



# Knowledge gaps in host–parasite interaction preclude accurate assessment of meat-borne exposure to *Toxoplasma gondii*



M. Crotta<sup>a,\*</sup>, G. Limon<sup>a</sup>, DP. Blake<sup>b</sup>, J. Guitian<sup>a</sup>

<sup>a</sup> Veterinary Epidemiology, Economics and Public Health Group, The Royal Veterinary College, Hawkshead Lane, North Mymms, AL9 7TA Hatfield, UK

<sup>b</sup> Pathology and Pathogen Biology, The Royal Veterinary College, Hawkshead Lane, North Mymms, AL9 7TA Hatfield, UK

## ARTICLE INFO

### Article history:

Received 19 July 2016

Received in revised form 15 November 2016

Accepted 17 December 2016

Available online 20 December 2016

### Keywords:

*Toxoplasma gondii*

Quantitative risk assessment

Probabilistic assessment

Food safety

Zoonotic disease

Meat, foodborne disease

## ABSTRACT

*Toxoplasma gondii* is recognized as a widely prevalent zoonotic parasite worldwide. Although several studies clearly identified meat products as an important source of *T. gondii* infections in humans, quantitative understanding of the risk posed to humans through the food chain is surprisingly scant. While probabilistic risk assessments for pathogens such as *Campylobacter jejuni*, *Listeria monocytogenes* or *Escherichia coli* have been well established, attempts to quantify the probability of human exposure to *T. gondii* through consumption of food products of animal origin are at early stages. The biological complexity of the life cycle of *T. gondii* and limited understanding of several fundamental aspects of the host/parasite interaction, require the adoption of numerous critical assumptions and significant simplifications. In this study, we present a hypothetical quantitative model for the assessment of human exposure to *T. gondii* through meat products. The model has been conceptualized to capture the dynamics leading to the presence of parasite in meat and, for illustrative purposes, used to estimate the probability of at least one viable cyst occurring in 100 g of fresh pork meat in England. Available data, including the results of a serological survey in pigs raised in England were used as a starting point to implement a probabilistic model and assess the fate of the parasite along the food chain. Uncertainty distributions were included to describe and account for the lack of knowledge where necessary. To quantify the impact of the key model inputs, sensitivity and scenario analyses were performed. The overall probability of 100 g of a hypothetical edible tissue containing at least 1 cyst was 5.54%. Sensitivity analysis indicated that the variables exerting the greater effect on the output mean were the number of cysts and number of bradyzoites per cyst. Under the best and the worst scenarios, the probability of a single portion of fresh pork meat containing at least 1 viable cyst resulted 1.14% and 9.97% indicating that the uncertainty and lack of data surrounding key input parameters of the model preclude accurate estimation of *T. gondii* exposure through consumption of meat products. The hypothetical model conceptualized here is coherent with current knowledge of the biology of the parasite. Simulation outputs clearly identify the key gaps in our knowledge of the host–parasite interaction that, when filled, will support quantitative assessments and much needed accurate estimates of the risk of human exposure.

© 2017 Elsevier B.V. All rights reserved.

## 1. Introduction

Toxoplasmosis is a worldwide distributed zoonotic disease caused by the protozoan parasite *Toxoplasma gondii*. The life cycle of *T. gondii* includes felines as the definitive host and mammals and birds as the most common intermediate hosts. Oocysts produced in the definitive host are excreted in faeces and sporulate in the environment, before being ingested by an intermediate or another definitive host. Following ingestion, sporozoites are released from the oocyst, developing into tachyzoites in an intermediate host and primarily targeting muscle or neural tissues where the parasite develops into a tissue cyst, the site of bradyzoite replication (Dubey, 1998). The number of bradyzoites

within a tissue cyst varies depending on the age and size of the cyst (Dubey et al., 1998). Except in instances of congenital or sexual transmission, blood transfusion or organ transplantation (Guerina et al., 1994), *T. gondii* is not passed from person to person. The ingestion of raw or undercooked meat containing viable cysts has been suggested to be one of the major sources of infection in Europe and North America (Guo et al., 2015a; Hoffmann et al., 2007; Scallan et al., 2011), very recently, the results of a case-control study in UK suggest an association between beef and toxoplasmosis, especially when the beef is cooked rare or medium rare (Said et al., 2017). In the United States, the US Centre for Disease Control and Prevention (CDC) has included toxoplasmosis in a group of five parasitic diseases (together with Chagas disease, cysticercosis, toxocariasis and trichomoniasis) that are considered public health priorities (CDC, 2016). At the global level, *T. gondii* was ranked in fourth position in a multicriteria-based risk

\* Corresponding author.

E-mail address: [mcrotta4@rvc.ac.uk](mailto:mcrotta4@rvc.ac.uk) (M. Crotta).

ranking of foodborne parasites compiled by the Food and Agriculture Organization (FAO)/World Health Organization (WHO) in 2014 (WHO/FAO, 2014). However, the ranking is the results of expert meetings and it should be considered as an overall “picture” that is representative of the information available at time, the criteria used for ranking and the weighting that were assigned to those criteria. Recently, a report published by the WHO on the global burden of foodborne diseases (WHO, 2015), ranked *T. gondii* in sixth position among 31 food-borne hazards with respect to the relative contribution of years of life lost due to premature mortality (YLL). Concern in relation to foodborne *T. gondii* infection has led agencies such as the UK Food Standards Agency (FSA) and the European Food Safety Authority (EFSA) to conduct consultations and issue scientific opinions on key aspects of the parasite-host interaction (FSA, 2012; Opsteegh et al., 2016). Information gained can be used to quantitatively estimate the probability of human exposure and/or infection through food consumption.

Increasingly, quantitative microbial risk assessment (QMRA) models that provide estimates of risk to human health (typically expressed as probability of infection and/or exposure) are used to support decisions on the management of food safety issues. The application of QMRA has improved the transparency and scientific basis of many regulatory decisions, including scenarios involving established or emerging foodborne pathogens (FAO/WHO, 1995). To date, four risk assessments of *T. gondii* exposure/infection have been published, two qualitative assessments (Guo et al., 2015a; Mie et al., 2008) and two QMRA (Guo et al., 2016; Opsteegh et al., 2011). In the first QMRA (Opsteegh et al., 2011), which aimed at exploring and quantifying the relative contribution of sheep, beef and pork meat products to *T. gondii* infections in humans, the biological complexity of the system combined with some uncertainties and incomplete evidence resulted in an estimate reliant upon a number of implicit and critical assumptions. In particular, the model assumed that the level of *T. gondii* contamination ( $\log_{10}$ -transformed bradyzoite/g) detected in sheep hearts by MC-PCR was the same as the level of contamination in sheep, beef and pig meat and that bradyzoites were homogeneously distributed throughout the meat of infected animals (as opposed to clustered into discrete tissue cysts). This QMRA also assumed that the overall probability of a meat portion being infected was the same as the proportion of animals with detectable antibodies (for pork and sheep products) or the proportion found positive by PCR (for beef). The infective dose for humans in this model was assumed to be the same as for mice. In the second study (Guo et al., 2016), *T. gondii* bradyzoite concentration in lamb muscle tissue was described based on a real-time PCR study of limb muscles from experimentally infected goats. As highlighted by the authors, bradyzoite concentration in muscle tissue from a naturally infected lamb might not be the same as that from experimentally infected goats. Although that model included a number of important improvements such as the inclusion of a formal human-derived dose-response model and detailed modeling of the steps along the food chain, the assumption of homogeneous dispersion of bradyzoites in meat was made by necessity. Recent experimental studies and epidemiological investigations have begun to fill some of these knowledge gaps, providing evidence on the relationship between the results of serological tests and presence of the parasite in meat in different meat-producing species, predilection tissues and the frequency of exposure in livestock animals across EU countries (Deng et al., 2016; Hosein et al., 2016; Opsteegh et al., 2016). Nonetheless, many key knowledge gaps surrounding assumptions highlighted in the previous QMRAs remain, continuing to undermine effective QMRA and limiting practical value for policy makers. In response, the development of a well-structured hypothetical model aimed at capturing the relevant biological parameters and defining the remaining knowledge gaps is now timely since the model can be used as the foundation for a formal QMRA as data for key parameters currently unknown become available. In the meantime, the relevance of the inputs involved and the impact of the uncertainty (i.e. lack of data/evidence) that characterizes some of them can be explicitly quantified by sensitivity analysis, with

the subsequent possibility of ranking those inputs by their effect on the output. Therefore, while purely hypothetical, this process does allow decision makers and researchers to prioritize further research.

Following these considerations, the objectives of the present work were to: (i) conceptualize and develop a hypothetical model to estimate the probability of human exposure to at least one viable cyst of *T. gondii* in a 100 g portion of pig meat, and (ii) parameterize the model with the latest evidence generated by experimental and epidemiological research and quantify the effects of remaining data gaps on the final estimate.

To this end, a probabilistic model for the assessment of human exposure to *T. gondii* from fresh pig meat was developed drawing upon recent data and evidence collected in England (Limon et al., in press).

## 2. Material and methods

The flowchart in Fig. 1 illustrates the steps and biological dynamics of the system that were reproduced in the stochastic model for the assessment of human exposure to *T. gondii* through a 100 g portion of pig meat. Briefly, the model has been structured in four main steps. The first and the second steps aim at estimating the proportion of pigs destined for human consumption that are seropositive to *T. gondii* (step 1) and the proportion of seropositive and seronegative animals being infected with viable cysts (step 2). The model continues with the estimation, in animals carrying viable cysts, of the number of viable cysts in 100 g of *T. gondii* election tissue (step 3). In the final step (step 4), the expected number of viable cysts in 100 g of meat is inferred from the number in 100 g of election tissue by using a ratio coefficient ( $\gamma$ ) expressing the number of cysts in the edible tissue of interest  $i$  as a function of the number of cysts in the predilection tissue.

### 2.1. Step 1. Seroprevalence of *T. gondii* in pigs

The outcome of this step is an estimate of the proportion of seropositive animals or seroprevalence ( $P_{SERA}^+$ ) in the target population given the number of animals tested as part of a survey ( $n$ ) and the number of animals found seropositive ( $s$ ).

For the illustrative purpose of this model, the seroprevalence of *T. gondii* infection in pigs in England was estimated based upon the serological results of a cross-sectional study conducted between January and July 2015 (Limon et al., in press). In that study, a total of 2071 pigs ( $n$ ) were sampled and tested for antibodies (IgG) specific for *T. gondii*. The modified agglutination test (MAT) was used and animals were considered seropositive when above the cut-off titre of 1:10. A total of 155 samples ( $s$ ) were found to be positive. The beta distribution:  $Beta(s + 1, n - s + 1)$  was used to describe the uncertainty in the proportion of seropositive pigs when estimated on the basis of the total number of animals tested ( $n$ ) and the total number of them found positive ( $s$ ).

### 2.2. Step 2. Proportion of animals with viable cysts

The purpose of this second step was to estimate the proportion of pigs carrying viable cysts among those found seropositive and seronegative in the previous step. Although in pigs the presence of detectable antibodies is known to correlate with the physical presence of the parasite in animal tissues, the correlation is not perfect (Opsteegh et al., 2016). For the purpose of a quantitative exposure assessment, it is important to discriminate the presence of viable and non-viable organisms. For this reason, in this step the probability of an animal being infected with viable cysts ( $PV_{cyst}$ ) is calculated. To this end, the results reported by Opsteegh et al. (2016) summarizing the overall percentage of detection of *T. gondii* in seropositive and seronegative animals were used. The 95% confidence intervals calculated for the percentages of detection in seropositive and seronegative pigs were used to parameterize the distributions describing the uncertainty in the conditional

Download English Version:

<https://daneshyari.com/en/article/5740582>

Download Persian Version:

<https://daneshyari.com/article/5740582>

[Daneshyari.com](https://daneshyari.com)