are closely monitored by public health organizations at national and local levels in order to provide warnings or damage control in the face of an outbreak. This monitoring includes tracking specific epidemiological data; identifying the population subgroups most important for transmission of an infection, estimating the components of vaccine effectiveness, and addressing biases in studies of the effectiveness of interventions (like vaccines) or risk factors for infection. The most important factor in controlling disease outbreaks is that detection is early, before the disease has a chance to spread. Research has shown that they key to detecting outbreaks early, sometimes even before they happen, is studying and understanding the relationship between a disease outbreak and the relevant risk factors.

The second step is to confirm the diagnosis, especially with pertussis, where the symptoms may indicate simply a bad cold. Once one case of pertussis is confirmed, it is vital to have all presumptive cases tested. Along with confirming the diagnosis is active case finding. It is the responsibility of the public health department to work with the school administration to reach out to students, and their families, who may have been exposed. No surveillance system is perfect, but continuously spreading information about what signs and symptoms to look out for, as well as directly contacting those likely to have been exposed are necessary active steps to controlling the spread. Providing and controlling information in the media is also extremely important. Lane County sent flyers to the schools, so parents would understand the outbreak and be advised as to how to safeguard their children, as well as to all local physicians and doctors' offices with notices to look out for symptoms that may be associated with pertussis.

Once two confirmed cases with a link have been established, the public health department begins to characterize them. Questions about person, place, and time become extremely relevant in trying to understand how the disease is entering the community. How old is the patient? Where do they live? Do they live alone? Have they been near babies or pregnant women in their third trimester? Are they in school? Have a job? When did they first become symptomatic? The more information of this nature that can be gathered informs what the course of the disease seems to be. This knowledge allows the department to begin formulating hypotheses about the outbreak beginning and ascertain certain risk factors to help understand where to focus to be most effective with the resources available to help stop the spread, such as antibiotics and vaccinations.

The epidemiological triad is explained by the CDC and is a tool used by epidemiologists and public health agents to explore the causes of infectious disease and the factors that allow it to spread. The three factors included in the triangle are agent, host, and environment, as depicted in the figure below, as well as an example epidemiological triad for pertussis.

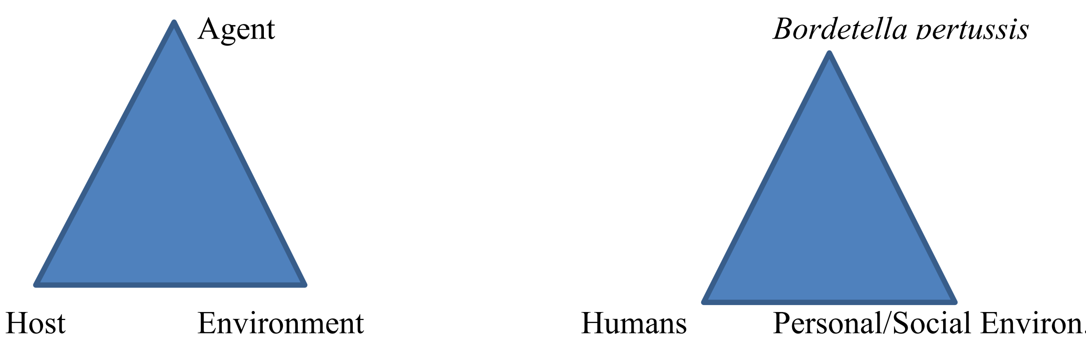

Figure 7: The Epidemiological Triad

Pertussis is only found in humans, so there are no other vectors or zoonotic reservoirs. The agent, the bacterium *Bordetella pertussis,* can survive 3-5 days on inanimate dry surfaces, 5 days on clothes, 2 days on paper, and 6 days on glass (Public Health Agency of Canada, 2014). Personal environment includes factors like body temperature (the bacteria prefers higher temperatures) or if one is a smoker (the bacteria binds better to the respiratory tracts of smokers than nonsmokers), and vaccine status (Bagaitkar, 2008). Social environment factors include being in vulnerable spaces like classrooms, where the demographic may include vaccinated and non-vaccinated persons. Once each factor has been researched, the next step is to determine how they are linked. In this example, the host (humans) are responsible for transmitting the agent (*Bordetella pertussis)* through highly contagious airborne droplets of respiratory mucous, or any exchange of saliva. The personal environment of a host will determine how likely they are to contract then transmit the disease, along with their social environment. The environment of the agent determines how far it will spread – in a community with herd immunity it may not have any real effect, but in a community like Lane County with lower vaccination rates the agent may spread rapidly.

The final step and true crux of the epidemiological triad is to determine how the public health department can intervene between two of these factors to potentially cease transmission or further spread, or otherwise disrupt the course of the disease. Vaccination serves as a block between agent and host, heavily enforced classroom etiquette about hand washing and coughing/sneezing into one's elbow could decrease agent transmission in social environments, or a host in a heavily immunized environment may inflict no damage on the greater community, to name a few examples. Another strategy employed in the midst of a disease outbreak is school exclusions. Lane County implements exclusion day, which in 2018 was February 21st. To reiterate, exclusion day means that any child who is either not up to date on their required immunizations or do not have approved exemptions on file with their school will be prohibited from attending until the can provide documentation for either of the two options. In the event of an outbreak, non-medical exemptions may not be held up, and those children are still excluded. In order to mitigate the number of children facing exclusion, the county offers a free walk in immunization clinic in the two days prior to exclusion day, with the hopes of making vaccinations as accessible as possible to the community.

Another way a public health department may approach an outbreak is by categorizing the issues into pre-event, event, and post-event phases. This design model is called the Haddon Matrix and is used commonly in the injury prevention field and can be applied to infectious disease (Haddon, 1970). This framework, like the epidemiological triangle, allows for the evaluation of the different factors and potential interventions. Before the event of an outbreak, the public health department wants to prevent the existence/release of an agent from a host or provide host protection (like a vaccine). During the event, the goal is to control the pattern of release, minimize damage/the amount of the agent present, and increase host resilience and control the interaction between the agent and the host. After the event (in this case the event could be the entire outbreak or just individual infection) the primary goal is to provide rapid treatment for the host(s). The table below is an example Haddon Matrix for the pertussis outbreak.

Pre- Event Issues	Event Issues	Post-Event Issues
-Lack of herd immunity -Negative attitudes about the vaccine/vaccine hesitancy -Waning efficacy of vaccine -Only one booster shot -High likelihood of disease reoccurrence (cyclical trends) -Symptoms look like the common cold	-Significant unvaccinated populations in schools -Parents sending unvaccinated children to school -Unvaccinated school children with younger siblings -Anger about school exclusions -Unknown disease origin	-Likelihood of reinfection -21-day incubation period -Evaluating the successes and failures of the public health response

Table 3: The Haddon Matrix

Implementing prevention and control measures is the seventh step in the unofficial protocol. Because pertussis is a vaccine preventable disease, vaccinations are the biggest prevention measure available. Also important for pertussis is promoting good hygiene practices (especially in the classroom) like washing hands and covering coughs. Antibiotics can serve as a control mechanism, as can isolation from others once infected to prevent the spread. Post – outbreak, the final step is to write a detailed comprehensive report and share it widely, a project that will hopefully be aided by this research. The report is important not just for Lane County knowledge, but the rest of the state and country as well. The two-and-a-half-page report was published on April 3, 2019. It included a methods section that clearly outlined the criteria for classifications of confirmed, presumptive, and suspect cases, as well as an overview of the guidelines for the follow up protocol for a confirmed case. The report confirmed that Lane County Public Health notified the public about the outbreak and risks of transmission through letters to parents, health alerts to clinicians, and press releases to the general public. The report offered data results on case numbers, common places of exposure, school exclusion rates, and the percentage of vaccinated people who still contracted the disease. It concluded that the 2018 outbreak was the largest in Lane County history to-date and reminded clinicians to be aware of the endemic nature of pertussis in Oregon, and always be on the lookout for signs and symptoms in patients.

Conclusion

The Lane County pertussis outbreak of 2018 was not the first of its kind, nor will it be the last. I learned from this research how important it is to study the patterns of an outbreak, and related matters like vaccine efficacy and tracking to inform the public health response. My review and analysis of the latest pertussis outbreak highlighted a few main themes that lend themselves to drawing preliminary conclusions about the outbreak. In review, due to the long (21 days) incubation period of the *Bordetella pertussis* bacteria, during which infected persons are contagious but asymptomatic, mixed with the initial cases presenting just after public schools came back from spring break, it was impossible to determine where this outbreak began. The infant age group, who are most vulnerable to the negative side effects of pertussis due to their small, underdeveloped lungs, had 11 cases but no fatalities. 52% of the cases were reported in adolescent and young adult patients from 11-18 years of age. It is not surprising that the majority of cases occurred in this age group, given that the outbreak began in the high schools and spread quickly throughout.

One of the most significant findings from this project was the effect of vaccine status on pertussis immunity. Of all the confirmed cases, 76% of people were up to date on their vaccinations, 6% were partially vaccinated, and 18% had no vaccine history for pertussis. It is likely that the outbreak started in the unvaccinated population and spread to those who had been vaccinated. These numbers clearly point out a need for an improvement in the pertussis vaccine, as the booster wanes midway through adolescence, leaving a very large portion of school aged children vulnerable.

It is difficult to accurately track all cases reported in an outbreak and updating personal profiles if a case goes from presumptive or suspect to confirmed can become confusing and challenging very quickly. Data collection and reporting accuracy had some limitations in regard to this project. The excel worksheet I was working from was not the official LCPH database, so the accuracy of all the case classifications from there is not absolute. I do not know with what regularity the public health nurses updated individual cases, for example if changes were made when a particular case went from presumptive to confirmed after a lab test. However, my results do align with the Lane County report published by the Oregon Health Authority, so it is safe to say that the discrepancies were likely very minimal. If research like this is to be done again, a more complete and accurate database should be used.

For future case tracking in pertussis outbreaks, it would be extremely helpful to further classify "partial" vaccinations and record the number of vaccinations one received in the pertussis series. Having this specific data would allow for more analysis of where the vaccine is most effective. Dates of when shots were administered would also be helpful in tracking the lifespan of immunity from each DTaP shot or Tdap booster. My research on vaccine resistance was somewhat inconclusive, but it did highlight what I believe are the main components parents take issue with; including potential health hazards from the vaccine as well as lack of long-term protection. These findings are relevant beyond just pertussis as well, all infectious disease outbreaks involve a similar pattern.

A lot of research done on pertussis is partnered with research on measles. Measles is similar to pertussis in that it is a highly contagious, vaccine preventable disease that has shown significant resurgence in the last decade, primarily due to waning vaccination rates in the general population. The same principles of public health responses apply to all infectious disease outbreaks. Promoting healthy prevention strategies like vaccinations and good hygiene, along with correcting the vast amount of misinformation about vaccines and maintaining public trust in the public health departments is critically important.

Pertussis outbreaks will happen again in Lane County – most likely in the next 3-5 years – and Lane County Public Health will be the agency to respond. This outbreak highlighted the need for higher community vaccination rates (especially in the schools), increased public awareness of pertussis signs and symptoms, collection of more detailed vaccination data, and accurate epidemiological analysis.

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