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An Overview of One Health Concept Focusing on Toxoplasmosis

Tek Sağlık Konseptinde Toxoplasmosis'e Genel Bir Bakış

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ABSTRACT

The "One Health" concept is a universal approach to sustainably balancing and optimizing the health of humans, animals, and ecosystems. This approach is based on the health of humans, domestic and wild animals, and plants in a wider environment in which self-renewable ecosystems exist, with essential characteristics of integration, unifying and holistic perspective. Toxoplasmosis, one of the most common zoonotic infections in both terrestrial and oceanic ecosystems in the world, is an ideal model disease for the "One Health" approach. Toxoplasmosis is a zoonotic disease caused by the obligate intracellular pathogen protozoan *Toxoplasma gondii*. In the life cycle of *T. gondii*, the definitive host is domestic cats and felines, and the intermediate hosts are all mammals (including humans), birds and reptiles. The infected cats have primary importance and play a crucial role in the contamination of habitats in the ecosystems with *T. gondii* oocysts. Thus, ecosystems with domestic cats and stray cats are contaminated with cat feces infected with *T. gondii* oocytes. *T. gondii* positivity has been scientifically demonstrated in all warm-blooded animals in terrestrial and aquatic habitats. The disease causes deaths and abortions in farm animals, resulting in great economic losses. However, the disease causes great problems in humans, especially pregnant women. During pregnancy, it may have effects such as congenital infections, lesions in the eye and brain of the fetus, premature birth, intrauterine growth retardation, fever, pneumonia, thrombocytopenia, ocular lesions, encephalitis, and abortion. The mechanism of death and abortion of the fetus in a pregnant woman infected with *T. gondii* occurs as a result of complete disruption of the maternal immune mechanism. The struggle against toxoplasmosis requires the universal collaboration and coordination of the World Organization for Animal Health, the World Health Organization and the World Food Organization in the "One Health" concept and integrative approaches of all responsible disciplines. Establishing universal environmental safety with the prevention and control of toxoplasmosis requires the annihilation of the feces of the infected cats using suitable techniques firstly. Then routinely, the monitoring and treatment of *T. gondii* positivity in cats, avoiding contact with contaminated foods and materials, and development of modern treatment and vaccine options. Particularly, mandatory monitoring or screening of *T. gondii* positivity during the pregnancy period in humans should be done. It would be beneficial to replace the French model, especially in the monitoring of disease in humans. In this article, the ecology of toxoplasmosis was reviewed at the base of the "One Health" concept.
Keywords: One health, ecology of toxoplasmosis, *Toxoplasma gondii*, pregnancy, prevention and control, interdisciplinary, struggle

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ÖZ

"Tek Sağlık" konsepti, insanların, hayvanların ve ekosistemlerin sağlığını sürdürülebilir bir şekilde dengelemeyi ve optimize etmeyi esas alan üniversal bir yaklaşımdır. Bu yaklaşım entegresyon, birleştirici ve holostik temel karakteristikleri ile insanların, evcil ve vahşi hayvanların, bitkilerin ve içerisinde kendi kendini yenileyebilir ekosistemlerin bulunduğu daha geniş bir çevrenin sağlığını esas alır. Dünyada hem karasal hem de okyanus ekosistemlerinde en yaygın zoonotik karakterli enfeksiyonlardan birisi olan Toxoplasmosis, "Tek Sağlık" konsepti için ideal model bir hastalıktır. Toxoplasmosis, zoonotik karakterli, zorunlu hücre içi patojen protozoon *Toxoplasma gondii*'nin meydana getirdiği bir hastalıktır. Hastalık etkeni *T. gondii*'nin hayat siklusunda son konağı evcil kedi ve kedigiller, ara konakları ise insan dahil tüm memeliler, kanatlı hayvanlar ve reptillerdir. Hastalık etkeni patojen *T. gondii*'nin hayat siklusunda kediler hem son konak hem de ara konak vazifesi gördükleri için, ekosistemin kontaminasyonundan da primer öneme sahiptirler. Dolayısıyla evcil kedilerin ve serbest dolaşan kedilerin bulunduğu ekosistemler, *T. gondii* oocytleriyle enfekte kedi dışkılarıyla kontamine olurlar. *Toxoplasma gondii* pozitifliği, karasal ve sucul habitatlarda tüm sıcakkanlılarda bilimsel çalışmalarla gösterilmiştir. Hastalık çiftlik hayvanlarında ölümlere ve abortlara yol açarak büyük ekonomik kayıplar oluşturur. Bununla beraber hastalık, insanlarda özellikle hamile kadınlarda büyük problemlere neden olmaktadır. Gebelikte *T. gondii* konjenital enfeksiyonları, fetüsün göz ve beyninde lezyonlar, prematüre doğum, intrauterin büyüme geriliği, ateş, pnömoni, trombositopeni, oküler lezyonlar, ensefalit ve abort gibi patolojik bozukluklara yol açar. *Toxoplasma gondii* ile enfekte bir gebede ölüm ve abort, maternal bağışıklık mekanizmasının tamamen bozulması sonucu şekillenmektedir. Toxoplasmosis'e karşı mücadele, üniversal boyutta Dünya Hayvan Sağlığı Teşkilatı, Dünya Sağlık Teşkilatı ve Dünya Gıda Teşkilatı'nın "Tek Sağlık" konseptinde koordinasyonunu ve tüm paydaş ülkelerde ulusal düzeyde ilgili tüm disiplinlerin bütünleştirici yaklaşımlarını gerektirir. Bu bağlamda özellikle hastalıktan korunma ve kontrolde, tekniğine uygun olarak çevre güvenliği için kedi dışkısının imhası, kedilerde pozitifliğin izlenmesi ve tedavisi, kontamine gıda ve malzemelerle temastan kaçınmak, modern tedavi ve aşı seçeneklerinin geliştirilmesi ve insan ve hayvanlarda hastalığın zorunlu izlenmesi/taraması gerekmektedir. Özellikle insanlarda hastalığın izlenmesinde Fransa modeline geçilmesinde yarar vardır. Bu makalede, "Tek Sağlık" konseptinde toxoplasmosis'in ekolojisi incelenmiştir.

Anahtar Kelimeler: Tek sağlık, toxoplasmosisin ekolojisi, *Toxoplasma gondii*, gebelik, korunma ve kontrol, disiplinlerarası, mücadele

INTRODUCTION

Pathogens like viruses, bacteria, parasites, fungi, and prions, pose significant threats to humans, animals, and plants, often leading to outbreaks of a wide variety of diseases with emerging and reemerging features (1,2) of which 75% are classified as reemerging zoonotic infections (3). The Outbreaks have appeared as sporadic, endemic, epidemic and pandemic in the history of epidemiology (2). Throughout history, humans facing adverse natural conditions and infectious diseases have been engaged in a continuous battle against these outbreaks. This ongoing battle has evolved into the modern "One Health" concept, which represents a significant step forward. International organizations such as the World Health Organization (WHO), the World Organization for Animal Health (OIE), and the Food and Agriculture Organization of the UN (FAO) coordinate the implementation of the "One Health" approach, with global-scale strategies developed to address these challenges. As a result, many zoonotic epidemics and pandemics have been effectively controlled. Toxoplasmosis is a zoonotic disease caused by the coccidian parasite *Toxoplasma gondii*. Cats have special importance in the ecology and epidemiology of toxoplasmosis, as they act as both final and intermediate hosts in the life cycle of *T. gondii*. This pathogen can be seen in all animals including the intermediate host human, mammals, poultry, and reptiles and causes abortions in intermediate mammalian hosts, with sheep being highly susceptible resulting in significant economic losses. Therefore, it is necessary to evaluate toxoplasmosis in the context of "environmental health, animal health and human health in a self-renewing ecosystem" with a holistic perspective. To effectively address toxoplasmosis, it is crucial to develop combat strategies and programs that involve all relevant stakeholders in a coordinated effort. However, before taking action, it is important to first analyze the connection between the ecosystem and toxoplasmosis from a human-centric perspective. Throughout human history, the interest to understand and control nature has always been high to mitigate increasing animal protein and energy demands destroying natural ecosystems including the oceans. Therefore, new holistic approaches should employed within the scope of the slogan "stop ecocide" and "to create self-renewing ecosystems on land and in the ocean, to produce healthy animals and functional animal products on the basis of herd health, and to reach safe food, healthy and happy people". In this context, the motto "One World, One Health" concept was developed by WHO.

The Chronological Development of the "One Health" Concept in Historical Periods

Although the concept of "One Health" was officially introduced in the early 2000s, its roots can be traced back to ancient times, as far back as the discovery of fire. Archaeologists have described the discovery of fire by humans as a complex process that took place over a long period. Although the discovery of fire is about 1.5 million years ago, its use with flint dates back to 400,000 years ago. However, the third phase, in which people use fire regularly, goes back to about 7,000 years ago (4). The fact that humans heat food with fire and then consume especially cooked animal products has generated the beginning of a new era for human nutrition (5). The domestication of cattle in the Neolithic Age around 14,000 years ago was another turning point in human history, as it led to the selective breeding of farm animals and the regular production and consumption of animal-based foods such as meat and milk. To protect human health, the consumption of animal products that have died from infectious diseases or are suspected to have died from such diseases has been abandoned. Therefore, humans have taken measures to prevent diseases of animal origin and protect their interests (6-8).

Following that, about 12,000 years ago, the cultivation of wheat and the initiation of agriculture became a new historical period in human nutrition. The consumption of agricultural products has also been an important step for human health. Additionally, humans utilized agricultural practices to generate animal feed, resulting in healthier livestock and better-quality animal products. The consumption of foods from animal and plant sources provided the "*adaptation to food and the formation of intestinal flora*" in the gastrointestinal tract of humans. This evolutionary adaptation has increased the resistance against food-borne diseases, so that people have been healthier and happier. This selective eating habit has continued until today (5,8). The period of human history that witnessed the transition to settled city life marked a crucial epoch in terms of health. Roughly 10,000 years ago, humans established communal city life, beginning with the earliest settlements such as Göbekli Tepe and Çatalhöyük in the "fertile crescent" region. This development had an important impact on the establishment of public health. Around 9,500 years ago, city people began to domesticate cats as a means of combating pests like mice in their immediate surroundings. This practice was the beginning of the "environmental sanitation period" in areas where people lived, which played a crucial role in maintaining good health (9).

The concept of "One Health" was based on scientific observations during the period of the Greek philosopher Hippocrates (460-370 BC). Hippocrates in his book titled "On Airs, Waters and Place" mentioned the necessity of "Air, Water and Soil" for optimum health and wrote the first information about "Environmental Health/Eco Health" (10). Over time, the concept of "One Health" has flourished through the acquisition of knowledge about diseases in the context of historical processes. In the Neolithic period, the relationships between arthropods such as flies, fleas, lice, and ticks and the diseases observed in humans and animals were noticed (11). Recently, archaeoentomology has focused on investigating ancient civilizations and their environments, particularly ancient human communities, with an emphasis on pest insects, preserved products, and mummies (12-17). In history, various Anatolian civilizations (eg; Ephesus, Hittite) have been destroyed by vectors (such as mosquitoes, ticks, fleas) and various vector-borne diseases including malaria, plague, Crimean Congo haemorrhagic fever, etc. (18). In the early stages of history, primarily plague pandemics (first: 541-750 in Egypt, the Middle East, Northern Europe; second: 1331-1855 in Central Asia and Europe; third: 1855-1960 in China, India, and the West Coast of the United States) were seen. At the same periods of history, it has been considered that the causes of many epidemic/pandemic diseases are microorganisms. However, since the microscope was not invented yet during the first and second Plague Pandemics, pathogens causing the disease could not be shown (19).

Ibn Sina, also known as Avicenna (980-1037) is renowned as one of the most notable Turkish philosophers in history. His influential work, "The Canon of Medicine" or "The Law of Medicine," included various aspects of medical knowledge. Within this extensive book, Ibn Sina provided a significant contribution to the field of epidemiology by defining the concept of the Plague and presenting an insightful approach to understanding disease transmission (20). In his book "The Canon of Medicine", Sina explored different aspects of medical science. The first treatise explored anatomy, while the second focused on the causes and symptoms of diseases. The third treatise incorporates topics such as hygiene, health, sickness, the inevitability of death, and the implementation of quarantine measures to prevent and control outbreaks (21). Giovanni Maria Lancisi, an Italian philosopher (1654 to 1720), was a prominent epidemiologist who researched how the physical environment contributes to the transmission of diseases among humans and animals (Figure 1).

With the invention of the microscope by Antonie van Leeuwenhoek (1632-1723), a new historical period called the "Microscopic Era" started. During this time, significant progress has been made in the field of pathogen diagnosis for human and animal diseases, disease identification, and the implementation of infection control strategies. Soon after this historical development, the world's first veterinary school was established by Claude Bourgelat in Lyon, France in 1762 (22). At the beginning of the 19th century, German Pathologist Rudolf Virchow (1821-1902) emphasized the importance of the strong link between human medicine and veterinary medicine and laid the foundation of the concept of "One Health" in the modern sense. Dr. Virchow used the term "Zoonosis/disease transmitted from animal to human" for the first time and demonstrated the importance of zoonotic pathogens and diseases with zoonotic characters with the famous phrase "*There is no dividing line between animal and human medicine - there should not be*" (23). The discovery of the

Figure 1. The history of the One Health in the world 1st period

Rabis vaccine in 1885 by Louis Pasteur was a step forward toward the "One Health" concept (24). Later, Sir William Osler (1849-1919) emphasized that similar thinking methods are required in both veterinary medicine and human medicine for optimal health in his work titled "Principles and Practice of Medicine" (25). In 1854, at a meeting of the London Epidemiological Society, John Snow presented two groundbreaking maps displaying the cholera epidemic and visually illustrating the spread of the disease. A few months later, Snow's maps were published in his book "On the Mode of Communication of Cholera." Nobel Prize-winning German physician Heinrich Hermann Robert Koch (1843-1910) successfully isolated the pathogens responsible for anthrax (1877), tuberculosis (1882) and cholera (1883) bacilli and also developed the "Koch Postulates". Dr. Koch has displayed very important scientific contributions to the concept of "One Health," both etiologically and epidemiologically (26). On the other hand, Scottish Medical Doctor Sir Patrick Manson (1844-1922) discovered the transmission of a human parasite (*Wuchereria bancrofti*) through mosquitoes in 1877. In the field of epidemiology, Dr. Manson made a significant contribution by describing a vector-borne disease for the first time which also contributed to the "One Health" concept. In addition, Dr. Manson proposed the theory that "*Malaria Can Be Transmitted by Mosquitoes*" which further advanced our understanding of how diseases can be transmitted (27). Victor Babes, a Romanian scientist discovered *Babesia bovis* in 1888, a parasite with zoonotic characteristics than Veterinary surgeon Curtis, along with his colleagues Theobald Smith and Fred Kilborne, identified a blood parasite in bovine erythrocytes and named the disease "Texas Fever" caused by *Pyrosome bigeminum* opened a new era in the epidemiology of tick-borne diseases (28). Soon after in 1897, Dr. Sir Ronald Ross (1857-1932) proved Dr. Manson's hypothesis that "*Malaria may be a vector-borne disease*" and discovered that Malaria was transmitted by mosquitoes. Thus, malaria took its place in the history of epidemiology as a mosquito-borne disease. These historical discoveries have ensured great scientific contributions to the "One Health" concept (29). The discovery of the BCG vaccine by two French Veterinary Surgeon and Bacteriologist Jean Marie Camile GUERIN and Albert CALMETTE was a significant advancement in the battle against epidemics, particularly tuberculosis (30).

Their invention in the 1920s made a tremendous contribution to the "One Health" concept, highlighting the interconnections between human and animal health. During the early stages of urban life and culture, advancements in city infrastructure such as "Sanitization" and "Modern Urbanization" studies, which date back to the bronze age (3000-1100 BC) and began with "Urban Hydrological Technologies," led to significant gains in the fight against contagious diseases. The establishment of public drinking water supply systems and sewer systems to carry off waste matter were revolutionary chronological developments that contributed to the "One Health" concept (31,32). Furthermore, works such as coagulation, flocculation, sedimentation, filtration (including microfiltration and ultrafiltration systems), and disinfection were essential in preventing aquatic pathogens and water-borne diseases, and legal standards were eventually established to guarantee these processes. The establishment of treatment units in the sewerage networks, the determination of standards, and the fact that they are guaranteed by legal regulations have also created revolutionary positive developments for "One Health" in terms of environmental, animal, and human health. In this context, John Laing Leal (1858-1914) disinfected drinking water by chlorinating it in 1908 in Jersey City, New Jersey (33) (Figure 2).

Figure 2. The history of the One Health in the world 2nd period

The "antibiotic age" brought about significant advancements in the fight against infectious diseases through the use of antibiotics, resulting in a new historical development period for the "One Health" concept. Alexander Fleming also explained in 1949 the fact that the wrong usage of antibiotics can lead to "Antimicrobial Resistance (AMR)". As an indicator of the fight against antimicrobial resistance, the European Veterinary Federation (FVE) initiated and conducted the Healthy Livestock project against AMR in 1975 (34). Subsequently, with the discovery of dichloro-diphenyl-trichloroethane, a highly toxic and persistent insecticide, by Swiss chemist Paul Hermann Müller (1899-1965), who was later awarded the Nobel Prize in Medicine, a new era began in the fight against pests and vector-borne diseases in 1939. However, shortly after, due to the excessive harmful effects of this chemical, its use was banned in 1970, which is highly significant from a "One Health" perspective (35). As an indication of this, the FVE launched the AMR and Healthy Livestock project in 1975 to combat AMR and provide education on it (36). Through this project, significant contributions were made to the interdisciplinary development of the "One Health" concept by regulating the use of antimicrobials in Veterinary Medicine. Contemporary Veterinarian Epidemiologist/parasitologist Calvin Schwabe (1927-2006) wrote a book titled "Veterinary Medicine and Human Health" in 1964 where he proposed "One Medicine Concept as Unified Approach to Human and Veterinary Health," particularly cooperation between Human Physicians and Veterinary Surgeons for the Control of Zoonotic diseases. In the book for the first time, Schwabe declared veterinary surgeons as the primer responsible professional of the "One Health" concept. With Schwabe's modern and up-to-date approach, the professionals involved in the interdisciplinary cooperation of the "One Health" concept have been clearly pointed out (37). *Toxoplasma gondii* is a zoonotic apicomplexan protozoan parasite, and it serves as a prime example of a modern approach to "One Health" practices. In the 1970s, Prof. Dr. Jitender Prakash Dubey, a veterinarian and parasitologist, identified *T. gondii* and conducted research on its life cycle, epidemiology, and ecology. His work has contributed to the formation of multidisciplinary collaborations between the fields of veterinary medicine and human medicine, which is essential to the "One Health" concept (38). In fact, since the mid-1900s, the collaboration between veterinary and human medicine has continued to strengthen worldwide, and similar cooperation examples have been observed in Turkey. In the Ottoman Institute of Bacteriology in İstanbul, Veterinarian Adil Mustafa Şehzadebaşı and French Medical Doctor Microbiologist Maurice Nicolle made a significant discovery in 1902, demonstrating that the Rinderpest virus could pass through filters. In 1915, Dr. Reşat Rıza Kor, developed the typhus vaccine at the Bacteriology Center in Istanbul, and it was first administered by Dr. İbrahim Refik Saydam (39). In 1929, Veterinary Ord. Prof. Dr. Süreyya Tahsin Aygün developed the "Universal Anthrax Vaccine," while in 1933, Veterinarian Captain Kemal Cemil and Prof. Dr. René Legroux collaborated on vaccine research at the Paris Pasteur Institute, resulting in the development of the "Anamorve" vaccine (40).

Simultaneously with these historical achievements of the "One Health" concept, it was realized that the relationship between diseases and environment is very important. American Environmental Microbiologist Dr. Rita Rossi Cowell (1934-) has worked on global waterborne infectious diseases and their impacts on global health with the perspective of "Climate and Global Distribution of Microorganisms". Her unique perspective has made a significant impact on the advancement of "One Health", particularly regarding the epidemiology of Vibrio cholerae, a pathogen that resides in aquatic environments and causes Cholera disease (41). The "resistance" of parasites to some chemicals used as pesticides, acaricides, and insecticides led to prohibitions that marked an important and historical beginning in the "One Health" approach to prevent ecological contamination. Unfortunately, despite these chemical bans, systems developed to meet increasing energy demands, such as nuclear power plants, coal-based thermal power plants, deep energy in oceans, and hydroelectric generation systems (HEPP) on rivers, cause serious ecocidal effects on ecosystems. These devastating situations lead to major environmental disasters in both terrestrial and marine systems, posing serious threats to human and animal health (42).

The solution to these global environmental problems lies in the "One Health" approach, which involves international collaborations using strong early warning systems and developing sustainable alternative energy sources. New approaches have been developed in the control and prevention of diseases due to the advancement and studies in the field of immunology. In 1996, Nobel Prize-winning Australian veterinarian Peter Charles Doherty (1940) and Swiss immunologist Rolf Martin Zinkernagel discovered "the mechanism of the immune system to recognize virus-infected cells," making a significant contribution to the concept of "One Health" (43).

The establishment of international organizations and their coordinated work have brought significant advantages in the control of diseases on a global scale. Some examples of international centers established chronologically include: the Food and Drug Administration in 1906, the League of Nations in 1920, the OIE in 1924, the FAO in 1943, the UN in 1945, the WHO in 1945, the United Nations International Children's Emergency Fund (UNICEF) in 1946, the Center for Disease Control and Prevention (CDC) in 1946, the United Nations (UN) Environment Program (UNEP) in 1972, the European Medicines Agency (EMA) in 1995, the European Food Safety Authority (EFSA) in 2002, the European Center for Disease Control (ECDC) in 2004, and the Institute of One Health (IOHR) in 2022 (Figure 3).

The joint work of veterinarians and human physicians has progressed significantly since the establishment of the Veterinary Public Health unit at CDC by Doctor Veterinarian James H. Steele in 1947 (35). Important studies for "One Health" have also been conducted in the following periods. The Manhattan Principles about "One World, One Health" (2004) have been an important development in terms of "One Health", as they focus on issues such as combating epizootic/epidemic diseases and developing holistic approaches such as protecting basic biodiversity and ecosystem integrity (44). Nobel Prize-winning American biologist and parasitologist William C. Campbell (1930) discovered a new therapy against Nematode infections in 2012 (45). Veterinary Parasitologist, Sir/Lord Prof. Dr. Ernest Jackson Lawson Soulsby (1926-2017) made significant contributions to institutionalizing the "One Health" approach. In honor of Sir Soulsby for his devoted work, The Soulsby Foundation was established in 2016 to internationally support research and other charitable activities related to promoting the "One Health" approach between the Medical and Veterinary professions (46). The historical progress of the concept of "One Health" has essentially been closely related to world politics. After the collapse of the Soviet Union in 1992,

Figure 3. The history of the One Health in the world 3rd period

a new era has begun. In 1994, the concept of "Globalization" was developed and applied in almost every field (eg "Global Economy", and "Global Trade"). In this context, WHO has also developed the concept of "Global Health". However, this approach left its place in the "One Health" concept in the early 2000s. Soon after, in 2002, WHO developed the slogan "One World One Health". The World Organization for Animal Health (OIE) also defined in 2020 the concept of "One Health" as "Ecosystem Health" (47).

In the modern era, cooperation and joint work between Epidemiologists and Virologist Veterinarians and Human Physicians, especially their coordinated work in the Scientific Committees established for special purposes, have provided important gains in the fight against epidemic diseases. In the global fight against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2/COVID-19), a zoonotic virus that caused a pandemic, strategies have been developed to combat the disease. This pandemic is the latest epidemic encountered in the history of humanity, and its economic losses cannot be calculated. The WHO announced the pandemic in March 2020. Human physicians, veterinarians, epidemiologists, virologists, public health specialists, and all health professionals have worked selflessly and coordinated at the highest level to combat the disease. Their work is the greatest example and achievement of the "One Health" concept.

In the Covid-19 pandemic, vaccines developed with "Subunit Vaccine Technology" reached the development of the "One Health" concept to the new age. During this process, the development of vaccines against Covid-19 by both human physicians and veterinarians and their widespread use in immunizing people have been historical successes in terms of "One Health". Turkish scientists have greatly contributed to the "One Health" concept by showing great success in the global fight against Covid-19. The inventors of the BIONTECH vaccine are Medical Doctors Prof. Dr. Uğur Şahin and his wife Prof. Dr. Özlem Türeci and the inventor of the TURKOVAC vaccine, Veterinarian Prof. Dr. Aykut Özdarendeli's contributions have been highly recognized. Also, the Crimean-Congo Vaccine was developed by Özdarendeli constitutes another important model study in terms of "One Health".

On October 17, 2022, the FAO, the UNEP, the WHO, and the OIE launched a new five-year (2022-2027) One Health Joint Action Plan. The plan outlines six steps to be taken to achieve its objectives.

These actions:

1. Developing "One Health" capacities to strengthen health systems.

2. Reducing the risk of emerging and re-emerging zoonotic outbreaks and pandemics.

3. Control and eradication of endemic zoonoses, tropical epidemics and vector-borne diseases.
4. Evaluation, management and reinforcement of food safety risks.
5. To curb the silent epidemic of AMR.
6. Integrating the Environment into "One Health" (48) (Figure 4).

In order to achieve sustainable goals in the "One Health" concept, scientific excellence, dissemination of knowledge, interdisciplinary coordinated management, creation of needed funds and advanced monitoring systems integrated with an early warning system are required. In addition to these, primary professional responsible veterinarians must establish strong collaborations with other responsible stakeholders, especially human physicians, in the development of sustainable alternative approaches, uncompromising biosecurity practices, and the preservation of ecological connections between habitats and integrity assurance. Ensuring the participation of the public in this cooperation will provide great convenience in obtaining successful results. In order to better understand the "One Health" concept developed in the New Millennium and to achieve the necessary gains for professionals to fulfill their responsibilities, this concept should be given as a "Compulsory Lesson" and "Course Information Packages" in the "National Core Curriculum" of faculties Veterinary, Medical, Dentistry, Pharmacy and Health Science. In addition, the UNESCO Eco Health/Environmental Health initiative supported the protection of the sea and oceans and the creation of the necessary culture for this with the slogan "One Earth-One Ocean (OEOO) (49). In Turkey, "Veterinary Public Health Departments" were established in Veterinary Medicine Faculties within the scope of the Council of Higher Education, UNESCO/ISCED Education Standard Classification. This development meets an important need and is very beneficial in creating an academic infrastructure for rapidly acquiring the "One Health" culture in higher education. The next step in developing the "One Health" approach, as seen in the United States and Europe, is to integrate "One Health" into the curricula of relevant higher education units. Today, in accordance with the "One Health" concept, the epidemiology of zoonotic infections is mainly evaluated together with their ecological factors and dynamics of the causative pathogens with enzootic characteristics. In this context, it is necessary to examine the ecology of *T. gondii*, which causes toxoplasmosis, one of the most common parasitic infectious diseases in the world.

Figure 4. The history of the One Health in the world 4th period

Epidemiology and Ecology of *Toxoplasma gondii*

Since cat act as both intermediate and final hosts in the life cycle of *T. gondii*, the ecosystem consistently gets contaminated with their infected feces. There is a close relationship between the contamination of ecosystems with *T. gondii* oocysts and the number of infected cats in a region. When the population of domestic cats in an area is higher than that of stray cats, the potential of contamination of ecosystems with *T. gondii* also increases. In the USA, a large number of domestic cats carry *T. gondii* throughout their lifecycle and each infected cat can release millions of oocysts. Epidemiological studies revealed that domestic cats are more likely to contaminate the environment than stray cats (50-53). It is important to note that *T. gondii* oocysts can remain infective for months or years in harsh natural conditions making it more difficult to control (51-54). It has been estimated that on the Morro coast of California in the United States, domestic and stray cats excrete approximately 77.6 and 30 tons of feces per year, leading to environmental contamination of over 4,500 oocysts/m^2 per year (55). The increase in the number of cats will increase the possibility of contamination of the environment with *T. gondii* oocysts increasing the likelihood of intermediate hosts such as humans, domestic animals, and wild animals getting infected with *T. gondii* oocytes, which in turn increases the likelihood of final host cats becoming infected. The inability to clearly understand the role of domestic cats in the spread of toxoplasmosis and the epidemiology of the disease in many ecosystems, and sometimes ignoring this critical situation, constitutes an important handicap in informing society accurately and adequately (56).

Animal care-feeding policies can have an impact on the number of stray cats and the risk of transmission of *T. gondii* by removing cats from open places (31,32). With a growing number of animal shelters, deliberate outdoor housing of cats will reduce the risk of transmission of *T. gondii* to humans, pets and wildlife (56). Determining the concentration of *T. gondii* oocysts in the environment is critical for assessing health risks in a holistic framework. Research showed that land, water and ocean can be contaminated with *T. gondii* and the survival of oocysts in soil may vary depending on geological and environmental characteristics such as soil temperature, texture and chemistry. Under optimal conditions, oocysts can survive for approximately four years (57-60). Factors such as the presence of water or humidity, cold temperatures (not freezing), and sufficient oxygen are essential for their longevity (61). To model the spread of oocysts in the soil to wider environments, it is important to consider factors such as the effect of rainwater, land use, and cat density. However, the environmental parameters responsible for the long-term infectivity of oocysts, their resistance, the extent of environmental contamination, and the survival time or infectivity of cysts following the intermediate host's death are not fully understood. The omnipresence of *T. gondii* oocysts and the ability to rapidly sporulate under suitable environmental conditions also increase the likelihood of infection for all at-risk species in the ecosystem (62).

The prevalence of *T. gondii* in some countries with very cold or hot climates tends to be lower in humans, while in countries with warm and humid climates is higher. In general, the prevalence of *T. gondii* infection appears to be higher in temperate regions of the world. The prevalence of the disease in humans has been reported to be 8-22% in the United States, with similar rates in the United Kingdom, and 30-90% in Central America, South America and Continental Europe (63-69). In Turkey, the seroprevalence of *T. gondii* in humans is 10-85% and the highest rate is in the Southeastern Anatolia Region; In a study conducted in Ankara, immunglobulin (Ig)G and IgM positivity were found to be 22.3% and 0.64%, respectively. 47% of women between the ages of 15-45 who came to Turkey from Syria and were likely to become pregnant were found to be *T. gondii* positive (70,71).

It has been reported that more than one million people are infected each year in the USA and approximately 2,839 people develop "ocular toxoplasmosis" annually. The economic loss caused by the disease is estimated to be approximately 3 billion USD. *Salmonella, Listeria,* and *T. gondii* are jointly responsible for more than 75% of food-related deaths in the United States (72); Scallan et al. (73) reported that *T. gondii* causes 8% of food-borne hospitalizations and 24% of deaths in the US. Although there are no routine screening programs for toxoplasmosis in the US, Canada, the Netherlands, Norway and England, all pregnant women are subject to screening programs in countries such as France, Belgium, Italy, Switzerland, Germany and Austria. In these countries, serological testing is mandatory every month or every three months to detect a possible new infection earlier if the screening results are negative (Table. 1).

The biggest challenge in the diagnosis of toxoplasmosis is the detection of acute infection and its differentiation from chronic infection. Detection of *Toxoplasma* infection can be made using serological tests (IgM and/or IgG), ultrasound scans (suspicious images) and amniocentesis. Since maternal infection does not always result in fetal death, it is important to determine the presence of fetal infection. Congenital toxoplasmosis can be detected in the fetus by using polymerase chain reaction for *T. gondii* DNA in amniotic fluid (70,74,75). Infections occurring in early pregnancy have minimal risk of fetal transmission (less than 6%). However, transmission rates in the third trimester can increase as much as 60% and 81% (76).

The One Health concept, with the slogan "One World, One Health," takes a holistic view of human, animal, plant, and environmental health at the local, global, and even space levels. In this context, if the historical development of toxoplasmosis, the transmission routes of the agent and its effects are known in all aspects, the disease can be better understood. In particular, it is encouraged to implement the necessary coordinated cooperation between professionals such as universities, state institutions (especially local governments), non-governmental organizations, politicians, doctors and veterinarians, and the public, to protect ecosystem health.

Discovery and Definition Processes of *Toxoplasma gondii*

Toxoplasma gondii was first discovered in 1908 by Nicolle and Manceaux in the tissues of *Ctenodactylus gundi*, a hamster-like rodent used in leishmaniasis research in Charles Nicolle's laboratory at the Pasteur Institute in Tunisia (77). The scientists first thought the parasite was a pyroplasm, but later realized that it was a newly discovered microorganism.

Table 1. Mandatory screening for toxoplasmosis in pregnant women by country

Country	No screening	All pregnant women are screened	Screening in pregnant women is optional	
Austria		X		Serological screening has been conducted for the first trimester since 1974. Seronegative women receive monthly follow-ups throughout their pregnancies.
Belgium		X		Serological screening is performed starting from the first trimester. Seronegative women receive monthly follow-ups throughout their pregnancies.
Bulgary			X	
Czech Republic			X	Serological screening is only available in specific regions and gynecological clinics. Screening is not covered by legal health insurance.
Denmark	X			Surveillance and screening were actively conducted between 1999 and 2007.
Estonia	X			
France		X		Serological screening is performed from the first trimester onwards. Seronegative women are followed up on a monthly basis throughout their pregnancies.
Germany			X	Screening is not covered by legal health insurance.
Hungary			X	
Island	X			Suspected cases are individually tested.
Ireland	X			If there are clinical indications, a Toxoplasma test is requested.
Malta	X			
Holland	X			
Norway	X			
Slovakia		X		Serological screening is conducted starting from the first trimester. Seronegative women receive monthly follow-ups throughout their pregnancies.
Slovenia		X		
Switzerland	X			Suspected cases or women at high risk of infection are individually tested.
United Kingdom of England	X			
Türkiye			X	Women can choose to have testing done prior to pregnancy based on their own preference

This new microorganism was named "*Toxoplasma gondii*" by Nicolle because of the morphological characteristics of the parasite and the host being *Ctenodactylus gundi*. However, later comments were made that this nomenclature was not made correctly and that the correct name of the parasite should be "*Toxoplasma gundii*". It has been suggested that the basis of these critical comments was related to mistakenly naming the host of the parasite as "*Ctenodactylus gondi*" instead of "*Ctenodactylus gundi*" (51,52). In the same year, Splendore (78) discovered the same parasite in a rabbit in Brazil and mistakenly identified it as *Leishmania* but did not name it as a species (79). About 30 years later, it has been suggested that organisms similar to *T. gondii* were found in other hosts, particularly in some bird species. Sabin and Olitsky (80) investigated the cause of unexpected encephalomyelitis while conducting a study on viruses in mice. They showed that this encephalitis was not caused by a virus and that the main cause was *T. gondii*. In the following years, Sabin and Feldman (81) found that humoral antibodies killed extracellular tachyzoites but not intracellular tachyzoites. In the next 50 years, it has been determined that protective immunity is largely mediated by lymphoid cells. On the other hand, in the pyrophosphate homeostasis of *T. gondii*, pyrophosphate-dependent phosphofructokinase plays a crucial role in regulating pyrophosphate levels, ensuring a balanced metabolism between breaking down and building up molecules. This allows the parasite to effectively utilize carbon nutrients obtained from host cells, enhancing its ability to thrive as a parasite. Additionally, pyrophosphate-dependent phosphofructokinase is vital for the parasite's growth and virulence in living organisms, while being absent in human hosts, presenting an opportunity for targeted drug development to treat toxoplasmosis (82).

Three dominant archetypal clonal lineages of *T. gondii* have been identified to date (83-86). Various atypical genotypes have also been found in America and China (87-89). Although there is no dominant genotype in the southern hemisphere, some genotypes are dominant in the northern hemisphere, notably genotypes 1 (type II clonal), 2 (type III) and 3 (type II variant) that make up the majority of isolates in Europe. Genotype 2 and Genotype 5 (both Genotype 4 and Genotype 5 are known as Genotype 12) are common in North America. Genotype 2 is dominant in Africa with Genotype 3 outside of North America; Genotype 9 and Genotype 10 are quite common in China (89-91). Some genotypes have been associated with increased virulence in humans and wildlife (92-95). Lorenzi et al. (96) compared the genomes of 62 isolates of conserved large haploblocks with different ancestral origins worldwide that may affect the spread, host range and pathogenicity of *T. gondii*. Among the clonal lineages, Lineage 1 to Lineage 4 were found to be the most widespread with very similar multilocus genotypes, high levels of linkage disequilibrium, and sparse recombination features.

The first study about toxoplasmosis in animals in Turkey was carried out by Akçay and colleagues (97,98). Later, Ekmen and Altıntaş (99), isolated *T. gondii* from a new borne kid with hydrocephaly for the first time. Yucesan et al. (100) inoculated the isolated strain of *T. gondii* in albino mice. The whole genome of this *T. gondii* strain was studied for the first time and registered in the NCBI database as *T. gondii* TR01.

T. gondii can reproduce sexually only in definitive host felines (101). Unsporulated oocysts are released by cats and transformed into the infective form after sporogony under suitable conditions in nature. Infective *T. gondii* oocysts can infect all warm-blooded hosts following oral contamination. The parasite can reproduce through schizogony in the tissues of the infected host. In the case of asexual reproduction, tachyzoite and bradyzoite are formed from sporozoites. While bradyzoites form tissue cysts in the intermediate host, the tachyzoite form goes to the host's tissues such as the heart, lungs and central nervous system, causing intrauterine infections. It can be transferred to the tissues of the fetus by transplacental transmission (102,103). When final host cats eat infected tissues of an intermediate host, sexual reproduction begins in the life cycle of *T. gondii.* One of the ways that facilitates the completion of the life cycle is the unusual behavior of the infected host with toxoplasmosis. For example, infected rodents lose their instinctive fear of cats and are attracted to cat urine (104,105). Host manipulations associated with *T. gondii* infection have also been observed or hypothesized in other intermediate host taxa, including primates and birds (106).

Toxoplasmosis in Humans

In recent studies, it has been shown that the main way of the spread of *T. gondii* is the contamination of the ecosystem with oocysts. Some of the primary and critical factors that increase the risk of human and animal infection include consuming meat that is raw or undercooked and infected with pathogens, disposing of cat feces contaminated with oocysts into sewage systems which can spread the disease to water bodies, drinking water that contains oocysts, eating vegetables grown in soil that is contaminated, or coming into contact with anything else that is contaminated with oocysts. Other means of transmission include receiving blood or organ transplants, being infected via intrauterine or transplacental transmission, or drinking unpasteurized milk that has been infected with the pathogen (103,107-110). Toxoplasmosis is the second leading cause of death among foodborne diseases in the USA. In humans, the presence or absence of symptoms at the time of infection does not provide information about whether the disease will occur later in life. The disease can be seen in individuals of all ages and can show an acute or chronic course (111-114). *T. gondii* infection after birth can have an asymptomatic course or it can affect other organs including the eyes causing fever and lymphadenopathy (115-118). The virulence of the disease varies depending on the individual's genetic characteristics, susceptibility, and the strain of the parasite (119). For example, it has been suggested that *T. gondii* genotypes found in French Guiana cause significant damage and even death in adult humans who are not immunocompromised (94). Reports suggest higher virulence in South American *toxoplasma* strains compared to strains from Europe and North America, leading to more severe ocular toxoplasmosis and acquired toxoplasmosis cases (120). It has been reported that an estimated 1.1 million people in the USA are infected with *T. gondii* each year and approximately 10.4% of the population is exposed to the parasite (121,122). The infection may cross the placenta and reach the fetus if the mother is infected during pregnancy, and it can proliferate in fetal tissues (123). In a congenital toxoplasmosis case, the infection may also induce lesions in the eyes and brain of the fetus or systemic pathological findings such as premature birth, intrauterine growth retardation, fever, pneumonia, and thrombocytopenia (124,125). Ocular lesions or signs of encephalitis in the fetus may include chorioretinitis, meningoencephalitis, hydrocephalus, microcephaly, or calcifications of necrosed areas; infants usually do not show clinical signs at birth, but deafness may occur later in life. If exposure to infection in pregnant women occurs after the first 6 months of pregnancy, the rate of transmission of the infection to the fetus is considerably reduced. The diagnosis of congenital toxoplasmosis can be made by serological tests which are the commonly used methods. Although toxoplasmosis is a treatable disease and transplacental transmission can be prevented by Spiramycin treatment, prevention is the best solution to combat *T. gondii*. It is important to note that Spiramycin cannot reverse the damage if the parasite has already passed the placenta and/or infection has induced any damage to the fetus (123). Latent and primary toxoplasmosis, as well as diseases that can be treated with corticosteroids, cytotoxic drugs, and tumor necrosis factor alpha antibody, can be particularly dangerous for individuals with compromised immune systems (125,126). Encephalitis develops in approximately one-third of individuals infected with both *T. gondii* and HIV (127). Regulatory T-cells (Treg) are very important in the maternal immune mechanism in pregnant women and abnormal pregnancy outcomes are mainly associated with Treg dysfunction (128-130). In addition to the regulatory functions of Tregs, the effects of the transcriptional factor Foxp3, which has a critical role, and the role of proinflammatory cytokines such as Macrophage Migration Inhibitory Factor (MIF) are also essential. During *T. gondii* infection, the pathogen may invade the placental tissue and impair maternal-fetal immune tolerance. This immune-pathological issue can cause maternal immune rejection, affect fetal growth, and lead to miscarriage and/or other pregnancy complications (131). Adverse pregnancy outcomes are associated with reduced Treg cell counts by apoptosis triggered by *T. gondii* infection (132). However, different susceptibility to *T. gondii* infection may occur during the first and third trimesters of pregnancy due to variations in MIF regulation. Such sensitivities have an important role in the initiation of the inflammatory response that may result in abortion and the activation of immunologic patterns. MIF, which triggers the activation of extracellular signal regulated-kinase (ERK1/2) and prostaglandin E2 (PGE2) by participating in the immune response against *T. gondii*, is an effective cytokine in pregnancy. This cytokine plays a major role in the inflammatory response and defense against the pathogen. Therefore, death and abortion in a pregnancy infected with *T. gondii* occur as a result of the complete disruption of the maternal immune mechanism (130,132).

Retinal toxoplasmosis is considered to be the leading cause of blindness in many parts of the World (133,134). It has been reported that ocular toxoplasmosis develops in approximately 5,000 people per year in the USA (122). Exposure to *T. gondii* has been associated with mental decline and overall increased disease symptoms in the elderly (135). In addition, *T. gondii* is associated with many neuropsychiatric disorders including anxiety, suicide attempts, depression, and schizophrenia (109,136-139). Although the mechanisms defining these relationships are not known for certain, they may be related to the immune response to tissue cysts and the presence of bradyzoite tissue cysts in the brain post-infection (111). In one study, *T. gondii* oocyst-specific IgG antibodies were found in 193/490 (43%) pregnant women's serum samples whereas in another study positive cases were found in 30 out of 340 (8.8%) samples in pigs. Twenty-four (80%) of these *T. gondii* positive 30 samples also gave oocyst-derived IgG positivity. The results of these serological studies also confirmed that the infection started with the ingestion of *T. gondii* oocysts (140,141). Oocysts of *T. gondii* can also be found in drinking water sources such as both small-scale wells and larger water reservoirs as well as removing hairs of pet animals (dog hair) or machines used for shaving dogs, etc. It has been suggested that it can also contaminate the surfaces of equipment (142–145). For all these reasons, the high risk of spreading and transmission of oocysts should be considered and should never be neglected.

Toxoplasma gondii in Pets and Farm Animals

Despite its high prevalence worldwide, toxoplasmosis in domestic cats cannot be distinguished clinically or asymptomatically. Among the clinical symptoms fever, ocular inflammation, anorexia, lethargy, pneumonia, abdominal pain, and discomfort in the central nervous system could be observed (52,111). Although clinical *T. gondii* infection is severe in domestic cats, it has been suggested that wild cats are at higher risk of infection than domestic cats (146). Pet dogs can also be infected with *T. gondii*. However, subclinical infection in dogs is more common than clinical infection (147,148). Respiratory, neuromuscular or gastrointestinal systems are affected by the disease in infected dogs, and clinical signs and even death may occur (147). Although free-range dogs are believed to be at higher risk, pet dogs can acquire *T. gondii* parasites from infected meat that is given uncooked or raw (149).

Common intermediate hosts for toxoplasmosis are sheep, goats, pigs and chickens. Cattle and horses are particularly resistant to the disease. The primary effect of congenital infection in sheep is the loss of offspring due to premature birth or stillbirth. Lambs born alive but infected usually show normal growth. However, if the infected meat of these animals is consumed, there is a risk to public health (147).

Abortion, stillbirth, weak offspring, and nonspecific clinical signs such as fever, loss of appetite, and weight loss are observed in small ruminants, pigs, and occasionally other livestock. The incubation period of toxoplasmosis is usually a few days until nonspecific clinical signs appear, and it can take days or weeks until abortion or stillbirth occurs. Definitive hosts, such as cats, usually do not display clinical signs, except for rare cases of diarrhea. Toxoplasmosis can also be seen in adult goats, and it is more severe compared to sheep. In goats, the congenital infection also results in the loss of offspring before or after birth (150). During both acute and chronic infections, tachyzoites can be transmitted through milk, including goat milk, as well as sheep and cattle milk. Drinking unpasteurized goat's milk has been identified as a risk factor for human infection in epidemiological surveys (151,152). Pigs can become infected with *T. gondii* by ingestion of infective oocysts through water and food, by transplacental passage of tachyzoites, and by ingestion of infected meat with *T. gondii* bradyzoite tissue cysts. Although adult pigs infected with *T. gondii* rarely show clinical signs, the meat of these infected pigs is a potential source of infection for humans. Young pigs infected with *T. gondii* can die from toxoplasmosis before they can enter the food chain for humans. Toxoplasmosis positivity is largely due to contamination of the environment with oocysts of the parasite. Free-roaming domestic cats have been identified as the major risk factor in the infection of farm animals (150). As a result, livestock shelters and facilities, which lack adequate biosecurity, pest and pest management practices, do not implement regular screening and control programs, and whose environment is not restricted, constitute important risk factors for animal infection (53,110).

Toxoplasmosis has been classified as a notifiable disease in certain countries as part of their efforts to prevent and control its spread. The disease is present in all types of animals in countries such as Latvia, Poland, and Switzerland, and Finland. In Germany, only certain animals, including pigs, dogs, and cats, are required to be reported if they carry the disease. On the other hand, in Austria, Denmark, Sweden and Turkey, notification is not obligatory. It is necessary to make standard regulations in this regard and to make reporting mandatory in all countries (153) (Table 2).

Toxoplasma gondii in Wild Animals

The transmission route of *T. gondii* in wild animals can be counted as ingestion of infected felines or their organ/tissue remains, consumption of infected intermediate host, ingestion of sporulated oocysts directly from the contaminated environment or transplacental transmission of tachyzoites from infected female to offspring. Transmission of *T. gondii* to carnivores and omnivores such as polar bears (*Ursus maritimus*), grizzly bears (*Ursus arctos*) and black bears (*Ursus americanus*) may occur through environmental contamination, predation of infected hosts and consumption of their meat or direct ingestion of sporulated infective oocysts (154,155).

T. gondii positivity obtained in serological studies on herbivores was associated with the density of domestic cats (156). For example, seroprevalence of toxoplasmosis in white-tailed deer (*Odocoileus virginianus*) among other terrestrial, wild herbivores infected with *T. gondii* was reported as 49.5% in suburbs and 66.1% in urban areas. On the other hand, Hawaiian geese (*Branta sandvicensis*) have a seroprevalence of 21-48% as a result of exposure to oocysts (107). The sero-epidemiological data indicates a rise in the prevalence of *T. gondii* oocysts in the environment, particularly in the soil, which is believed to be linked to an increase in the number of domestic cats (157-159).

The geographic and taxonomic prevalence of infection in marine mammals is explained by the transport of oocysts from land to sea, primarily by rainwater and sewage waters (160-163). Infection of the endangered southern sea otter (*Enhydra lutris nereis*) with *T. gondii* is associated with the land-to-sea transport of infected domestic or wild cat feces (164-166). Unfortunately, this transmission route, which is completely contrary to the normal mechanism of the ecosystem, has also been confirmed for other marine mammals (166,167). Similar genotypes of *T. gondii* have been detected in tissues from sea otters, terrestrial wildlife animals such as lynx, mountain lions, wild canids, and wild domestic cats sharing the California coast (156,168,169).

Table 2. Mandatory reporting of toxoplasmosis in animals by country

Country	Mandatory reporting requirement
Letonia	Mandatory
Poland	Mandatory
Switzerland	Mandatory
Finland	Mandatory, except for rabbits and rodents.
Germany	Mandatory in pigs, dogs, and cats.
Austria	Not mandatory
Denmark	Not mandatory
Sweden	Not mandatory
Türkiye	Not mandatory

Shapiro et al. (165) showed that invisible polymers play a critical role in the transmission of *T. gondii* in food webs through particle aggregates and biofilms, also increase parasite retention in snails grazing on algae, and facilitate infection of sea otters. At land-to-sea coastal exposure, phocids, otariids, mustelids, and some threatened and endangered marine mammals are also affected (170-176). However, data on *T. gondii* positivity from cetacean deaths are limited compared to those obtained through autopsies of terrestrial animals.

Protection and Control Practices

Fecal samples of domestic cats should be periodically monitored for *T. gondii* oocyst positivity. It should also be ensured that these cats do not hunt mice and birds. Domestic cats should not be given uncooked meat or giblets (177). To ensure effective biosecurity measures during tasks such as changing cat litter at home, it is essential to wear gloves as a preventive measure against potential contamination. It is especially important for pregnant women or for those preparing for pregnancy to be more meticulous in this process (178). In any case, the litter used by the cat to defecate should be kept in a microwave oven at 75 °C so that possible *T. gondii* oocysts are destroyed. Then it should be disposed of following the medical waste category and procedure (179). The same control practices should be carried out with high precaution in shelters where cats are kept in groups in the municipality-responsible areas. Sand areas of children's playgrounds, where stray cats are likely to defecate should also be subjected to the same process periodically (53). It is believed that these disciplinary control practices will significantly reduce the contamination of the environment and ecosystem with *T. gondii* oocysts. If a cat is diagnosed positive for *T. gondii* oocyst either by microscopic examination of the stool sample or by advanced laboratory methods, it should be treated with Spiramycin. In addition, post-treatment status should be monitored. At this point, to protect and guarantee the integrity of Animal Health/Public Health/Ecosystem Health with a holistic perspective, diagnosis and treatment expenses of cats in the fight against *T. gondii* should be evaluated within the National Health Program and government subvention should be provided for necessary expenses. Effective management of *T. gondii* contamination within the ecosystem can be achieved through the collaborative, disciplined and diligent efforts of all parties involved in the control initiatives led by municipalities (180). This will ensure that the potential impact of *T. gondii* oocysts on the environment is minimized to a significant degree that ultimately resulting in herd health in animals, community health in humans (eliminating the disadvantage of *T. gondii* positivity in organ, bone marrow and blood transfusions) and ecosystem health (181). On the other hand, contact between animals, especially felines and rodents, must be prevented. Vaccination of livestock against *T. gondii* at a young age can be effective in preventing the formation of tissue cysts if they become infected later in life. This preventive measure can help reduce the risk of human exposure to *T. gondii* through the consumption of infected meat. At the same time, routine analyzes should be performed to monitor the presence of *T. gondii* in meat or meat products (182). In addition, meat and giblets type foods should be consumed after they have been sufficiently cooked. For this purpose, cooking or smoking at 72-74 °C or freezing at -20 °C will neutralize the bradyzoites in meat cysts. It is very important to wash hands thoroughly after touching raw meat and vegetables (183). Another factor that should be considered is that the cutting boards, containers and tools that the raw food comes into contact with should be washed with soapy water. The food given to cats must be cooked and only dry or canned foods are suggested. Water resources have also played a very important role in the transmission of *T. gondii*. Therefore, the mixing of water sources contaminated with infected cat feces into drinking water should be prevented and adequate and effective measures should be taken. Especially in rural areas, old and expired water tanks should be renewed and careful sanitation should be done at regular intervals (179). To prevent "water-borne *T. gondii* transmission," it is advisable to utilize control methods similar to those employed in the epidemiology and ecology of Tularemia. While working with the soil, it is necessary to use gloves and to wash hands with soap and water immediately after gardening to prevent any possibility of contamination of infected soil with cat feces (184). In this way, the potential risk of contamination can be prevented. Trespassing of cats in the warehouses where the food of butchery animals is stored and contamination of the food with cat feces should be prevented and feed storage areas should be protected following biosecurity rules. One of the important areas that can cause contamination is animal slaughterhouses. Utmost care should be taken to ensure that the giblets of animals slaughtered in slaughterhouses and infected with *T. gondii* are not thrown into the environment or given to animals uncontrollably after slaughter. Organs and tissues that cannot be consumed as a result of slaughter in slaughterhouses should be destroyed by cremation. In this way, a possible slaughterhouse toxoplasmosis contamination is prevented.

Vaccination and New Treatment Options

In the fight against Toxoplasmosis, it is very important to obtain strong immunity through vaccination. Developing a vaccine that can be used in final or intermediate host animals and providing immunization with vaccination will also constitute one of the most effective solutions for protection and control against toxoplasmosis. Currently, a vaccine containing tachyzoites of *T. gondii* S48 strain has been developed to prevent abortions caused by toxoplasmosis in sheep and goats. It has been reported that this vaccine, which can be found in Europe and New Zealand, reduces fetal damage but does not prevent fetal infections, and sheep vaccinated with S48 strain can remain immune for at least 18 months (182). This live vaccine poses a risk to pregnant animals. Therefore, it is recommended to apply at least 3 weeks before mating. Pregnant sheep should not be vaccinated. Breeding lambs are vaccinated with the basic vaccine when they are 4-5 months old. It should be noted that the basic vaccine should be administered as a single dose at least 4 weeks before mating. It is recommended that the vaccine booster be administered after 2 years, at least 3 weeks before mating (185). It has also been reported that immunity against *T. gondii* is formed in mice and rats immunized using *T. gondii* recombinant tachyzoite antigens and plasmid DNA encoding tachyzoite antigens (186,187).

There is currently no preventive vaccination program against toxoplasmosis in Türkiye. The Parasitology Department at Erciyes University's Faculty of Veterinary Medicine is conducting a research project on the development of an exosome-based vaccine candidate for toxoplasmosis. The vaccine is produced using tachyzoites grown in BeWo cell cultures, which are derived from human placenta choriocarcinoma. The study has yielded promising preliminary outcomes (188). In addition to these developments, it is considered that new methods and new options can be produced in the treatment of toxoplasmosis in light of the information produced by molecular techniques. In this context, in a study conducted at Erciyes University Faculty of Medicine, Department of Parasitology, it was proven that "Nitroflurane inhibits *T. gondii* infection by affecting genes in the Toll-Like Receptor pathway". With this new treatment option, the possibility of developing new preparations with fewer side effects as an alternative method in the treatment of the disease has been considered a promising development (189). In light of these studies, the possibility of producing an effective vaccine and/or vaccine candidates, drug and/or drug candidates for the future in the fight against toxoplasmosis raises hope.

Planning One Health Intervention

One Health approach focuses on interdisciplinary collaborations to solve problems related to animal, human, environmental, and plant health (190). According to One Health concept, effective monitoring of the prevalence of *T. gondii* has great importance. In the USA, toxoplasmosis is not a nationally notifiable disease. Therefore, its exact prevalence is not known (64,65,191). For the same reason, although the prevalence of toxoplasmosis is very high in other countries such as Brazil, the incidence of congenital disease in children can only be put forward hypothetically (192). Toxoplasmosis screening in pregnant women and newborns is available in the US. However, these congenital toxoplasmosis screening programs lag behind regular screenings in many countries (74). In addition, screening programs for congenital toxoplasmosis alone may miss a large part of the infected population. Therefore, it is important to apply "Advanced Integrated Toxoplasmosis Screening Programs" in the fight against this disease. Advanced Toxoplasmosis Screening Programs will generate more data in reducing risks and developing more sensitive tools. Integrating human, pet and wildlife data allows for better assessment of risk and better control methods. On the other hand, regional and global interaction can further facilitate the local, regional and global spread of pathogens by affecting endangered animal populations. Human-induced environmental changes, travel, globalization and trade may facilitate the spread of *T. gondii* in human populations, as well as other zoonotic animal parasites. Given that majority of human infectious diseases are of animal origin (zoonotic), it is clear that there is a need to integrate human-animal-ecosystem health within a common framework. This holistic approach has essentially emerged as a basic necessity. Increasing global problems, including environmental change, loss of biodiversity, fragmentation of habitat and the emergence of infectious diseases, and the convergence of the global great danger day by day, require integrative approaches that go beyond the disciplinary boundaries of the "One Health" concept. In this integration, it is suggested that not only governmental institutions, universities and other institutions take part, but also new tasks should be given to them in the creation of new international organizations (177,193,194).

Interdisciplinary Collaborations

Simple solutions are rarely seen in addressing regional or global ecological and environmental problems. A versatile, interdisciplinary "One Health" approach is required in the ecology of infectious diseases. The "One Health" approach can also be applied against Toxoplasmosis as it has been applied during wildlife parasitic zoonosis surveillance in Australia (195) and/or studies of *Echinococcus spp* in North America (196), and Sri Lanka (197). "One Health" approach was also implemented against some foodborne parasitic diseases caused by *Cryptosporidium* spp., *Giardia duodenalis*, *Cyclospora cayetanensis* and *T. gondii* in other developed countries (195).

In the last 10 years, new tools and institutional initiatives have been developed to evaluate and monitor emerging pathogens. In this context, knowledge of ecosystems existing in nature, epidemiology of diseases, ecological modeling of disease and web-based analytics have emerged. New types of integrated ecological health assessment are implemented; these include certain biomedical diagnostic tools and environmental indicator studies. Other innovations include the development of non-invasive physiological and behavioral monitoring techniques for the conditions of low-income countries, the adaptation of modern molecular biological and biomedical techniques, the design of population-level disease monitoring strategies, and the creation of ecosystem-based health and preventive species surveillance approaches (198).

Mathematical modeling, predictive tools, and new prevention strategies for emerging infectious diseases have evolved tremendously over the past decade. These exciting tools now enable advanced detection and diagnosis of diseases and disease symptoms (153,177,199)

A data-based decision-support tool should be created to help physicians, experts, and managers for action and intervention. Veterinarians, Physicians, Epidemiologists, geographic modelers, public health officials, and sociobiologists must collectively choose the right model to implement a rigorous approach to etiological agents in disease epidemiology (198).

It is known that *T. gondii* is affected by environmental conditions and measures to reduce exposure also positively affect ecosystem health. The environmental parameters responsible for the long-term survival and resistance of the parasite in the oocyst form, or the survival as well as the infectivity of tissue cysts from an infected animal that has died in the wild, are not fully understood. The "One Health" approach is also critical to filling such knowledge gaps. For this purpose, joint studies of professionals from a wide range of disciplines have been proposed (200).

Integrative Studies

In addition to the occurrence of acute infection, congenital infection and some other important negative health problems due to toxoplasmosis in humans, it has been suggested that there is a close relationship between the increased number of fatal traffic accidents and *T. gondii* positivity in recent years (201,202). In the epidemiology of toxoplasmosis, several investigations including surveys are needed to assess risk and to integrate data by developing control methods. Environmental contamination rather than meat consumption has been shown to be a more common and important route for infection epidemiologically (81,149,147,150). Therefore, to understand the risk of transmission, land use and outdoor cat management policies need to be expanded, developed and modeled. At this point, the relations between the Animal Shelter Policies of local governments and the increase in the number of stray cats and the resulting oocyst loads should be considered as basic issues and solutions should be developed in this regard. For this purpose, research can be done with integrative project studies. For example, platforms can be created where interdisciplinary teams can perform field and laboratory studies, spatial, geographical and other mathematical modeling, and integrated applications of veterinary medicine and human medicine. Considering that 1/3 of the world's population is *T. gondii* positive, legislation and/or regulatory arrangements for risk reduction and increasing demands for food safety require rapid diagnosis of *T. gondii* infections. For this purpose, it has been emphasized that there is an urgent need for the development and standardization of safe diagnostic tests with rapid results (203). Such tests need to be previously performed with comparable specificity and sensitivity experiments in a range of animal species to provide an accurate estimate of the risks of transmission of toxoplasmosis to humans. Most farm animals naturally infected with *T. gondii* (with the exception of suspected beef) have been shown to carry bradyzoites in their meat (204). Chopped or minced meat can be contaminated by mixing other types of meat during these processes. Thus, the epidemiological link between raw beef consumption and outbreaks of *T. gondii* infection can be explained by such process contamination (64). The relationship between raw meat consumption and toxoplasmosis has been reported in Korea, the USA, France, French Guiana, and New Zealand (203). In these countries, effective screening processes are applied to meat offered to consumers, along with new standard tests that may be useful for the control of *T. gondii* positivity. Especially at the point of monitoring and control of the disease, it is necessary to carry out such practices effectively throughout the world (205).

Conclusion

The "One Health" concept, which started with the widespread use of fire in the history of modern humans, has reached its current level as a result of its continuous development. Today, the level of "One Health" concept has evolved to the level of "Safe Food", which is produced with the principle of the "Functional Animal Product Production" process, especially based on "Healthy Food" and defined with the characteristics of "Functional Food", personalized and compatible with the immune mechanism of the person. On this basis, the "One Health" concept emphasized the necessity of establishing a solid and absolute organic bridge between disciplines connecting human health, animal health and ecosystem health. In this context, the fight against toxoplasmosis requires integrative approaches that transcend the boundaries of disciplines. This integration is for managing and controlling disease and creating new approaches. Identifying the complexity of Toxoplasmosis prevention and management requires the development of a quick and easy reference control panel system, a combination of health and ecological markers. Interdisciplinary, integrative research and capacity building are key elements in the creation of "One Health" interventions for toxoplasmosis. Innovative methodologies that make information flow between stakeholders feasible must address this major challenge facing society, wildlife and ecosystems globally in a consensus and sustainable manner (177). The "One Health" approach to the epidemiology and control of toxoplasmosis requires practical, sustainable and effective solutions with a precise understanding of local socioeconomic and cultural factors, as well as a solid understanding of local, regional, national and international health and environmental policies. The "One Health" approach offers great opportunities for professionals who practice "Environmental Health - Animal Health - Human Health" holism to provide "Concurrent Benefits". Ultimately for the health of both terrestrial and ocean ecosystems regarding toxoplasmosis, the first step is eliminating the feces of infected cats using appropriate techniques. Secondly, regular monitoring and treatment of *T. gondii* positivity in cats is a necessity. Additionally, contact with contaminated food and materials should be avoided. Advances in modern treatment and vaccine options should be continued. Mandatory monitoring or screening for *T. gondii* positivity in humans during pregnancy is essential, particularly the implementation of the French model for human disease monitoring may provide positive outcomes.

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