Master of Public Health

Integrative Learning Experience Report

CHARACTERIZATION OF TOXOPLASMOSIS REPORTING AND SURVEILLANCE IN THE UNITED STATES

by

Jayden Henry Alexander McCall

MPH Candidate

submitted in partial fulfillment of the requirements for the degree

MASTER OF PUBLIC HEALTH

Graduate Committee:
Justin Kastner, PhD
Paige Adams, DVM, PhD
Nancy Muturi, PhD
Waithaka Mwangi, PhD

Public Health Agency Site:
Parasitic Diseases Branch, Centers for Disease Control and Prevention
May 24 – August 13, 2021

Site Preceptor:
Anne Straily, DVM, MPH, DACVPM

KANSAS STATE UNIVERSITY
Manhattan, Kansas

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Summary/Abstract

This *online* experience was completed with Dr. Anne Straily from the Parasitic Diseases Branch of the Centers for Disease Control and Prevention (CDC) during the Summer of 2021. As part of this field experience, the author assisted Dr. Straily with a study investigating the surveillance systems for toxoplasmosis in states where this disease is currently categorized as "reportable." Toxoplasmosis is a disease caused by the protozoan species *Toxoplasma gondii* and generally only causes clinical disease in immunocompromised individuals and children of mothers infected during gestation. This study sought to determine if toxoplasmosis would be a good candidate to become a nationally notifiable disease with the CDC. This allowed the author to use skills from several classes from the MPH coursework as well as expand on crucial writing and communication skills when preparing the results for publication and presentation to relevant individuals both within and outside the host agency. During this time, the author was also able to be a part of several other functions of this branch of the CDC, including monthly meetings and other events to learn more about their various projects and global reach. In addition to the author's responsibilities with the CDC, he separately engaged in various teaching opportunities with his faculty mentor, Dr. Justin Kastner. This included a lecture to undergraduate students about the risks of toxoplasmosis and a lecture to graduate students about the trade-policy implications of African Swine Fever Virus over the past century (a topic that combined aspects of the author's public health, veterinary, and PhD research-related knowledge). This experience, while primarily completed virtually due to the COVID-19 pandemic, was a rewarding opportunity for the author to learn more about how a federal public health agency like the CDC operates, to apply techniques learned from the MPH coursework regarding surveillance systems, and to gain experience in teaching future public health professionals and veterinarians.

Subject Keywords: Toxoplasmosis, surveillance systems, Centers for Disease Control and Prevention, parasitic diseases, reportable diseases

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Chapter 1 - Background to Toxoplasmosis in the US Context

Toxoplasmosis is a disease caused by the protozoan parasite *Toxoplasma gondii*. Felines are the primary host species, but *T. gondii* infects humans and other species by ingesting oocysts released by adult *T. gondii*. Fecal-oral transmission (consuming contaminated food or water) or eating improperly cooked encysted meat (from a *T. gondii*-infected animal with cysts in its tissue) are the most common transmission mechanisms. Toxoplasmosis is the 2nd leading cause of death from foodborne illness, responsible for an estimated 327 deaths annually in the United States (Scallan et al., 2011). In addition to foodborne transmission, vertical transmission (children infected as a result of the mother being infected during pregnancy) and transplantation (tissue cysts being moved into a new host via an organ transplant) have garnered additional attention in recent years. With this in mind, some countries such as France have developed maternal screening systems, testing pregnant mothers for toxoplasmosis monthly during pregnancy. This allows for more successful intervention in the case of maternal infection, during which treatment can be most successful in preventing congenital toxoplasmosis. If a similar system were to be implemented in the US, it is estimated that it would save $2.5 billion per year due to decreased disease burden and associated medical costs (Stillwaggon et al., 2011).

This disease is most significant for neonates and immunocompromised individuals. While in the immunocompetent population, 90% of infected individuals are asymptomatic (Montoya & Liesenfeld, 2004) (symptomatic individuals generally present with flu-like and self-limiting disease), immunocompromised people and children infected *in utero* show a greatly increased risk of severe encephalitis, chorioretinitis, and even death. Due to the ubiquity of the symptoms (or absence of symptoms in the majority of the population), it is likely that this disease goes underreported by physicians. In an outbreak at a horse stable in Atlanta, Georgia, in 1977, of the 25 physicians who saw clinically affected patients from the outbreak, only three correctly diagnosed it as toxoplasmosis (Dubey, 2021).

Modern diagnostic testing has greatly improved the proper diagnosis of this disease, but some challenges still remain. Standard case definitions require both clinical symptomatic and laboratory confirmation components. While the previously described clinical presentation sets the basis for diagnosis, serology, histopathology, and sequence analysis generally act to confirm the likelihood of infection. Detection of *T. gondii* in tissue or by polymerase chain reaction (PCR) is generally a confirmatory laboratory result and indicative of active infection. Serology is a less optimal diagnostic tool, especially when attempting to deduce if the infection

is ongoing or has passed. IgM antibodies tend to peak early in an infection before dropping off within a couple of weeks (although this has been shown to be inconsistent, with some reports of IgM titers remaining elevated for up to 18 months) (Dhakal et al., 2015). IgG antibodies tend to peak a few weeks later, but maintain a higher titer for longer periods of time; a positive IgG titer may or may not be detected well during an acute infection, but it will likely be detectable much later in the disease process or in chronic infections. Sequential testing is required for confirmatory diagnosis due to the change over time in antibody titers and general unreliability of individual titers. However, a newer serology testing method known as avidity testing has become available in reference laboratories such as the Dr. Jack S. Remington Laboratory. With this testing, IgG antibodies bind to the target antigens and then are exposed to urea. If they are low avidity, they will dissociate in the presence of urea while high avidity samples will remain bound. A low IgG avidity demonstrates an acute infection, while a higher avidity indicates a chronic infection (Teimouri et al., 2020).

The CDC provides definitions for reportable and notifiable diseases. Reportable diseases are those for which state health departments “work with healthcare providers, laboratories, hospitals, and other partners to get the information needed to monitor, control, and prevent” (*What Is Case Surveillance?*, 2021) these diseases. Notifiable diseases are those for which data is voluntarily collected by the CDC from the reporting states to monitor disease burden at a regional and/or national level. At the present time, toxoplasmosis is considered a reportable disease in 8 states (Nebraska, Arkansas, Pennsylvania, Minnesota, Wisconsin, Kentucky, Delaware, and Hawaii). Therefore, each of these states collect case data from physicians and laboratories in their respective states who identify cases of toxoplasmosis. This information is not collected by the CDC or any other federal agencies at this time (as they would be if the disease were made notifiable).

The division of power and responsibilities between state and federal governments can offer many pros and cons. For example, by delegating surveillance to the state level, states can quickly learn the best way to perform surveillance and relay that information to the federal level (i.e. the CDC) to advise strategies to improve efficiency in this process (Srinivasan et al., 2012). States often have dedicated individuals assigned to surveillance of certain diseases, providing a more focused approach to these systems. However, this may also be seen as an inefficiency, as it may result in hiring of single-disease focused personnel at the state level to facilitate these types of surveillance systems. A national project aimed at porcine reproductive and respiratory syndrome virus (PRRSV) has given further insight into regional differences in disease surveillance within a national system. In the Morrison’s Swine Health Monitoring Project

(MSHMP), data is voluntarily collected from swine producers and veterinarians within certain regions across the country concerning PRRSV incidence and disease outbreaks. While it has been seen as a net positive in disease monitoring and decreasing the annual financial burden of the disease, regional variations were noted as a concern. This is due to the seasonality of PRRSV as well as variable compliance within certain regions (Perez et al., 2019). Overall, it was beneficial to have a central agency (in this case, the MSHMP) to guide regional programs. The federal government could operate in a similar, central-support role for regional/state surveillance systems of other diseases such as toxoplasmosis. These regional/state discrepancies in disease surveillance can even be seen in the current COVID-19 pandemic. As of the writing of this document (November 2021), several states have reduced the frequency of reporting their county or state-level COVID-19 case numbers, citing staffing issues and privacy concerns (Bauer, 2021). This lack of updated data can have severe consequences, especially for immunocompromised individuals who use this information on a daily basis to determine their own risk and make choices associated with that risk determination.

Parasitic diseases present some unique challenges for preventive medicine as compared to diseases caused by bacterial and viral pathogens. For example, many parasites infect hosts for long enough to reproduce and complete a life cycle before leaving and moving onto the next host. To facilitate this, they modify and block the host's immune response long enough to complete these needs. This is one reason that there are not the same preventive medicine options widely available as there are with other diseases. The primary means of prevention of parasitic diseases are a matter of practicing good hygiene (washing hands regularly and properly) and food safety (including cooking food to an adequate temperature). In human medicine (and for the most part, in veterinary medicine as well) the only medical intervention for parasites is treatment once the burden has been diagnosed.

Vaccine development for parasitic diseases is a challenging endeavor. This is due to the difficulty of stimulating an adequate immune response against the parasite itself, the wide antigenic variation, and the potential for limited return on investment into development (Knox & Redmond, 2006). While there are currently no human toxoplasmosis vaccines available, there is a modified live vaccine available for sheep and goats in parts of Europe and New Zealand. It uses organisms in the tachyzoite stage which are attenuated through passages in mice to stimulate a protective and long-lasting immune response in their livestock hosts. The benefit of this vaccine design is that these organisms cannot enter the bradyzoite stage (which is involved in the tissue encystation that causes persistent infection in the host). Due to the strong protective immunity stimulated by this vaccination, this protection will last for the whole life of the

animal (Tizard, 2021). No human toxoplasmosis vaccines are currently available, although there are several promising candidates in development. Important goals in the development of effective toxoplasmosis vaccines include antigen identification, protective immune response characterization, and live-attenuated vector identification (Rezaei et al., 2019; Foroutan et al., 2018). The hope is that with this type of preventive medicine being made available, the deleterious effects of chronic and acute cases of toxoplasmosis as well as congenital toxoplasmosis in neonates may be avoided. It is unclear exactly why parasitic vaccines tend to lag so far behind viral and bacterial diseases, but it is thought to be a result of the generally greater mortality and severe clinical signs associated with those two classes of pathogens versus the generally mild/chronic effects of many parasitic diseases. Additionally, severe parasitic disease is primarily seen in low-income countries and preventable with proper hygiene, so the financial return from investment in parasitic vaccines may be difficult to realize.

Several major sources of information are available to professionals operating in the One Health field. Notable among those are the CDC website (www.cdc.gov), the *Control of Communicable Diseases Manual* (CCDM) published by the American Public Health Association (APHA), and *The Merck Veterinary Manual* (especially for those working in the veterinary public health field). All of these sources were of value to the author during this field experience and provide important information regarding toxoplasmosis (among other diseases). They include everything from clinical signs to transmission routes to risk factors. However, in the case of toxoplasmosis, information regarding disease burden in these sources and among others shows some inconsistency. For example, the CDC website states that 11% of the US population over the age of 6 has had toxoplasmosis, with that number being as high as 60% in other parts of the world (*CDC - Toxoplasmosis - Epidemiology & Risk Factors*, 2019). The *Merck Veterinary Manual* cites “up to 60% of individuals have IgG titers against toxoplasmosis” (Aiello & Moses, 2016, p. 686), a value similar to that provided by the CDC but with the additional focus on how those numbers are determined based on serology.

The lack of reliable prevalence data is a major driver for the study pursued as a part of this field experience. With toxoplasmosis only being reportable in the aforementioned 8 states, it is difficult to apprehend the true impact of this disease in the United States. The goal was to determine if toxoplasmosis is a good candidate to become a nationally notifiable disease so that its national disease burden could be better determined. For this field experience, the author worked with Dr. Anne Straily in the Parasitic Diseases Branch of the CDC. Dr. Straily received her DVM from Kansas State University and her MPH from the University of Kansas. She also recently became board-certified in Preventive Medicine (Epidemiology). While this project was

completed online, the author was able to interact with other individuals within the Parasitic Diseases Branch through several monthly meetings to learn more about what this portion of the CDC does and what other projects were ongoing.

Chapter 2 - Learning Objectives and Project Description

During the Summer of 2021, the author completed an online field experience due to limitations caused by the COVID-19 pandemic. After meeting Dr. Anne Straily from the CDC during a virtual Vet Student Day hosted by the CDC in January 2021, work began on developing a plan for a field experience helping with a toxoplasmosis surveillance study. Dr. Straily is a veterinarian who graduated from KSU and also received her MPH from the University of Kansas. She has worked for the Parasitic Diseases Branch of the CDC for several years. This experience allowed the author to combine knowledge from the MPH and DVM curriculum to achieve the following learning objectives and complete the associated activities:

2.1 Learning Objectives:

1. To learn about surveillance systems and how they are used by states to monitor toxoplasmosis disease burden
2. To gain a better understanding and first-hand experience in how the CDC monitors diseases in the United States
3. To write a report summarizing the findings of the study and to share the results with personnel at the CDC

2.2 Field Experience Activities:

1. The author worked with the field experience mentor to develop a written report summarizing the findings of the study.
2. The author developed a presentation that summarized the study findings to share with CDC personnel which contained a recommendation for reportability requirements for the future regarding toxoplasmosis.
3. The author developed a presentation for undergraduate students about the risks of toxoplasmosis.
4. The author interviewed the field experience mentor regarding her involvement in the authorship of a toxoplasmosis chapter of the CCDM.

The accompanying Applied Practice Experience (APE) document specifies the various products developed throughout this field experience. These products include the following:

1. Portfolio product no. 1A: “Characterization of public health surveillance and reporting of human toxoplasmosis in the United States” (9)
2. Portfolio product no. 1B: Slide deck developed for presentation of study results to CDC Parasitic Diseases Branch (11)
3. Portfolio product no. 2: Slide deck and class lecture regarding toxoplasmosis (12)
4. Portfolio product no. 3: CCDM article in the *One Health Newsletter* (12)

These four products appear in the appendix to this Integrated Learning Experience (ILE) report.

Chapter 3 - Reflection, Analysis and Key Observations

This chapter devotes time, reflection, and analysis of specific experiences, insights, and "new knowledge" gained by the author. There was much learned during the online field experience with Dr. Straily; in addition, the author's major advisor (Dr. Kastner) and the author have regularly dialogued about what was both experienced and, significantly, *learned* during these last several months.

Portfolio product no. 1A: "Characterization of public health surveillance and reporting of human toxoplasmosis in the United States"

Background on This Product

This report was designed to act as a culmination of the findings of the study, including recommendations regarding whether or not toxoplasmosis should be made a nationally notifiable disease. The written format of this report is designed to be published in a journal relating to public health and/or zoonoses. As such, the general target audience would be those individuals who work in the public health landscape, especially in terms of policy change and disease surveillance.

During the study, the state public health veterinarians of the eight states for which toxoplasmosis is reportable were contacted to schedule an interview to discuss their respective toxoplasmosis surveillance systems. The interviews were based on a nine-question questionnaire, displayed in Table 3.1. This questionnaire acted to ensure that all relevant aspects of toxoplasmosis surveillance were investigated equally between all states so that comparisons could be made.

Table 3.1: *The nine question-template used in all interviews of state officials to gather information on their respective toxoplasmosis surveillance systems.*

1) When was toxoplasmosis made reportable in your state?
2) What are the reasons that toxoplasmosis was made reportable?
3) How was the case definition developed?
4) What, if any, public health actions do you take after a case is confirmed?
5) Who is responsible for reporting cases in your state / how are you typically notified of cases?
6) Do you currently collect non-human data for toxoplasmosis surveillance? If yes, please explain.
7) Do any programs in your state focus on screening pregnant women and/or infants born to infected mothers? If yes, please provide a brief description of the programs.
8) How are the collected data utilized? How are the results disseminated?
9) Have there been any changes to the surveillance for toxoplasmosis since it began in your state? If yes, please explain

After initial attempts to contact and schedule interviews, officials from six out of the eight states were available for discussion (Minnesota, Arkansas, Wisconsin, Nebraska, Pennsylvania, and Kentucky). Responses from all interviewed officials were recorded and results included in the draft manuscript. The manuscript also includes a Discussion section wherein the findings from the interviews were further evaluated to gain an understanding of the limitations of surveillance systems currently in use for toxoplasmosis. This was an important part of the process to develop a recommendation regarding whether or not toxoplasmosis should become a nationally notifiable disease.

Experiential Learning Gained Developing This Product

During this process, the author was introduced to state public health veterinarians and other public health personnel during the interviews with the 6 participating states. This allowed the author to gain a greater understanding of the responsibilities of public health professionals engaged in disease surveillance at the state level. Additionally, their responses to the questionnaire highlighted priorities within surveillance systems which these professionals should be aware of, including why the disease is being monitored, how case data is gathered and recorded, and what is done with that information once it is compiled.

Some great insight into the federal side of surveillance was gained during this experience as well. In working with Dr. Straily at the CDC, the author gained an understanding of what a federal agency such as the CDC would be focused on when compiling data collected from state surveillance systems. This includes case numbers/trends (spatial and temporal), source identification, and support/information offered to healthcare providers and state health departments.

Portfolio product no. 1B: Slide deck developed for presentation of study results to CDC Parasitic Diseases Branch

Background on This Product

This presentation was prepared for a biweekly meeting of the Parasitic Diseases Branch of the CDC on August 26, 2021. The goal of the presentation was to provide the results of the study to all personnel within the Parasitic Diseases Branch. With the majority of the personnel having an advanced knowledge of parasitic diseases and their surveillance (such as toxoplasmosis), less background information was provided in the presentation and more focus was given towards conveying the findings of the study to inform policy. Essentially, all information from Portfolio product no. 1A was summarized within the presentation, including the results as well as relevant interpretations and considerations identified.

Experiential Learning Gained Developing This Product

With the intended audience of this presentation being more experienced in knowledge of parasitic organisms and their surveillance, this activity challenged the author to provide additional detailed information regarding the disease. Additionally, the author was able to envision additional considerations regarding the results of the study from a public health professional's perspective. For example, a weak point revealed by background research as well as interview results was that physicians may not be adequately identifying suspect toxoplasmosis cases, indicating that reported toxoplasmosis numbers may be much lower than actual numbers due to lack of diagnosis. One proposed way for the CDC to intervene and provide support was to provide more education for physicians regarding toxoplasmosis diagnostic options to improve proper screening for this disease.

Portfolio product no. 2: Slide deck and class lecture regarding toxoplasmosis

Background on This Product

This presentation was developed for Dr. Kastner's undergraduate *Environmental and Public Health* course (DMP 314). The focus of the presentation was toxoplasmosis and the environmental health considerations for the disease. Given the lack of experience in the intended audience, this presentation included much more background information regarding toxoplasmosis than did Portfolio product no. 1B. Additionally, with a focus of the class being environmental health, the author highlighted risk factors for the disease with environmental causes. These included food safety, proper food handling and preparation, as well as at-risk populations such as pregnant women and immunocompromised individuals.

Experiential Learning Gained Developing This Product

As the author has an interest in teaching as a part of his career, this presentation gave the author an opportunity to practice giving lectures to college students. In addition to this, the author also developed quiz questions to provide to the students after the lecture to further hone their learning and to ensure that they received all relevant information from the presentation.

Portfolio product no. 3: CCDM article in the *One Health Newsletter*

Background on This Product

This article was produced to provide interested future public health professionals and readers of the *One Health Newsletter* with relevant sources to use in their career. The focus of the article was the *Control of Communicable Diseases Manual* (CCDM) produced by the American Public Health Association (APHA). This resource is used by Dr. Kastner in his previously mentioned undergraduate public health course and Dr. Straily is also an author for this publication. To prepare the article, Dr. Straily was interviewed by the author and Dr. Kastner to learn more about her experience with its publication and more about the publication itself. While the CCDM was the focus, the article also included brief information regarding the *Yellow Book, Red Book,* and *The Merck Veterinary Manual*, all of which are regularly used by public health professionals in various fields.

Experiential Learning Gained Developing This Product

Through the experience of preparing for and writing this article, the author became more aware of various resources available to public health professionals. More specifically, the author obtained a copy of the CCDM to learn more about how it may be used, especially in regards to learning more about toxoplasmosis. This resource was used as a primary source for information when developing all previously described products. The information gained from preparing this article equipped the author to share with not only other public health students but also other veterinary students the value that the CCDM provides. By highlighting the value of the CCDM, the author has sought to "equip" his fellow veterinary students with resources other than just, for example, *The Merck Veterinary Manual*.

Additional Reflection: Observation of State-Federal Disease-Reporting

This study demonstrated to the author an in-depth and immersive view of disease surveillance, especially in regards to the reportability of diseases. As the focus of the study was to determine whether or not toxoplasmosis was an acceptable candidate to become nationally notifiable, the author first needed to gain an understanding of the differences between these two distinctions (reportable vs. nationally notifiable). Briefly, reportable diseases are those for which states choose to collect data regarding disease prevalence within their states. They require case numbers to be reported to their state health department (generally using case definitions that they must develop) and use that data to develop policy within their states. When a disease becomes nationally notifiable, the primary difference is that states listing the disease as reportable then also voluntarily give their case data to a federal agency (generally the CDC).

This process can be an excellent way to monitor disease both regionally and at a national level. However, it also opens itself up for many inconsistencies. Especially when a disease is just classified as reportable, it is left up to the states to develop their own case definitions most of the time. This makes it very difficult to determine accurate numbers as many of these definitions may classify cases differently and may be missing some individuals. While this is commonly corrected under a nationally notifiable system (which generally provides a case definition developed by the CDC to be applied in the reportable states), nationally notifiable diseases are not without their own challenges.

Nationally notifiable diseases generally require additional personnel to be employed at the federal agency to collect and record data from reporting states. Additionally, the participating states are still not required to submit their data to the CDC. This data is still provided voluntarily.

If only a few states in separate regions are providing data, it does not provide much benefit within a nationally notifiable disease reporting system to truly perform an analysis about the state of a disease within a region or nation.

Additional Reflection: Perception of Role of Veterinarian at CDC in Public Health

During weekly meetings held via Zoom with Dr. Straily, the author was able to gain a greater understanding of the roles and responsibilities of a veterinarian operating in the public health field with a federal agency such as the CDC. Dr Straily shared with the author about other projects within the Parasitic Diseases Division which she was involved with, including projects related to a variety of zoonotic, parasitic diseases. In addition to this, the author was able to see how a veterinarian may work with human health professionals within the CDC (an agency which primarily focuses on human diseases/zoonoses) and the specific strengths that a veterinarian can bring to a public health-oriented group. This includes having a deeper knowledge and understanding of the interactions between parasites/diseases and their human and/or animal hosts.

In addition to the weekly meetings with Dr. Straily, the author also engaged in other activities within the CDC. These included biweekly meetings within the Parasitic Diseases Division as well as the monthly Zoonoses and One Health Updates (ZOHU) meetings. In the Parasitic Diseases biweekly meetings, the author was able to learn about other projects occurring within the division, specifically focused on parasitic diseases, such as toxoplasmosis. This gave the author the opportunity to not only see other veterinarians operating in this role, but also observe how other human health professionals worked together on these projects. While the ZOHU meetings were broader than just parasitic diseases, it also showed an even wider range of ways that a veterinarian may be involved in both diseases of human health and animal health. It also helped to capture the vast reach of the CDC, showcasing projects from around the world and with many different diseases, some of which not being focused on within the veterinary curriculum.

As a part of the study conducted with Dr. Straily, the author had several conversations regarding what the role of a veterinarian at the CDC would be in the case of diseases that may become nationally notifiable in the future (as this was the purpose of the study). This included compiling data from all reporting states, travelling to sites of disease outbreak to monitor disease burden, and offering technical support to health departments within relevant states or other countries.

Additional Reflection: MPH Coursework That Was Most Helpful

Several courses within the MPH program were especially noteworthy as providing additional value during the author's time working on this field experience. These courses included *Principles of Veterinary Immunology* (DMP 705), *Introduction to One Health* (DMP 710), *Multidisciplinary Thought and Presentation* (DMP 815), and *Social/Behavioral Aspects of Public Health* (MPH 818).

Principles of Veterinary Immunology is part of the first-year veterinary curriculum. However, it holds immense value from a public health perspective as well. Notably, the author found relevance to this study in the analysis of diagnostic results as a component of the case definitions provided by states. Serology is the backbone of the laboratory diagnosis portion of case definitions for toxoplasmosis (although the laboratory criteria vary among states). Discussion of both when immunoglobulins can be expected to be elevated in the presence of disease as well as diagnostic testing options in DMP 705 were both beneficial in comparing the differing serology-based case definitions provided by states. Additionally, reference laboratories have begun using a more accurate type of serological testing known as avidity testing. An understanding of how immunoglobulins bind target antigens and how that binding can be altered is essential to developing new serological diagnostic approaches such as this one.

Introduction to One Health is especially relevant for zoonotic diseases such as toxoplasmosis. While the study was more focused on toxoplasmosis in humans, an understanding of how the animal hosts are involved in the infection cycle is important as well, especially in guiding recommendations to prevent human exposure and infection. This course also provided benefit in preparing Portfolio product no. 2, focusing on the environmental factors involved in disease transmission pertaining to toxoplasmosis.

Multidisciplinary Thought and Presentation was a central source of technical skills during the author's field experience, specifically when it came to the writing and presentation-preparation portions. This class gave practical tips for both preparing technical reports such as Portfolio product no. 1A and 3 as well as the presentations seen in Portfolio product no. 1B and 2. Having practiced these skills when taking this course in Summer 2020 made applying these skills during the field experience much less daunting.

Social/Behavioral Aspects of Public Health offered some new viewpoints regarding public health in general. This course encourages students to think beyond just the medical component of public health and consider more of the socioeconomic components. In the case of toxoplasmosis, there are several ways in which these factors can be considered. For example, while reference laboratories seem to be the optimal way to accurately diagnose an individual's

current state of infection, this type of diagnostic testing is not always covered by health insurance, requiring several hundred dollars to be paid out of pocket. This excludes impoverished communities from having access to this type of accurate diagnostic testing and may even be a cause for underreporting of this and other diseases.

Chapter 4 - Competencies

Student Attainment of MPH Foundational Competencies

The author gained a valuable background in several essential public health-related skill sets through the coursework which was then applied and expanded on during the field experience. Table 4.1 describes the five competencies covered through the field experience as well as how they were achieved via the deliverables that were produced.

Table 4.1 Summary of MPH Foundational Competencies

Number and Competency		Description
4	Interpret results of data analysis for public health research, policy or practice	After completing interviews with the state public health officials, the author evaluated their responses to gain a better understanding of their surveillance systems. He was able to compare and contrast these responses to learn more about differences amongst how these states monitor toxoplasmosis burden. These responses were aggregated and described in the draft publication (Portfolio product no. 1A).
12	Discuss multiple dimensions of the policy-making process, including the roles of ethics and evidence	A component of the data interpretation and interview process described above included asking states when and how they began reporting toxoplasmosis burden within their state. This helped the author to learn more about the process that went into developing the policies regarding toxoplasmosis reporting in each state as well as to identify common themes in this process as described in Portfolio product no. 1A.
15	Evaluate policies for their impact on public health and health equity	By interviewing public health officials from six different states, the author was able to learn about how each of these states perform toxoplasmosis surveillance. In doing so, he was also able to identify some ways in which this reporting process may not be equitable. For example, some of the laboratory testing utilized by some states is very expensive and not covered by insurance. This may exclude a large part of the population from having access to this type of testing, an important distinction noted in the publication as part of Portfolio product no. 1A.
19	Communicate audience-appropriate public health content, both in writing and through oral presentation	The author was able to write a final report on the findings of this investigation (Portfolio product no. 1A). In addition to this, he gave a presentation to the PDM branch of the CDC regarding the findings of this investigation (Portfolio product no. 1B). This audience was overall very knowledgeable both on toxoplasmosis itself as well as surveillance of this and other parasitic diseases. The author also gave a presentation to an undergraduate *Environmental and Public Health* class about toxoplasmosis (Portfolio product no. 2), which allowed him to change his delivery toward an audience that had less

		experience and prior knowledge about toxoplasmosis.
21	Perform effectively on interprofessional teams	Throughout this process, I was able to meet several people from different teams within the CDC and the PDM branch. This allowed me to meet with people from a variety of different professional backgrounds which provided me a great learning environment. In both of the publications (Portfolio products no. 1A and 3), the author worked with Dr. Straily and the state public health veterinarians interviewed to gain insight into the material from a variety of viewpoints and backgrounds.

Below, Table 4.2 displays all of the Foundational Competencies within the program and the associated coursework within which these competencies are taught.

Table 4.1 MPH Foundational Competencies and Course Taught In

22 Public Health Foundational Competencies Course Mapping	MPH 701	MPH 720	MPH 754	MPH 802	MPH 818
Evidence-based Approaches to Public Health					
1. Apply epidemiological methods to the breadth of settings and situations in public health practice	x		x		
2. Select quantitative and qualitative data collection methods appropriate for a given public health context	x	x	x		
3. Analyze quantitative and qualitative data using biostatistics, informatics, computer-based programming and software, as appropriate	x	x	x		
4. Interpret results of data analysis for public health research, policy or practice	x		x		
Public Health and Health Care Systems					
5. Compare the organization, structure and function of health care, public health and regulatory systems across national and international settings		x			
6. Discuss the means by which structural bias, social inequities and racism undermine health and create challenges to achieving health equity at organizational, community and societal levels					x
Planning and Management to Promote Health					
7. Assess population needs, assets and capacities that affect communities' health		x		x	
8. Apply awareness of cultural values and practices to the design or implementation of public health policies or programs					x
9. Design a population-based policy, program, project or intervention			x		
10. Explain basic principles and tools of budget and resource management		x	x		

22 Public Health Foundational Competencies Course Mapping	MPH 701	MPH 720	MPH 754	MPH 802	MPH 818
11. Select methods to evaluate public health programs	x	x	x		
Policy in Public Health					
12. Discuss multiple dimensions of the policy-making process, including the roles of ethics and evidence		x	x	x	
13. Propose strategies to identify stakeholders and build coalitions and partnerships for influencing public health outcomes		x		x	
14. Advocate for political, social or economic policies and programs that will improve health in diverse populations		x			x
15. Evaluate policies for their impact on public health and health equity		x		x	
Leadership					
16. Apply principles of leadership, governance and management, which include creating a vision, empowering others, fostering collaboration and guiding decision making		x			x
17. Apply negotiation and mediation skills to address organizational or community challenges		x			
Communication					
18. Select communication strategies for different audiences and sectors	DMP 815, FNDH 880 or KIN 796				
19. Communicate audience-appropriate public health content, both in writing and through oral presentation	DMP 815, FNDH 880 or KIN 796				
20. Describe the importance of cultural competence in communicating public health content		x			x
Interprofessional Practice					
21. Perform effectively on interprofessional teams		x			x
Systems Thinking					
22. Apply systems thinking tools to a public health issue			x	x	

Student Attainment of MPH Emphasis Area Competencies

The author's emphasis area is Infectious Diseases and Zoonoses. This emphasis pairs well with his interest in veterinary medicine and disease control/surveillance. The field experience helped to reinforce several concepts learned in class, with toxoplasmosis being the primary zoonotic disease focused on in the course of this study. Table 4.3 below describes the ways in which the author enhanced his skills during this experience pertaining to understanding pathogens and how to monitor and combat their corresponding disease.

Table 4.2 Summary of MPH Emphasis Area Competencies

MPH Emphasis Area: Infectious Diseases and Zoonoses		
Number and Competency		**Description**
1	Pathogens/Pathogenic mechanisms	While toxoplasmosis doesn't cause any clinical signs in most cases, in those that do, there are severe inflammatory signs, generally in the nervous system. Once an individual is infected, the organisms move through the body via the blood/lymphatic system and encyst somewhere in the body. Depending on where the cysts develop generally indicates the associated inflammatory signs. Two of the most severe manifestations include encephalitis (cysts in/near the brain) and chorioretinitis (cysts in the eye).
2	Host response to pathogens/immunology	An important distinction in the disease prevalence of human toxoplasmosis is that it is much more likely to cause systemic disease in immunocompromised individuals. The majority (90%) of immunocompetent individuals infected with *T. gondii* will show no symptoms (Montoya & Liesenfeld, 2004). Many states interviewed had developed differential case definitions which accounted for the range in symptoms displayed between these two populations.
3	Environmental/ecological influences	When preparing the presentation as part of Portfolio product no. 2, the author performed extensive literature analysis to identify and describe the environmental influences and risk factors for toxoplasmosis. Additionally, the CCDM was one of the primary sources for this and other important background information regarding toxoplasmosis. Through this, he was able to explain the importance of fecal-oral transmission as a source of infection as well as the importance of proper food handling to reduce risk of infection.
4	Disease surveillance	Since the primary goal of this study was to gain a better understanding of current toxoplasmosis surveillance systems utilized in the United States, the author was able to learn more about these as well as how these systems work in general. This is a subject that he had learned about in several courses in the MPH program. Through this study, the author also learned about several different diagnostic options used by states either through commercial or reference laboratories.
5	Disease vectors	While cats are the primary vector for *T. gondii,* the main way that it infects humans is through improper food handling/hand washing (Heymann, 2015). Cooking potentially infected meat fully and washing

		vegetables are two important food handling steps which can be taken to reduce the risk of toxoplasmosis. There are no insect vectors of this disease, and the main way of getting it from cats is from fecal-oral transmission (contamination of hands from cleaning cat litter or working in contaminated soil).

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Appendix

1. Portfolio product no. 1A: “Characterization of public health surveillance and reporting of human toxoplasmosis in the United States”
2. Portfolio product no. 1B: Slide deck developed for presentation of study results to CDC Parasitic Diseases Branch
3. Portfolio product no. 2: Slide deck and class lecture regarding toxoplasmosis
4. Portfolio product no. 3: CCDM article in the *One Health Newsletter*

Characterization of public health surveillance and reporting of human toxoplasmosis in the United States

Jayden McCall[1], Anne Straily[2]

1. Kansas State University College of Veterinary Medicine, Department of Pathobiology, Manhattan, KS 66506
2. Division of Parasitic Diseases and Malaria, Parasitic Diseases Branch, Centers for Disease Control and Prevention, Atlanta, GA

Introduction

Toxoplasmosis is caused by infection with the zoonotic protozoan parasite *Toxoplasma gondii*. Individuals can be infected from a variety of sources, including fecal-oral contamination from cats, consumption of contaminated undercooked meat, contaminated unwashed fruits or vegetables, contaminated water, and unpasteurized milk; vertical transmission from an infected mother, and organ transplants. In immunocompetent individuals, the disease tends to have minor clinical signs (flu-like symptoms), if any. Typically, disease is more severe among immunocompromised individuals, who can develop neurological disease which can be fatal. Additionally, the risk posed to fetuses from mothers infected during development is another major threat. These children infected in utero may be subject to a wide range of symptoms including ocular infection, cranial deformities, or death (stillbirth or miscarriage). Despite the potential severity of the disease and multitude of potential transmission routes, there is currently no national public health surveillance data available for toxoplasmosis in the United States as it is not a nationally notifiable disease. However, 8 states have classified toxoplasmosis as a reportable disease and gather information from cases reported in each of their states. This study sought to learn why states made toxoplasmosis reportable, how they define cases, and what they do with the data produced in their state to better inform public health decision making with regard to whether toxoplasmosis should be designated a nationally notifiable disease.

Materials and Methods

States where toxoplasmosis is reportable were identified using the State Reportable Conditions Assessment (SRCA) query tool on the Council for State and Territorial Epidemiologists (CSTE) website (https://www.cste.org/group/SRCAQueryRes) and supplemented by reviewing reportable diseases lists accessed from state public health websites for the inclusion of toxoplasmosis. CSTE's definitions of explicit and implicit reporting were used to classify states: if toxoplasmosis was mentioned by name in the state's laws or reportable condition lists and case definitions and surveillance criteria for toxoplasmosis were available then the state was categorized as "explicitly reportable"; if toxoplasmosis was not specifically listed as reportable but would be considered reportable under general language in the jurisdiction's laws, such as for reporting outbreaks or clusters of public health importance then the state was considered "implicitly reportable".

A brief questionnaire of 9 questions was developed to gather all intended information for the study (Table 1). State public health veterinarians (SPHVs) were contacted via email and invited

to participate either in an interview over Zoom or to simply complete the questionnaire and return it. This activity was reviewed by the CDC's Center for Global Health and determined to be non-research. Responses from the questionnaire were aggregated and results of descriptive analyses are presented.

Table 1. *The 9 question-template used in all interviews of state officials to gather information on their respective toxoplasmosis surveillance systems.*

1) When was toxoplasmosis made reportable in your state?
2) What are the reasons that toxoplasmosis was made reportable?
3) How was the case definition developed?
4) What, if any, public health actions do you take after a case is confirmed?
5) Who is responsible for reporting cases in your state / how are you typically notified of cases?
6) Do you currently collect non-human data for toxoplasmosis surveillance? If yes, please explain.
7) Do any programs in your state focus on screening pregnant women and/or infants born to infected mothers? If yes, please provide a brief description of the programs.
8) How are the collected data utilized? How are the results disseminated?
9) Have there been any changes to the surveillance for toxoplasmosis since it began in your state? If yes, please explain.

Results

As of April 2021, eight states conduct surveillance for toxoplasmosis. The following states were identified as having toxoplasmosis listed as explicitly reportable using the CSTE SRCA tool: Pennsylvania, Arkansas, Wisconsin, Minnesota, and Hawaii. Upon searching state health department websites, Kentucky, Delaware, and Nebraska were also added to this list. Of the eight identified states, public health personnel from six agreed to participate and were interviewed: Kentucky, Minnesota, Wisconsin, Nebraska, Philadelphia, and Arkansas. Delaware declined and a contact for Hawaii was not able to be located for interview and as such, these two states were omitted from this analysis.

None of the interviewed state personnel were able to identify a specific date for when toxoplasmosis became reportable in their state. One state suggested that it may have been in the 1970s. It was commonly noted among all states that toxoplasmosis had been reportable for as long as could be remembered. Likewise, since no one interviewed was present when toxoplasmosis was made reportable, no one knew exactly what prompted adding it to the reportable diseases list, or if any significant changes had been made over time.

Several different reasons were offered for why toxoplasmosis was made reportable. Among the most frequently reported was the goal of identifying the source of infection (3/6). This was followed by the effect of toxoplasmosis on pregnancy and states who responded with "unknown" (2/6), and then by states focusing on outbreak identification. Response options were not mutually exclusive and some states included a combination of these responses.

When asked how their case definition was developed, many states did not have a clear answer and were not able to find information to answer this question. However, those that did generally used a combination of clinical and laboratory components, as is standard for surveillance case definitions (Table 2). For example, the case definition from Kentucky and Wisconsin specified that a confirmed case would be a patient with matching clinical signs and laboratory confirmation achieved through *T. gondii* detection in tissue/body fluids, significant antibody titer change, and/or positive polymerase chain reaction (PCR) test. Probable cases in those same states were defined as those presenting with the expected clinical signs but with only a single positive antibody titer. Pennsylvania, Arkansas, and Minnesota provided a very similar case definition; however, they had a paired antibody titer change in the "supportive" or "probable" laboratory evidence category. Notably, Minnesota refers to the Palo Alto (now the Dr. Jack S. Remington Laboratory for Specialty Diagnostics) toxoplasmosis reference laboratory in the discussion of their serology testing for cases.

The majority of states (5/6) indicated that they would gather a history from the patient (looking specifically at exposure history and clinical signs). Based on this information, they would then work to investigate potential outbreaks depending on the source, if identified. After gaining a proper history from the patient, most states (5/6) also indicated that they would provide education regarding proper sanitation and prevention strategies regarding toxoplasmosis, especially for immunocompromised or pregnant mothers. Two states (Pennsylvania and Minnesota) indicated that they would also get similar information from the patient's physician/primary care provider (PCP) or infection control nurse (Pennsylvania).

All states interviewed identified laboratories as their primary reporting source. Physicians are generally the front line against toxoplasmosis, as they are responsible for coordinating laboratory testing for their patients showing toxoplasmosis symptoms. However, in Minnesota, veterinarians and veterinary diagnostic labs may also report cases to the state health department in "certain circumstances". None of the states interviewed collected non-human data as part of their surveillance for toxoplasmosis.

No states reported having formal maternal screening programs for toxoplasmosis. However, in Minnesota, the SPHV noted that maternal screening is frequently recorded as a reason for testing on case report forms submitted to the state health department.

Half of states (3/6) prepared public reports from their collected data. This information was generally posted to their website and made accessible for the general public. Two states reported that they prepared "in-house" reports, indicating that while they did compile their surveillance data, the distribution of those reports was restricted to within the agency and not shared publicly through their website or other avenues. Finally, one state (Kentucky) reported that they only

updated toxoplasmosis case counts in the annual disease tables along with other diseases surveyed within their state, which are available on the state health department website.

Discussion

For those states where toxoplasmosis is currently reportable, it appears to be a legacy disease; none of the individuals who were interviewed could pinpoint why or when it was made reportable in their state. This produced other issues with our interview as several questions were focused on aspects related to this information (such as why it was made reportable and if any changes had been made since it was made reportable). It seems likely that these states made it reportable around the same time (estimated by some to be in the 1970s), but the reasoning for this is unclear. There is perhaps evidence of a common event preceding reportability in these states in that Kentucky and Wisconsin share a nearly identical case definition. It is possible that there was a case definition offered from CSTE or CDC at that time that was used and modified by these states around the same time, but we were unable to find historical evidence of this.

As with many other aspects of these interviews, we found that some of the case definitions had several commonalities. For example, they all incorporated PCR and histopathology as a part of the laboratory evidence of their case definitions, likely because these types of testing are readily available at multiple commercial laboratories and rarely display false positive results (Contini, 2008). There were also important differences in the laboratory criteria and clinical case definitions, as well as the case classifications. The most prominent difference was in the way that serological testing definitions were applied. While many states identified that paired or sequential antibody testing would qualify a case as confirmed (with individual titers only being suggestive), neither Pennsylvania nor Arkansas had any allowance for serology results in their confirmed case definition. Additionally, Minnesota was the only state to identify a reference laboratory as a distinct source for laboratory criteria in their surveillance case definition. Not all states provided distinctions in clinical symptoms based on immunocompetency or age of the patient at time of infection. All states except for Arkansas provided this contrast and reported similar differences in symptoms amongst these populations. Notably, Pennsylvania even noted a difference in time of infection during pregnancy with different clinical symptoms. Minnesota was the only state to classify cases based on symptoms and laboratory diagnostic definitions for latent infections.

With all of these minor differences between definitions, there would be immense benefit in having a common case definition for all states to use. This would typically be a result of the disease being made nationally notifiable so that a case definition could be applied to all cases being voluntarily reported to the CDC. With a common case definition, this would ensure that no individuals are missed by the irregularity of the several different case definitions currently in use in states as described in Table 2.

Serology may not be the best indicator of active infection, unless additional and more specialized testing is done (for example at a reference laboratory). Once infected, people remain infected presumably for life and likely maintain detectable antibody levels, even without reverting to or showing signs of active disease (latent/chronic infections). Commercially

available serology tests, which typically examine immunoglobulin (Ig) G and IgM antibody levels, cannot reliably differentiate acute from chronic infection. IgM may remain elevated for 18 months or more following infection (Dhakal et al., 2015) and IgG may be present during acute infections (Teimouri et al., 2020). Advanced serological tests, like IgG avidity testing or IgA or IgE antibody levels, available only through a reference laboratory, are required to differentiate acute from chronic infections on the basis of serology alone. This is an important and necessary distinction for public health departments to make: investing time and resources into further investigation of a person with a latent/chronic infection acquired at some point in the distant past to attempt to identify a source would be unlikely to yield actionable information that could be used to prevent additional illnesses, if a source could be identified at all. A more accurate diagnostic tool could be PCR, as DNA would only be readily detectable among patients with active infections, but this is likely more fruitful in immunocompromised patients. Several states indicated that PCR was a confirmatory laboratory diagnostic test as part of their case definition. Serology, however, still seemed to be a primary source for investigation across all states. The testing provided by the Dr. Jack S. Remington Laboratory is beneficial in differentiating acute and chronic cases of toxoplasmosis, especially among pregnant mothers to help determine the risk to their unborn children. However, this advanced testing may be financially out of reach of many patients: the test panels cost anywhere from $330-811 USD (*Fee Schedule | Sutter Health*, 2018) and cannot be billed to a patient's health insurance provider. While this type of testing was only reported by Minnesota in their surveillance efforts when indicated, this financial barrier alone may be prohibitive in proper surveillance and may not allow all individuals affected by toxoplasmosis to receive appropriate testing and treatment. It is difficult to say whether commercial testing alone results in over-treatment or under-treatment. Based on the discrepancy in determining current activity of disease (acute versus chronic) described above from commercial testing, a larger focus on reference laboratory testing would at least provide more clear diagnostic outcomes, allowing for more accurate diagnosis and treatment.

Toxoplasmosis is likely underdiagnosed in the United States, as approximately 90% of infections among immunocompetent persons are generally asymptomatic or non-specific and are self-limiting (Montoya & Liesenfeld, 2004), there is no national maternal screening program, and most infants born with congenital toxoplasmosis appear normal at birth (Dubey, 2016). Physician awareness of toxoplasmosis may also be low, resulting in missed opportunities for diagnosis and case identification. For example, in an outbreak of toxoplasmosis in Atlanta, Georgia in 1977, only 3 out of the 25 physicians involved were able to correctly diagnose the patient with toxoplasmosis (Dubey, 2021). In another, more recent example, toxoplasmosis was not considered as a differential diagnosis in a recent outbreak documented in Wisconsin until the physician consulted with the state health department (Schumacher et al., 2021). As described previously, physicians are the front line in the reporting process in all of the states interviewed. This is an important commonality, because these physicians may act as a limitation in the evaluation of toxoplasmosis prevalence. While this is understandable as toxoplasmosis is a disease with a wide, non-specific set of symptoms, it does show a weakness in the current structure of surveillance employed in these states. This weakness may be overcome with increased training and awareness surrounding toxoplasmosis diagnosis for medical professionals.

Multiple approaches may be taken to achieve this. For one, the Association of American Medical Colleges (AAMC) may be able to encourage toxoplasmosis education during medical school for future practitioners. Additionally, the CDC can provide increased guidance for proper diagnostics through both website resources as well as annual or semi-annual trainings offered to current or future practitioners. Another step that would help would again be the implementation of a common case definition. This would allow not only better assessment of disease burden, but would also provide another resource for practitioners to use to adequately diagnose cases of this disease.

Toxoplasmosis poses some unique challenges for public health surveillance. First, among immunocompetent people, disease is largely asymptomatic. Once a person is infected, they remain infected presumably for life, so they may always have detectable antibody titers. Even if acute infections could be easily identified, it is very difficult to definitively identify the source of exposure with this disease. *Toxoplasma gondii* is ubiquitous, with multiple transmission pathways that could result in human infection. Even with a thorough and complete patient history, any number of sources could have attributed to the patient's exposure to *T. gondii.* In outbreak scenarios it may be easier to find a common source but in the case of seemingly sporadic cases among individuals, it can be much more difficult to identify one lone cause.

One of the primary goals of this study was to investigate if toxoplasmosis should be considered as a candidate to become a nationally notifiable disease. With this change, a standardized case definition would be developed and implemented and all states where the illness is made reportable would voluntarily submit case data to the CDC. This information could be used to evaluate disease burden, identify outbreaks, monitor regional differences in disease prevalence, identify potential interventions, and evaluate their success. Based on the results of this investigation, toxoplasmosis does not appear to be an acceptable candidate for this designation at this time. Participating states did not feel that toxoplasmosis was a major priority within their health departments, with some even considering removing it from their current surveillance systems following our evaluation.

This study is subject to several limitations. Not all eight states could be interviewed, and although the six that participated described relatively similar surveillance systems it is unknown what type of system Hawaii and Delaware have in place or how they operate. This evaluation was conducted during the ongoing COVID-19 pandemic, and more specifically during the delta variant surge, which may have affected state health department personnel's viewpoint on the relative importance of toxoplasmosis.

Conclusion

It is the authors' opinion at this time based on the data gathered through this study that toxoplasmosis is not a good candidate to be made nationally notifiable. While it is very likely an underreported disease, there does not appear to be ample concern or burden within the states where it is currently reportable to justify the creation of a passive surveillance system at the national level. The majority of states that were interviewed gave very similar responses to all questions asked, suggesting some consistency in the structure and efficacy of their current

surveillance strategies. However, many states indicated that their primary public health response is simply educating at-risk populations such as the immunocompromised and pregnant women about the danger of toxoplasmosis. This strategy would appear to be one which many individuals involved in public health (physicians, health department personnel, etc.) could support and enhance to help protect our nation's population from the effects of toxoplasmosis.

Conflicts of Interest

The authors have no conflicts of interest to report.

Acknowledgments

Table 2. Surveillance case definitions for toxoplasmosis from each of the six states included in the evaluation; clinical case criteria, laboratory criteria, and case classifications are included. *States and corresponding clinical definition with laboratory diagnosis methods. Included in the laboratory methods portion are clarifiers to show if a case is considered "suspect"/ "probable" or "confirmatory". Some states identified different clinical definitions based on age or immune status of the patient as well.*

State	Clinical Criteria	Laboratory Criteria	Case Classification
Arkansas	Cervical lymphadenopathy and/or flu-like illness and/or ocular infection with vision loss	• Elevated *T. gondii*-specific IgG, IgM, IgA, and/or IgE titers (presumptive) • Isolation of *T. gondii* in blood/fluids; detection of tachyzoites in tissue; and/or detection using PCR (confirmatory)	• Confirmed – A clinically compatible case with confirmatory laboratory results • Probable – a clinically compatible case with laboratory results indicative of presumptive infection
Kentucky	Fever, lymphadenopathy, and/or lymphocytosis. Immunocompromised persons: above, plus myocarditis, pneumonia, and/or cerebral signs Infection during pregnancy: congenital anomalies or infant mortality	• Single antibody titer (suspect) • Significant change in paired specimen antibody titers; demonstration of *T. gondii* in tissues/fluids; detection by PCR; and/or specific IgM or increasing titer in sera in congenital infection (confirmed)	• Confirmed – a clinically compatible illness that is laboratory confirmed; clinical diagnosis and laboratory confirmation • Probable – a clinically compatible illness that is laboratory suspect
Minnesota	Immunocompetent: Ranging from asymptomatic to flu-like symptoms, fever, lymphadenopathy, and/or chorioretinitis. Immunocompromised: Encephalitis and/or chorioretinitis Latent: No symptoms required.	• Individual positive IgM test with/without positive IgG test from commercial laboratory (suspect) • *T. gondii* in tissue; positive PCR; and/or confirmatory testing at reference lab (positive IgM and/or low IgG avidity test) (confirmed) • Positive IgG or IgM from commercial laboratory with no symptoms OR reference lab results indicating past infection (negative	•

		IgM/positive IgG/high IgG avidity) (latent)	
Nebraska	Fever, lymphadenopathy, malaise, lymphocytosis, and/or elevated liver enzymes. Immunocompromised: Chorioretinitis, myocarditis, pneumonia, and/or encephalitis. Mothers infected during pregnancy: Infant death or congenital abnormalities. Neonatal: Fever, rash, jaundice, and/or chorioretinitis	• Detection of *T. gondii* in tissue or by PCR; and/or IgG/IgM change in paired serology (confirmed)	•
Pennsylvania	Immunocompetent: lymphadenopathy and/or ocular infection (uveitis) Immunodeficient: encephalitic symptoms with or without pulmonary/cardiac involvement Newborn infants (early pregnancy infection): fever, lymphadenopathy, microcephaly, megalocephaly, rash, and/or anemia Newborn infants (3^{rd} trimester infection): ocular complications/developmental days in later life	• Sequential sera displaying four-fold rise in *T. gondii*-specific IgG antibody titer (supportive) • Demonstration of *T. gondii* organisms in tissue; demonstration of tachyzoites in tissue by histopathology; and/or positive PCR (confirmatory)	• Confirmed: a case that meets the clinical case definition and is laboratory confirmed • Probable: a case that meets the clinical case definition and has only supportive laboratory results • Suspect: a case that meets clinical case definition and has other laboratory test results, or no laboratory testing was performed
Wisconsin	Fever, lymphadenopathy, and/or lymphocytosis. Immunocompromised: Above, plus myocarditis, pneumonia, and/or cerebral signs Infection during pregnancy: Congenital anomalies or infant mortality	• Change in paired specimen antibody titer; demonstration of *T. gondii* in tissues/fluids; detection by PCR; and/or specific IgM or increasing titer in sera in congenital infection (confirmed)	•

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Centers for Disease Control and Prevention

Toxoplasmosis Reporting and Surveillance Characteristics in the United States

Jayden McCall and Anne Straily, DVM, MPH, DACVPM (Epi)

August 26, 2021

Toxoplasmosis: Why it's Important

- 10.4% seroprevalence in USA
- Wide variety of sources (improperly cooked/washed foods, cat feces, etc)
  - Additionally, vertical transmission (from infected mother) and transplants
  - 4th leading cause of hospitalization and 2nd leading cause of death due to foodborne illness
- Not currently nationally notifiable
  - Reportable in 8 states

States with Toxoplasmosis Listed as Reportable

- Wisconsin
- Minnesota
- Arkansas
- Kentucky
- Nebraska
- Pennsylvania
- Delaware
  - Not interviewed
- Hawaii
  - Not interviewed

Questionnaire

1. When was toxoplasmosis made reportable in your state?
2. What are the reasons that toxoplasmosis was made reportable?
3. How was the case definition developed?
4. What, if any, public health actions do you take after a case is confirmed?
5. Who is responsible for reporting cases in your state / how are you typically notified of cases?
6. Do you currently collect non-human data for toxoplasmosis surveillance? If yes, please explain.
7. Do any programs in your state focus on screening pregnant women and/or infants born to infected mothers? If yes, please provide a brief description of the programs.
8. How are the collected data utilized? How are the results disseminated?
9. Have there been any changes to the surveillance for toxoplasmosis since it began in your state? If yes, please explain
10. Are you willing to partner with CDC and other states where toxoplasmosis is reportable on a review of U.S. toxoplasmosis public health surveillance?

When was toxoplasmosis made reportable in your state?

- **No state was able to identify a specific date**
  - **AR officials found evidence of it being some time in the 1970s**
  - **Kentucky and Wisconsin have nearly identical case definition**
- **Had been reportable "as long as anyone could remember"**
  - **Has been in place longer than any officials at any agencies interviewed**

What are the reasons that toxoplasmosis was made reportable?

- **3/6 focused on source of infection**
  - **Can be difficult due to variety of possible sources**
- **2/6 focused on effects on pregnancy**
- **2/6 "unknown"**
- **Some had a combination of these responses**

How was the case definition developed?

State	Clinical Case Definition	Laboratory Criteria
Arkansas	Cervical lymphadenopathy and/or ocular infection with vision loss	• Elevated *T. gondii*-specific IgG, IgM, IgA, and/or IgE titers (probable) • Isolation of *T. gondii* in blood/fluids; detection of tachyzoites in tissue; and/or detection using PCR (confirmed)
Kentucky	Fever, lymphadenopathy, and/or lymphocytosis. Immunocompromised: Above, plus myocarditis, pneumonia, and/or cerebral signs Infection during pregnancy: Congenital anomalies or infant mortality	• Single antibody titer (suspect) • Change in paired specimen antibody titer; demonstration of *T. gondii* in tissues/fluids; detection by PCR; and/or specific IgM or increasing titer in sera in congenital infection (confirmed)
Minnesota	PENDING	• *T. gondii* in tissue; positive PCR; and/or confirmatory testing (testing at Palo Alto reference lab, described below) (confirmed)
Nebraska	Fever, lymphadenopathy, malaise, lymphocytosis, and/or elevated liver enzymes. Immunocompromised: Chorioretinitis, myocarditis, pneumonia, and/or encephalitis. Mothers infected during pregnancy: Infant death or congenital abnormalities. Neonatal: Fever, rash, jaundice, and/or chorioretinitis	• Detection of *T. gondii* in tissue or by PCR; and/or IgG/IgM change in paired serology (confirmed)
Pennsylvania	Immunocompetent: Lymphadenopathy and/or ocular infection (uveitis) Immunodeficient: Encephalitic symptoms with or without pulmonary/cardiac involvement Newborn infants (1st trimester infection): Fever; lymphadenopathy; microcephaly; megalocephaly; rash; and/or anemia Newborn infants (3rd trimester infection): Ocular complications/developmental days in later life	• Sequential sera displaying four-fold rise in *T. gondii* –specific IgG antibody titer (supportive) • Demonstration of *T. gondii* organisms in tissue; demonstration of tachyzoites in tissue by histopathology; and/or positive PCR (confirmatory)
Wisconsin	Fever, lymphadenopathy, and/or lymphocytosis. Immunocompromised: Above, plus myocarditis, pneumonia, and/or cerebral signs Infection during pregnancy: Congenital anomalies or infant mortality	• Change in paired specimen antibody titer; demonstration of *T. gondii* in tissues/fluids; detection by PCR; and/or specific IgM or increasing titer in sera in congenital infection (confirmed)

What, if any, public health actions do you take after a case is confirmed?

- **Most states gained case history from patient or PCP**
  - **Followed by investigation to identify infection source and education for patient**

Who is responsible for reporting cases in your state / how are you typically notified of cases?

- **All states: physicians and laboratories responsible for reporting**
  - **Laboratory results electronically sent to state agency for case follow-up**
  - **States indicated that laboratories are primary source of case reports**
  - **In MN, veterinarians/vet diagnostic labs may report in "certain circumstances"**
- **Limitations:**
  - **Physicians must think to include toxoplasmosis as differential**
    - **3/25 patients diagnosed correctly in Atlanta outbreak in 1977 (Dubey, 2021)**
  - **Serology**
    - **IgG and IgM tests cannot differentiate chronic vs acute cases**
    - **IgM also gives false positives (FDA has given warning on this!)**
  - **Cost of testing**
    - **Advanced testing at reference lab needed to differentiate acute from chronic may not be covered by insurance and may be unaffordable for some patients**

Do you currently collect non-human data for toxoplasmosis surveillance?

- **No states collected non-human data**

Do any programs in your state focus on screening pregnant women and/or infants born to infected mothers?

- **No formal screening programs were available in any states**

How are the collected data utilized? How are the results disseminated?

- 3/6 states produced public reports (results shared on website)
- 2/6 states produced "in-house" reports
  - Kept within agency, not shared publicly
- One state (Kentucky) updated toxoplasmosis in annual disease tables
  - On state health department website

Have there been any changes to the surveillance for toxoplasmosis since it began in your state?

- Difficult to say as no states could identify when reporting began

Conclusion

- **Lots of common trends between current reportable states**
- **Doesn't appear to be significant evidence to suggest making nationally notifiable**
  - Some states considering dropping reporting programs
    - May be seen as unnecessary drain on resources
    - Public health action in response to a single case is limited
      - If chronic case, source is very difficult to identify
- **Continue to focus on providing education, especially for vulnerable individuals**
  - Educate individuals of risks regarding toxoplasmosis
    - Once individuals are infected, education not as beneficial
  - Also provide education to physicians to better detect toxoplasmosis

For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

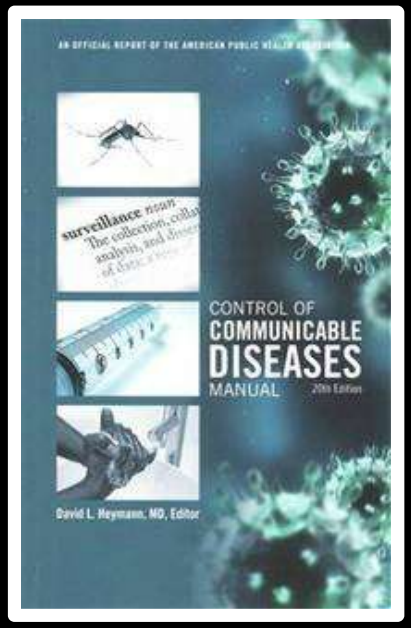
Module 9: An(other) illustration of a zoonotic environmental health threat

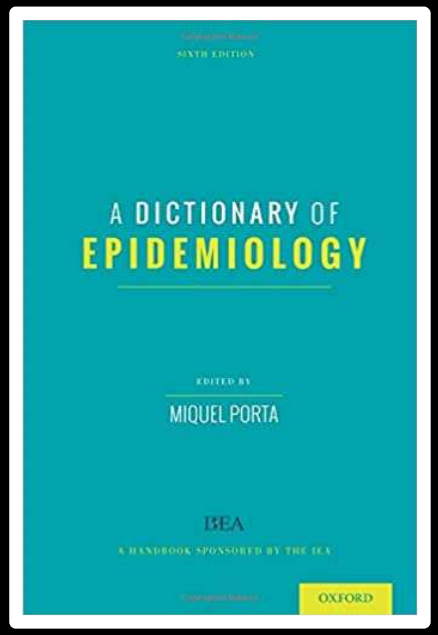
DMP 314 *Environmental and Public Health*

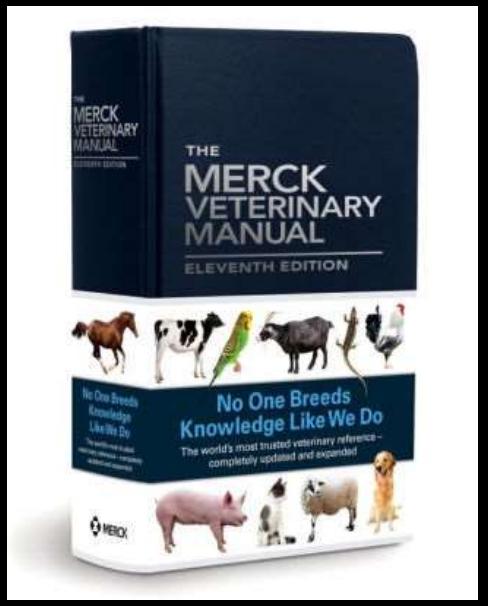
About Me

- 3rd year veterinary student
  - Also in MPH and PhD programs
- Undergrad at KSU (Microbiology)
- From Valley Center, KS
- Career goal: Work as VMO at NBAF
  - Continue teaching at KSU CVM
  - Vaccine development
- Doing summer project with CDC about toxoplasmosis reporting in USA
  - Mentor (Anne Straily, DVM, MPH) is a author/editor for the CCDM!

Public Health Resources







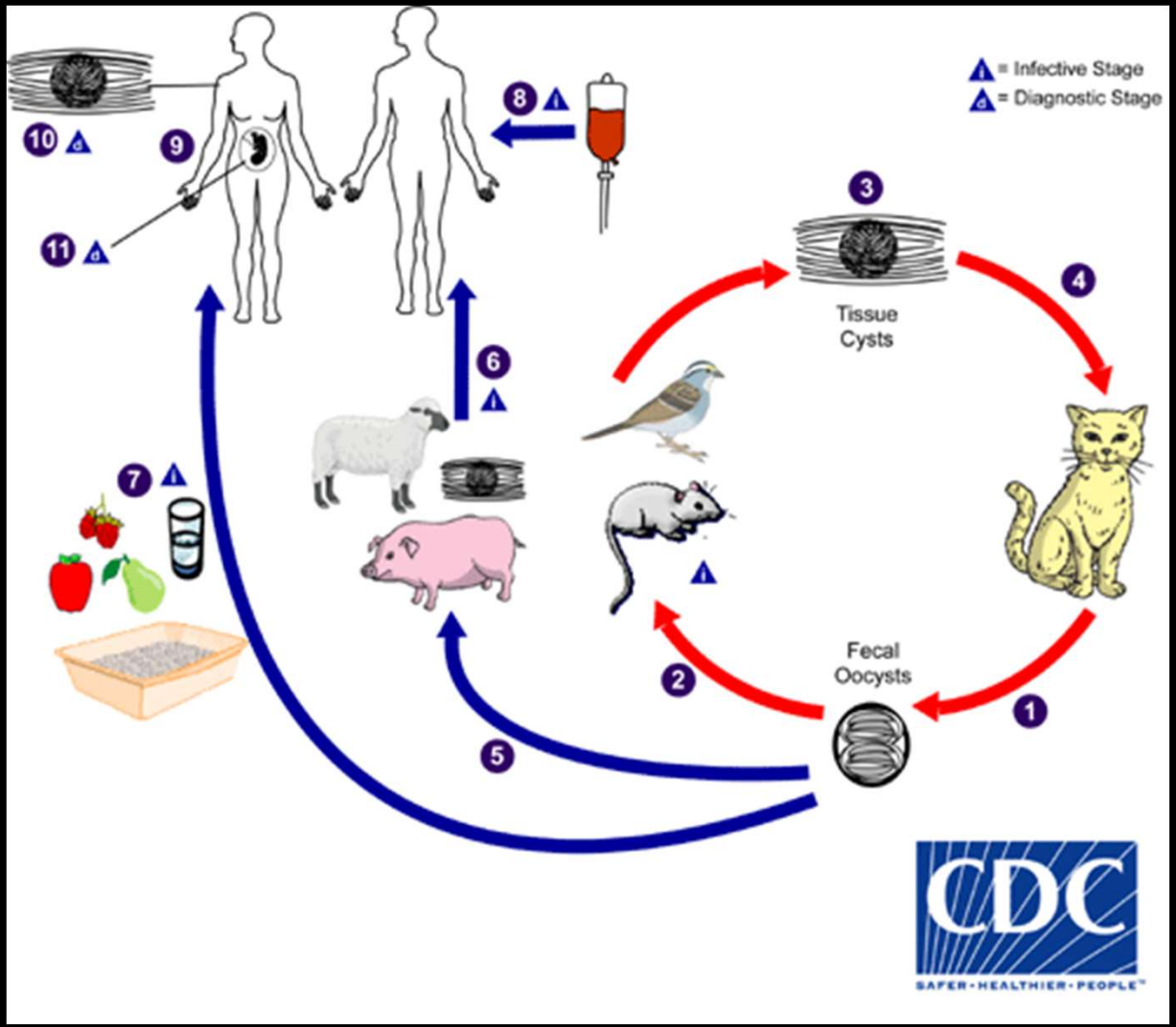
- CCDM (20th edition)
- *A Dictionary of Epidemiology*
- *CDC website (cdc.gov)*
- *Merck Veterinary Manual*

What is toxoplasmosis?

- Infection with *Toxoplasma gondii*
  - Protozoan parasite
    - However, differs in several ways from *Cryptosporidium sp.*
  - “foreign entity living at the expense of the host”
- One of five “neglected parasitic diseases”
  - Toxoplasmosis, Chagas, Neurocysticercosis, Trichomoniasis, and Toxocariasis
    - Diseases with potentially greater than realized impact
    - High prevalence

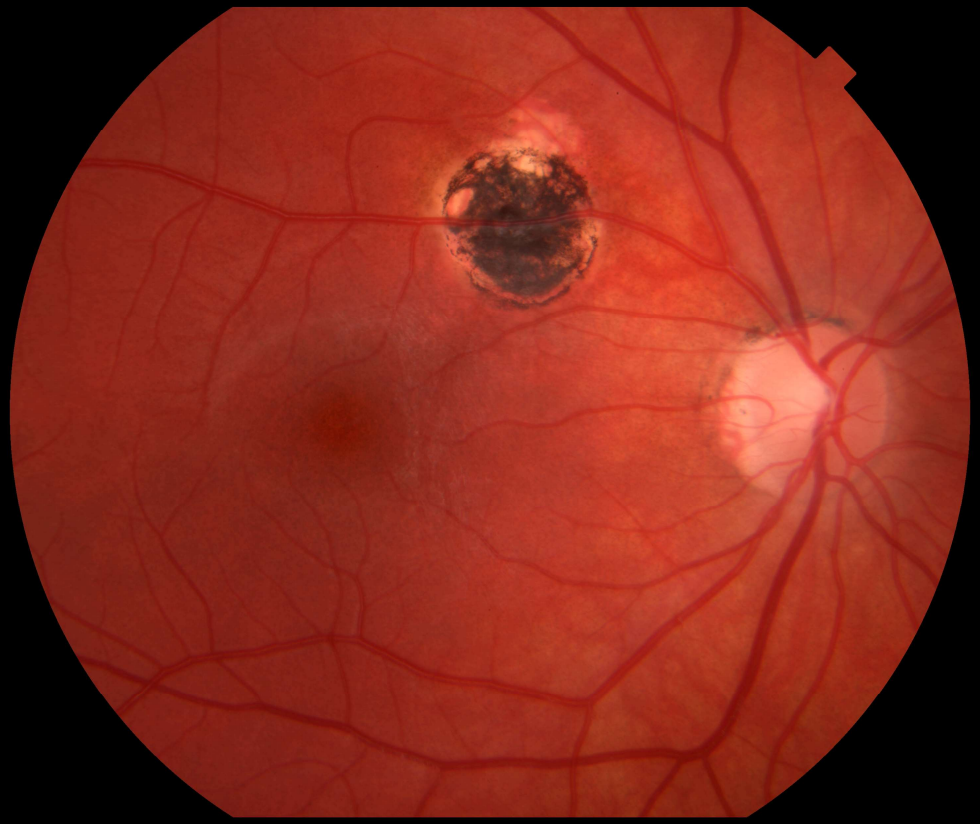
https://microbewiki.kenyon.edu/index.php/Toxoplasmosis

Life Cycle


= Infective Stage
= Diagnostic Stage
Tissue Cysts
Fecal Oocysts
1
2
3
4
5
6
7
8
9
10
11
CDC
SAFER·HEALTHIER·PEOPLE™

Symptoms

- Primarily in immunocompromised individuals (HIV+)
- Generally flu-like
  - Lymphadenopathy/fever
- Complications during pregnancy:
  - Early: Neurological defects (hydrocephaly/microcephaly) or abortion
  - Late: More mild manifestations (chorioretinitis)
- May persist/reactivate (cysts)



https://www.merckmanuals.com/professional/infectious-diseases/extraintestinal-protozoa/toxoplasmosis

Prevalence

- 11% seroprevalence in US (CDC)
  - 30% infected worldwide
- Few cases reported per year
  - Only 8 states have it listed as “reportable”
    - NOT nationally notifiable
- 3/25 physicians correctly diagnosed in US stable outbreak (1977)

Teutsch SM, Juranek DD, Sulzer A, Dubey JP, Sikes RK. Epidemic toxoplasmosis
associated with infected cats. N Engl J Med. 1979;300:695–9.

But this is an Environmental Health class, right?

Routes of Exposure

- Fecal-oral route
  - Cat feces (only species who sheds oocysts)
  - Improperly cooked meat (cysts in tissue)
  - Improperly washed vegetables
  - Gardening (soil)
- Vertical transmission
  - Infected mother to fetus
- Transplants

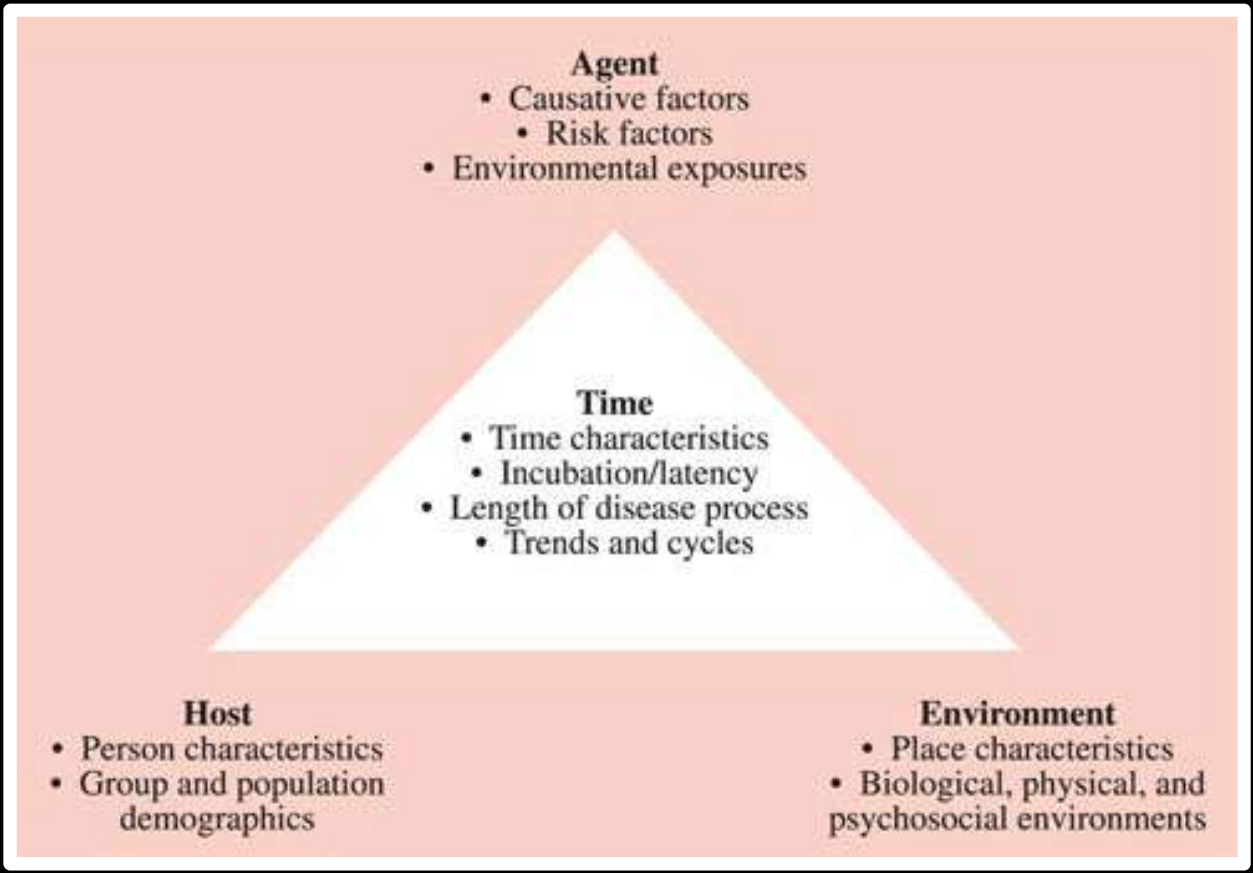
Food Safety

- A leading cause of death due to foodborne illness
  - Cook meat according to specifications
    - ESPECIALLY game meat
  - Wash vegetables thoroughly
  - Wash hands after gardening

Prevention

- Pregnant women/immunocompromised especially should protect themselves
  - Avoid changing cat litter (or wear gloves/wash hands)
  - Cook meat accordingly
  - Wear gloves/wash hands after gardening
- Don’t allow cats to hunt
- Keep sandboxes covered

The Epidemiological Triad



The Epidemiological Triad, according to R.E. Miller

Questions?

jaydenmccall@vet.k-state.edu

Resourcefulness, resources, and the CCDM: An essential for practitioners of veterinary public health

By: Jayden McCall and Justin Kastner, with files from Anne Straily

Submitted to: The editors, *One Health Newsletter*

The *Control of Communicable Diseases Manual* (CCDM) is a resource that describes many important features (such as pathogen/agent information, clinical signs, and prevention measures) for hundreds of infectious diseases. To compile such a vast wealth of information, the American Public Health Association (APHA) calls on experts in the field to help provide material for the CCDM. One such expert is Dr. Anne Straily, a veterinarian who graduated from Kansas State University and now studies toxoplasmosis (along with several other parasitic diseases) at the Centers for Disease Control and Prevention (CDC). Dr. Straily has assisted with the most recent online edition of the CCDM (specifically in the toxoplasmosis chapter updated in 2020).

The CCDM is especially useful for individuals working in public health settings and medical practitioners (primarily those working in human health), and has been available since 1917, with new editions periodically released (the online version is even updated annually). Additionally, it serves as a good resource for individuals early in their careers to establish a solid knowledge base. Dr. Justin Kastner, a K-State faculty member who teaches one of K-State's new undergraduate public health courses (DMP 314 *Environmental and Public Health*), is so convinced of the long-term usefulness of the CCDM that he requires his students to purchase it for the course. This idea of "resourcing" students with texts, such as the CCDM, is something which Dr. Straily values. She says, "You don't need to know everything, but you do need to know where to look for it." Indeed, this type of resource can be useful for human health practitioners to screen various communicable diseases, thus aiding with more accurate diagnoses.

While the original version is utilized by a wide range of public health professionals, there are two other versions of the CCDM for specific audiences (one for laboratory practice and one for clinical practice). Some similarly useful resources for individuals and practitioners in different domains of public health and veterinary public health include the so-called and so-titled *Yellow Book*, *Red Book*, and *The Merck Veterinary Manual*. The *Yellow Book* (a resource produced by the CDC) is geared towards travelers' health and can be useful when planning trips abroad and educating people before travelling. The *Red Book* is a resource produced by the American Academy of Pediatrics (AAP) and provides information regarding infectious diseases in children. Finally, *The Merck Veterinary Manual* serves as a primary resource for veterinary professionals. It includes information on infectious and non-infectious animal diseases. This resource has been available since 1955, and has been perpetually available in several subsequent editions since that time. Despite working in the veterinary field for over a decade, Dr. Straily says that she still uses *The Merck Veterinary Manual* in her professional career!

In the past year and a half, public health has been brought into the limelight more so than ever before. Interestingly, coronaviruses are described briefly in the most recent edition of the CCDM in the "Common Cold and Other Acute Viral Respiratory Diseases" section. When asked about her expectations regarding coronaviruses in future editions, Dr. Straily anticipates that the CCDM may devote a new section entirely to the agent responsible for the current pandemic (SARS-CoV-2), or it may just receive more attention and information in the chapter coronaviruses are already housed in. At the time of this article's publication, COVID-19 has already received its own place in the online version of the CCDM. In any case, if history is any indication, the CCDM will prove to be an essential resource for many public health practitioners.

This summer, one of the authors (Jayden McCall, a DVM-PhD-MPH student) worked with Dr. Straily on a project to characterize toxoplasmosis surveillance systems in several states in the US. While this project was virtually facilitated, he was able to learn about many other projects superintended at the CDC, especially within the Parasitic Diseases Branch, which he worked with. This was part of Jayden's Applied Practice Experience, the culminating project for his master of public health degree.

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The following sources are provided along with the websites at which each book can be purchased.

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