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INTERNATIONAL JOURNAL OF Agricultural Science and Food Technology

Mini Review

Impact of Toxoplasmosis on domestic animal production and its significance in the risk of human infection in China

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Received: 17 October, 2022 Accepted: 26 October, 2022 Published: 27 October, 2022

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Introduction

Toxoplasma gondii is a ubiquitous zoonotic food-borne parasite [1]. Nearly one-third of the world's population has been exposed to the parasite, with prevalence ranging from ~10% to 50% depending on the geographical area. Human infection is usually asymptomatic in immunocompetent individuals and may remain for life, but in immunocompromised persons, the infection might be fatal [2]. Parasites may result in serious consequences for pregnant women. Primary infection during pregnancy can lead to spontaneous abortion, fetal death, stillbirth, and congenitally infected offspring. Infants with preexisting infections may be born with neurological disorders such as mental retardation, deafness, and/or eye lesions [3].

Three stages in the life cycle of T.gondii may invade humans and animals. They are tachyzoites (present as clusters or clones in acute infections), bradyzoites (in the form of chronic infections that arise from tissue cysts), and sporozoites (produced during sexual reproduction in the form of oocysts) [4]. Tachyzoites, duplicating asexually, are crescent-shaped and enter the cell by active penetration of the cytoplasmic membrane or phagocytosis by host cells, then change shape to become oval and are surrounded by the parasite vacuolar membrane (PV) from the host cells, thereby protecting them

from host immunity [5], constituting the mechanism of immune evasion of the parasite. Bradyzoites proliferate slowly in tissue cysts, which are more common in nerve and muscle tissues. Intact tissue cysts may accompany the host for a long term and may not cause prominent harm to the host. Felids shed their oocysts after ingesting the parasite at any stage of infection [6]. The tissue cysts subsequently release bradyzoites, which can penetrate the small intestinal epithelium and cause massive reproduction [7].

It has been known that almost all warm-blooded vertebrates act as the intermediate hosts of T.gondii [8]. Humans get the infection through ingestion of bradyzoites present in undercooked meat, raw milk, or oocysts present in foods or water sources contaminated with feces of domestic cats, or even in marine mollusks due to the accumulation of oocysts when soil contaminated with T.gondii flows into the ocean [9-11].

Infection of livestock and poultry products due to contamination with Toxoplasma cysts

T.gondii presents a major challenge to the livestock industry as it is responsible for the stillbirths, miscarriages, postnatal mortality and fetal malformations of farm animals. Toxoplasma infection in domestic animals is common in China. Several

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Citation: Wang R, Wu M, Wang P, Shen J, Du J (2022) Impact of Toxoplasmosis on domestic animal production and its significance in the risk of human infection in China. Int J Agric Sc Food Technol 8(4): 273-276. DOI: https://dx.doi.org/10.17352/2455-815X.000177

outbreaks of toxoplasmosis were reported on a pig farm in Shandong province years ago. These outbreaks of deadly toxoplasmosis were presumed to be linked to the misuse of feeds contaminated with cat fecal oocysts [9]. Research has shown that pigs raised on indoor farms have a lower risk of Toxoplasma infection compared to outdoor farms (Table 1) [12]. Toxoplasmosis in sheep has the greatest impact on humans [13] since people prefer to eat half-cooked lamb in some minorities of China [14]. Toxoplasmosis is also a major cause of abortions in goats and sheep in the early stages of development being infected with T. gondii, leading to miscarriages [15]. Children in rural areas prefer to drink raw goat milk, which is thought to be more digestible than cow's milk. Goat milk contaminated with Toxoplasma can be detrimental to the health of children [16]. Rabbits are also a source of Toxoplasma infection in humans [17]. Humans can be affected not only by consuming undercooked rabbit meat but by slaughtering and processing undercooked or raw rabbit meat and by being contaminated with oocysts in the hands and mouth.

For the poultry, *T.gondii* was detected in brain samples from 588 domestic ducks from the Hunan province of the south of China in 2019. The prevalence of *Toxoplasma* infection was 7.7% (45/588), which was much higher than that of wild ducks in the Czech Republic [18]. It has been estimated that China produced and consumed 9 444 400 tons of ducks in 2019, accounting for 70% of the global totality. The best-selling duck products in China, it has triggered the consideration of duck meat products for human health [18]. In the soil contamination survey, *T.gondii* oocysts were detected in the soil of free-range farms, and the rate of serological positivity of chicken for *T.gondii* was higher in free-range farms compared to regular farms (Tables 2,3) [19]. Traditionally, free-range chickens are thought to be more nutritious and have better taste, but they are more likely to get exposure to *Toxoplasma* from contaminated soil [20].

Toxoplasmosis in domestic animals not only causes huge economic losses but is responsible for posing a threat to public health. According to the national wide investigation in China, the seropositive rate of Toxoplasma infection in the general population is about 7%, which is lower than that in other parts of the world. A population investigation showed that serum antibodies against T.gondii were detectable in 2.6% of women and 25% of pregnant women in Thailand [21]. In Central America, South America, and continental Europe, the estimated range of people infected with toxoplasmosis is 30 to 90% [22]. The highest rate of Toxoplasma infection occurs in Brazil and other South American countries. Generally, the serum-positive rate in Europe and North America, and Africa as well, is higher than that in Asia. The seroprevalence of Toxoplasma infection in cats previously reported in Asian countries also varies, with the highest in Vietnam (Table 4) [21]. Eating habits, consuming not-well-cooked meats, for instance, might be responsible for the difference in susceptibility to T.gondii infection. Thus, due to the large population at risk, healthy and reasonable feeding and processing of foodborne animals and pet breeding are of great significance.

There are existing surveillance procedures for pregnancy and congenital toxoplasmosis. The primary prevention

Table 1: Effect of farm type on *Toxoplasma* infection of slaughter pigs in the Netherlands.

Type of pig farm	Total pigs (n)	Seropositive pigs (n)	Positive rates (%)
Free-range(outdoor)	635	30	4.7
Conventional(indoor)	621	0	0

Table 2: Contamination of T. gondii in the soil collected from different farms in China

Type of farms	No. of samples examined (n)	Positive (n)	Positive rate (%)
Free-range farms(outdoor)	350	7	2
Scale farms (indoor)	350	0	0

Table 3: Detection of T. gondii in chickens in China.

Type of chicken sources	Total chickens (n)	Seropositive chickens (n)	Positive rate (%)
Farms with Toxoplasma positive in soil	250	194	77.6
Farms with Toxoplasma negative in soil	100	41	41

Table 4: Seroprevalence of Toxoplasma infection in cats reported in Asian countries.

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Prevalence (%)	Method	Reference
25.2	ELISA	[23]
21.3	MAT	[24]
59.4	IH	[25]
35.3	MAT	[26]
6.0	LAT	[27]
5.4	LAT	[28]
15.3	ELISA	[29]
15.8	ELISA	[30]
2.2	ELISA	[31]
14.5	IFAT	[32]
41.3	ELISA	[33]
60.0	LAT	[34]
62.8	ELISA	[35]
30.7	ELISA	[36]
6.5	IFAT	[21]
72.3	LAT	[37]
	Prevalence (%) 25.2 21.3 59.4 35.3 6.0 5.4 15.3 15.8 2.2 14.5 41.3 60.0 62.8 30.7 6.5	25.2 ELISA 21.3 MAT 59.4 IH 35.3 MAT 6.0 LAT 5.4 LAT 15.3 ELISA 15.3 ELISA 15.8 ELISA 14.5 IFAT 41.3 ELISA 60.0 LAT 63.0 ELISA 64.1 IFAT 65.1 IFAT

ELISA : Enzyme-Linked Immunosorbent Assay; IFAT : Indirect Fluorescence Antibody Test; IH: Indirect Hemagglutination; LAT: Latex Agglutination Test; MAT: Modified Latex Agglutination Test

measures have reduced the risk of exposure to the parasite through popular education of the women before gestation for *Toxoplasma* infection. Secondary prevention includes serological screening for *Toxoplasma* infection before and during pregnancy and the measure has been routinely taken in China for decades although it is not compulsory. More important measures for control of the disease include proper husbandry of livestock and appropriate processing of meat ware before marketing. Final preventive measures are accurate diagnosis and treatment of children with congenital toxoplasmosis [38]. This strategy has been implemented in various ways among countries. France uses a maternal screening program, while Denmark and Poland use a strategy based on newborn screening. In 2006, in the city of Londrina, Paraná (PR), the

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Acquired and Congenital *Toxoplasma* Surveillance Program, based on serological screening during prenatal care, primary prevention measures, and early diagnosis and treatment of pregnant women and children, is into effect [39]. Till now no vaccines are available for practical use in domestic animals and humans although the attenuated live tachyzoites Toxovax[™] (S48) have been successfully developed and used in sheep and goats for the prevention of reproductive failure [40]. Recombinant vaccines, including DNA and parasite-derived molecules such as SAGs, ROPs, GRAs, and MICs are under investigation in the laboratory [41,42].

Treatment for T. gondii and resistance mechanisms

The lack of a convenient method for detecting intracellular T.gondii reagents and the lack of understanding of the metabolic and biological characteristics of the parasite have kept the drug treatment of toxoplasmosis from being groundbreaking. There are several standardized treatment protocols available today for different populations. In pregnant women, if acute infection is suspected and maternal infection is confirmed but the fetus is not yet infected, spiramycin should be offered for fetal prophylaxis [43]. Spiramycin has been widely used in the treatment of acute Toxoplasma infection acquired during pregnancy due to its low toxicity and inability to cross the placenta. Congenital toxoplasmosis can be treated with a combination of ethacridine, sulfadiazine, and calcium folinic acid [44]. Sulfamethoxazole Sulfadoxine-pyrimethamine and ethamethoxine are Toxoplasma antagonists of folic acid, inhibiting the proliferation of the parasite. They mainly inhabit the tachyzoite stage of T. gondii.

Conclusion

Toxoplasma gondii can cause diseases in domesticated animals leading to losses in the farming industry and also is a source of infection in humans. Therefore, scientific and rational improvement in animal feeding management, meat inspection and quarantine, food processing, and cooking can significantly reduce the infection of animals. This mini-review focuses on the effects of toxoplasmosis on livestock and poultry, leading to enlightenment on the control of toxoplasmosis in humans. Preventive measures for toxoplasmosis are involved in all aspects of the life cycle of T.gondii, such as cleaning the cat litter and properly handling cat faeces to disinfect the source of oocysts and minimize contamination of fields. Pregnant women should be especially careful to stay away from pet cats with Toxoplasma infections. The meat products for consumption should be deep-frozen before they hit shelves and thoroughly cooked. Fruits and vegetables need to be completely washed with clean water.

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