Toxomoplasmosis in Hawai'i

A Review and Evaluation
Of Its Implications

PREPARED FOR:
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EXECUTIVE SUMMARY

Infections caused by *Toxoplasma gondii* (Nicolle and Manceax, 1908) are called Toxoplasmosis. These infections are widespread among humans and animals and occur only where cats are found. Human infections are usually mild and/or completely asymptomatic and are therefore undetected and under reported. In a few instances the infections can result in blindness, mental retardation and death to children who become infected in the womb **(Congenital Toxoplasmosis).** A devastating illness may also develop with Acquired Immune Deficiency Syndrome (AIDS) or among patients receiving immunosuppressive therapy in preparation for organ transplants or for tumor therapy.

It is estimated that more than 500 million people are infected by *T. gondii*. The prevalence of infections ranges from 0 to 90% worldwide[1]. Among adults in the U.S. and the United Kingdom, it is estimated that about 30% are infected, but in continental Europe, the estimates of infections are higher, ranging from 50 to 80%. Wallace et. al.[23] estimated that about 60% of the adults in Hawai`i were infected with *T. gondii*. Wherever epidemiological surveys have been conducted, the trend shows a steady increase in the prevalence of antibodies with increasing age and with greater prevalence, the earlier the rise. Prevalence of infection varies among ethnic groups and is due to differences in sanitation and cooking habits related to cultural practices rather than to genetic differences. Toxoplasmosis is more common in warm-humid climates and in low-lying areas than in cold climates and mountainous regions.

Prior to 1970, it was well documented that the greater majority of human infections caused by *T. gondii* occurred as a result of consuming raw or undercooked meat of infected animals. However, undercooked or raw meat could not account for all human infections or herbivores that became infected and thereby served as the source of infections. The discovery

of the sexual stages of *T. gondii* in the cat and the resultant production of a resistant oocyst was the missing piece of the puzzle related to infecting herbivores, omnivores and unaccounted human illnesses. The oocysts can remain infective for as long as a year or longer in warm-humid conditions and in low-lying areas. Infections caused by the sexually produced form occur as a result of ingesting oocysts deposited into the environment through the cat feces.

The references cited about toxoplasmosis in Hawai`i may be dated since they discussed problems evident in 1970. The most significant change since 1970 are the environmental sanitation improvements and the significant increases in the human and cat (feral and domestic cats) populations that have occurred in Hawai`i. Cultural and demographic changes have occurred but appear to be of little significance in relation to toxoplasmosis. Because of the significant environmental improvement and the growing social changes in Hawai`i's society, several key questions and concerns come to mind such as: Have improvements in community sanitation resulted in the creation of a human population that has become susceptible to infections by *T. gondii*? Have new societal changes deviated to the point where former cultural practices that afforded a level of protection against infection to *T. gondii* become compromised? And has the recent proliferation of feral cat colonies in public parks increased the risk for infection? If the answer is yes to any of the questions, then there is a potential for increased risk for infection by *T. gondii*. Should we be concerned? What should we be doing?

Stray and feral cats are emerging as a public health nuisance in Hawai`i. These stray and feral cats have caused problems that require intervention by programs in the Environmental Health Services Division. It is recognized that cats roam and defecate at will, resulting in a potential public health risk of exposure to parasite infested feces. The Department of Health attempted to resolve this problem through amendments to Hawai`i Administrative Rule, Chapter

11-26. The measure was defeated by organized protests by feral cat activists who argued that the proposed amendments were not necessary as their solution to the problem was more humane. They argued that their trap, neuter and release program was the appropriate solution. The Department of Health attempted to justify the proposed amendments based on nuisances and had no solid public health basis. Hence, one of the reasons for this review was to determine whether infections by Toxoplasma still exists in Hawai`i and to develop a public health basis to control feral and stray cats in Hawai`i if the infections continue to exist.

For these reasons, this review was undertaken. The intent of this review is to accomplish the following:

- Provide facts and useful information on toxoplasmosis worldwide and for Hawai`i.
- Identify current risks and possible solutions and
- Provide recommended course(s) of action.

This review includes the following parts: Executive Summary, Facts About the Parasite and the Illness, Identification and Analysis of Risk Factors that may Support the Perpetuation of Toxoplasmosis in Hawai`i, Identification of Possible Solutions, and Conclusions and Recommendations.

A few risk factors were identified that require follow up actions by the Department of Health in order to minimize infections caused by *T. gondii* and to protect the public. With respect to current infections, we have evidence that infections continue to occur in Hawai`i although the data is preliminary and insufficient to determine the prevalence. The highest identified risk factor is a holistic risk factor combining the feral cat population and public parks.

Several recommendations focusing on disease monitoring and prevention and on the feral cat population were made, including the following:

- Adopting proposed amendments to Hawaii Administrative Rules, Chapter 11-26, to control feral cats in public parks;
- Drafting and supporting proposed county ordinances prohibiting or controlling feral cat colonies in newly established 'green spaces' in new developments;
- Drafting and supporting statutory or county ordinance related to 'domestication of cat law' similar to the dog leash law;
- Promoting stepped up monitoring of newborn babies for *Toxoplasma* infection so medical intervention can occur at the earliest possible time (Epidemiology Branch in its' "Communicable Disease Publication");
- Developing health education material on this subject for the general public;
- Encouraging park administrators to improve sanitation in public parks to reduce the abundance of natural intermediate and transport hosts in public parks; and
- Consideration for conducting limited research or survey on the enzootic potential of toxoplasmal infections at certain public parks with feral cat colonies.

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INTRODUCTION AND PURPOSE

Toxoplasmosis is one of the most common parasitic infections of humans and other warm-blooded animals. The parasite that causes the infection is *Toxoplasma gondii*. The protozoan parasite is found throughout the world wherever cats exist. It has been estimated that over 500 million people are infected by *T. gondii*, with the greater majority of infections being asymptomatic. In most adults it does not cause serious illness, but it can cause blindness, mental retardation and death to children who become infected in the womb (**Congenital Toxoplasmosis**). A devastating illness may develop among patients with Acquired Immune Deficiency Syndrome (AIDS) or among patients given immunosuppressive therapy for organ transplantation or tumor therapy. Other warm-blooded animals are similarly affected and the clinical spectrum of toxoplasmosis found in humans is also found in domestic animals such as sheep, goats and pigs. In these important domestic animals, abortion and neonatal mortality due to toxoplasmosis cause significant economic losses.

The most extensive review of this disease was published recently by Dubey and Beattie[1]. This review included citation of only 1150 original references from the more than 15,000 references listed world wide on this topic. Frenkel[2] also conducted a review of toxoplasmosis. The review by Frenkel[2] focused on human infections and its prevention based on facts gleaned from the discovery of the parasites' complete life cycle. Besides relying on the above mentioned reviews, papers written or co-authored by G.D. Wallace and others who conducted research about this disease in Hawai`i and other tropical areas including Pacific islands have been reviewed. Finally, I have included pertinent citations of the complex life cycle of *T. gondii* by Dubey, et.al.[3,4], Hutchinson et. al.[5] and Wallace[6,7] who pioneered the research leading to the

discovery and confirmation of the parasites' sexual stage in the early 1970's. These references provide for a comprehensive understanding of infections caused by the parasite as well as its epidemiology.

Stray and feral cats are emerging in Hawai`i as a public health nuisance that requires frequent intervention by programs within the Environmental Health Services Division. These stray and feral cats defecate at will on private and public property, exposing individuals and the public to a potential source of infection. Cat feces are known to contain numerous parasites that could infect humans of which *T. gondii* was considered to be one of the most serious. The Department of Health attempted to promulgate an amendment to the Hawai`i Administrative Rules, Chapter 11-26, proposing control of cats in public parks. The proposal was unsuccessful because of the strong objections from animal rights and feral cat activists who challenged the adoption of such a rule as inhumane and unnecessary. The feral cat activists argued that their solution of trap, neuter and release was more humane. The Department of Health attempted to justify the proposed amendments based on nuisances and had no solid public health basis. Therefore, one of the major reasons for this review was to determine whether a public health concern existed and to develop a public health basis if such a concern did exist.

In addition, this review was conducted for the purposes of determining the extent of knowledge available on this disease; whether further research in Hawai`i needs to be conducted; and how current knowledge about the disease affects our ability to understand and minimize human infections.

THE PARASITE – HISTORY AND DESCRIPTION

Toxoplasma gondii (Nicolle and Manceaux, 1908) is a protozoan parasite of the domestic cat, *Felis catus*, and other related wild cats of the Family Felidae[1,8]. This parasite has an unusually wide range of intermediate hosts. A description and proposed systematic placement of *T. gondii* with other Apicomplexa sporozoans was published by Nicolle and Manceaux in 1908 from specimens recovered from a laboratory rodent, *Ctenodactylus gundi* (Rodentia: Cricetidae). The name *Toxoplasma* is a Greek derivation from the crescent shape of its infective cell (toxon = arc; plasma = form). The specific name *gondii* is derived from the name of the host from which the parasite was first isolated. This initial manuscript by Nicolle and Manceaux described what is currently known as the asexual form of *T. gondii.* Although their description was of a typical asexual form of a sporozoan including possession of complex ring like tubular and filamentous organelles at the apical end (visible only with the electron microscope), it lacked a description of the sexual stages typically associated with Apicomplexa sporozoans. The function of the apical complex was uncertain but could have been necessary for entry into the host cell. We know from current knowledge that the life cycle of a generalized sporozoan involves an asexual and a sexual phase[8]. A thorough discussion of the life cycle including its sexual and asexual stages will come later.

Because of the incomplete knowledge of this parasite's life cycle and the lack of the intracellular sexual stages in the description of *T. gondii* by Nicolle and Manceaux, their classification for this parasite remained confused for many years. The asexual form of the parasite was also isolated in laboratory rabbits; in domestic animals such as goats, sheep, pigs,

dogs; and in humans by various investigators. The researchers who isolated these asexual forms from the various animals suspected blood-sucking arthropod transmission of *T. gondii*.

Prior to 1970, it was well documented that carnivore and human infections occurred as a result of consuming raw or undercooked meat infected with *T. gondii* cysts. However, undercooked or raw meat from infected animals could not account for all human infections and especially for herbivores that became infected and whose meat infected humans and other carnivores or omnivores. It was obvious that the chain of infection was missing key links. The earlier researchers theorized either arthropod vectored transmission or some kind of contact with infected pet dogs.

The discovery of the sexual stages of *T. gondii* by experimentally infecting cats with infected tissues and isolation of the resistant oocyst in cat feces was achieved by Dubey, et.al.[3,4] and Hutchinson et. al.[5] , while Wallace[6] was the first to isolate the oocysts from naturally infected cats on Oahu. Wallace's[6,7] findings under natural conditions confirmed the experimental results achieved by Dubey et.al.[3,4] and Hutchinson et. al.[5]. These significant discoveries in the parasite's life cycle resulted in a better understanding of the natural history of the disease and established its current classification as a sporozoan[5] belonging to the Family Eimeriidae (Family Sarcocystidae[8]). The Family Eimeriidae (Family Sarcocystidae[8]) include many species that cause infections of medical and veterinary importance. Finally, the findings that cats were the definitive host negated the earlier myth that dogs were some how responsible for the transmission of toxoplasmosis.

THE PARASITE--LIFE CYCLE

To better understand the disease, the complexity of infections and the various modes of transmission, it is necessary to know the life cycle of the organism. The bulk of information related to this paper was abstracted from references of Dubey and Beattie[1]; Dubey et. al.[3,4], Hutchinson et. al.[5], Frenkel[2] and Levine[8].

A brief description of a generalized life cycle of sporozoans involves the following. The asexual phase starts after the initial invasion of the host by the infective stage called a sporozoite. The sporozoite undergoes asexual multiplication by endodyogeny (intracellular multiple fission or schizogony). In this type of multiple fission the nucleus divides several times by mitosis before the cytoplasm divides forming two daughter cells called merozoites. Merozoites continue schizogony (intracellular multiple fission) for several generations but eventually start the **sexual phase** as gametes (sexual forms) are formed. The gametes fuse to form a zygote (fertilized egg = 2 sets of genes or diploids). The zygote undergoes meiosis (reduction/division to form the haploid or animal with single set of genes) to form oocysts which contain the sporozoites or invasive form.

The life cycle of *Toxoplasma gondii* is more complex than the generic life cycle described earlier. The life cycle is heteroxenous with the asexual phase occurring in one of its multitude of intermediate hosts (more than 200 species of mammals and birds) and the sexual phase occurring in the definitive or complete host (the domestic cat and related felines). The sexual cycle occurs only in cats and the resultant oocyst can remain viable in the environment for

a considerable length of time provided that ideal environmental conditions for survival of moisture and warmth are present.

There are three stages of *T. gondii* that cause infections in intermediate hosts (in this term, intermediate hosts could also include cats): tachyzoites (in pseudocysts or clones), bradyzoites (in tissue cysts) and sporozoites (in oocysts). In some references, the multiplying infective stages, i.e. tachyzoites and bradyzoites, are sometimes collectively referred to as trophozoites or merozoites with no further differentiation.

The term "tachyzoites" was coined by Frenkel to describe the rapidly dividing forms multiplying in any cell of the intermediate host and non-intestinal epithelial cell of the definitive host. Host cells containing numerous tachyzoites are called **clones, terminal colonies, groups or pseudocysts.** During this stage of growth the host may or may not manifest clinical symptoms as the process of cellular destruction may or may not cause localized necrosis, resulting in mild to severe fever that depends on several factors such as dose of infection and tissue affected. In acute infections, tachyzoites may be found free in the blood or in peritoneal exudates.

The bradyzoites are structurally similar to tachyzoites. Whereas the tachyzoite multiplies rapidly, the bradyzoite multiplies slowly within a protective tissue cyst. A tissue cyst is a collection of bradyzoites within a well-defined parasitic membrane. The parasitic membrane encasing the bradyzoites is resistant to enzymatic digestion which differentiates this stage from clones or groups.

Host tissues most commonly invaded during the asexual stages include neurons, microglia, endothelium, liver parenchymal cells, lung and glandular epithelial cells, cardiac and skeletal muscle cells, fetal membranes and leukocytes.

The sexual phase requires the formation of distinct sexual stages, followed by their eventual combination to form the oocyst. The sexually distinct gametes are the products of coccidian gametogony. The ingested tissue cysts (bradyzoites) undergo several generations of intracellular multiplication stages in the epithelial cells of the villi of the small intestines of cats (specifically goes through five structurally or morphologically distinct forms simply called type A to type F by Dubey et. al[3,4]). The 'male' gamete is a small biflagellate organism and is called a microgamete while the 'female' is significantly larger without motility and is called the macrogamont. (NOTE: Hutchinson et. al.[5] described the microgamete as a small biflagellate organism with a small rudimentary flagellum). The product of the penetration of the biflagellate microgamete into the macrogamont and the fusion of their individual nuclei is the zygote. The oocyst is the developed zygote that has completed meiosis within a two-layered wall. The unsporulated oocyst contains a sporont or inner mass filling the oocyst. Upon sporulation, the sporont divides into two round bodies called sporoblasts, which later elongate to form sporocysts. Within each sporocyst develop four sporozoites. Sporulation occurs only after the oocysts are shed in cat feces. The speed of sporulation depends upon temperature, humidity and aeration and usually is complete after 1 – 5 days, after which it becomes infective to intermediate hosts (NOTE: Unsporulated oocysts cannot cause an infection).

THE PARASITE -- HOSTS

Domestic and wild cats are the definitive or final host of *T. gondii* and are the only known hosts in which the intracellular sexual cycle of the parasite can occur (see Appendix Table 1 for a list of Felines recorded as definitive hosts or possible definitive hosts). Cats shed oocysts after ingesting any of the 3 infectious stages of *T. gondii*: tachyzoites, bradyzoites, or sporozoites. Prepatent periods (time to the shedding of oocysts after initial infection) vary according to the stage of *T. gondii* consumed[3,4,5,6] : 3 to 10 days after ingesting tissue cysts (bradyzoites); 19 days or longer after ingesting tachyzoites; and 20 days or longer after ingesting oocysts. Less than 50% of cats shed oocysts after ingesting tachyzoites or oocysts, whereas nearly 100% of cats shed oocysts after ingesting tissue cysts (bradyzoites), **(NOTE:** an infected cat can shed as many as a million or more oocysts as a result of infection). In some rare circumstances, a few cats can be re-infected and shed oocysts but only after more than two months following a previous infection.

Most other warm-blooded animals are capable of serving as intermediate hosts when tachyzoites, bradyzoites or sporozoites are ingested and replicated by intracellular fission and form tissue cysts (see Appendix Table 2 and 3 for a list of mammals and birds, respectively). Chickens, goats, pigs and sheep are the most important intermediate hosts that can infect humans. Rodents and birds on the other hand are the most important intermediate hosts that are common preys of cats and therefore the source of infection. Certain species such as the domestic dog and domestic bovines (cattle) were previously suspected as definitive host or to play a greater role in human infections. Dogs are readily infected but infections are primarily

asymptomatic and do not result in the production of oocysts as in cats. Cattle on the other hand are not readily infected and are therefore not considered efficient intermediate hosts.

THE PARASITE -- EPIZOOTIOLOGY

Fundamental to transmission of *T. gondii* is the cat, and this term includes all felines. Dubey and Beattie[1] abstracted references related to wild feline infections and shedding of oocysts (see Appendix Table 1). An infected cat may shed millions of oocysts in its feces. These are not immediately infectious, but must first sporulate outside the body of the host; a process which usually takes from 1 to 5 days, depending on temperature, moisture and other environmental conditions. As a rule, the duration of excretion is from 1 to 3 weeks and is rarely repeated due to the rising levels of anti-*Toxoplasma* antibodies, although it may be re-stimulated by malnutrition, by infection with *Isospora felis*, or by administration of cortisone.

According to Dubey and Beattie[1] the proportion of cats excreting oocysts at any one moment is not high, being usually not more than 2% in most countries, but a cat may shed millions of oocysts. Wallace[6,7] isolated oocysts from 5 to 8% of cat feces examined. Wallace[6,7] attributed the low recovery of oocysts to the large number of young kittens in his sample population and reasoned that young kittens were unable to hunt and capture available prey such as rats and birds because of their small size. Ruiz and Frenkel[9] were able to recover a higher percentage of cats shedding oocysts (23%) in Costa Rica due to the multiplicity of sanitary problems and extremely large population of cats. Further, Ruiz and Frenkel [9] found that 64% of

cats shedding oocysts were kittens and they reasoned that the kittens were able to easily capture infected mice that were lethargic due to infection.

The oocysts are very hardy, capable of surviving in the soil for a year or more, so the danger of infection is obvious. Moreover, oocysts can be brought to the surface by coprophagic invertebrates such as filth flies, cockroaches, earthworms, snails, slugs and by climatic conditions such as rain[1,2,6,7,9,10,11,12,13]. Contrary to these facts it has been said that the cat is a clean animal that licks its fur clean and buries its feces. Up to a point this is true, but it would be more correct to say "hides its feces", and kittens do not even do this.

How do cats become infected with *T. gondii*? Transplacental transmission in cats rarely occurs. Cats can be infected by ingesting oocysts of *T. gondii*, but experiments have shown that these are much less potent sources of infection for cats than tissue cysts[3,4,5,6]. Further evidence in favor of this is that infection is most common in kittens and occurs when they begin to hunt birds and small mammals[6,13]. **(A corollary is that there is greater risk of acquiring infection from kittens than from mature cats.)**

The extent of *T. gondii* infection in cats will depend on the availability of infected birds and small mammals which, in turn, become infected by ingesting oocysts shed by cats[6,13] (see Appendix Tables 2 and 3). In theory, infections would be greater in country cats than in town cats, **and in stray cats than pet cats**. As expected from this reciprocal infection, its extent among cats parallels its extent in birds and small mammals. Contrary to this theory, Ruiz and Frenkel [9,13] found no difference in infections between town and rural cats. They found that the

majority of "town cats" in Costa Rica were strays and were allowed to roam in and out of homes as well as between homes to scavenge for food or to hunt for food as well as to defecate wherever they desired to do so. Rats, mice and birds were commonly infected by large amounts of infected cat feces, and in turn were readily available as food for the "town cats" in Costa Rica. Finally, they found that mice appeared to be the easiest to infect and also the easiest to catch for food, especially by the large population of kittens in Costa Rica. According to Dubey and Beattie[1], infection in rats appears to be more common than in mice. Wallace[12] isolated *T. gondii* from 8% of rats in Hawai`i, but a kitten would have to be very brave to tackle these animals. It would be more likely for the kitten to eat a carcass brought by its mother. Ruiz and Frenkel[13] found that mice may play a greater role than rats in Costa Rica. They indicated that mice, when infected, become lethargic and become easy prey for even small kittens.

Herbivores and omnivores are infected by *T. gondii* as a result of ingestion of oocysts/ soil-oocysts, ingestion of food contaminated with oocysts deposited by infected cat feces, or ingestion of food indirectly contaminated with oocysts by contaminated transport hosts (see Appendix Tables 4 and 5 for lists of transport hosts). Strong circumstantial evidence for transmission of oocysts through this manner has been documented. The documents show higher prevalence in sheep that grazed in valleys where cats, and hence, oocysts, are numerous, than on hills where cats are uncommon; pigs fed contaminated soil; and sheep fed contaminated grain or grazed on pasture contaminated with cat feces[1]. The role of the cat in the spread of *T. gondii* infection was also substantiated by Wallace[14] and Wallace et. al.[15,16], and Durfee et. al.[17] when they found human infection prevalent on Pacific atolls and Borneo on which there were cats, but virtually absent where there were no cats.

HUMAN ILLNESSES -- HISTORY

The role of the parasite as a human pathogen was not widely known until 1937 when Wolf and Cowen[18] reported congenital *T. gondii* infection in humans. Their report stimulated considerable interest in human toxoplasmosis and, within 5 years, Sabin had characterized the four most consistent clinical features of severe infections caused by congenital toxoplasmosis. These features included the tetrad of deformity of the skull, convulsions, chorioretinitis and cerebral calcification (**NOTE:** Later clinical cases indicate that not all of the four clinical features need to be present in all infections). The development of the "dye test" by Sabin and Feldman[19] was and still is the key to the proliferation of our knowledge of toxoplasmosis. Their interpretation of test results indicated that an asymptomatic mother who gave birth to a congenitally infected child had anti-*Toxoplasma* antibody titers of 1 : 256 to 1 : 16,384 for 2 – 5 years after the probable onset of infection by *T. gondii* (NOTE: high antibody titers are generally indicative of active parasitic multiplication in tissues by the tachyzoite stage. The tachyzoite stage is the form of the parasite that can be passed on to the fetus via the umbilical cord). Further, titers of 1 : 16 to 1 : 64 were found in those with a history of infection 6 – 7 years earlier or longer (NOTE: lower titers are generally indicative of a past infection and the lowering of the antibody titer occurs when the actively multiplying tachyzoite stage becomes encased within tissue membrane which results in the formation of the tissue cysts stage called the bradyzoite). The Sabin-Feldman dye test is the most specific serological test for toxoplasmosis available for identifying human infections. Wallace[20] improved on the performance and results of the Sabin-Feldman dye test by the addition of sodium citrate in accessory factor of serum samples.

Confirmation of the existence of toxoplasmosis in Hawai`i was not recognized until 1953 when Tilden[21] reported a fatal case of congenital toxoplasmosis related to a low birth weight Filipino that died at 19 hours of age with massive destruction of the brain. In the same year, Stitt and Levine[22] conducted a retrospective examination of several suspected cases of toxoplasmosis in Hawai`i. They attempted to correlate the new dye test with suspected cases of congenital toxoplasmosis in Hawai`i based on clinical manifestations of ophthalmologic (eye infections) or central nervous system disorders (possibly learning disability or mental retardation) of obscure origin. They found that 15 of 29 suspected cases with confirmed chorioretinitis had sera positive for antibody in the mothers and patients as confirmed with the assistance of Dr. Feldman. Later reports by Wallace et al[23] and Philip and Wallace[24] described 11 latent infections and 9 congenital infections, respectively. In the study of 11 latent infections[23], eight had lymphadenopathy and 3 had chorioretinitis. In the study of nine congenital toxoplasmosis cases by Philip and Wallace[24], the mother of one of the nine cases reported the consumption of undercooked goat meat.

Other scientists using the Sabin-Feldman "dye test" were able to demonstrate that toxoplasmosis was a common infection in man throughout the world. However as discussed earlier, the main route of transmission remained a mystery. Due to these pioneer medical and veterinary researchers, we can now make certain statements about human infections.

It is now evident that *T. gondii* usually infects the definitive and various intermediate hosts (the term hosts includes humans and other warm-blooded animals in which the organism can multiply, cause an infection, and produce long-lasting tissue cysts) without producing

clinical symptoms (asymptomatic). With regards to human infections, only rarely does the infection cause severe clinical manifestations and such severe infections are generally related to congenitally acquired infections or in immune deficient individuals. Hence, it is understandable why human infections may be under reported.

Among immune deficient individuals, primary infection may include cerebral signs, pneumonia, generalized skeletal muscle involvement, myocarditis, a maculopapular rash, and death. Dormant organisms from earlier infection can reactivate as in AIDS patients among whom cerebral toxoplasmosis occurs, most often resulting in death. Among patients with impaired immunity due to lymph node tumors or due to treatment mainly with corticosteroids and cytotoxic agents, reactivated toxoplasmosis has been observed especially in the brain and eyes.

One of the most common forms of human infection is a naturally acquired infection that is generally mild or totally asymptomatic. Natural infections are probably acquired by the ingestion of tissue cysts in infected meat, oocysts from cat feces contaminated food, by oocysts from soil contamination, or by direct contact with infective cat feces. Infections generally occur and progress as follows. The bradyzoites from the tissue cysts or sporozoites from the oocysts penetrate the intestinal epithelium and multiply in the intestine. The parasite may spread locally to mesenteric lymph nodes and to distant organs by invasion of the lymphatic system and blood. Focal areas of necrosis may develop in many organs. The clinical picture may include fever, pneumonia, and inflammation in heart muscle, liver and skin rash, all of which persist for days to weeks. With the development of antibodies, the parasitemia decreases but tissue cysts remain

viable for long periods of time, possibly for the infected person's lifetime. Further, the clinical picture is determined by the extent of injury to these organs, especially vital organs such as the brain, eye, heart and adrenals. The necrosis is caused by the intracellular growth of tachyzoites. The host may die of acute toxoplasmosis but more often recovers with acquisition of immunity coincident with the appearance of antibodies.

On the other hand, some natural infection can result in more severe clinical manifestations. In these rare instances, the parasite is transmitted through the placenta from a naturally infected mother to her baby while the fetus is developing in the womb. This kind of infection is called congenital toxoplasmosis and the infections can be severe or mild. The severe form results in still birth or serious post-natal illness (meningo encephalomyelitis = brain fever, or micro and/or hydrocephalus = water in the brain) or myocarditis and death during early infancy. The milder form of congenital toxoplasmosis has no manifestations at birth but infection of the brain and eye (chorioretinitis) may occur in later years and therefore give the clinical impressions of an acquired infection.

To alleviate fears with respect to congenital toxoplasmosis, Harrison[25] indicates that most women infected during pregnancy gave birth to uninfected babies. About one third of these women will transmit the infection to the babies. Only about 15% of women infected in the first trimester transmit infection, but neonatal disease is most severe, often resulting in stillbirth or neonatal death from extreme complications. Sixty-five percent of women infected in the third trimester transmit infection to the baby, but the infant usually is asymptomatic at birth. Frenkel[2] stated that only about 0.33% of births will result in death or optical and brain impairments.

Further, Frenkel estimated that of the 0.33% infections at birth 5 – 15% may die; 8 – 10% may have severe brain or eye damage; 10 – 13% may have moderate to severe visual handicaps; and that 58 – 72 % may be asymptomatic at birth with a proportion developing chorioretinitis as children or young adults.

As to why some individuals become ill due to toxoplasmosis, whereas others remain well, is not fully understood even to this day. Age, host species, strain of *T. gondii,* number of parasites, and route of administration may account for some of these differences.

HUMAN ILLNESS -- TRANSMISSION (EPIDEMIOLOGY)

T. gondii infection in humans is widespread throughout the world. Approximately one half billion people have antibodies to *T. gondii*. Infection in humans varies in different geographical areas of a country. Causes of these variations are not completely understood. Environmental conditions may determine the degree of natural spread of *T. gondii* infection. Infections are more prevalent in warm climates and in low-lying areas than in cold climates and mountain regions[1] and in humid areas rather than dry areas. This is probably related to conditions favoring sporulation and survival of the oocysts in the environment. Wallace[6,7,10,11,12,14], and Wallace et. al.[15,16] conducted several studies on Pacific islands and concluded that infections occurred only on those islands which had cats and where other intermediate and transport hosts were present and capable of sustaining the natural life cycle of *Toxoplasma* infections. Durfee et. al[17] made similar observations in Borneo as they found human infections only in villages where cats were present. Ruiz and Frenkel[9,13] and Frenkel and Ruiz[26]

made similar observations and their findings related to human infections due to exposure to cat feces in the homes in Costa Rica were significant and irrefutable.

Cultural habits and hygiene of people may play a role, especially with respect to cooking and eating habits of the different ethnic groups. Wallace et. al.[27,28] published several studies conducted on Pacific islands with different ethnic groups and his findings confirm that infections were related to culture and cooking habits of the different cultures (Chinese and Japanese were identified as the lowest risks while others with more primitive cultures as associated with Pacific Island nations or European related cultures were high risks). Ruiz and Frenkel[13] and Frenkel and Ruiz[26] showed that the culture of Costa Ricans was tolerant to cats primarily out of fear of bad luck from killing cats. Despite their dislike for cats, people would often feed them food scraps such as raw chicken entrails and head, thereby perpetuating infections of toxoplasmosis. It is not known what proportion of human *T. gondii* infection is due to eating raw or undercooked meat containing tissue cysts and what proportion is due to oocysts on unwashed hands or vegetables. With respect to transmission from raw or undercooked infected meat, Dubey and Beattie[1] abstracted and described the classical study conducted in a Paris Tuberculosis Sanitarium. The epidemiologic evidence of that study indicated that not only can *T. gondii* be transmitted by the ingestion of infected raw meat, it also showed that infection is common in localities where consumption of raw or undercooked meat is common. Hence, in Paris, where it is customary to eat raw or rare meat, over 80% of the adult population had antibodies for toxoplasmosis. Philip and Wallace[24] studied nine cases of congenital toxoplasmosis in Hawai`i. The significant finding in this 1974 report was that Filipino mothers were at risk of giving birth to infected children and, further, one of the cases was directly related to the consumption of undercooked goat meat by the

Filipino mother. A similar observation was made by Durfee et.al.[17] as they associated infections in humans in South Kalimantan (Borneo) with the consumption of 'sate' or undercooked goat meat. Al-Nakib et.al.[29] also observed that eastern Mediterranean Arab women had higher *Toxoplasma* antibodies than Gulf Arab women and the difference was attributed to the consumption of undercooked lamb by the eastern Mediterranean women. It seems likely that where cats are free-roaming and defecate around and even in houses, oocysts will be the main source of human infection[1,9,10,11,12,13,14,15,16,26]. However, in large cities where cats are better controlled and where raw or undercooked meat is eaten, the latter would be the source of human infections.

Arthropods may serve as important "transport" hosts of oocysts. The term 'transport hosts' merely refers to the ability for certain animals to carry the infective stage (oocysts) from materials that they normally feed on to food stuffs of humans or intermediate hosts (see Appendix Tables 4 and 5 for lists of transport hosts). Wallace[10,11,12] showed that the house fly, *Musca domestica,* oriental blowfly, *Chrysomya megacephala,* Madeira cockroach. *Rhyparobia (Leucophaea) maderae*, and the Amercian cockroach, *Periplaneta americana*, could serve as transport host readily for at least 1-3 days.

Additionally, several studies conducted by Wallace[14] and Wallace et. al.[15,16] in the Pacific alluded to the potential for infections via food contamination by these transport hosts. Ruiz and Frenkel[13] attempted to replicate findings made by Wallace[10,11,12] and were unable to isolate oocysts from flies and cockroaches but showed significant numbers of oocysts in earthworms. Levine[8] and Wallace[12] also included cold blooded vertebrates such as lizards,

geckos, skinks, etc. as potential transport/intermediate hosts. **It is important to note that toxoplasmosis can also occur in 'clusters' as well as individually. Several outbreaks of toxoplasmosis have occurred. Four outbreaks will be discussed, each with a distinct feature.**

Teutsch et. al.[30] described an outbreak that occurred at a riding stable in Atlanta, Georgia in 1977. Thirty-seven patrons of the stable were ill or had serologic evidence of infection by *T. gondii*. Investigation concluded that the outbreak occurred as a result of ingestion of oocysts by one of two ways: (1) oocysts stirred up in dust by the horses in the enclosed arena might have been inhaled; or (2) the oocysts were ingested via indirect oocyst contamination of food or beverage. A significant feature of the outbreak was that **95% of those that were infected had clinical symptoms of infection.**

Stagno et. al.[31] described an outbreak of involving 10 of thirty members of an extended family in Alabama. The index patient had unusual and severe clinical manifestation resembling a dual infection. The index case was finally "cured" months after it was concluded that the infections were caused by *T. gondii* and *Toxocara.* The outbreak of toxoplasmosis was confined largely to pre-school aged children. Of the 11 children, seven (68%) were sero positive, six of whom had acute-phase titers of ≥1024 to *Toxoplasma.* Geophagia was associated statistically with acute toxoplasmosis among the children; it also increased the risk of infection with *Toxocara* and other enteroparasites. Epidemiologic evidence indicates that this outbreak was probably caused by ingesting oocysts from cat feces deposited by an infected cat in the children's outdoor play area. Similar to the earlier described outbreak, **7 of the 10 infected**

individuals displayed clinical manifestations requiring treatment that is contrary to generalized mild and/or completely asymptomtic infection.

Benenson et. al[32] described an outbreak of acute toxoplasmosis that occurred in a battalion of U. S. Army soldiers that were infected during a training exercise in Panama in 1979. Epidemiologic evidence indicated that the infections resulted from the ingestion of stream water contaminated with *T. gondii*. In this instance, the unusual feature was that this occurred in the jungle where domestic cats were not present. It is believed that the infective source was a wild jungle cat, most probably the Jaguar.

Miller, et. al[33] reported that seven human infections were circumstantially attributed to the accidental ingestion of oocysts during their laboratory research on toxoplasmosis. Those accidentally infected included the three authors of that paper, one assistant and three other investigators. All were sero-negative prior to working with oocysts. Within one year or sooner higher antibody levels were observed. Two had mild flu-like symptoms and one had swelling of the mid cervical lymph nodes that persisted for 4 months during which the antibody rose from 1 : 32 to 1 : 2000. All of those infected had worked many years prior with the tachyzoite and bradyzoite stages with no sero conversions.

These outbreaks discussed are by no means all of the outbreaks documented. Each outbreak describes a different means of human infection that was caused by oocysts. These studies strongly suggest that where cats are present, people need to be aware that infections of toxoplasmosis can occur.

HUMAN ILLNESS -- DIAGNOSIS

Diagnosis is made by biologic, serologic, or histologic methods or by some combination of them. Clinical signs of toxoplasmosis are nonspecific and cannot be depended upon for a definite diagnosis. *T. gondii* can be isolated from patients by inoculation of laboratory animals and tissue culture with secretions, excretions, body fluids and tissue samples taken by biopsy from patients. Diagnosis can also be made by finding *T. gondii* in host tissue removed by biopsy or at necropsy and microscopic examination of impression smears stained with Geimsa. Finding *T. gondii* antibody can aid diagnosis. Numerous serologic procedures used to detect humoral antibodies are described in Dubey and Beattie [1]. The description includes eight methods for detecting humoral antibodies, a discussion on detecting circulating antigens, detecting *T. gondii* by immunoperoxidase staining, skin tests, and anti-specific lymphocyte transformation.

Since the most severe infections result from congenital infections, early diagnosis in child-bearing age females and/or pregnant females should be considered. Dubey and Beattie[1] discussed individual screening of pregnant females and displayed a tabulated program for mass screening of pregnant females. The procedure for testing pregnant females calls for individual serum testing during various phases of pregnancy. If results are negative, there is no risk for mother and fetus, but testing and monitoring will continue for the duration of pregnancy. On the other hand, if test results indicate recent or past infections, potential risks to mother and fetus are identified. If a recent infection is detected, necessary prophylactic treatment for the infected mother and possible postnatal examination and treatment for the infant are prescribed. The testing continues throughout pregnancy regardless of negative test results.

Another diagnostic option that may be less threatening or alarming would be to immediately test newly born infants for possible *Toxoplasma* infections as was done by Philips and Wallace in1974[24]. Any positive test result could then result in the initiation of immediate treatment to reduce damage to the child.

HUMAN ILLNESS -- TREATMENT

The following treatment regimen for infections was abstracted from Harrison[25] and Benenson[34]. Sulfonamides and pyrimethamine (Daraprim) are two drugs widely used for therapy of toxoplasmosis. These two drugs act synergistically by blocking the metabolic pathway involving *p*-aminobenzoid acid and the folic-folinic acid cycle, respectively. These two drugs are usually well tolerated, but sometimes thromobocytopenia and/or leukopenia may develop. These effects can be overcome by giving patients folinic acid and yeast without interfering with treatment, because the vertebrate host can utilize pre-synthesized folinic acid while *Toxoplasma* cannot.

HUMAN ILLNESS -- PREVENTION AND CONTROL

To prevent infection of human beings by *T. gondii*, hands should be washed thoroughly with soap and water after handling meat. All cutting boards, sink tops, knives, and other materials coming in contact with uncooked meat should be washed with soap and water because the stages of *T. gondii* in meat are killed by hot water. Meat of any animal should be cooked to 70°C before human or animal consumption, and tasting meat while cooking or seasoning

homemade sausages should be avoided. Pregnant women, especially, should avoid contact with cats, soil, and raw meat. Pet cats should be fed only dry, canned, or cooked food. The cat litter should be emptied every day, preferably not by a pregnant woman. Dried cat litter should not be shaken so as to avoid dispersal of oocysts in the air. Gloves should be worn while gardening. Vegetables should be washed thoroughly before eating because they may have been contaminated with cat feces. Expectant mothers should be aware of the dangers of toxoplasmosis.

To prevent infection in cats, they should never be fed undercooked meat, viscera, or bones, and efforts should be made to keep cats indoors to prevent their hunting. Because cats cannot utilize plant sources of vitamin A, some owners feed raw liver to improve the coat of their cat. This practice should be discontinued because *T. gondii* tissue cysts frequently are found in the liver of food animals and because cat foods contain most of the essential nutrients, there is no need to feed raw meat to cats. Trash cans also should be covered to prevent scavenging. Although freezing can kill most *T. gondii* tissue cysts, it cannot be relied on to kill them all. Cats should be spayed to control the feline population on farms.

SPECIAL TECHNIQUES

Dubey and Beattie[1] described numerous special techniques useful for isolation and identification of *T. gondii*. Specifically, they had lengthy discussions on cultivation techniques for the various stages of the parasite, cryopreservation techniques, and for isolation and examination of cat feces for *T. gondii* oocysts.

Proper identification of *T. gondii* oocysts in feces of cats is important from a public health viewpoint. Detection of oocysts is possible using any of the standard fecal flotation techniques. However, the use of salt solutions over 1.18 sp is not recommended because the distortion produced in the oocysts makes identification difficult. The method recommended by Dubey and Beattie[1] is detailed in their text (pp.33-35).

RISK FACTORS THAT MAY SUPPORT TOXOPLASMOSIS IN HAWAI`I

The breadth of knowledge concerning infections caused by *Toxoplasma* and its transmission suggest a need to scrutinize certain risk relationships. In the process of scrutinizing risk relationships, we need to ask whether the prevention of the infection is worth the cost of implementing preventative measures and the diligence required to successfully implement the preventative measures. The ranking of the risk factors that have been utilized in this review is based on the health concern related to the risk factor and allows for increasing or decreasing the ranking through considering whether the risk factor can be controlled (reduces ranking) or cannot be controlled (increases ranking).

The identification of risk factors in no way should be used as a measuring stick for predicting actual human infections. This exercise merely identifies factors that could lead to infections either individually or collectively as is the case with any vector-borne disease. The mere presence of the disease organism or the presence of the disease vector should not result in the conclusion that such a vector borne disease will occur. For example, a report received by the Epidemiology Branch that a human case of malaria was reported to the department should not

trigger any alarm of a malaria outbreak, since we know that malaria patients suffer periodic relapses and we do not have the malaria vector in Hawai`i. It does not mean that we should not investigate whether the infection was locally acquired or not. Similarly, we should not cause an alarm by telling the people of Hawai`i that an epidemic of West Nile Virus is imminent in Hawai`i since the vector, *Culex quinquefasciatus*, is present in Hawai`i. The fact remains that the epidemic cannot occur without the virus. It does not mean that we should not remain alert to the possible introduction of the virus into Hawai`i via migratory birds or pet birds, etc. Similarly, with this exercise in risk identification one should refrain from making conclusions on any single risk factor but should look at the risk factors collectively before coming to any conclusion.

CURRENT INFECTIONS IN HAWAI`I (PRELIMINARY)

What is the public health significance of toxoplasmosis in Hawai`i? As an endemic infection with an apparent high prevalence, unknown morbidity and mortality, toxoplasmosis should be of little direct importance to adults. However, the occurrence of congenital infection and naturally acquired acute cases that occur post-birth cause concern. Table 6 (Appended) is an extension of Frenkel's[2] Table 5 and its basic assumptions. Table 6 is the estimated consequence to 17 babies infected at birth with *Toxoplasma gondii* in Hawai`i, annually based on an infection rate of 1/1000 pregnancies with 17,326 deliveries per year (1997 Hawaii birth rates per Office of Health Information). The results of extending Frenkel's[2] assumptions would indicate that **a major concern may not be warranted** because of the small numbers of estimated cases that could occur in Hawai`i. However, I am uncertain whether Frenkel's assumptions and model

accurately describe the situation in Hawai`i now. Finally, **I do not feel that any case of congenital toxoplasmosis is considered an acceptable risk for Hawai`i because of the potential future medical costs and possible health consequences**. Appended Tables 7, 8, and 9 show the results of tabulating preliminary raw data on *Toxoplasma* infections in Hawai`i between July, 1999 to May, 2000 based on serologic test results submitted by one laboratory in Hawai`i. Table 7 shows four cases that I have arbitrarily called congenital toxoplasmosis based on the age of the patient (newborn infant). Three cases show significant levels of IgG antibodies and one that is IgM negative but not confirmed negative (may need a IgG negative to confirm negativity). One of the cases has a highly significant titers of 7856 (IgG) and 4.76 (IgM) which is indicative of an active infection while the other two IgG positive cases are probably indicative of an older infection passed on to the fetus from its mother. Comparing the estimated cases for Hawai`i in Table 6 with the preliminary report of cases tabulated in Table 7, the results appear to be comparable or expected. This conclusion is tentative since it is based on the fact that the actual cases were only reported from a single laboratory in Hawai`i and may not be representative of the whole picture, including facts related to how the infection occurred. Finally, I am assuming that the overall results could be equivalent or higher if all laboratories in Hawai`i submitted test results. Tables 8 and 9 are cases in adult males and females, respectively, with males having 13 cases and the females having 12 cases. The only remarkable result was one male case showed significant titers indicating a recently acquired or relapse from a chronic infection. These preliminary findings were included only for the purposes of showing that the infections continue to occur in Hawai`i.

The defect in utilizing raw data is that infection rates cannot be determined since the raw data is indicative only of the numerator of the rate equation. Hence this kind of raw data requires careful explanation and the data should not be compared with prevalence rates such as the 60% estimated infection rate expressed by Wallace et.al.[22].

We know that infections continue to occur in Hawai`i. The question is, do we need further medical interventions? **I do believe that this review has shown that we have more than ample diagnostic and treatment capabilities but what may be lacking is systematic monitoring and review of cases**. This review could possibly stimulate physician awareness that this disease continues to exist and they need to be on the lookout for them.

IDENTIFICATION OF RISK FACTORS

Since we have evidence that the infections still exist in Hawai`i, we need to examine other risk factors that may be present in Hawai`i. We also need to examine how these risk factors could impact future infections, what can be done to control the risk factors, and whether it is worth the effort to pursue the control of these risk factors individually or collectively. The following is a list of risk factors that could sustain toxoplasmosis in Hawai`i:

- Ideal climate and environment
- Domestic and feral cat populations
- Feral cats in public parks
- Natural population of intermediate hosts
- Natural population of transport hosts

- Increasing immune suppressed population
- Social and cultural changes – influence on human susceptibility and advocating for animal rights
- Improved environmental sanitation
- Increased urbanization & increased "green space"
- Lack of concerted public health education
- Lack of vaccine to immunize cats
- Lack of laws to control feral cats or enforce 'domestication of cats'
- Other health risks associated with cats

ANALYSIS OF IDENTIFIED RISK FACTORS

The following are analysis and recommendation for each of the identified risk factors:

- **Ideal Climate and Environment** --- Dubey and Beattie[1], Dubey et.al.[3,4], Frenkel[2], and Wallace[6,7,10,11,12,13,14,15,16] and Ruiz and Frenkel[9,13] have stated that the ideal habitat for *T. gondii* is a place with warm temperatures, ample humidity to enable the oocysts to survive and sporulate, and frequent rainfall to support vegetation which afford protection for exposed oocysts. Many places in Hawai`i fit the description of the ideal environment for sustaining the life cycle of the parasite, hence the environment of Hawai`i is identified as a **Very High Risk Factor**. Although this is an identified very high risk factor, human intervention cannot alter the climatic variables necessary to maintain infections. Hence **no recommendation for altering the environment can be made.**

➢ **Domestic and Feral Cat Populations** --- It was stated earlier in this review that **domestic and wild cats are the definitive hosts of *T. gondii* and are the only known hosts in which the intracellular sexual cycle of the parasite can occur. Further, it was also stated earlier that infections occur only where cats are established. It can therefore be concluded that *Toxoplasma* infections could be eradicated if there were no cats. However, it is not the intent of this review to suggest or recommend the eradication of cats.** Dubey and Beattie[1] stated that populations of cats excreting oocysts at any given time is about 2%. Dubey, et. al.[3] indicated that 45% of stray cats in Kansas City had significant levels of antibody titer for toxoplasmosis which indicated these seropositives cats had already defecated infected oocysts. Wallace[6,7] had estimated the number of domestic cats and feral cats in Hawai`i as 30,000 each. Current estimates provided by an official of the Hawaiian Humane Society in Honolulu is that we have 115,800 house cats owned on O`ahu and **this number does not include feral or stray cats**. Unfortunately, not all house cats are maintained completely indoors. Many are allowed outside of the homes. The cat problem created by house cats that are allowed to stray will be discussed in a later section.

Some feral cats have been registered by the Humane Society as owned by an individual but not housed by that individual. To arrive at an approximation of the stray and feral cats in Hawai`i we must make certain assumptions. If we use the 40% to 50% estimates identified previously[3,6,7] **we may estimate that the feral or stray cat population in Honolulu may now be as high as 80,000 or more cats**. My understanding from discussions with the Society official is that 'owned stray or feral cats' may be spayed/neutered prior to release to the registered owner, hence the population of registered 'owned stray or feral cats' maybe incapable of reproducing and could be diminished by attrition. In theory, it appears to be a

sound policy; however, in reality, not all registered feral or stray cats are spayed/neutered and the number of new stray cats continues to increase as more strays occur from abandonment by its previous 'unregistered owner'. Such a practice of abandoning animals is both cruel to the animal and contrary to sound public health policy. Anecdotally, it is believed that feral cat colonies have been increasing especially in public parks and are "being maintained by several individuals or groups". The **anecdotal statement needs verification** and if found to be true, feral cat colonies in public parks maybe unacceptable.

The current cat populations on O`ahu which include domestic and stray cats now total close to 200,000 cats; this is more than three times the population estimated in the 1970's by Wallace[6,7]. It maybe concluded that the source of infective oocysts has also theoretically more than tripled. Based on the increased cat population and its concomitant public health risk, the cat population is ranked as a **Very High Risk Factor.** The risk factor is exacerbated as controls for both domestic and stray cats are very limited to non-existent, resulting in public nuisance complaints that are difficult to resolve. These kinds of nuisance complaints are difficult to resolve because of the lack of clear legal authority to control cats, lack of clearly defined owner responsibility for their cats, or a lack of will to enforce by the landowner. It is therefore evident from the public health perspective, that additional statutory or other legal authorities need to be available to protect the publics' health. **Further action that should be pursued by the department includes adoption of a proposed amendment to Hawai`i Administrative Rule, Chapter 11 – 26, related to control of feral cats. Additionally the department should encourage the counties to adopt a county ordinance for greater control of domestic cats or owner responsibility.**

- **Feral Cats in Public Parks ---** As was indicated in the earlier discussion, the population of feral cats was estimated to have more than tripled on O`ahu since the 1970's. Further, feral cats were anecdotally identified as an increasing concern in certain public parks. It was concluded in the earlier discussion related to the increasing cat population on O`ahu that the increasing feral cat population and its related public health concerns were a **Very High Risk Factor.** If the anecdotal statement that feral cats in certain public parks are increasing can be verified, they become the **Highest Collective Risk Factor and Require Further Attention and Action from a 'holistic public health perspective'.** Public parks that are populated by feral cat colonies, especially those that are at the lower elevations, are ideal **Enzootic Ecosystems** for the perpetuation of the life cycle of the parasites. The environmental conditions are ideal (warm and humid) as cited by numerous references. Natural sources of intermediate and transport hosts are generally abundant and may be accidentally or purposefully enhanced or amplified by anthropogenic activities. For example, picnickers may purposely feed wild birds. Their improperly discarded garbage may become food and breeding media for domestic rats, mice, filth flies, and cockroaches. Skinks and geckos dependent on natural populations of insects and small arthropods as their food source will become abundant as the insect population (transport hosts) increases. Earthworm, snail, and slug populations are increased because of landscaping work to beautify the parks. Finally, the presence of feral cat colonies in combination with the ideal environment and the natural source of intermediate and transport hosts merits the dubious title of an **Ideal Enzootic Ecosystem** which provides the necessary components for sustaining toxoplasmosis in public parks. The potential for human infections to occur is probably the highest in publicly owned and operated parks than any other single location in

Hawai`i. Why? The combination of the above conditions and of picnickers who may be totally uneducated about necessary precautions for preventing infections by infected cat oocysts poses a high risk factor. Finally, as far as this writer knows, there has been no concerted effort by park officials to pick-up cat feces that have been reported anecdotally to be abundant in parks. It may be only one feral cat that may be infected at any moment and may be shedding infected oocysts in parks. **But the fact remains that even a single infected cat can shed a million or more oocysts and even one oocyst may be sufficient to cause an infection in certain susceptible humans, especially children playing in soil contaminated with infected oocysts. Finally, should human cases or an outbreak such as the outbreak of toxoplasmosis in pre-school age children with geophagic tendencies[31] be traced to a public park, the economic liability to government could be staggering and may even result in deterring potential tourists from visiting Hawai`i.** A large number of risk factors identified herein are controllable. One requires that laws or rules be available to enable certain controls to be effected such as the prohibition or greater control of feral cat colonies in publicly owned parks. **I recommend follow up including proposed statute or Administrative Rule amendment(s) that prohibits or places controls on feral cat colonies in public parks. Further, I recommend that the department consider conducting surveys at certain public parks to confirm these risk factors.**

- **Natural Populations of Intermediate Hosts** --- Two types of intermediate hosts exist in Hawai`i. The first type includes those species of warm-blooded animals that are purposefully raised for human consumption and are known to be intermediate hosts of toxoplasmosis. These include domestic pigs, goats, sheep, chickens and pigeons. The

second type of intermediate host includes wild animals, some of which may be consumed by humans and those that are not consumed by humans. The wild animals that could be consumed or 'handled' by humans (especially hunters) include wild pigs, wild goats, wild sheep, feral pigeons, feral chickens and wild doves. The wild animals that are not consumed by humans include rats, mice, mongooses, and the numerous introduced birds (various species of finches and other passerine birds) that have since escaped and established feral populations. The estimated numbers of the above are unknown but inquiries with the State Department of Agriculture (Animal Division), State DLNR (Wildlife Division), Audubon Society, etc. may provide some numerical estimate. This is rated a **Moderate Risk Factor, especially with respect to the consumption of undercooked or raw infected meat by humans and the perpetuation of enzootic infections (cat cycle) as this review has already indicated**[1,2,6,7,14,15,16]. However, this moderate risk factor can be partially negated through public education, provided that efforts are made to educate the public about handling and consuming naturally infected wild animals and even domestic animals. The moderate risk factor related to the perpetuation of the enzootic cat cycle by wild rodents and birds can be controlled. The specific controls require that vector be controlled (transport hosts), the county ordinances prohibiting the feeding of wild birds (intermediate hosts) be enforced, and the quarantine regulations related to the importation of pet birds into Hawai`i be enforced. **I recommend further action focused on health education for the general public and hunters and reminding state and county agencies about stricter enforcement of their rules or ordinances.**

- **Natural Population of Transport Hosts** --- Transport hosts are those species of animals that can mechanically carry the oocysts externally or internally but play no part in increasing the numbers of parasites (no multiplication occurs in these species). Wallace [6,7,10,11,12,14,15,16] indicated that **coprophagus** arthropods such as the housefly, oriental blowfly, American cockroach, and Madeira cockroach could play an important role in the transport of oocysts onto unprotected foods. Woke et.al.[35] indicated that certain ticks and the body lice carried toxoplasmal organism. Wallace[12] studied geckos as possible carriers. Although the study was inconclusive, it is still strongly believed that these reptiles are capable of carrying oocysts. The mode of transmission of oocysts by these transport hosts may be more important for remote and rural areas of the state where primitive living conditions and sanitation may still exist although very unlikely. The greatest concern for transmission of infection by these transport hosts is for picnickers who leave their food unprotected from mechanically infected flies, cockroaches and lizards at publicly owned and operated parks. The rating for this identified risk factor is **Low.** Reducing fly and cockroach populations is relatively simply and merely requires stricter enforcement of existing sanitary rules such as requiring frequent pick-up and disposal of refuse, sanitary maintenance of refuse containers and frequent cleanup of park facilities. Public park administrators need to be reminded of their sanitary responsibilities. Education of the public is necessary to minimize infections. **Recommend necessary follow up with Park Administrators and public health education for the general public.**

- **Increasing Immune Suppressed Population** --- It is my belief that the population of HIV positive patients continues to grow but at what rate is unknown. The number of AIDS

cases has declined from a high of 2,420 to not more than 1,437 (as of July 31, 2000) due to the death of patients. It would be extremely difficult to get accurate information on the number of HIV cases because HIV positive cases are not required to be reported to the department and the department is notified only when an HIV positive case becomes an AIDS patient*. The number of patients with suppressed immune systems due to organ transplantation and/or under therapy for tumor and/or other ailments is unknown. It is my opinion that these numbers are increasing annually since organ transplants are becoming common in Hawai`i and nationally and the number of patients being treated with immunosuppressive chemicals are also rising. Being that these groups collectively represent the greatest human risk to fatal infection by *T. gondii*, the rank for this risk factor is **High.**

Despite the high risk, I do feel that health education about avoiding consumption of infected meats and foods, avoiding contact with cat feces, and other preventive behaviors could negate the risk. **Recommend follow up discussion with the Communicable Disease Division, and the Health Education Branch about available education material and the dissemination of these materials. No other action is necessary.**

- **Social and Cultural Changes --- influence on human susceptibility and advocation for animal rights** --- I am simply examining whether social and cultural changes have affected the susceptibility of human populations and behavior of animal rights or feral cat activists. We have come to accept the fact that these kinds of changes occurs

*The source of this information was made available to me from the department's STD/AIDS branch.

with younger generations or with people who may disagree with accepted policy, thinking or behavior of an older generation or the greater majority of those in power. These are generally changes in values that may often be in conflict with "established" sense of values. It is by no means anything demeaning or derogatory but simply changes that must be accepted regardless of any personal belief. Social changes may include a greater desire to 'protect the underdog' that a greater majority or mainstream individuals may have considered undesirable (animal rights activists and feral cat advocates). We need to recognize that despite our concern for public health, animal rights or feral cat activists have a similar concern for the rights of animals as expressed by Howard.[37] Cultural changes on the other hand are merely not accepting the mores, behavior, beliefs, teachings, practices etc. of the older generation and may even include deviation from traditional dress or foods. Wallace[27] expressed concerns in the 1970's that future infections caused by *T. gondii* may increase due to the "westernizing" of Hawai`i's culture (especially traditional Japanese and Chinese cultures who were identified as low risk). He felt that changes could result in exposing more people to infections related to the consumption of undercooked meats as is favored by the Europeans and by many U.S. adults. These in themselves are **Not Risks Factors.** These could become risk factors if the changes that occur go counter to preventive measures discussed earlier for minimizing toxoplasmosis. For example, if the Department of Health meetings for developing a better understanding with the feral cat activists regarding the control of feral cats in public parks are not successful, the department could see their objections as an unacceptable risk factor. This is especially true if the feral cat activists refuse to recognize the Department's concern about the public health significance of *Toxoplasma* infections that may be related to feral cats. Hence the Department would be

in its rights to proceed to amend statutes or rules to prohibit feral cats in public parks to negate the high risks afforded by feral cats in public parks. It is this reviewer's belief that compromises to the proposed rule can be agreed upon by all parties involved if the currently existing barriers between the Department of Health, feral cat activists and others are dissolved[37].

- **Improved Environmental Sanitation** ---Wallace[27] felt that the higher standard of living in future years with improved sanitation and reduced exposures to oocysts may result in an increase in the number of females susceptible to infection by *T. gondii* when reaching child-bearing age. **Whether the improved sanitation has resulted in a 'oocyst cleaner environment' is questionable. It may be possible that the current environment may contain more oocysts because of the significant increase in cat population contrary to the vision held by Wallace[27].** The major environmental sanitation improvements in existence include municipal and privately operated sewage and garbage collection and disposal systems, highly regulated and monitored drinking water systems, controlled zoning which separates urban and agriculture zones, and significantly improved housing, etc. In general, a significantly cleaner and safer environment. It is uncertain whether any of these significant environmental improvements contributed to the reduction of exposure to toxoplasmosis other than drinking water quality and zoning requirements for separating agriculture from urban areas. With respect to an 'oocyst cleaner environment' which Wallace[27] may have envisioned, it is my opinion that it is probably contrary, especially in one of the highest public health risk situations, i.e. public parks. It is my belief that further improvements to environmental sanitation are necessary to address the risk factors associated

with cat feces and oocysts in public parks which is an area that I identified as a very high collective risk factor, especially when associated with feral cat colonies.

I believe that the public perceives that government is almighty and can easily correct problems through the enforcement of existing laws. Environmental sanitation laws, i.e. Chapter 322, Hawai'i Revised Statutes, have been in existence since the late 1800's and nuisance problems with animals and animal droppings, although significantly improved, are not totally attributable to the enforcement of Chapter 322, HRS. In reality, the recent attempt by the Vector Control Branch to amend its Administrative Rule to "take care of the feral cat problem" was government's first attempt to correct a potential public health problem. The Vector Control Branch's attempt failed because the citizens who may have been concerned about feral cat nuisances never attended public hearings to support the proposed rule change. Further, the general public who may have been concerned about feral cat nuisances were absent during the 2000 Legislative hearing when the Department of Health was being chastised by the Legislators for attempting to regulate feral cats through the proposed rule changes to Chapter 11-26. The proposed amendment had a great deal of merit but unfortunately lacked a sound public health basis to negate the objections of feral cat activists and may have also lacked the assumed support of the general public. **Enforcement of Chapter 322, HRS, or the proposed amendments to HAR Chapter 11-26 can be a viable practical solution for improvement of current animal nuisance problems if a sound public health basis is established and the support of the affected individuals and groups is acquired**. Law enforcement generally tends to polarize rather than bring together groups and individuals to resolve a "community-wide problem". Further, law enforcement takes a long time to be effective and may not result in the desired

permanent behavioral changes. I rank further improvements to environmental sanitation as A High Risk Factor. **Further improvement to environmental sanitation (as a means for controlling Toxoplasmosis) can be achieved by the adoption of amendments to Hawai`i Administrative Rules, Chapter 11-26. It is recommended that the Vector Control Branch proceeds slowly and develops a partnership and understanding between the feral cat activists and the advocates for cat control. It is further recommended that the Vector Control Branch assimilate salient parts of this technical review as a public health basis for amending Chapter 11-26.**

- **Increased Urbanization and Increased 'Green Space'** --- Urbanization as an independent entity could result in the decline of toxoplasmosis. It has been stated several times by Dubey and Beattie[1], Dubey et.al.[3,4] and, Frenkel[2] that cats and toxoplasmosis are human problems in the country rather than in the cities. Why? Primarily because a typical city has little or no exposed moist soil which can maintain infected oocysts whereas in the country, especially on farm lands a great deal of moist soil is available for maintaining infective oocysts. Certain county land use policy requires developers to insure that adequate 'green space' is part of any new development. It is my understanding that 'green space' in these development terms means parks that eventually become publicly owned and operated. I already discussed the problems associated with publicly owned parks and the potential for these parks to become homes for feral cats and foci for transmission of toxoplasmosis. If the public were aware that their child or themselves could become infected with an acute infection of toxoplasmosis in a publicly owned and operated park, the state could then be liable for not taking appropriate actions. Increased urbanization and concomitant increase in

green space as a condition for new development is highly desirable but is given a rank of **Low Risk Factor if implemented per se.** This ranking as a low risk factor may be negated if the county land use requirements stipulates that the 'green space' is for public usage only and not for maintaining feral cat colonies. **It is therefore recommended that the department strongly advocate for the inclusion of the above stipulations as a policy or rule for new urban developments with 'green spaces'.**

- **Lack of Concerted Public Health Education** --- I believe that the Department of Health has been remiss about making continuous or periodic efforts at educating the public with respect to toxoplasmosis. I believe this occurred because only a few cases were being diagnosed or reported; however, as pointed out in this review, the majority of infections is mild or completely asymptomatic. The fact remains that the earlier survey by Wallace estimated that 60% of adults in Hawai`i were infected by *T. gondii*. If that estimate is still accurate, public health education on a continuous basis must be provided to insure that the severe forms of infection by *T. gondii* are minimized or prevented. (See Appendix; Tables 7, 8, and 9 are current infections to the newborn baby as well as to adult male and females in Hawai`i as reported by only one commercial laboratory in Hawai`i). Education efforts should be focused primarily at persons with suppressed immune systems, i.e. HIV positive individuals; those patients undergoing therapy that requires use of cytotoxic drugs; those patients receiving treatments which may cause their immune systems to be suppressed; hunters; and to pregnant females. **This is a High Risk Factor especially for persons with immune suppressed systems and for pregnant females. It is recommended that the Department provide continuous health education especially to those named above.**

- **Lack of Vaccine to Immunize Cats** --- Dubey and Beattie[1] and Frenkel[2] discussed the merits of a cat vaccine that would render cats as immune to infection by *T. gondii* and in theory could possibly 'eradicate' this disease. However, to date, no vaccine has been developed. Dubey and Beattie[1] and Frenkel[2] also discussed the problem of vaccinating cats. How do we vaccinate all cats to 'eradicate' this disease? With the current stray and feral cat problems in Hawai`i and elsewhere, the task for immunizing all cats via a vaccine is a nearly impossible task. This ranks as **a High Risk Factor.** It is desirable to have a vaccine to eradicate this disease but the problems and costs of developing, manufacturing and administering a vaccine makes it impractical to pursue.

- **Lack of Laws to Control Feral Cats or Enforce "Domestication of Cats"** --- As discussed earlier, the population of domestic cats has more than tripled on O`ahu from approximately 30,000 in the 1960's to 115,800 as of July, 2000. If we assume that at least 50% of these are strictly indoor cats, we then have approximately 55,000 cats that are allowed to stray. The number of actual stray cats in the urban environment (not public parks) is then estimated to be 55,000 domestic cats that are allowed to stray plus an estimated 50% of the 80,000 feral cats or approximately 95,000 stray cats roaming urban and suburban neighborhoods. Again, that estimate indicates that the stray cat population has more than tripled from the 1970 estimates by Wallace[6,7], resulting in the generation of public complaints. Complaints related to stray cats include but are not limited to the deposition of cat feces, cat sounds emanating as a result of ritual mating behavior, damage to land and structure, and the deposition of cat ectoparasites (fleas, ticks, mites, etc.) on private and

public property. The most significant complaint from the public health perspective is the unlawful deposition of cat feces that can serve as the source of infective *Toxoplasma* oocysts on private and public property and the resultant exposure of an unsuspecting susceptible individual to this source of infection. This is rated as a **High Public Health Risk Factor primarily because control of stray domestic cats has no legal basis.** We already discussed laws controlling feral cats in public parks and recommended that Vector Control Branch pursue amending HAR Chapter 11-26 cautiously and logically. With respect to laws related to "domestication of cats", I visualize a "Cat Leash Law" that is structured on the same lines as the "Dog Leash Law" and makes cats running loose in public areas subject to the same penalties as unleashed dogs. For that matter, we should be asking the question "Why are dogs prohibited from running loose in public areas" while cats are allowed despite the fact that they are carriers of parasites that could infect humans? Dubey and Beattie[1], Dubey et.al.[3,4], Frenkel[2], and Wallace[6,7] state that cats that are strictly maintained within homes and not allowed to hunt birds and rats outside the homes are rarely infected with *T. gondii* and hence are not sources of infections to their household members. On the other hand, house cats that are allowed to go outside to hunt and feed on birds and rats are frequently infected and may be a source of infection to their household members. It is my understanding that the logic used for the successful adoption of the dog leash laws included the potential for dog attacks resulting in liabilities to the owner as well as the potential for human diseases being introduced in their respective household. The diseases considered included **Larval migrans (from nematode worms) introduced through dog feces and Rabies (a disease with high fatality rates and severe infections that require intense human treatments).** With the cat leash law we are making an additional argument about **the possible introduction of**

toxoplasmosis into the household. The technical discourse that occurred earlier clearly indicate that toxoplasmosis can be severe and even fatal. The high cat population in Hawai`i combined with the potential for domestic and stray cats to become sources of *Toxoplasma* infections ranks this currently uncontrolled factor as a **High Risk Factor. The broad ethical question concerns the publics' right to protection from sources of infection. An infectious cat exposes not only his owners but neighbors who choose not to own pets. We should take the initiative and propose that counties adopt a "cat leash law" similar to the dog leash law.**

- **Other Health Risks Associated With Cats** --- The previous section further expanded our knowledge about the public health risks concerning *Toxoplasma* infections. The focus on the need to either limit the movement of the definitive host of the infection (cats) or to prohibit/control the colonization of feral cats in the highest risk area, i.e. public parks, were discussed at length. It is important to know that cats are hosts for numerous other human infections which include the following:

  - Leptospirosis
  - Murine Typhus
  - Plague
  - Rabies
  - Cat Scratch Fever (Bartonellosis)
  - Ehrlichiosis
  - Salmonellosis
  - Hookworms

Preliminary data from the Epidemiology Branch show that **infections in Hawai`i continue to occur. The potential for infection to the highest risk populations (pregnant females, HIV positive individuals, and immune suppressed patients) remains as a moderate risk.**

Analysis of twelve risk factors that could contribute to the maintenance of *Toxoplasma* infections in Hawai`i resulted in identifying several risk factors that collectively require some degree of follow up. **The major risk factors that need further attention focus on the definitive host --- the domestic cat --- and more specifically to feral or undomesticated cats (strays).**

The following are recommendations for taking further actions to address moderate to high risk factors with no current solution and pose a threat to public health. The recommendations include:

(1) **Adopting proposed amendments to HAR, Chapter 11-26, to control feral cats in public parks;**

(2) **Drafting and supporting proposed county ordinance(s) prohibiting feral cat colonies in newly established 'green spaces' in new developments;**

(3) **Drafting and supporting statutory or county ordinance(s) related to "domestication of cat law" similar to the dog leash law;**

(4) **Promoting stepped up monitoring of new born babies for *Toxoplasma* infection so medical intervention can occur at the earliest time possible (Epidemiology Branch in its "Communicable Disease Publication");**

(5) **Developing health education material on this subject for the general public;**

(6) **Encouraging park administrators to improve sanitation in public parks to reduce the abundance of natural intermediate and transport hosts in public parks; and**

(7) **Consideration for conducting limited research on the enzootic potential of toxoplasmal infections at certain public parks with large feral cat colonies.**

The conclusions and recommendations made herein are strictly those of this writer and do not require the Department of Health to implement any of the recommendations contained herein.

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TABLE 1. List of definitive hosts of Toxoplasma gondii recorded in references.

Common Name	Scientific Name	Country Locate	References
Domestic Cat	Felis catus	Worldwide	D, F, H, L, R, W
Bobcat	Lynx rufus	U.S.A.	D, F, L
Cheetah	Acinonyx jubatas	Zoo - U.S.A.	D, F, L
Iriomote Cate	Prionailurus iriomotensis	Japan (Ryuku Isle)	D
Jaguar	Panthera onca	Central America	D, F, L
Mountain Lion (Puma)	Felis concolor	U.S.A.	D, F, L
Ocelot	Felis pardalis	Brazil, Central America	D, L
Pallas Cat	Felis manul	Zoo - U.S.A.	D
-------	Felis cola cola	Argentina	D
-------	Felis eira	Argentina	D
-------	Oncifelis geofrayi	Argentina	D
-------	Felis pardinoides	Brazil	D

References: [a]

D = Dubey. et.al[1, 3, 4]
F = Frenkel[2] and Frenkel and Ruiz[26]
H = Hutchinson et.al[5]
L = Levine[8]
R = Ruiz & Frenkel[9,13]
W = Wallace[6, 7]

TABLE 2. List of mammals recorded as intermediate hosts of Toxoplasma gondii that are found in Hawaii.

Common Name	Scientific Name	Develop Tissue Cysts
ORDER: ARTIODACTYLORIDA		
Cattle	Bos taurus	Rarely or short duration
Bison	Bison bison	Rarely
Water buffalo	Bubalus bubalis	Rarely
Goat	Capra hircus	Readily infected; cysts numerous
Sheep	Ovis auries	Readily infected; cysts numerous
Moliflon sheep	Ovis museman	Occasionally
Pig	Sus serofa	Readily infected; cysts numerous
Axis deer	Axis axis	Occasionally
ORDER: RODENTORIDA		
Guinea pig	Cavia porcellus	Readily infected
Hamster	Cricetus cricetus	Readily infected
Polynesian rat	Rattus exulans	Readily infected
Norway rat	Rattus norvegicus	Readily infected
Black rat	Rattus rattus	Readily infected
Mouse	Mus musculus	Readily infected
ORDER: CARNIVORIDA		
Dog	Canis familiaris	Short duration
Mongoose	Herpestes auropunctatus	Occasionally
ORDER: LAGOMORPHORIDA		
Rabbit	Oryctolagus cuniculus	Occasionally

TABLE 3. List of birds recorded as intermediate hosts of Toxoplasma gondii that are found in Hawaii.

Common Name	Scientific Name	Develop Tissue Cysts
ORDER: GALLORIDA		
Chicken	Gallus gallus	Readily develop cysts
Japanese Quail	Coturnix japonica	Readily develop cysts
Guinea Fowl	Numida meleagris	Occasionally
ORDER: COLUMBORIDA		
Pigeon	Columba livia	Readily develop cysts
Barred Doe	Geopelia striata	Readily develop cysts
Spotted Dove	Streptopelia chinerisis	Readily develop cysts
ORDER: PASSERORIDA		
Sparrow	Passer domesticus	Readily develop cysts
Canary	Serinus canarius	Readily develop cysts
Cardinals	Paroaria calcullata	Readily develop cysts
Mynah	Acridotheres tristis	Occasionally
Finches	-------	Maybe
Rice birds	Munia nisonia	Maybe
ORDER: ANSERORIDA		
Duck	Anas platyrhynchos	Readily develop cysts
Goose	Anser anser	Occasionally

TABLE 4. List of non-mammalian vertebrates recorded as potential transport hosts of Toxoplasma gondii that are found in Hawaii.

Common Name	Scientific Name	Reference[a]
Mourning gecko	Lepiclodacylus luqubris	L, R, W
Fox gecko	Hemidactylus garnoti	L, R, W
Stump-toed gecko	Gehyra mutilata	L, R, W
Hawaiian gecko	Hemiphyllodactylus typhus	W
Skink		L, R, W
Chameleons		L
	Anole	L

References[a]

L = Levine[8]
R = Ruiz and Frenkel[9, 13]
W = Wallace[7, 12]

TABLE 5. List of invertebrates recorded as potential transport hosts of Toxoplasma gondii that are found in Hawaii.

Common Name	Scientific Name	Reference
House fly	Musca domestica	R, W
Blow fly	Chrysomya megacephala	W
Madeira cockroach	Leucophaea maderae	R, W
American cockroach	Periplaneta americana	W
Australian cockroach	Periplaneta australaisae	R
Snails	Bradybuena similarus	R, W, A
	Subulina octona	A
Slugs	Veronicella alfe	R, W
Earthworm	Pheretina spp.	R, W

A = Alicata[36]
R = Ruiz and Frenkel[9, 13]
W = Wallace[7, 10, 11, 12]

TABLE 6. Estimated consequences to 17 (3,000) toxoplasmic babies born in Hawaii (the U.S.) per year, based on an infection rate of 1/1000 pregnancies with 17,326[1/] (3 million) deliveries per year. (NOTE: This is an extension of Frenkel's[2/] Table 5 as applicable to Hawaii).

% Affected	Affect/Consequence	Frenkel's [2/] U.S. Estimate of No. of babies Affected	Hawaii's Estimate Using Frenkel's [2/] Assumptions
5 - 15%	Will die	150 - 450 babies	0.8 - 2.6 babies
8 - 10 %	Have severe brain damage	240 - 300 children	1.4 - 1.7 children
10 - 31%	Will have moderate to severe visual handicaps	300 - 390 children	1.7 - 2.2 children
58 - 72%	Will be asymptomatic at birth with a proportion developing active retino-choroiditis as children or young adults	1,700 - 2,150 children or young adults	10.0 - 12.4 children or young adults

[1/] Hawaii birth rate = 17,326 per Dr. Alvin Nonaka, DOH, Office of Health Status Monitoring based on 1997 data.

[2/] Frenkel, J.K. 1973. Toxoplasma in and around us. Bioscience, 23(6): 343-351.

TABLE 7. Congenital Toxoplasmosis infections that were identified in Hawaii between July, 1999 to May, 2000 based on serologic test results conducted by one laboratory in Hawaii.
(NOTE: data is preliminary and does not reflect infection rates in Hawaii).

SEX[1/]	Age	IgG Titer [2/]	IgM Titer [3/]	Remarks
F	0 (Newborn)	----	0.32	Test result read as negative but needs confirmed IgG negative to be "True negative"
F	0 (Newborn)	127	----	Reflective of an old infection passed to fetus by the mother.
M	0 (Newborn)	70	----	Reflective of an old infection passed to fetus by the mother.
F	0 (Newborn)	7,857	4.76	Congenital infection. May have clinical symptoms.

1/ SEX. F = female; M = male

2/ IgG Titer. <6 = No infection; >6 and <1000 = positive; >1000 = current infection

3/ IgM Titer. <0.9 = Negative; >1.10 = positive
NOTE: IgM Negative could be false negative and should be verified with IgG test.

TABLE 8. Toxoplasma infections that were detected in male patients in Hawaii between July, 1999 to May, 2000 based on serologic test results conducted by one laboratory in Hawaii.
(NOTE: data is preliminary and does not reflect infection rates in Hawaii -- simply -- this is the only current data available).

Age	IgG Titer [1/]	IgM Titer [2/]	Remarks
59	122	----	Old infection
82	156	----	Old infection
59	110	----	Old infection
48	42		Old infection
52	23		Old infection
50	282	----	Old infection
41	----	2.04	Inconclusive, need IgG titer
62	282	----	Old infection
32	67	----	Old infection
52	1,708	2.29	Recent infection
56	345	----	Old infection
20	189	----	Old infection
85	280	0.64	Chronic infection
13			

[1/] IgG titer less than 6 = no infection; titer in excess of 6 = positive

[2/] IgM titer less than 0.9 = negative; and if titer is 1.10 or greater = positive
Note: IgM negative could be a false negative and should be verified with an IgG test.

TABLE 9. Toxoplasma infections that were detected in female patients in Hawaii between July, 1999 to May, 2000 based on serologic test results conducted by one laboratory in Hawaii.
(NOTE: data is preliminary and does not reflect infection rates in Hawaii -- simply -- this is the only current data available).

Age	IgG Titer [1]	IgM Titer [2]	Remarks
40	353	0.47	Chronic infection
26	-----	1.41	Inconclusive, need IgG titer
19	370	-----	Old infection
29	317	-----	Old infection
43	373	-----	Old infection
50	69	-----	Old infection
25	353	0.79	Chronic infection
23	232	-----	Old infection
36	30	-----	Old infection
26	59	-----	Old infection
25	-----	2.57	Inconclusive, need IgG titer
24	297	-----	Old infection
30	0	1.57	False positive
13			

[1] IgG titer less than 6 = no infection; titer in excess of 6 = positive

[2] IgM titer less than 0.9 = negative; and if titer is 1.10 or greater = positive
Note: IgM negative could be a false negative and should be verified with an IgG test.