

**Post-consultation DRAFT**

**ADVISORY COMMITTEE ON THE  
MICROBIOLOGICAL SAFETY OF FOOD**

***AD HOC* GROUP ON VULNERABLE GROUPS**

**Risk profile in relation to toxoplasma in the food chain**

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## Summary

1. In this report the *Ad Hoc* Group has reviewed the evidence on toxoplasmosis in humans and animals in the UK to produce a risk profile for toxoplasma in the food chain. This follows a request from the FSA to consider whether current evidence indicates a food safety issue that needs to be addressed, which food sources are most likely to present a significant risk and what further investigations may be necessary to obtain robust data on UK prevalence and foodborne sources of toxoplasmosis.

2. In December 2006 and March 2007 the FSA sought the views of the ACMSF on the significance of toxoplasmosis in the UK. The issue was referred to the *Ad Hoc* Group on Vulnerable Groups who met in December 2008 to begin their considerations on toxoplasma in the food chain. The Group met seven times over a period of 28 months.

3. The Group used as a starting point for their report a review of the current situation on toxoplasmosis in the UK completed for the FSA by Dr Judith Hilton. The Group also considered information on the prevalence of toxoplasmosis in humans, estimates of the burden of disease in the UK and other countries, seroprevalence data in farmed and non-farmed animals and studies on the presence and survival of toxoplasma in foods. In order to review the relative importance of different sources they considered published information from outbreak reports and case control studies and the group also reviewed the consumer advice given by different countries in relation to reducing the risk of becoming infected with toxoplasma.

4. Key conclusions and recommendation arising from the work of the group were:

- Although the majority of cases of toxoplasmosis will occur in the immunocompetent, the largest burden of disease is likely to be associated with infection of immunocompromised individuals among whom symptoms are more severe and potentially life-threatening. Accurate figures are not available but it is estimated that 350,000 people become infected with toxoplasma each year in the UK, of which 10-20% are symptomatic. Whilst the lack of accurate data for overall incidence and severity of symptoms is a barrier to achieving accurate estimates of the burden of disease and economic impact in the UK, it seems reasonable to proceed on the basis of assessments made in the USA and Netherlands that the costs of the relatively small proportion of cases with severe disease make toxoplasmosis one of the most costly of gastro-intestinal infections. This would justify further work to assess the importance of the foodborne route of infection, to identify the most important risks and appropriate risk management measures, and to refine the burden of disease assessment. As healthy individuals may go on to become immune-compromised later in life it is also important to consider the potential burden of latent infection of the immune-competent population. It is recommended that risk management strategies could be focused on relevant sub-populations.

- Susceptibility of intermediate hosts to toxoplasma infection varies according to species with seroprevalence data indicating that infection is most common in sheep, pigs and wild game. Cattle appear to be relatively resistant to infection. There is a very small amount of data on meat contamination in the UK but (other than a recent serological survey in sheep) virtually none on the presence of the parasite in farm animals reared in the UK. Further data on seroprevalence in farm animals would be useful in monitoring the effectiveness of control measures in animal husbandry and testing of a larger range of meat samples would be useful in identifying the main sources of risk. Further studies are therefore recommended to establish seroprevalence in UK livestock species
- Toxoplasma has been found in a wide variety of meats. However based on the available, limited evidence, beef and housed chicken appear less commonly infected, than other meat. Tachyzoites and bradyzoites are relatively fragile whereas oocysts and tissue cysts are relatively resistant to food preparation and processing. Washing of salads and vegetables may remove some surface contamination of oocysts, whereas inactivation of the more resistant tissue cyst requires adequate cooking. Curing of meats may inactivate tissue cysts, depending on the process used. It would significantly assist risk assessment if further studies were undertaken to determine the prevalence and concentration of toxoplasma contamination in meat and other foods in the UK and to assess the effect of a number of microbiological reduction/destruction processes e.g. salad washing, milk fermentation and various meat curing methods on toxoplasma. It is also recommended that methods are developed to assess the number and distribution of viable tissue cysts in a range of edible tissue.
- Oocyst contamination of the environment is an important risk factor in infection and consumption of undercooked meat is also likely to be an important risk factor for pregnant women and immune-compromised groups. However the relative contribution of food associated toxoplasma infection is not well-defined and not known in the UK. None of the case control studies has involved cases in the UK. Given the variability in seroprevalence across Europe, differences in food handling and consumption, and in climate, a case control study in the UK should be considered. The utility of studies that seek to exploit recently reported methods that can distinguish sporocysts from tissue cysts as source of infection should also be considered.
- There is variation in the consumer advice given by different countries in relation to toxoplasmosis. The current UK advice to pregnant women should be reviewed in the light of current knowledge, and the advice given by other countries. The need for similar advice for other immune-compromised groups should also be considered. Advice to the immune-competent population should not be ignored.

5. The assessments made and conclusions reached by the Group reflect evidence oral and written drawn from the scientific community, government departments and Agencies, EFSA and the scientific literature. The Group's full conclusions, identified data gaps and recommendations are brought together at the end of this report. The ACMSF accepts full responsibility for the final content of the report.

6. This report was subject to a 12 week public consultation. The actions taken to address consultation comments can be found in the consultation response table. A number of the consultation comments received related to risk management and these were passed to the FSA for consideration as they are outside the remit of the ACMSF and this report.

## 1. Background

1.1 Information on the incidence of toxoplasmosis in the UK population and the risk of infection associated with food sources is limited. Evidence suggests that infection of food producing animals (animals reared for meat) with the parasite *Toxoplasma gondii* may be common. Recent research, in the Netherlands<sup>1</sup> and the US<sup>2</sup>, has estimated that the disease burden due to toxoplasmosis may be more significant than previously thought and may be greater than several other foodborne pathogens due to the severity of the disease.

1.2 The FSA therefore sought the view of the ACMSF, in December 2006, on the significance of toxoplasmosis disease in the UK, the foodborne risks and whether there was a need for further investigation. After an initial discussion and a subsequent presentation in March 2007 by Public Health Wales/HPA giving an overview of human toxoplasmosis in UK, US and the Netherlands, the subject was referred to the *Ad Hoc* Group on Vulnerable Groups.

1.3 The ACMSF asked the *Ad Hoc* Group to:

- Review the current evidence on toxoplasmosis in humans and animals in the UK;
- Consider whether the evidence indicates a food safety issue that needs to be addressed and which food sources are likely to present a significant risk;
- Discuss what further investigations/surveillance may be necessary to obtain robust data on UK prevalence and foodborne sources of toxoplasmosis;
- Consider whether there is a need to revise current food safety advice;
- Suggest any other aspects that require consideration.

### The ACMSF's approach to its work

1.4 The *Ad Hoc* Group met seven times from December 2008 to April 2011 to consider evidence relating to toxoplasma in the UK. The Group used as its starting point a review undertaken for the FSA by Dr Judith Hilton of the current situation on toxoplasmosis and recent research.

1.5 Membership of the Group is shown in Annex I.

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<sup>1</sup> Kemmeren JM, Mangen MJ-J, van Duynhoven YTHP, Havelaar AH. Priority setting of food borne pathogens. RIVM report 330080001/2006. Available from <http://www.rivm.nl/bibliotheek/rapporten/330080001.html>

<sup>2</sup> Mead PS, Slutsker L, Dietz V, McCaig LF, Bresee JS, Shapiro C, Griffin PM, Tauxe RV. Food-related illness and death in the United States. *Emerging Infectious Diseases* 1999; 5(5): 607–625.

## 2. Introduction

2.1 The causative agent of toxoplasmosis is an intra-cellular protozoan, *Toxoplasma gondii* (hereafter referred to as toxoplasma), which is widely prevalent in humans, warm-blooded animals and birds throughout the world.

2.2 The cat is the only definitive host in which sexual reproduction of the parasite occurs in the intestine, resulting in the shedding of oocysts into the environment. Following sporulation of the oocysts, ingestion by humans and other animals results in release of sporozoites in the intestine. These penetrate the intestinal wall and migrate throughout the body, where they may invade a variety of tissues and cells, including muscle, hepatocytes, cells of the heart and central nervous system. Following multiplication in the cells, the parasite forms tissue cysts. These contain bradyzoites within a cyst wall which is partly of host and partly of parasitic origin. The bradyzoites have a low metabolic activity but tissue cysts break down periodically to release bradyzoites, which induce further cyst formation. Consequently, the tissue cyst burden constantly evolves over the lifetime of the host.

2.3 Tissue cysts are highly infectious for humans and other animals, who may thus acquire infection by consuming meat and offal. Humans may also acquire infection by transmission from a pregnant woman to her unborn baby. This occurs when a pregnant woman acquires primary infection. Infection of the foetus is due to tachyzoites in the maternal circulation which may cross the placenta to the foetus for a period of several weeks, during the acute phase of her illness. The lifecycle of toxoplasma is shown in figure 1.

2.4 The relative importance of ingestion of oocysts from contaminated environments versus tissue cysts from the consumption of meat and offal is unclear. This report will consider information on the epidemiology of this pathogen, including data on sources of infection and routes of transmission, together with the available information on disease burden, which is needed to assess the priority that should be given to reducing foodborne toxoplasmosis in the UK.

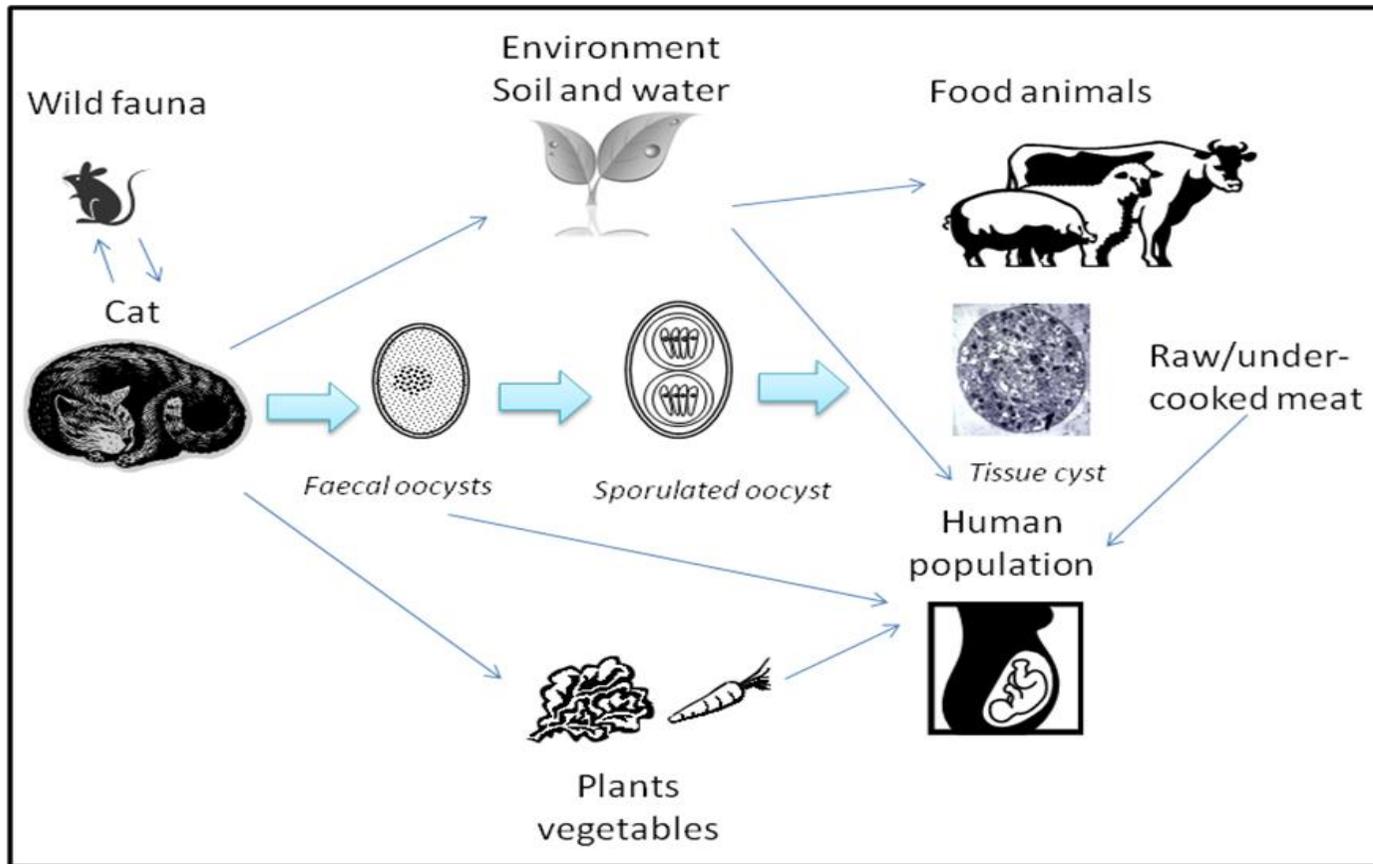


Figure 1: Life cycle and transmission of *Toxoplasma gondii*

### 3. The organism

3.1 *Toxoplasma gondii* has three infectious stages: (1) tachyzoites, (2) bradyzoites in tissue cysts, and (3) sporozoites contained in oocysts.

3.2 Tachyzoites are the rapidly multiplying stage of the parasite found in intermediate hosts, such as humans, after primary infection (figure 2). They are responsible for congenital infection and may also be involved in infections acquired from transplants, blood products that are high in white cell fractions, or in laboratory accidents.

3.3 Parasitaemia is short-lived after primary infection and these sources are infrequently involved in horizontal transmission of infection. Hence, whilst the presence of tachyzoites in donor tissue is the usual source of infection in bone marrow transplant recipients, this is a rare event which only occurs when the donor has asymptomatic parasitaemia at the time of harvest. In recipients of solid organ grafts, life-threatening toxoplasmosis is most often acquired through the reactivation of viable tissue cysts from the donor organ in a recipient with no prior infection with the parasite. Tachyzoites are rarely the source of infection in this patient group.



**Figure 2: Tachyzoites**

3.4 Tachyzoites can also be found in milk from intermediate hosts, including sheep, cattle,<sup>3</sup> and goats.<sup>4</sup> Human cases have only been linked directly to consumption of goat's milk, although risk factor studies have suggested an association with drinking milk in Poland<sup>5</sup> and with camel milk in the Sudan.<sup>6</sup>

<sup>3</sup> Esteban-Redondo I, Innes EA. *Toxoplasma gondii* infection in sheep and cattle. *Comp. Immun. Microbiol. Infect. Dis* 1997; 20(2):191-196.

<sup>4</sup> Elsheikha HM. Congenital toxoplasmosis: Priorities for further health promotion action. *Public Health*. 2008;122: 335-353

<sup>5</sup> Paul M. Potential risk factors for *Toxoplasma gondii* infection in cases with recently acquired toxoplasmosis. *Przegl Epidemiol*; 1998; 52:447-54

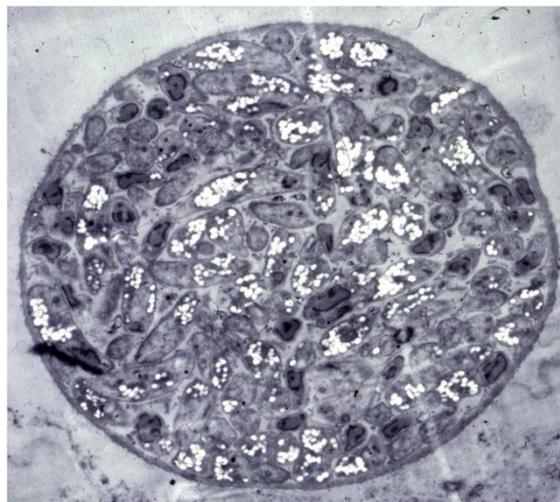
<sup>6</sup> Elamin EA et al. Prevalence of *Toxoplasma gondii* antibodies in pastoral camels (*Camelus dromedarius*) in the Butana plains, mid-Eastern Sudan. *Vet Parasitol* 1992; 43: 171-5

Tachyzoites are sensitive to proteolytic enzymes and are usually destroyed by gastric digestion. However, they have been shown to survive for up to 2 hours in acid pepsin solutions and oral application of high doses of tachyzoites has been shown to produce infection in mice and cats. It has also been suggested that tachyzoites may enter the host by penetration of the mucosal tissue thus bypassing the stomach, and this route of transmission has been suggested for a case of acquisition by a breast-fed infant.

3.5 Tachyzoites have been found in saliva, sputum, urine, tears and semen, as well as in raw eggs from experimentally but not naturally infected hens<sup>7</sup>, and there is no evidence of these being associated with horizontal transmission of infection.

3.6 Most horizontal transmission is thus thought to be acquired by consumption of tissue cysts in meat and offal, or of oocysts shed by cats into soil or water courses.

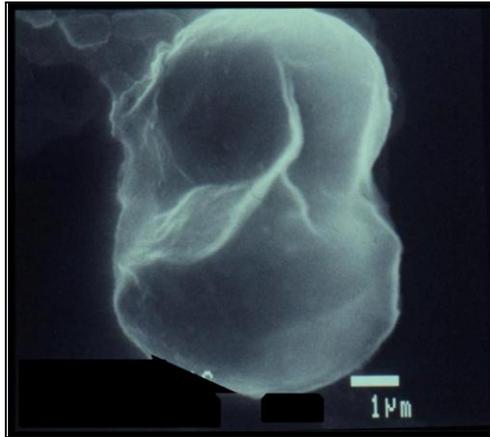
3.7 As immunity develops after primary infection, tissue cysts are formed (figure 3). Whilst these do produce a host reaction, as evidenced by the long-term persistence of toxoplasma-specific IgG, this immune reaction does not lead to the elimination of the organism from the host. Tissue cysts can be found in brain, muscles, heart and viscera. They contain bradyzoites which are released after consumption of tissue cysts in meat from infected animals. Bradyzoites are more resistant to digestive enzymes than tachyzoites but less resistant to environmental conditions than oocysts, remaining infectious for up to three weeks at 1-4°C. Bradyzoites are normally killed by freezing at minus 12°C. Similarly, they may survive curing, depending on the conditions used. They are killed by temperatures  $\geq 67^{\circ}\text{C}$  and by gamma irradiation.



**Figure 3: Tissue cyst**

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<sup>7</sup> Jacobs L, Melton ML. Toxoplasmosis in chickens. *J. Parasitol* 1966; 52: 1158-1162



**Figure 4: Oocyst**

3.8 Oocysts are shed during primary infection in cats (figure 4). Male and female gametes are produced in the epithelial cells of the small intestine and, after fertilisation of the female gamete by the male gamete, a protective wall is formed producing the oocyst. At the time of shedding, oocysts are non-infective, but they sporulate within 1-5 days on exposure to air. Sporulation is inhibited by anaerobic conditions, by heat at approximately 50°C (see Table 4) and by temperatures of 4°C or lower. Sporulated oocysts are very resistant to environmental conditions, particularly in moist soil or sand, where they retain infectivity for up to 18 months. They can remain viable in surface water for prolonged periods. They lose infectivity during drying, remaining infective for at least 30 days at 100% relative humidity but for less than 3 days at 0-37% relative humidity. They are relatively resistant to freezing although some killing is observed at minus 21°C. They are killed within 1-2 minutes by heating to 55-60°C. They are highly impermeable and therefore very resistant to disinfectants.

3.9 Oocysts in the environment may cause direct infection in humans through ingestion of soil or contaminated raw fruit and vegetables. They also give rise to infection in herbivores and hence may lead to formation of tissue cysts in farm animals. Flies and other insects have also been shown to transmit oocysts to food.

## 4. Human toxoplasmosis: clinical disease

4.1 Most human infections in those with no immune suppression are asymptomatic. Most sources state that only 10-20% are symptomatic, although a review of outbreaks of toxoplasmosis<sup>8</sup> has suggested that up to a further 50% may experience mild symptoms. In those with symptoms, the disease most commonly presents in immunocompetent patients with a glandular fever or flu-like illness and may involve lymphadenopathy, low grade fever, generalised malaise, mild to extreme tiredness and muscle pain. Links between toxoplasmosis infection and behavioural changes and other neurological conditions in mammalian hosts, including humans, have been proposed. However, there is insufficient evidence to draw any firm conclusions at this time.<sup>9</sup> Toxoplasma infections have been estimated to cause 3 to 7% of clinically significant cases of lymphadenopathy. However, severe disease may arise as a result of congenital infection, and of infection or reactivation in people who are immunocompromised.

4.2 Congenital infection may result in intrauterine death or in chorioretinitis, hydrocephalus, convulsions and intracerebral calcification. Whilst affected infants may be born without symptoms, a significant proportion will later develop ocular disease.

4.3 More severe primary infection or reactivation is associated with conditions resulting in compromised immunity, such as AIDS and Hodgkin's disease<sup>10</sup>, in patients on immunosuppressive therapy and in recipients of organ or bone marrow transplants. In these groups infection may result in chorioretinitis or toxoplasma encephalitis. Toxoplasma encephalitis, with or without CNS lesions, is the most common manifestation of toxoplasmosis in individuals with AIDS and may occur in up to 50% of those with other forms of immunodeficiency<sup>11</sup>. Pulmonary toxoplasmosis (pneumonitis) may also occur in patients with AIDS who are not receiving appropriate anti-HIV drugs or primary prophylaxis for toxoplasmosis.

4.4 There is no effective human vaccine to protect against toxoplasma infection nor is there likely to be one in the near future.

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<sup>8</sup> Ho-Yen DO. Clinical Features. In: Ho-Yen D.O. and Joss, A.W.L. (eds) *Human Toxoplasmosis*, Oxford University Press, Oxford, 1992. pp 56-78

<sup>9</sup> Flegr J, Hrdy I. Influence of chronic toxoplasmosis on some human personality factors. *Folia Parasitol (Praha)*. 1994; 41(2):122-6.

<sup>10</sup> Girdwood, RWA. "Protozoan" infections in the immunocompromised patient – the parasites and their diagnosis. *J. Med. Microbiol.* 1989; 30: 3-16 provides longer list of immunocompromising states: pregnancy, age, congenital immunological defects, chronic infections (including HIV), malnutrition, neoplasia, therapeutic suppression, collagen-vascular diseases, surgery (e.g. splenectomy)

<sup>11</sup> This is an unreferenced statement from the emedicine article on toxoplasmosis, the author of which is Murat Hökelek, MD, PhD, Technical Consultant of Parasitology Laboratory, Associate Professor, Department of Clinical Microbiology, Ondokuz Mayıs University Medical School, Turkey

## 5. Human cases: prevalence

5.1 80-90% of cases of toxoplasma infection are asymptomatic and the majority of the remainder have only mild, self-limiting symptoms. Thus, reports of acute symptomatic toxoplasma infection (toxoplasmosis) do not provide a reliable basis for assessing overall disease incidence. However, determining the prevalence of antibodies to toxoplasma in the normal population provides an alternative for estimating the number of cases and disease burden.

5.2 In the UK, surveillance of toxoplasmosis-related human disease is mainly derived from specimens referred to reference laboratories for investigation.

5.3 Surveillance based upon referrals to the reference laboratory are likely to represent an underestimate of the true incidence of disease. In the immunocompetent, in particular, where laboratory diagnosis is based on routine serological tests, samples are referred only where primary testing is equivocal or where confirmation will help exclude other diagnoses that might require significant clinical intervention, eg lymphoma.

5.4 In clinically vulnerable groups referral of patients is typically more common. Therefore, underestimates are likely to be less since specialist testing offered by reference units can support diagnosis and significantly inform clinical management. In suspected CNS toxoplasmosis in HIV/AIDS, for example, treatment for toxoplasmosis may be initiated on the basis of diagnostic imaging, but further specialist laboratory testing for confirmatory purposes and to exclude differential diagnoses, is often undertaken.

5.5 Nevertheless, since most toxoplasma infections of the immunocompetent population are asymptomatic or associated with mild to moderate, non-specific signs and symptoms, even primary laboratory investigation may not be undertaken. Further, routine pre- or post-natal screening for toxoplasmosis is not undertaken in the UK and, as the great majority of maternal and congenital infections are asymptomatic, most of these cases will also not be identified.

5.6 Toxoplasma seroprevalence is known to vary geographically and with age. Whilst antibodies are found in 20-40% of adults in the UK and USA, seroprevalence is higher in Central Europe, South and Central America, and in West Africa (50-80%) and similar or lower in South East Asia, China and Korea (4-39%) and Scandinavia (11-28%). In the early 1990s, seroprevalence in Europe varied from 8.1% in the UK to 77.4% in the former Yugoslavia. Climate, and consumption of raw meat, meat from animals farmed outdoors or frozen meat may be factors that contribute to these variations. Seropositivity also varies within countries. For example, in studies of military recruits in the USA, seropositivity ranged from 3% to 13%, being highest in those from rural or small town backgrounds and lowest in those from urban or suburban areas. In the UK, it is reported to be highest in Northern Ireland and lowest in England and Scotland (Figure 5). UK

seroprevalence is generally higher in the west and lower in the east of the country.

5.7 Data showing the variation in seropositivity with age are available from a number of countries. For example, in the Netherlands, it was found to range from 20% at 25 years of age to 60% at 50 years. In a country with a lower overall prevalence, Japan, seropositivity in the 20-29 year old age group was 3%, increasing to 40% in those over 70 years of age. Data from three studies carried out around 1989-1992 in Sheffield<sup>12</sup>, the East of England<sup>13</sup> and Wales provide some limited data on seroprevalence in women of child-bearing age ranging from 8-10% in England to 22% in Wales, whereas a prevalence of 50% has been found in the over 50s.<sup>14</sup> Similar seroprevalence results have been found in Scotland.<sup>15, 16</sup>

5.8 These apparent variations in seroprevalence within England and Wales have been confirmed in a systematic study of blood donor sera collected from throughout the British Isles during 1990-1991 (Figure 5).

5.9 In order to investigate the relationship between age and seroprevalence of a wider age-range, these data were combined with those from individuals of known age less than 20 and older than 60 yrs collected for routine investigation of diseases of non-infectious aetiology by hospital chemical pathology departments located within the same regions as the blood donors (Figure 6).

5.10 The data from the blood donor seroprevalence study confirm:

- Mean levels of infection among blood donors were found to range from 11-40% among the UK population with a slightly higher level of infection in males (23.0%) than females (20.7%).
- Significant geographical variation in levels of infection was identified with higher seroprevalence in the Western British Isles than in the East. There also appears to be a marked correlation between urbanisation and seroprevalence, with larger population centres tending to have lower levels of infection.
- A clear positive relationship between age and seroprevalence was confirmed in all centres but we also find this relationship may not be strictly linear. These data cannot discriminate between the two contrasting interpretations; that toxoplasmosis incidence is falling over time, or that

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<sup>12</sup> Zadik PM et al. Low incidence of primary infection with toxoplasma in pregnant women in Sheffield: a seroconversion study. *Br J Obstet Gynaecol* 1995; 102: 608-10

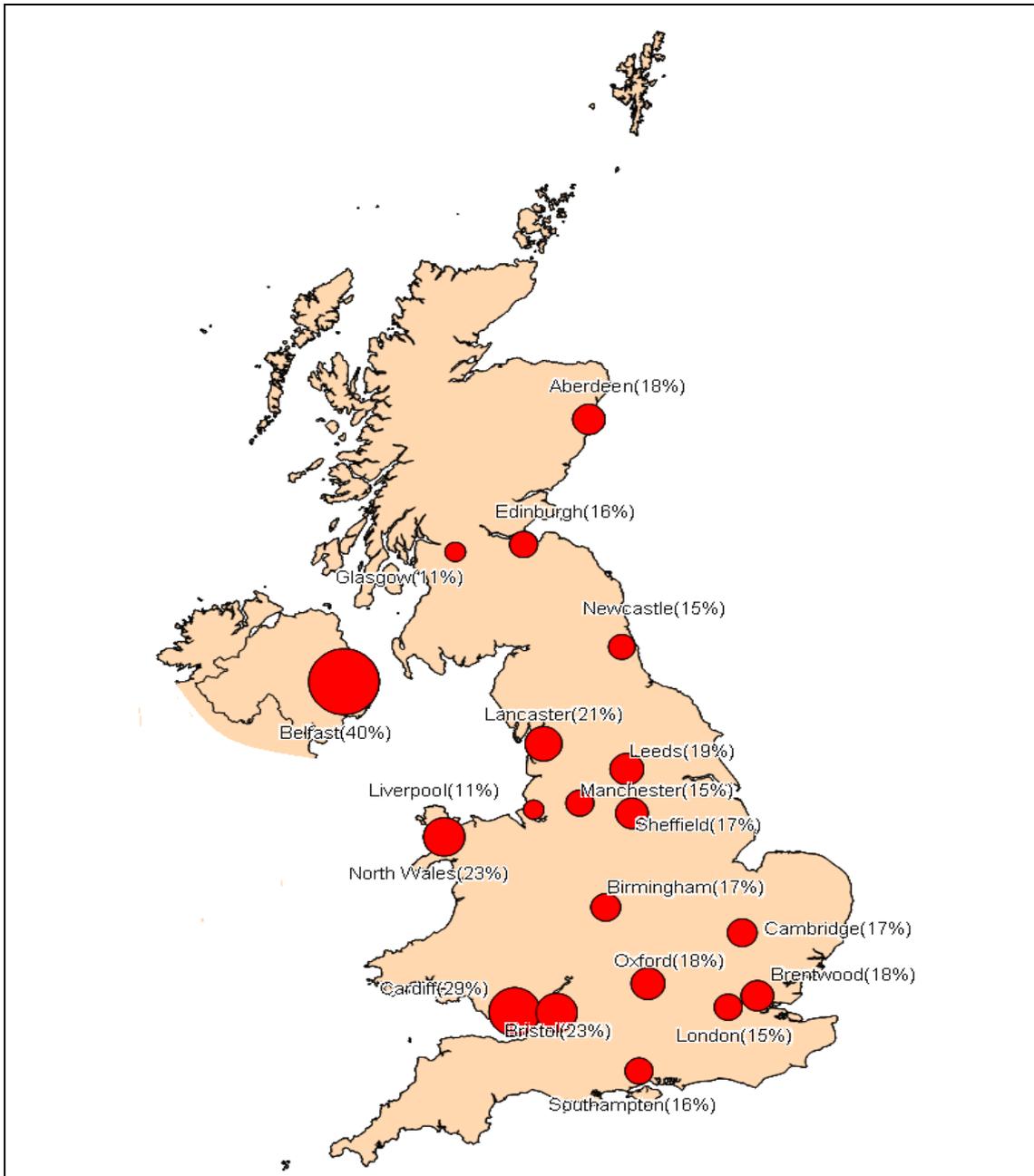
<sup>13</sup> Allain JP et al. Epidemiological study of latent and recent infection by *Toxoplasma gondii* in pregnant women from a regional population in the UK. *J Infect* 1998; 36: 189-196

<sup>14</sup> Toxoplasma Reference Unit, Public Health Wales, Edward Guy, personal communication

<sup>15</sup> Williams et al. Congenital toxoplasmosis: a prospective survey in the West of Scotland. *Journal of Infection* 1981; 3: 219-229

<sup>16</sup> Joss et al. Simultaneous serological screening for congenital cytomegalovirus and toxoplasma infection. *Public Health* 1988; 102: 409-417.

incidence increases with age. An additional study collecting comparable data but carried out one or more decades later would be required to investigate this further.



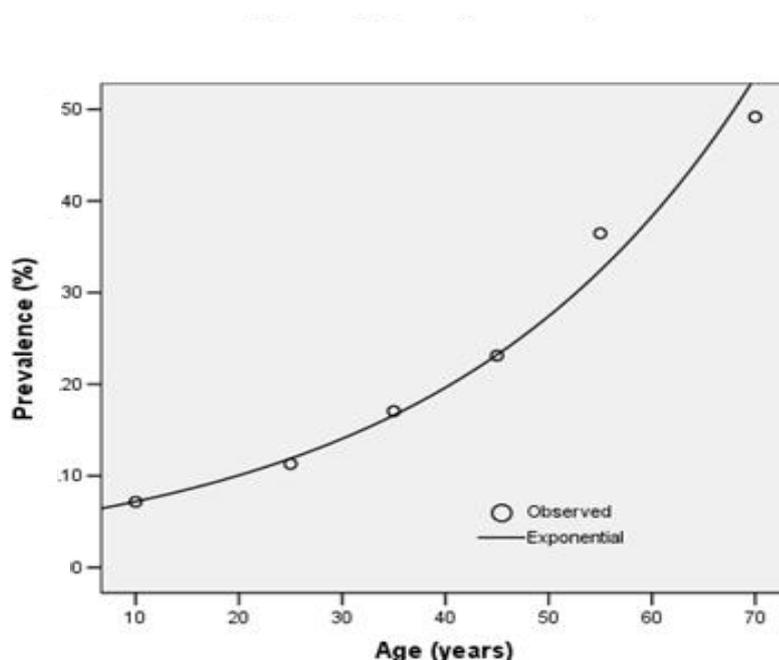
**Figure 5: Seroprevalence among Blood Donors<sup>14</sup>**

Approximately 400 sera from each centre (50 male & 50 female from each of the 4 decades 20-29 yrs to 50-59 yrs) were tested using the Dye test. The area of the red circles is proportional to seroprevalence at each blood donor centre.

5.11 Where data are available, there is evidence of a sharp decrease in seroprevalence over the last 40 years in many populations. For example, in

1960 there was a seroprevalence of 82% in France, falling to 44% in 2003.<sup>17</sup> This decrease is in part attributable to a decrease in infection in childhood, probably associated with increased standards of living, and has also been linked to changes in meat husbandry and consumption. As discussed above, no information is currently available to determine whether, and to what extent, seroprevalence may have changed in the UK over recent years.

5.12 Changes in seroprevalence with age provide a basis for estimating seroconversion rates and hence the incidence of infection. A systematic review of 15 studies in 1996 found annual seroconversion rates of 0.24 – 1.6% in Europe and 0.2 – 0.6% in the US<sup>18</sup>.



**Figure 6: Seroprevalence in the UK and Age<sup>14</sup>**

The data from the blood donors shown in Figure 5 were combined with data from individuals of known age less than 20 and older than 60 yrs collected for routine investigation of diseases of non-infectious aetiology by hospital chemical pathology departments located within the same regions as the blood donors.

5.13 The limited studies of seroconversion during pregnancy in the UK have shown lower rates even than those reported from Scandinavia, with rates below 0.1%. The data presented in Figure 6 gives an estimated

<sup>17</sup> AFSSA (Agence Française de Sécurité Sanitaire des Aliments) Report (2005). Toxoplasmose: état des connaissances et évaluation du risque lié à l'alimentation

<sup>18</sup> Eskild A, Oxman A, Magnus P, Bjørndal A, Bakketeig LS. (1996). Screening for toxoplasmosis in pregnancy: what is the evidence of reducing a health problem? *J Med Screen* 1996; 3: 188-194.

seroconversion rate of 0.2% in those aged 20 and 0.8% in those aged 70 and are comparable with those reported in the USA, of up to 0.6%. As stated in paragraph 5.10, the significance of these findings requires repeated surveillance to clarify. On this basis, a total number of 350,000 cases would be estimated to occur each year, of which 35,000-70,000 would be symptomatic. Reference laboratory data in the UK reported 356 cases of acute toxoplasmosis. This represents approximately 0.5-1% of the number of symptomatic infections estimated from apparent seroconversion data. This is a lower proportion of infections than that captured by passive surveillance in the USA where around 6% of the estimated 225,000 symptomatic cases are reported. This finding is expected since referral of suspected acute toxoplasmosis is not routine. Referral of samples is more frequent, however, from vulnerable groups where specialist testing is required to achieve a definitive diagnosis and support clinical management. These will include the immunosuppressed and immunodeficient, pregnant women and the unborn child/infant.

**Table 1. Annual incidence of toxoplasma cases identified by the Toxoplasma Reference Unit (TRU) during the period January-December 2009<sup>19</sup>**

<b>Clinical Scenario</b>	<b>Symptoms/Status</b>	<b>No. Cases</b>
Immunocompetent	Acute systemic (lymphadenopathy, 'flu')	202
	Pregnant women	38
	Ocular disease	55
	Other	61
HIV		98
Organ transplant	Donor/ Recipient	15
Congenital toxoplasmosis		8
<b>Total</b>		<b>477</b>

<sup>19</sup> Health Protection Agency. *Toxoplasma gondii* infections diagnosed by the Toxoplasma Reference Unit, England and Wales: weeks 1-52/2009. *Health Protection Report* 4(6) 12 February 2010. Available at: <http://www.hpa.org.uk/hpr/archives/2010/hpr0610.pdf> and Dr D Ho-Yen, Scottish Toxoplasma Reference Laboratory, personal communication.

## 6. Burden of disease

6.1 In order to establish the priority for further work to establish the role of foodborne transmission of toxoplasma, evidence on the burden of disease needs to be considered and, where necessary, further data may be needed to complete the picture and assess trends. The burden of disease is a reflection of both the numbers of infected individuals and the severity of the infection.

6.2 In assessing the disease burden, it is clear that there is such a great difference between expected and reported cases of acute toxoplasmosis in the immunocompetent, that this will have to be based on estimates of disease incidence rather than disease reports. In immunocompetent people the majority of cases are asymptomatic. Of the rest, the majority experience a glandular fever-like illness. Whilst these make up the majority of cases of what appears to be a common infection possibly affecting 0.6% of the UK population each year and with half the population showing signs of past infection by the age of 50, disease severity is low and, since the infection is also self-limiting, the burden of disease per case will be relatively low. However, in key vulnerable groups such as the immunosuppressed, immunodeficient, and infection acquired in pregnancy resulting in congenital infection, severe or life-threatening disease can result and so the burden of disease per case will be significantly higher.

6.3 Both the overall burden of disease to the UK population and the contribution from each of the clinical groups affected will depend upon a combination of disease severity, duration, and the number of cases that occur. Thus, a precise measure will require the application of quantitative analytical methods of the kind undertaken elsewhere<sup>1</sup>. No such study has been carried out in the UK but studies of disease burden elsewhere have concluded that the relatively small proportion of cases with congenital toxoplasmosis, encephalitis and chorioretinitis account for most of the disease burden due both to the more severe immediate symptoms and the risk of longer term, and potentially life-long, sequelae.

### Congenital toxoplasmosis

6.4 Since congenital toxoplasmosis is a consequence of primary maternal infection, incidence will depend directly upon both seroprevalence in women of childbearing potential and the seroconversion rate ie the lower the seroprevalence in this group, the higher will be the proportion of cases susceptible to primary infection. Where maternal infection is acquired during pregnancy, the risk of transmission is greatest in late pregnancy. For example, a study in the Netherlands<sup>20</sup> showed 9% transmission from mother to child in the first trimester, increasing to 59% in the third trimester. Similar transmission rates have been recorded in the USA, whilst in France transmission rates as high as 80% have been found at the end of the third trimester. In contrast, the severity of disease is greatest where the infection is transmitted to the unborn child in early pregnancy.

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<sup>20</sup> Montoya JG and Liesenfeld O (2004) Toxoplasmosis. *Lancet* 2004 ;363 (9425) :1965-76

6.5 Worldwide, it is estimated that primary maternal infection occurs in 0.1 – 0.8% of pregnancies, resulting in 1-120 cases of congenital toxoplasmosis per 10,000 births. Although a high proportion of pregnant women in the UK are seronegative (90%), a 1995 study in England yielded a low rate of 0.023% seroconversion during pregnancy.<sup>12</sup> Based on data from other countries suggesting that transmission occurs in 30-40% of cases, this would suggest that there are around 40-60 cases of congenital toxoplasmosis per year. However, in a 1994 paper<sup>21</sup>, the number of cases of congenital toxoplasmosis in the UK was estimated as being 243-2428. This was based on data showing that congenital toxoplasmosis occurs in 0.03-0.3% of live births. The 1995 study in England reported above was, however, carried out in only a single region. Based upon the data presented earlier confirming that regional variations exist in levels of infection across the UK, extrapolation of these data to the national level is difficult. However, in a subsequent national study carried out between 2002 and 2004<sup>22</sup>, 22 cases of congenital toxoplasmosis were identified (mean incidence 11 cases per annum). This is equivalent to a cumulative incidence for England and Wales of 3.4/100 000 live births (95% CI 2.4 to 4.8), of whom 2 (9%) were stillborn, 7 (32%) live births had intracranial abnormalities and/or developmental delay (5 of whom had retinochoroiditis), and 10 (45%) had retinochoroiditis with no other abnormalities reported.

6.6 Of pregnancies in which transmission of toxoplasma occurs, around 4 - 10% result in abortion, stillbirth or neonatal death whilst 65-85% of babies are asymptomatic at birth. The proportion of cases with symptoms at birth varies from study to study and results are expressed in different terms so that comparison between studies is difficult (Table 2). The most common effects are CNS abnormalities (3-20%), chorioretinitis (4-15%), intracranial calcifications (10-12%) and hydrocephalus (2%). Figures from Europe show that, in the longer term, 1-2% suffer from learning difficulties and 4-27% from retinochoroidal lesions, whilst studies in the USA<sup>23</sup> suggest that, by 20 years of age, 53% suffer from visual impairment and 73% from mild to severe learning difficulties.

**Table 2. Outcomes of congenital toxoplasma and proportion of associated cases (data taken from several different studies).**

Sequelae at birth	CNS abnormalities	3-20%
	Chorioretinitis	4-15%
	Intracranial calcifications	10-12%
	Hydrocephalus	2%
“Longer-term” complications	Learning difficulties	1-2%
	Retinochoroidal lesions	4-27%
Complications at age 20 years	Visual impairment	53%
	Mild to severe learning difficulties	73%

<sup>21</sup> Roberts T, Murrell KD, Marks S. Economic losses caused by foodborne parasitic disease. *Parasitology Today* 1994; 10: 419-423

<sup>22</sup> Gilbert et al, *Arch Dis Child* 2006;91:495-498

<sup>23</sup> Roberts T. and Frenkel JK. Estimating income losses and other preventable costs caused by congenital toxoplasmosis in people in the United States. *JAVMA*, 1990; 196: 249-256

6.7 Data from the UK are limited. Over a 2 year period of enhanced surveillance in 2002-04, 22 cases of congenital toxoplasmosis were reported in England and Wales<sup>22</sup>. If it is estimated that 15-35% of cases are symptomatic at birth, this would equate to a maximum of 30-75 cases of congenital toxoplasmosis a year in total. However, this figure may be an over-estimate because some of the 22 cases reported in the study only became apparent several years after birth.

### Ocular toxoplasmosis

6.8 Based on data from Canada<sup>24</sup>, the proportion of cases of toxoplasmosis with chorioretinitis ranges from 0.3 – 0.7%. The majority of cases occur in 10 – 35 year olds and most references suggest that the majority of cases are due to reactivation of subclinical congenital toxoplasmosis. However the incidence of eye disease following acquired infection has been estimated to be as high as 25% in certain regions of Brazil<sup>25</sup> and a UK study has suggested that 50% of cases follow congenital and 50% follow acquired infection.<sup>26</sup>

6.9 An incidence rate of 0.4 per 100,000 has been calculated for patients born in Britain<sup>27</sup>, culminating in a life-time risk of 18 per 100,000. Most of these cases were acquired, and comparison with the seroprevalence data from the UK yields a risk of ocular toxoplasmosis following acquired toxoplasmosis that is much lower than the estimated 0.3% from Canada. The incidence of ocular toxoplasmosis in the UK also varies by racial origin. For example, it is higher in those of West African origin than in Caucasians<sup>28</sup>.

6.10 It is not known if these differences reflect differences in genetic susceptibility, parasite strain variation or exposure.

6.11 The US study mentioned above<sup>21</sup> includes data related to the cost of eye disease in congenital toxoplasmosis. However, it is not possible to use this data as a basis for calculating the likely cost of chorioretinitis due to acquired toxoplasmosis.

### Toxoplasmosis in recipients of organ grafts

6.12 There is a relative paucity of information in this group although a review of the available information found that encephalitis was the most common

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<sup>24</sup> Burnett AJ et al. Multiple cases of acquired toxoplasmosis retinitis presenting in an outbreak. *Ophthalmology*, 1998; 105:1032-1037

<sup>25</sup> Glasner PD. et al. An unusually high prevalence of ocular toxoplasmosis in Southern Brazil. *Am. J. Ophthalmol.* 1992; 114: 133-144

<sup>26</sup> Stanford MR, Tan HK, Gilbert RE. Toxoplasmic retinochoroiditis presenting in childhood: clinical findings in a UK survey. *Br J Ophthalmol.* 2006 Dec; 90(12):1464-7.

<sup>27</sup> Gilbert RE et al. Incidence of symptomatic toxoplasma eye disease: aetiology and public health implications. *Epidemiol. Infect.* 1999; 123: 283-289

<sup>28</sup> Gilbert RE, Stanford MR, Jackson H, Holliman RE and Saunders MD. Incidence of acute symptomatic toxoplasma retinochoroiditis in South London according to country of birth. *British Medical Journal* 1995; 310: 1037-1040

type of infection.<sup>29</sup> Infections associated with renal, liver and bone marrow transplants are considered to be rare (0.44% mean for bone marrow transplants). On the other hand, there is a significant incidence of infection for seronegative heart transplantees receiving a graft from a seropositive donor with around 60% showing evidence of infection in the absence of appropriate prophylaxis. However, whilst seronegative recipients of heart transplants from seropositive donors are at risk of acquiring life-threatening infection, such symptomatic infections are rare as a result of prospective screening and the selective use of anti-parasite prophylaxis.

6.13 No data on estimated costs of infection or UK-specific data have been found.

#### AIDS related toxoplasmosis

6.14 In the US, toxoplasma encephalitis develops in up to 7% of AIDS patients (n = 4000) annually<sup>30</sup>, although the incidence declined from 1992 to 1997. In New Zealand it was estimated that 30% of seropositive patients with AIDS developed toxoplasma encephalitis<sup>31</sup>, although this figure has now been significantly reduced by the widespread use of Highly Active Antiretroviral Therapy (HAART). Toxoplasmosis in AIDS is rarely seen in patients with a CD4 count >200 and is most common in those with a CD4 count <100<sup>32</sup>.

6.15 Other forms of toxoplasmosis in patients with AIDS include ocular disease, which has already been considered above, and pulmonary disease for which no data have been found. The cost of toxoplasma encephalitis in the USA has been estimated to be \$23-106m.<sup>21</sup>

6.16 No UK-specific cost data have been found.

#### Toxoplasmosis and behavioural change

6.17 Some studies have concluded there is an association between toxoplasmosis and behavioural patterns and illnesses such as schizophrenia. However, there is insufficient evidence to quantify the burden of disease that may result from such cases.

#### Total burden of disease

6.18 Toxoplasmosis has been assessed as causing the highest disease burden of seven foodborne pathogens in the Netherlands, mainly due to stillbirths and chorioretinitis in congenital toxoplasmosis and chorioretinitis in

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<sup>29</sup> Smith JL. Long-term consequences of foodborne toxoplasmosis: effects on the unborn, the immunocompromised, the elderly, and the immunocompetent. *Journal of Food Protection*, 1997; 60: 1595-1611

<sup>30</sup> Schwartzman JD. Toxoplasmosis. *Current Infectious Disease Reports* 2001; 3: 85-89

<sup>31</sup> Lake R et al. Risk Profile: *Toxoplasma gondii* in red meat. Report to the New Zealand Food Safety Authority FW0138, 2002.

<sup>32</sup> Montoya JG, Remington JS. Toxoplasmosis. In: Mandell GL, Bennett JE, Dolin R, editors. *Principles and Practice of Infectious Diseases*, Philadelphia: Churchill Livingstone, 2000. pp 2858-88

acquired infection. In France, it was estimated to be the third most common cause of death from foodborne illness. In the USA, it has been estimated to cause 0.9% of all cases of foodborne illness, 8.0% of hospitalisations (ranked fourth) and 24% of deaths (ranked second), based on an estimate that 50% of cases are foodborne (note that the rationale for choice of this figure is not explained in the paper)<sup>33</sup>.

6.19 In the USA, the economic costs of congenital infection and infection in AIDS patients has been estimated to be \$0.4 – 8.8 billion.<sup>21</sup> Work on the total costs of toxoplasmosis in the Netherlands is currently close to completion.<sup>34</sup>

6.20 In the UK, based on seroprevalence data, it is estimated that there are a total of around 350,000 cases a year, only 35,000 – 70,000 of which are symptomatic.

6.21 In 1994, the number of cases of congenital toxoplasmosis in the UK was estimated as being 243-2428, although other data suggest that the number of cases could be an order of magnitude smaller. The cost was estimated to be \$1.2–12m.<sup>21</sup>

6.22 Based on data from Canada<sup>24</sup>, the incidence of ocular toxoplasmosis in the UK could be 1050-2450 cases a year. However, given the data from the UK study mentioned previously<sup>27</sup>, this is likely to be an overestimate.

6.23 There are limited UK data on toxoplasmosis in AIDS patients and cases in organ graft recipients. An estimate that toxoplasma encephalitis occurs in 7% of AIDS patients would translate into 35 cases in the UK (based on an incidence of 500 new cases of AIDS per year). This does not include cases of pulmonary disease. In 2009 the Health Protection Agency reported toxoplasmosis in 81 HIV cases. Cases in organ graft recipients are likely to be rare.

6.24 Putting these estimates for ocular toxoplasmosis and toxoplasma encephalitis together with the estimated number of cases of congenital toxoplasmosis, they could account for up to 5000 cases, (7-14% of symptomatic cases).

6.25 The only data on costs in the UK are for congenital toxoplasmosis. Whilst there are data from the USA on the estimated cost of toxoplasma encephalitis in AIDS patients, this cannot be used to estimate UK costs, and no data are available on other types of toxoplasmosis.

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<sup>33</sup> Scallan E, Hoekstra RM, Angulo FJ, Tauxe RV, Widdowson M-A, Roy SL, Jones JL and Griffin PM. Foodborne illness acquired in the United States – Major Pathogens. *Emerging Infectious Diseases* 2010; 17 (1): 7- 15.

<sup>34</sup> John Coia – personal communication

## Gaps in current knowledge relevant to a UK risk assessment

6.26 The overall surveillance of cases of clinical toxoplasmosis in the UK is sub-optimal such that any current risk assessment must be based largely on estimates rather than reports of disease.

6.27 The accuracy of current reporting of incidence of congenital toxoplasmosis is not confirmed. In particular, routine surveillance is based primarily upon cases where either the pregnant mother or child is symptomatic. Detection rates among the asymptomatic, which probably account for the majority of congenital infections, are likely to be low.

6.28 Maternal infection rate, mother-to-foetus transmission rate and rate of disease affection of neonates & infants in the UK have not been studied systematically. Overall, the health costs of congenital toxoplasmosis have not been accurately estimated.

6.29 The relative contribution of congenital and acquired toxoplasma infection to the burden of ocular disease is uncertain. There is some evidence to suggest racial differences in the prevalence of ocular toxoplasmosis but this has not been adequately explored. In this context, it is not known if these racial differences reflect genetic susceptibility to infection or variation in the virulence of endemic strains of *T. gondii*. The health costs of ocular toxoplasmosis in the UK have not been accurately defined.

6.30 The current incidence of organ-graft associated toxoplasmosis is likely to be low and may be reducing but the actual numbers are not recorded.

6.31 The incidence of HIV associated toxoplasmosis may have fallen with the introduction of HAART, anti-parasitic prophylaxis and maintenance therapy after an acute disease episode but there has been no systematic national study.

6.32 The current incidence of behavioural change associated with toxoplasma is unknown.

6.33 The relative importance of toxoplasmosis in terms of disease burden and compared to other food-borne pathogens is not well established.

## Summary and Conclusions to Sections 4-6

6.34 Other than pregnant women, most infections of the immune competent are asymptomatic or associated with only a mild to moderate, self-limiting illness. However, severe disease can occur in immunocompromised individuals such as the foetus, organ graft recipients and individuals with AIDS or cancer.

6.35 Accurate figures are not available but it is estimated that 350,000 people become infected with toxoplasma each year in the UK, of which 10-20% are symptomatic.

6.36 Based on seroprevalence studies among UK blood donors, levels of toxoplasma infection within the UK appear to fall within the range of those reported elsewhere in Europe and North America.

6.37 It appears that geographical variation in levels of toxoplasma infection may occur within the UK. This has implications for the comparison and extrapolation of individual local studies.

6.38 Toxoplasmosis is a notifiable disease in Scotland but neither a notifiable nor reportable disease in the rest of the UK. Routine surveillance data alone are unlikely to provide an accurate measure of overall incidence. This may be the case particularly in the immunocompetent since the self-limiting and mild to moderate nature of the resulting illness in this group may result in many infected individuals not being identified by the healthcare system.

6.39 Toxoplasmosis in vulnerable clinical groups is, however, typically more severe and often requires specialist investigation. Thus, while reporting of such cases is still likely to result in an underestimate of incidence, such cases are more likely to be reported.

6.40 Although the majority of cases of toxoplasmosis will occur in the immunocompetent, the largest burden of disease is likely to be associated with infection of immunocompromised individuals among whom symptoms are more severe and potentially life-threatening.

6.41 The lack of accurate data for overall incidence and severity of symptoms associated with toxoplasma infection is a barrier to achieving accurate estimates of burden of disease and economic impact in the UK.

6.42 There are some data indicating a sharp decrease in the prevalence of toxoplasma over the last 40 years in some countries but there are no accurate trend data for the UK.

6.43 The relative contribution of the different foodborne routes is important and is considered in Section 9.

#### Recommendations arising from Sections 5 and 6

6.44 We note that the current data on prevalence and burden of disease are incomplete and we recommend that consideration is given as to how the existing data gaps regarding both the prevalence and burden of disease can be addressed.

6.45 A number of risk assessments or risk profiles have been produced but all highlight a number of data gaps and the difficulty in filling them. There is, however, general agreement that the costs of the relatively small proportion of cases with severe disease make toxoplasmosis one of the most costly of gastro-intestinal infections. Whilst there are not enough data to carry out a full assessment of the burden of disease in the UK, it seems reasonable to

proceed on the basis of the assessments made in the USA and Netherlands. We recommend further work to assess the importance of the foodborne route, to identify the most important risks and appropriate risk management measures, and to refine the burden of disease assessment.

6.46 The disease burden associated with toxoplasmosis in the UK mainly reflects infection of immune-compromised individuals including the unborn child. Consequently, risk management strategies could be focused on relevant sub-populations. However, as healthy individuals may go on to become immune-compromised later in life it is also important to consider the potential burden of latent infection of the immune-competent population.

## 7. Sources of infection

7.1 The main sources of infection are meat, other foods, water and the environment. Before considering evidence regarding the relative importance of these sources, information on carriage in farm animals, pets and wild animals is considered.

7.2 While studies based upon seroprevalence and detection of toxoplasma in food samples by nucleic acid testing (NAT) can be helpful in assessing comparative risk both between species and groups of animals from different locations or reared under different conditions, translation of such data into any direct measures of risk is highly problematic. Both seroprevalence and non-quantitative NAT provide no data either on the number of toxoplasma cells present, or on any reduction in their viability following slaughter caused by physical factors or manufacturing processes. This, together with insufficient data on the inoculum size required to cause toxoplasmosis, significantly complicates any direct measurement of risk that can be undertaken with these data alone.

### Farm animals

7.3 Most data on prevalence in animals are based on serological studies. In response to natural infection, most seropositive farm animals have been shown to harbour infectious parasites, with the exception of cattle.<sup>35</sup>

7.4 Comparison of serology results from different studies is difficult due to variation in serological techniques and choice of threshold for positive cut-off. Differences in farming and husbandry methods (both within and between countries) and climatic conditions will also introduce biases into the results. However, despite this, when a number of studies from various countries are looked at, an overall pattern does begin to emerge, and median seroprevalence based on review of the literature may give some indication as to the relative importance of each species in human infections: 30% sheep, 24% pork, 13% cattle, and 7% equine.

7.5 These figures may reflect a variety of factors such as:

- Species susceptibility
- Likelihood of being extensively husbanded (in Europe, pigs and poultry are more intensively farmed, which places barriers to infection from the environment and cats). However, the growing tendency to less intensive systems may impact on this.

7.6 Where data are available, cysts have been found in 25-80% of seropositive animals, based on bioassays in cats or mice.

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<sup>35</sup> Kijlstra A, Jongert E. *Toxoplasma*-safe meat: close to reality? *Trends in Parasitology*. 2008; 25 (1): 18-22.

## Sheep

7.7 Toxoplasma is the second most commonly diagnosed cause of abortion and is a significant cause of economic loss to the UK sheep industry. It has been estimated that the loss of over 0.5 million lambs each year due to toxoplasmosis costs the UK sheep industry £12-24 million.<sup>36</sup> Data from the Veterinary Laboratories Agency indicate that in England and Wales in 2009, toxoplasmosis accounted for 204 (23%) of 904 ovine abortion cases where a diagnosis was reached.

7.8 Licensed vaccines are available in the UK for the control of toxoplasma abortion in sheep although it is not known precisely what percentage of the national flock is vaccinated. However, in a recent survey of 3049 breeding ewes in Great Britain, 6.2% of animals were reportedly vaccinated against toxoplasma, 57.2% were unvaccinated and 36.5% were of unknown vaccination status.<sup>37</sup>

7.9 Vaccination of female breeding sheep prior to mating is primarily intended to protect against early embryonic death, abortion and neonatal mortality, rather than to reduce the tissue cyst load that may enter the food chain. Although the effect of vaccination on tissue cyst formation is not known, the development of a livestock vaccine with the potential to reduce tissue cyst numbers is highly desirable.

7.10 Tissue cysts are most commonly found in brain and skeletal muscle of infected sheep. Few studies have looked at prevalence of tissue cysts in slaughtered sheep destined for human consumption.

7.11 Sheep acquire the infection through ingestion of oocysts on pasture or concentrate feed that has been contaminated by cat faeces. The relative proportions of concentrate feed and grass in the diet will vary according to slaughter age. Lambs in the UK are generally slaughtered from 10 weeks of age (Easter lamb) to 50 weeks (stores).

7.12 Vertical transmission from ewe to lamb may play a role in the maintenance of toxoplasma in a flock.<sup>38</sup> It has been estimated that fewer than 2% of sheep become congenitally infected.<sup>39</sup>

7.13 Toxoplasmosis accounts for approximately 5-10% of abortions in goats in France. Toxoplasma has been detected in milk of naturally infected dairy goats. No data are available for goat meat.

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<sup>36</sup> Defra. Summary profile for toxoplasmosis.

Available:<http://www.defra.gov.uk/foodfarm/farmanimal/diseases/vetsurveillance/profiles/documents/sp-toxoplasmosis.pdf>/. Last accessed 05/01/11

<sup>37</sup> Paul Hutchinson, personal communication.

<sup>38</sup> Duncanson P, Terry RS, Smith JE, Hide G. High levels of congenital transmission of *Toxoplasma gondii* in a commercial sheep flock. *International Journal for Parasitology*. 2001; 31: 1699-1703.

<sup>39</sup> Dubey JP. Toxoplasmosis in sheep – The last 20 years. *Veterinary Parasitology*. 2009; Doi:10.1016/j.vetpar.2009.02.026

7.14 Sheep and goats generally have the highest seroprevalence for toxoplasmosis in most recent studies. Seroprevalences of up to 90% have been found in sheep in some European countries and a recent large-scale screening of sheep farms<sup>40</sup> has shown that 3.4% of sheep were shedding toxoplasma in their milk.

7.15 In New Zealand in the 1980s, an incidence of toxoplasmosis in young ewes was reported to be up to 30%, with up to 90% of ewes being seropositive by 2 years of age. However, use of a vaccine has now reduced this figure. Seroprevalence in goats can be as high as 77%. A UK study in 1990 showed a seroprevalence of 29% in farmed sheep<sup>41</sup> but no data have been found for goats.

7.16 A serological survey of toxoplasmosis is currently being conducted on 3539 blood samples taken from breeding ewes throughout Great Britain as part of a structured seroprevalence study of *Brucella melitensis* infection. Initial results indicate an animal prevalence from natural infection of 68.6% (CI: 67.8-69.4%) and a between flock prevalence of 100% (CI: 98.7-100%).<sup>37</sup>

### Pigs

7.17 Historically, pig meat was generally considered to be the highest risk food for transmission of toxoplasmosis, with up to 90% seropositivity in studies carried out in the 1960s. These results should be interpreted with caution however, as earlier tests are likely to have had poor sensitivity/specificity, and changes in husbandry mean they are not necessarily applicable today.

7.18 The presence of cats, rodents and birds on pig farms and cannibalistic behaviour in pigs are cited as risk factors for toxoplasma infection in pigs.<sup>17</sup>

7.19 Over subsequent decades, changes in husbandry, particularly intensive farm management with indoor rearing of pigs, have reduced exposure of pigs to these risk factors. This may explain the marked reduction in seroprevalence during this time with figures of < 1% in fattening pigs being recorded in a number of European countries. The AFSSA report<sup>17</sup> supports the view that seroprevalence is lower in intensively reared animals (both in fattening pigs and sows).

7.20 More recently, changes to more outdoor farming systems may have resulted in an increase in seroprevalence due to increased exposure to other animals and the environment. For example, in Germany, a study published in 2008<sup>42</sup> showed that 3.9% of finishing pigs were seropositive, including 11.7% of organic finishing pigs, whilst 31.6% of sows were seropositive. This

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<sup>40</sup> Fusco G et al. *Toxoplasma gondii* in sheep from the Campania region (Italy). *Vet.parasitol.* 2007; 149: 271-274

<sup>41</sup> Samad MA, Clarkson MJ. Seroconversion to natural *Toxoplasma gondii* infection during the reproductive cycle and its effect on reproduction in sheep. *Bangladesh Vet J*, 1994; 28: 1-6

<sup>42</sup> De Buhr K. *Toxoplasma gondii* seroprevalence –current results in German swine herds. *Archiv für Lebensmittelhygiene* 2008; 59: 5-8

contrasts with <1% of finishing pigs and 18% of sows in studies in the 1990s. No data for the UK have been found.

### Cattle

7.21 Evidence of infection with toxoplasma based on seropositivity is less common in cattle and buffaloes (0-20%), although higher seroprevalences have been recorded, such as 43% in cattle in Portugal. No serological data are available for the UK. Moreover most studies of cattle have failed to detect viable tissue cysts.

7.22 Toxoplasma has only rarely been isolated from naturally infected cattle. There have been no published cases of isolation of the parasite from naturally infected cattle in Europe, US or Australia.

7.23 There is no evidence to suggest that toxoplasma is excreted in the milk of naturally infected cattle.

### Poultry

7.24 Data on poultry and other species of domestic fowl are sparse. In the developing world seroprevalence may be up to 65% in free-range chickens and tissue cysts have been found in 81% of seropositive birds<sup>43</sup>. However, in developed countries broiler chickens tend to be intensively reared and have a short life span, but no recent data are available on seroprevalence in these birds. Based on older data, seroprevalences of 1-10% have been reported.

7.25 The feeding behaviour of poultry species makes them highly susceptible to infection by oocysts and data from experimental infection studies suggest that cysts are located mainly in brain and heart tissue of poultry and rarely in muscle. Isolation of toxoplasma from chicken eggs following natural infection has never been reported.

### Deer

7.26 The largest study of deer in Europe (involving 760 animals) suggested a seroprevalence of 34% (7.7% in Red deer compared to 34% in Roe deer).<sup>17</sup>

### Horses

7.27 Two European serological studies have been reported. A Swedish study suggested a prevalence of 1% in 219 horses (ELISA) while in the Czech Republic, 7.7% of 2886 horses tested positive using the Sabin-Feldman dye test.<sup>17</sup>

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<sup>43</sup> Kijlstra A, Jongert E. Control of the risk of human toxoplasmosis transmitted by meat. *International Journal for Parasitology* 2008; 38: 1359-1370

7.28 Very few studies have looked at detection of toxoplasma in muscle tissue of naturally infected animals. A study in the US in 1979, which used mouse and cat bioassay, reported detection of the parasite in 7 (1.4%) of 500 slaughtered animals.

7.29 Experimental studies have shown tissue cysts persisting in horses for at least 15 months after inoculation.

### Rabbits

7.30 Proven to be susceptible experimentally but there are no prevalence data for naturally acquired infection in farmed or pet rabbits.

7.31 Estimates of seroprevalence in wild rabbits vary greatly, from 53% of 366 wild rabbits in the Czech republic to 5.9% of 187 rabbits tested in France.

7.32 In another Czech study, toxoplasma was isolated from tissues of 5% of 293 rabbits sampled.

### Other species

7.33 Evidence of toxoplasmosis in several other species whose meat may be consumed has been provided by seroprevalence studies. Examples include wild boar (8-38%), and kangaroos (22%).<sup>43</sup>

### Wild animals and pets

7.34 Evidence of environmental contamination is reflected in seroprevalence data in grazing animals and in a range of wild animals. Estimates of seroprevalence obtained from several studies are summarised in Table 3 below.

7.35 The predatory and scavenging behaviour of foxes suggests that seroprevalence in this species could be an indicator of prevalence in other local wildlife.

7.36 Toxoplasma can be found in most species of wild birds although seroprevalence and frequency of parasite isolation varies between studies. Results of serological surveys in birds should be interpreted with caution as some tests do not detect antibodies in all species. Antibodies to related parasites such as Atoxoplasma and Sarcocystis may cause cross-reaction in serological tests.

**Table 3. Seroprevalence in wild animals, UK<sup>(44)</sup> and non-UK**

<b>Species</b>	<b>Seroprevalence</b>	
Mink <i>Mustela vison</i>	23/26	88.5%
Stoat <i>Mustela ermineae</i>	2/3	66.6%
Foxes		18%-98% <sup>17</sup>
Eurasian otter <i>Lutra lutra</i>	57/141	40.4%
Weasel <i>Mustela nivalis</i>	2/6	33.3%
Crow		30%
Polecat <i>Mustela putorius</i>	5/17	29.4%
Hedgehogs		27%
Pigeon		10%
Moles		6%
Small rodents		<1% <sup>17</sup>

### Marine mammals

7.37 Toxoplasma infection has been reported in a number of marine mammal species<sup>45</sup> indicating that the organism has entered the marine environment.

7.38 Serological studies (carried out mainly in North America) have indicated generally high seroprevalences in a number of species.

7.39 It is possible that the parasite is harboured by marine crustaceans and molluscs after oocysts in soil are leached into seawater although toxoplasma has not been isolated from shellfish in the natural environment. Oocysts in cat faeces could also be discharged via domestic sewage systems into the sea, where they are capable of survival and sporulation.

7.40 It has been suggested that marine mammals could act as sentinel species for toxoplasma in the marine environment. A survey in California revealed 52% of 305 freshly dead sea otters as seropositive for toxoplasma. Sea otters do not prey on known intermediate hosts for toxoplasma and vertical transmission appears to play a minor role in this species. Resistant

<sup>44</sup> Forman D, Guy E. Personal Communication, Toxoplasma Reference Laboratory (England and Wales) and Swansea University

<sup>45</sup> Dubey JP et al. *T.gondii*, *N.caninum*, *S.neurona* and *S.canis*-like infections in marine mammals. *Veterinary Parasitology*. 2003; 116 (4): 275-296.

oocysts (possibly concentrated in bivalve molluscs) would therefore appear to be the most likely source of infection.<sup>46</sup>

7.41 Results of seroprevalence studies in some marine mammal species are shown in Table 4.

**Table 4: Seroprevalence in terrestrial and marine mammals in UK waters<sup>47,48</sup>**

Marine species	Seroprevalence	
Common dolphin <i>Delphinus delphis</i>	15/44	34.1%
Harbour Porpoise <i>Phocoena phocoena</i>	2/135	1.5%
Striped dolphin <i>Stenella coeruleoalba</i>	0/9	0%

### Cats

7.42 Cats are the definitive host of the parasite. A cat may shed up to 10 million oocysts/day for up to 14 days after primary infection. Oocyst shedding depends on the source of infection in that cats infected by tissue cysts all shed oocysts whereas oocysts are shed by only 30-50% of cats infected by oocysts<sup>49</sup>. It is thought that about 1% of domestic cats are excreting oocysts at any one time. Although shedding is usually suppressed by an effective immune response this immunity may not be life-long and cats may shed further oocysts when re-challenged several years after primary infection.<sup>50</sup>

7.43 In experimental trials vaccines using a live mutant strain of bradyzoite (T-263) have been shown to induce significant immunity against oocyst shedding in cats.<sup>51</sup>

7.44 A survey of 51 cats on 22 sheep farms in south-west England in 1987 revealed that 47% were seropositive for toxoplasma. There was no evidence

<sup>46</sup> Conrad PA et al. Transmission of *Toxoplasma*: clues from the study of sea otters as sentinels of *Toxoplasma gondii* flow into the marine environment. *International Journal for Parasitology*. 2005; 35 (11-12): 1155-1168.

<sup>47</sup> Forman D, West N, Powell M, Francis J, Guy E. *Toxoplasma* in cetaceans around the British Isles. *Veterinary Record* 2007;161:279

<sup>48</sup> Forman D, West N, Francis J, Guy E. The sero-prevalence of *Toxoplasma gondii* in British marine mammals. *Mem Inst Cruz* 2009; 104:296-8.

<sup>49</sup> Tenter AM et al. *Toxoplasma gondii*: from animals to humans. *International Journal for Parasitology* 2000; 30: 1217-1258

<sup>50</sup> Innes EA, Bartley PM, Buxton D, Katzer F. Ovine Toxoplasmosis. *Parasitology* 2009; 136: 1887-1894.

<sup>51</sup> Innes EA, Bartley PM, Maley S, Katzer F, Buxton D. Veterinary vaccines against *Toxoplasma gondii*. *Mem Inst Oswaldo Cruz*, Rio de Janeiro, 2009;104(2): 246-251.

of oocysts in the faeces of any of the cats using the McMaster slide technique.<sup>52</sup>

7.45 Globally, the seroprevalence of toxoplasma in cats ranges from 5.4% to 90% and is higher in wild and stray cats than domestic pets. Seroprevalence increases with age, although due to immunity acquired after initial infection it is primarily young kittens that excrete oocysts.<sup>53 54</sup>

7.46 Uncertainty exists as to whether co-infection with Feline Immunodeficiency Virus (FIV) or Feline Leukemia Virus (FeLV) increases the likelihood of infection and/or shedding of oocysts by cats. Three studies suggest that seroprevalence is not greater in cats infected with FIV, while one study shows the opposite. Experimentally, FIV infection does not alter the duration of oocyst excretion or resistance to re-infection. (The seroprevalence of FeLV and FIV in the UK stray cat population has been estimated to be about 3.5% and 10.4% respectively.<sup>55</sup>

7.47 Should an effective vaccine for cats become available this may have a significant effect on the burden of human disease. Development of such a vaccine may be informed by modelling studies.

#### Gaps in current knowledge relevant to a UK risk assessment

7.48 Seroprevalence data for UK-reared livestock is limited and the prevalence of viable parasites in these species is unknown. Indeed an EFSA Opinion published in October 2011 identified *Toxoplasma gondii* as one of the priority targets for official controls on pig meat due to its prevalence and impact on human health.<sup>56</sup>

7.49 The relationship between seropositivity in animals and the number of viable tissue cysts in edible tissue is not known.

7.50 Vaccines based on live attenuated strains of tachyzoites are effective in reducing morbidity in sheep but it is not known whether vaccination has any effect on the formation of tissue cysts.

7.51 Studies in UK wild animals species are currently not able to determine the usefulness of any of these as sentinel species.

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<sup>52</sup> Gethings PM, Stephens GL, Wills JM, Howard P, Balfour AH, Wright AI, Morgan KL. Prevalence of Chlamydia, toxoplasma, toxocara and ringworm in farm cats in south-west England. *Veterinary Record*. 1987; 121: 213-216.

<sup>53</sup> De Craeye S, Francart A, Chabauty J, De Vriendt V, Van Gucht S, Leroux I, Jongert E. Prevalence of *Toxoplasma gondii* infection in Belgian house cats. *Veterinary Parasitology*. 2008; 157: 128–132.

<sup>54</sup> Dubey JP, Jones JL. *Toxoplasma gondii* infection in humans and animals in the United States. *International Journal for Parasitology* . 2008; 38: 1257–1278.

<sup>55</sup> Muirden A. Prevalence of feline leukaemia virus and antibodies to feline immunodeficiency virus and feline coronavirus in stray cats sent to an RSPCA hospital. *Veterinary Record*. 2002; 150(20): 621-625.

<sup>56</sup> <http://www.efsa.europa.eu/en/topics/topic/meatinspection.htm>

## Summary and Conclusions to Section 7

7.52 Susceptibility of intermediate hosts to toxoplasma infection varies according to species. Seroprevalence data indicates that infection is most common in sheep, pigs and wild game. Cattle appear to be relatively resistant to infection.

7.53 Toxoplasma is the second most common cause of infectious abortion affecting sheep in the UK and is a significant cause of economic loss to the UK sheep industry.

7.54 Infection in sheep is usually acquired via oocyst contaminated feed, pasture and water. Sub-clinical congenital infection is rare.

7.55 Initial results from a survey of sheep flocks in Great Britain in 2009 indicate a between flock seroprevalence of 100% and a seroprevalence of approximately 69% at the individual animal level.

7.56 Consumer demand for outdoor reared meat, particularly pork, is likely to result in increased animal exposure to the parasite.

7.57 Serological studies in marine mammals indicate that toxoplasma has entered the marine environment. It is hypothesized that invertebrate species may act as carrier hosts for oocysts.

7.58 There is a very small amount of data on meat contamination in the UK but virtually none on the presence of the parasite in farm animals reared in the UK. However, there are data on farm animal infection in a number of countries from which we obtain meat, which would need to be included in any risk assessment. Further data on seroprevalence in farm animals would also be useful in monitoring the effectiveness of control measures in animal husbandry. Testing of a larger range of meat samples would also be useful in identifying the main sources of risk.

## Recommendations

7.59 Further studies are required to establish seroprevalence in UK livestock species. This data would be useful in the assessment of different husbandry practices on the likelihood of infection and also to inform risk management measures.

7.60 It is recommended that methods are developed to assess the number and distribution of viable tissue cysts in a range of edible tissues.

7.61 Further studies are needed to enable us to relate the outcomes of seroprevalence studies to prevalence and levels of viable tissue cysts in edible tissues (or to determine that this is not practical or possible).

## 8. Food studies

8.1 There is no standardised method for detecting oocysts on or in foods, nor is there a molecular method for detecting viable organisms in meats. Reports of the detection of viable cysts are based on *in vivo* studies.

8.2 *Toxoplasma* has been found in a wide variety of meat from lambs, goats, pigs and game whilst beef appears less commonly contaminated. Based on the available limited evidence in Europe, chicken rarely contains viable cysts (see section 7). The presence of cysts depends on age, time spent indoors, farm hygiene and the tissues concerned (non-skeletal-muscle is more frequently infected than skeletal muscle).

8.3 A summary of bioassay studies from several countries (1956-1981) indicated *Toxoplasma* infection in 13% of 7185 samples of naturally contaminated pork.<sup>57</sup>

8.4 A recent study in the USA showed no evidence of oocysts being shed by cats fed on chicken or beef samples<sup>58</sup> whilst 0.38% of pork samples gave evidence of transmission of infection to cats. Viable *Toxoplasma gondii* has also been found in fresh pork sausages from Brazil<sup>59</sup>.

8.5 PCR studies on a small number of UK meat products gave an overall prevalence of 38%, including 25% of beef samples, 33% of pork samples and 67% of lamb samples. These studies cannot determine cyst viability. In a study of 67 cured meat samples in the UK, viable parasites were found in 1 sample (1.5%).<sup>60</sup>

8.6 Bivalve molluscs are another potential source of foodborne infection. Although there is no direct evidence for this as a source of human infection, toxoplasmosis in sea otters in California, which has resulted in significant mortality, has been linked to their consumption of bivalve molluscs, which had entrapped oocysts in their gills/tissues.

8.7 6/9 (66%) samples of lamb sourced from a butcher in Manchester tested positive for *Toxoplasma* by PCR.<sup>61</sup> These samples were mainly processed meat products and therefore may have contained mixed meat derived from other animals.

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<sup>57</sup> Dubey JP. A review of toxoplasmosis in pigs. *Veterinary parasitology*. 1986; 19: 181-223

<sup>58</sup> Dubey JP, Hill DE, Jones JL et al. Prevalence of viable *Toxoplasma gondii* in beef, chicken and pork from retail meat stores in the United States: Risk assessment to consumers. *J. Parasitol* 2005; 91: 1082-1093

<sup>59</sup> Dias RAF, Navarro IT, Ruffolo BB et al. *Toxoplasma gondii* in fresh pork sausage and seroprevalence in butchers from factories in Londrina, Parana State, Brazil. *Rev. Inst. Med. Trop. S. Paulo* 2005; 47: 185-189

<sup>60</sup> Detection of *Toxoplasma gondii* in cured meats. Warneskulasuriya MR, Johnson JD, Holliman RE. *International Journal of Food Microbiology*, 1998; 45: 211-215

<sup>61</sup> Aspinall TV, Marlee D, Hyde JE, Sims PFG. Prevalence of *Toxoplasma gondii* in commercial meat products as monitored by polymerase chain reaction – food for thought? *International Journal for Parasitology*. 2002; 32: 1193–1199.

## Survival in foods

8.8 Control strategies for food require an understanding of the survival of the key infective stages of *Toxoplasma gondii* (oocysts, tachyzoites and tissue cysts) under different conditions. In general, tissue cysts will be the principal hazard in raw meats, tachyzoites may be a potential hazard in milk, and oocysts may be a hazard on agricultural crops and water.

8.9 Limited data exist on the survival of the organism in foods but the recent AFSSA risk assessment summarised many of the published studies on the survival of the organism under different physico-chemical conditions and these are summarised in the following section and in Table 5.

### 8.10 Unsporulated oocysts:

- Unsporulated oocysts: Sporulation of oocysts occurs within 1-5 days at ambient temperature and therefore oocysts contaminating foods are most likely to be sporulated.
- Notwithstanding this, the effect of temperature on sporulation of oocysts is summarised in Table 4. Dubey<sup>62</sup> reported that unsporulated oocysts were killed by exposure to 37°C for 24 hours.
- Salt does not prevent sporulation of oocysts with sporulation occurring in water at 1.5% and 3.2% NaCl.
- Anaerobic conditions appear to inhibit sporulation of oocysts.

### 8.11 Sporulated oocysts:

- Sporulated oocysts are highly resistant to adverse physico-chemical conditions. (See Table 4 for the effect of temperature.)
- Low pH has little effect on sporulated oocysts, surviving in inorganic acids e.g. sulphuric acid (pH <1) for over a year. Storage in alkali (sodium hydroxide, 6%, pH  $\geq$ 12) inactivated a suspension of oocysts in 24 hours and a 2-log reduction in infectivity was achieved after 1 hour (10% NaOH, pH  $\geq$  12).
- Oocysts survive for long periods in salt water (>6 months at ambient temperature or at 4°C).
- Disinfectants have little or no effect on oocyst viability. Levels of 2, 20 and 200ppm chlorine had no effect on oocyst viability. Ethanol (99%) for 24h has been reported to be required to kill oocysts. Similarly, oocysts were

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<sup>62</sup> Dubey JP, Toxoplasmosis of animals and humans. 2<sup>nd</sup> ed. 2010. CRC Press.

destroyed by a 4 day exposure (but not after 48 hours) to a 10% solution of formalin.

#### 8.12 Tissue cysts:

- Tissue cysts are more susceptible to inactivation by extremes in temperature although they can survive for extended periods at low temperature. Relatively mild pasteurisation is required to destroy tissue cysts and temperatures of 67°C and above will render contaminated meat safe.
- Survival of tissue cysts in the presence of salt (sodium chloride) is variable and dependent on the salt concentration and storage temperature. Salt concentrations of 6% have been found to be lethal to tissue cysts, although low temperatures (4°C) were shown to aid survival with cysts remaining viable for 56 days, 49 days and 21 days in 0.85%, 2% and 3.3% NaCl, respectively.
- Tissue cysts lost infectivity in pork sausages made with 2% and 2.5% salt and stored under refrigeration for 48 hours but not after 24 hours.
- Common curing salts can be effective at rendering tissue cysts non infective based on bioassays. When stored at 4°C, tissue cysts in pork became non infective in a number of curing salt solutions including, for example, the following; sodium tripolyphosphate (0.5%) + sodium chloride (2%) (after 7d, 28d and 45d), sodium chloride (1%) (after 45d but not after 7d or 28d) or sodium lactate (2%) (after 7d, 28d and 45d).

8.13 Bradyzoites, inside tissue cysts, have been reported to lose their infectivity after storage at low pH (<1, HCl) for 2 hours.

#### 8.14 Tachyzoites:

- Limited information is available on the survival of tachyzoites although they are reported to be susceptible to freezing and are destroyed by pasteurisation.
- Low pH (<1, HCl) destroyed tachyzoites after 25 minutes.
- Tachyzoites have been shown to survive for 7 days at 4°C in cow's milk.<sup>8.15</sup> The effect of novel food preparation methods on the viability of toxoplasma has not been studied.

**Table 5: The effect of temperature on toxoplasma<sup>17, 62</sup>**

Infective stage	Controlling factor	Conditions	Effect	Comments	
Oocyst (unsporulated)	High Temperature	60-70°C for 10 seconds	Loss of sporulation	By microscopy	
		55°C for 30s			
		50°C for 10 minutes			
		90°C for 30s	Loss of infectivity		Animal bioassay
		80°C for 1 min			
	Low Temperature	4°C for 6-11 weeks	Inhibition of sporulation	In cat faeces	
-21°C for 1 day		Loss of sporulation			
-6°C for 7d					
Oocysts (sporulated)	High temperature	40°C for 28d	Loss of viability		
		45°C for 1d	Infectivity retained		
		50°C for 1 hour			
		60°C for 1 min	Survival		
		35°C for 32d			
		40°C for 9d			
		45°C for 3d			
	50°C for 1 hour				
	Low temperature	-21°C for 28d	Survival		
		-10°C for 106d	Infectivity retained		
		-5°C for 106d			
		4°C for 18 months			
		4°C for 8wk		On rasp-berries and blackberries	
Tissue cysts	Low temperature	-12°C for 3d	Loss of infectivity	Experi-mentally infected pork – bioassay	
		4°C for 7wk	Infectivity retained	Crushed mouse brain	
		4°C for 3wk		Meat carcasses	
	High temperature	58°C for 9.5min ≥67°C	Loss of viability		
Bradyzoites	High temperature	D <sub>49</sub> 53.5min* D <sub>55</sub> 5.8min D <sub>61</sub> 3.8min	Loss of viability		
Tachyzoites	Low temperature	4°C for 1 week	Survival	Milk	
	High temperature	45°C for 30min	Infectivity retained	Mouse bioassay	
		50°C for 30min	Loss of viability		

\*: D<sub>x</sub> value is the time taken at the specified temperature (x) to reduce the initial population by a factor of 10 or 90% or 1-log unit.

## Gaps in current knowledge relevant to a UK risk assessment

8.16 There is limited data on the prevalence of toxoplasma in foods in the UK and virtually no data on the concentration of food contamination (i.e. level of cysts per gram in food).

8.17 Data are also limited on the survival of toxoplasma in certain foods, particularly salad vegetables and milk. This may be particularly relevant with respect to understanding the effect of washing salad vegetables, during fermentation and ripening of cheeses, particularly those made with raw milk, and various meat curing methods.

## Summary and Conclusions to Section 8

8.18 There is no standardised method for detecting oocysts on or in foods, nor is there a molecular method for detecting viable organisms in foods. Reports of the detection of viable cysts are based on *in vivo* studies.

8.19 Toxoplasma has been found in a wide variety of meats. However based on the available, limited evidence, beef and housed chicken appear less commonly infected, than other meat. This may broadly mirror the findings of studies of a range of live animals (see Section 7).

8.20 Tachyzoites and bradyzoites are relatively fragile whereas oocysts and tissue cysts are relatively resistant to food preparation and processing. Thus washing of salads and vegetables may remove some surface contamination of oocysts, whereas inactivation of the more resistant tissue cyst requires adequate cooking. Curing of meats may be effective in removing viability, depending on the process used. The effect of novel food preparation methods is not established.

## Recommendations

8.21 Notwithstanding the inherent difficulties, it would significantly assist risk assessment if further studies were undertaken to determine the prevalence and/or concentration of toxoplasma contamination in meat and other foods in the UK (see also recommendation 7.60 on method development).

8.22 Studies to assess the effect of a number of microbiological reduction/destruction processes e.g. salad washing, milk fermentation and various meat curing methods on toxoplasma would assist risk assessment. Similarly the effect of novel food preparation methods on the viability of toxoplasma should be assessed.

## 9. Foodborne versus other routes

9.1 The relative role of consumption of cysts in undercooked meat products and intake of oocysts from soil or water contaminated by cat faeces is not known for certain since the source of infection cannot be distinguished from disease manifestations, nor are there widely available laboratory tests to distinguish an infection due to oocysts from one due to tissue cysts.

9.2 A recently published study reports a method that can distinguish recent infection resulting from exposure to sporozoites from recent infection resulting from exposure to tissue cysts<sup>63</sup>. If confirmed this approach may prove useful in discriminating between sources of acute infection in the human population. Utilising this technique one US study reported that more than 70% of infections are related to unrecognized oocyst exposure.<sup>64</sup>

9.3 Some initial pointers may be gained from outbreak data. Of 17 outbreaks reported in a 1993 review<sup>65</sup>, 13 were linked to consumption of raw or rare meat or raw goat's milk. Two of the remaining outbreaks were associated with geophagy, one with inhalation of organisms in a riding stable and one was waterborne. The fact that 24-47% of vegetarians are seropositive also supports the importance of environmental sources of infection, although it is not clear how many of these will have eaten meat or raw goat's milk.

9.4 The main source of information on the relative importance of different routes of transmission comes from case control studies. Four European studies, which show a mixture of food and environmental factors in countries with both low and high seroprevalences, are summarised below. Where available, population attributable fractions (PAF) are quoted which represent the contribution of a risk factor to a disease. They are calculated by determining the proportional reduction in population disease or mortality that would occur if exposure to a risk factor were reduced to an alternative ideal exposure scenario. In other cases, odds ratios (OR) are given which are used to assess the relative risk of a particular disease if a certain exposure is present, they tell you how much more likely it is that someone exposed to a factor will develop the disease as compared to someone not exposed.

9.5 In 1992-1994, a study of 37,000 pregnant women was carried out in Norway<sup>66</sup>, a low prevalence country. A total of 69 maternal infections were identified. The main risk factors identified were consumption of raw or undercooked minced meat (PAF 0.29), consumption of unwashed raw vegetables or fruits (PAF 0.28) and consumption of raw or undercooked

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<sup>63</sup> Hill D, Coss C, Dubey JP et al. Identification of a sporozoite-specific antigen from *Toxoplasma gondii*. *J. Parasitol.* 2011; 97(2): 328-337.

<sup>64</sup> Boyer K, Hill D, Mui Ernest et al. Unrecognized ingestion of *Toxoplasma gondii* oocysts leads to congenital toxoplasmosis and causes epidemics in North America. *Clinical Infectious Diseases.* 2011; 53(11): 1081-9.

<sup>65</sup> Smith JL. Documented outbreaks of toxoplasmosis: transmission of *Toxoplasma gondii* to humans. *Journal of Food Protection*, 1993; 56: 630-639

<sup>66</sup> Kapperud G. et al Risk factors for *Toxoplasma gondii* infection in pregnancy. *American Journal of Epidemiology*, 1995; 144: 405-412

mutton (PAF 0.22). Other significant risk factors all related to food with the exception of cleaning cat litter trays (PAF 0.16).

9.6 A study of pregnancy-associated toxoplasmosis in Naples<sup>67</sup> during the same time period identified a PAF of 0.48 for significant food exposures (eating cured pork and raw meat). Whilst cat ownership was not significantly associated with infection, gardening was a significant factor in the univariate analysis (OR 2.0; 95% CI 1.1 – 3.7) and was thought to merit further investigation.

9.7 A case control study from France<sup>68</sup>, a high prevalence country, published in 1999 and involving 80 cases found that consumption of undercooked beef (OR 5.5; 95% CI 1.1-27) was a significant risk factor whilst consumption of undercooked mutton or lamb had an OR of 3.1 in the multivariate analysis, although this just failed to reach statistical significance at the 5% level (95% CI 0.85-14).

9.8 A European multicentre study<sup>69</sup> carried out in 6 centres in 1994-1995 investigated risk factors in 252 women infected during pregnancy. After controlling for confounding factors, consumption of raw or undercooked beef, lamb and other meats (but not pork) were significant risk factors, giving a PAF of 0.3 – 0.6. Consumption of unpasteurised milk or milk products was significant in the univariate but not in the multivariate analysis. Other significant risk factors were travel (OR 2.33; 95% CI 1.3 - 4.1) and contact with soil (OR 1.81; 95% CI 1.2 – 2.7). However, it should be noted this study failed to consider the role of unwashed salads and vegetables in the transmission of toxoplasmosis.<sup>70</sup>

9.9 Whilst the study showed no difference between the centres with regard to the ORs, there were differences in the PAFs. For example, lamb/other meat was more important in North and Central Europe, whilst salami was more important in Milan, Naples and Brussels (PAF 0.1-0.14) than in Copenhagen, Oslo and Lausanne (0.03 -0.05). Milk was a significant risk factor in Lausanne (0.14) but not in other centres ( $\leq 0.05$ ), whilst soil contact was less important in Italy (0.06-0.07) than elsewhere (0.16-0.17). 14-49% of cases were not explained by the variables that were found to be significant.

9.10 Comparing these results with other data, the authors commented that the attenuation of the pork risk was possibly due to indoor rearing and freezing of meat, that the salami risk may be increased because it contains non-skeletal muscle and may be from older animals farmed outdoors, and that

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<sup>67</sup> Buffolano W. et al Risk factors for recent toxoplasma infection in pregnant women in Naples. *Epidemol. Infect.* 1996; 16; 347-351

<sup>68</sup> Baril L. et al. Control of the risk of human toxoplasmosis transmitted by meat. *International Journal for Parasitology*, 1999; 38: 1359-1370

<sup>69</sup> Cook AJC. et al. Sources of toxoplasma infection in pregnant women: European multicentre case-control study. *BMJ* 2000; 321: 142-7

<sup>70</sup> Commentary: Congenital Toxoplasmosis – Further thought for food. Holliman RE *BMJ* 2000; 321: 147

beef could be important because of the large amounts consumed even if fewer cysts are present.

Summary of evidence for the importance of food as a source of human toxoplasmosis (with acknowledgement to Kijlstra<sup>43</sup>)

9.11 Four large case-control studies have identified consumption of undercooked meat as the most important risk factor for pregnant women with the largest and most geographically comprehensive study estimating it to account for 30-60% of cases. Whilst only a small number of outbreaks have been reported, the majority of these were linked to consumption of raw or undercooked meat or raw goat milk. However, risk factors reflecting environmental contamination were also identified in the case control studies. This, added to the fact that strict vegetarians become infected with toxoplasma, shows that oocyst contamination of the environment can play an important part in infection.

9.12 The observed decline in toxoplasma seroprevalence noted in many developed countries over recent decades has been attributed largely to factors associated with risks from meat. Modern farming systems, including housed management, have resulted in a reduction in the incidence of tissue cysts in meat and more meat is now frozen prior to consumption.

9.13 The occurrence of waterborne outbreaks support a continuing role for oocysts in human infection but a recent study<sup>71</sup> has shown that oocyst contamination of the environment is largely restricted to cat defaecation sites. Moreover, less than 0.9% of cats have been found to actively shed toxoplasma-like oocysts. Although it is generally assumed that raw vegetables are a source of infection in humans, no experimental data are available to support this route of infection. However, one study has shown that berries experimentally spiked with oocysts can transmit toxoplasma infection to mice<sup>72</sup> and consumption of unwashed fruit and vegetables has been found to be a risk factor in one of the case control studies.

Gaps in current knowledge relevant to a UK risk assessment

9.14 The relative contribution of food associated with toxoplasma infection is not well-defined, and not known in the UK.

9.15 Although it is generally assumed that raw vegetables are a source of infection in humans, no experimental data are available to assess this assumption.

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<sup>71</sup> Afonso E et al. Spatial distribution of soil contamination by *Toxoplasma gondii* in relation to cat defaecation behaviour in an urban area. *Int. J. Parasitol.* 2008; 38: 1017-1023

<sup>72</sup> Kniel KE. et al. Examination of attachment and survival of *Toxoplasma gondii* oocysts on raspberries and blackberries. *J. Parasitol.* 2002; 88: 790-793

## Summary and Conclusions to Section 9

9.16 The source of infection cannot be determined from disease manifestations.

9.17 Standard laboratory tests cannot distinguish an infection due to oocysts from one due to tissue cysts. Assays developed more recently may help to address this issue.

9.18 Consumption of undercooked meat is likely to be an important risk factor for pregnant women and immune-compromised groups.

9.19 Oocyst contamination of the environment is an important risk factor in infection.

## Recommendations

9.20 None of the case control studies has involved cases in the UK. Given the variability in seroprevalence across Europe, differences in food handling and consumption, and in climate, a case control study in the UK should be considered. However, it is worth noting that none of the case control studies provides evidence of environmental sources being more important than food as a source of human infection.

9.21 Studies that seek to exploit recently reported methods that can distinguish sporocysts from tissue cysts as source of infection should be considered.

9.22 If a case control or other studies confirm food as an important source of infection and control measures are identified, better data are required on the incidence of human infection and its complications in the UK as a baseline for subsequent comparison.

## 10. Consumer Advice

10.1 Current Government advice<sup>73</sup> to pregnant women and those with immune deficiencies to reduce the risk of becoming infected with toxoplasma is:

- **Wear gloves when gardening, particularly when handling soil.** Also, be sure to wash your hands thoroughly afterwards with soap and hot water.
- **Do not eat raw, or undercooked, meat,** particularly lamb, pork, and venison, including any ready-prepared chilled meals. Cook all red meat until no trace of pinkness remains and the juices run clear, and do not taste meat before it is fully cooked. Wash your hands thoroughly after handling raw meat.
- **Avoid sheep and their newborns** during the lambing season if you are at extra risk. Although unlikely, an infected sheep or its newborn lamb could pass the infection to you at this time.
- **Wash all kitchenware thoroughly** after preparing raw meat.
- **Wash all fruits and vegetables** before cooking and eating, including ready-prepared salads.
- **Avoid un-pasteurised goat's milk** or products that are made from it.
- **Do not handle or adopt stray cats.**
- **Avoid cat faeces in cat litter or soil.** Wear gloves if you are changing a cat litter tray, and if you are pregnant, or immune deficient, ask someone else to do this for you. Wash your hands thoroughly afterwards.
- **Feed your cat dried, or canned, cat food,** rather than raw meat.

10.2 Examples of consumer advice in other countries is shown in Table 6 with full details given in Annex III.

10.3 As most disease in the immune-compromised arises from infection acquired whilst immune-competent, the importance of effective consumer advice for the immune-competent should not be overlooked.

### Conclusions to Section 10

10.4 There is variation in the consumer advice given by different countries.

### Recommendations

10.5 The current UK advice to pregnant women should be reviewed in the light of current knowledge, and the advice given by other countries.

10.6 In reviewing the advice to pregnant women, the need for similar advice for other immune-compromised groups should also be considered. Advice to the immune-competent population should not be ignored.

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<sup>73</sup> On NHS Choices website:

<http://www.nhs.uk/Conditions/Toxoplasmosis/Pages/Prevention.aspx> last accessed 20/4/2011

**Table 6: Summary of advice to consumers on toxoplasmosis and other foodborne pathogens**

The recommendations below represent the common guidance/ advice provided by Austria, Finland, France, Germany, Luxemburg, Ireland, Sweden, Switzerland, the United Kingdom (UK) and the United States (US) to the public. This guidance is targeted at pregnant women and individuals with a weakened immune system to prevent exposure to and infection with a range of pathogens including toxoplasma. Key: • = included in national guidance; clear box = not included in national guidance.

Austria	Finland	France	Germany	Luxemburg	Ireland	Sweden	Switzerland	UK	US	Advice given
<b>Recommended advice in relation to food preparation and consumption</b>										
•	•	•	•	•	•	•		•	•	Wash and/or peel fruits and raw vegetables (including salads) well before use.
•	•	•	•	•	•	•	•	•	•	Wash hands thoroughly with soap and water before and after handling food.
•	•			•						Prepare raw meats, raw eggs and raw vegetables on different work surfaces; do not use the same utensils with raw and cooked foods.
•		•		•		•	•	•	•	Thoroughly clean the work area, cutting boards and utensils immediately after use.
•				•						Keep pets, insects and rodents away from the kitchen and off food.
•	•	•	•	•	•	•	•	•	•	Do not eat raw or incompletely-cooked meat or raw eggs. Always cook these foods thoroughly before eating.
•					•	•				Do not drink unpasteurised (raw) milk or milk products.
•				•		•				Do not eat foods past their expiry date.
				•	•					Cooked food and leftovers should be stored in the fridge and reheated thoroughly before eating.
<b>Recommended advice in relation to food storage</b>										
•				•	•				•	Avoid cross-contamination between raw and ready-to-eat foods in the fridge by keeping them stored separately.
•				•						Clean the refrigerator regularly (once a week is recommended)
•				•						Check the temperature of the refrigerator and the freezer regularly and don't break the cold chain.

Austria	Finland	France	Germany	Luxembourg	Ireland	Sweden	Switzerland	UK	US	Advice given
<b>Recommended advice in relation to personal hygiene</b>										
•	•	•	•	•	•	•		•	•	Regular, thorough hand washing (with soap and water) before and after food preparation, after handling raw meat, after animal contact, after touching soil, sand or cat litter, and after visiting the toilet.
<b>Recommended advice in relation to gardening and cat care</b>										
				•				•	•	Do not feed cats raw meat
•	•	•	•	•	•	•	•	•	•	Wash hands thoroughly after contact with animals
			•					•	•	Avoid contact with cat faeces
		•		•				•	•	Have someone else (who is not in the vulnerable group) change the litter box. If you have to clean it wear disposable gloves and wash your hands thoroughly with soap and warm water afterwards
		•						•		Cat litter should be changed daily
				•		•		•	•	Wear gloves when gardening, touching soil or handling sand from a sandbox. Wash your hands with soap and warm water afterwards

## Summary

It is widely recommended (by the majority of the countries outlined) that basic hygiene measures are strictly followed, that pregnant women and immunosuppressed individuals avoid contact with any materials which could be contaminated with cat faeces such as cat litter, garden soil and sand boxes. If contact with these materials is unavoidable it is recommended that protective clothing such as gloves are worn. It is advised that meat should always be well cooked and that raw or incompletely-cooked meat and unpasteurised milk or milk products should not be consumed. Raw meat products should be stored at the correct temperatures and separated from ready-to-eat foods to prevent cross contamination. Fruits, salads and vegetables should be washed and/or peeled before consumption and expiration dates should be followed.

## Advice not reiterated in other text

Some of the advice provided by certain countries was not reiterated in the guidance provided by others, these solitary suggestions are outlined below:

- Austria advised pregnant women not to consume raw seafood, Mettwurst and fermented sausages, sliced sausage packaged in foil,

cold smoked/fermented fish. Austria also advised pregnant women not to consume soft or lubricated cheese, or at least remove the rind before consumption and that after hand washing clean towels, possibly single use towels, should be used for drying hands.

- The US advised that pregnant women should avoid stray cats, not get a new cat during pregnancy, ensure indoor cats remain indoors and should remain especially cautious if outdoor cats are brought indoors. It was also advised that sandboxes were covered and that untreated water should not be consumed, particularly when travelling in less-developed countries.
- Sweden advised pregnant women to avoid mould- ripened or washed rind cheese, even if it is made of pasteurised milk, giving examples such as brie, gorgonzola, chèvre, vacherol and taleggio. It was advised however, that cheese used in cooking that has been heated until it is bubbling is quite safe to eat. It was advised that only newly made or newly packaged Gravad, smoked fish and sushi products should be consumed and that dried, cold-smoked or gravat meat, such as Parma ham or salami should be frozen for three days before eating.
- Finland advised that irrigation water quality has to be perfect and that wild and domestic animal access to growing areas and surface water should be restricted to prevent contamination.
- France advised that microwaving food does not guarantee that the parasite has been destroyed effectively and that litter trays should be cleaned using boiling water as bleach does not provide any extra guarantee.
- Germany advised that food with clumps of earth attached, like potatoes and carrots should be stored separately from other foods.
- The UK advised avoiding unpasteurised goat's milk and milk products and avoiding sheep and their newborns during the lambing season.

## 11. Summary of Data Gaps, Conclusions and Recommendations

### Data gaps

11.1 The overall surveillance of cases of clinical toxoplasmosis in the UK is sub-optimal such that any current risk assessment must be based largely on estimates rather than reports of disease.

11.2 The accuracy of current reporting of incidence of congenital toxoplasmosis is not confirmed. In particular, routine surveillance is based primarily upon cases where either the pregnant mother or child is symptomatic. Detection rates among the asymptomatic, which probably account for the majority of congenital infections, are likely to be low.

11.3 Maternal infection rate, mother-to-foetus transmission rate and rate of disease affection of neonates & infants in the UK have not been studied systematically. Overall, the health costs of congenital toxoplasmosis have not been accurately estimated.

11.4 The relative contribution of congenital and acquired toxoplasma infection to the burden of ocular disease is uncertain. There is some evidence to suggest racial differences in the prevalence of ocular toxoplasmosis but this has not been adequately explored. In this context, it is not known if these racial differences reflect genetic susceptibility to infection or variation in the virulence of endemic strains of *T. gondii*. The health costs of ocular toxoplasmosis in the UK have not been accurately defined.

11.5 The current incidence of organ-graft associated toxoplasmosis is likely to be low and may be reducing but the actual numbers are not recorded.

11.6 The incidence of HIV associated toxoplasmosis may have fallen with the introduction of HAART, anti-parasitic prophylaxis and maintenance therapy after an acute disease episode but there has been no systematic national study.

11.7 The current incidence of behavioural change associated with toxoplasma is unknown.

11.8 The relative importance of toxoplasmosis in terms of disease burden and compared to other food-borne pathogens is not well established.

11.9 Seroprevalence data for UK-reared livestock is limited and the prevalence of viable parasites in these species is unknown. Indeed an EFSA Opinion published in October 2011 identified *Toxoplasma gondii* as one of the priority targets for official controls on pig meat due to its prevalence and impact on human health.<sup>74</sup>

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<sup>74</sup> <http://www.efsa.europa.eu/en/topics/topic/meatinspection.htm>

11.10 The relationship between seropositivity in animals and the number of viable tissue cysts in edible tissue is not known.

11.11 Vaccines based on live attenuated strains of tachyzoites are effective in reducing morbidity in sheep but it is not known whether vaccination has any effect on the formation of tissue cysts.

11.12 Studies in UK wild animals species are currently not able to determine the usefulness of any of these as sentinel species.

11.13 There is limited data on the prevalence of toxoplasma in foods in the UK and virtually no data on the concentration of food contamination (i.e. level of cysts per gram in food).

11.14 Data are also limited on the survival of toxoplasma in certain foods, particularly salad vegetables and milk. This may be particularly relevant with respect to understanding the effect of washing salad vegetables, during fermentation and ripening of cheeses, particularly those made with raw milk, and various meat curing methods.

11.15 The relative contribution of food associated with toxoplasma infection is not well-defined, and not known in the UK.

11.16 Although it is generally assumed that raw vegetables are a source of infection in humans, no experimental data are available to assess this assumption.

## **Conclusions**

11.17 Other than pregnant women, most infections of the immune competent are asymptomatic or associated with only a mild to moderate, self-limiting illness. However, severe disease can occur in immunocompromised individuals such as the foetus, organ graft recipients and individuals with AIDS or cancer.

11.18 Accurate figures are not available but it is estimated that 350,000 people become infected with toxoplasma each year in the UK, of which 10-20% are symptomatic.

11.19 Based on seroprevalence studies among UK blood donors, levels of toxoplasma infection within the UK appear to fall within the range of those reported elsewhere in Europe and North America.

11.20 It appears that geographical variation in levels of toxoplasma infection may occur within the UK. This has implications for the comparison and extrapolation of individual local studies.

11.21 Toxoplasmosis is a notifiable disease in Scotland but neither a notifiable nor reportable disease in the rest of the UK. Routine surveillance data alone

are unlikely to provide an accurate measure of overall incidence. This may be the case particularly in the immunocompetent since the self-limiting and mild to moderate nature of the resulting illness in this group may result in many infected individuals not being identified by the healthcare system.

11.22 Toxoplasmosis in vulnerable clinical groups is, however, typically more severe and often requires specialist investigation. Thus, while reporting of such cases is still likely to result in an underestimate of incidence, such cases are more likely to be reported.

11.23 Although the majority of cases of toxoplasmosis will occur in the immunocompetent, the largest burden of disease is likely to be associated with infection of immunocompromised individuals among whom symptoms are more severe and potentially life-threatening.

11.24 The lack of accurate data for overall incidence and severity of symptoms associated with toxoplasma infection is a barrier to achieving accurate estimates of burden of disease and economic impact in the UK.

11.25 There are some data indicating a sharp decrease in the prevalence of toxoplasma over the last 40 years in some countries but there are no accurate trend data for the UK.

11.26 The relative contribution of foodborne routes is important and is considered in Section 9.

11.27 Susceptibility of intermediate hosts to toxoplasma infection varies according to species. Seroprevalence data indicates that infection is most common in sheep, pigs and wild game. Cattle appear to be relatively resistant to infection.

11.28 Toxoplasma is the second most common cause of infectious abortion affecting sheep in the UK and is a significant cause of economic loss to the UK sheep industry.

11.29 Infection in sheep is usually acquired via oocyst contaminated feed, pasture and water. Sub-clinical congenital infection is rare.

11.30 Initial results from a survey of sheep flocks in Great Britain in 2009 indicate a between flock seroprevalence of 100% and a seroprevalence of approximately 69% at the individual animal level.

11.31 Consumer demand for outdoor reared meat, particularly pork, is likely to result in increased animal exposure to the parasite.

11.32 Serological studies in marine mammals indicate that toxoplasma has entered the marine environment. It is hypothesized that invertebrate species may act as carrier hosts for oocysts.

11.33 There is a very small amount of data on meat contamination in the UK but virtually none on the presence of the parasite in farm animals reared in the UK. However, there are data on farm animal infection in a number of countries from which we obtain meat, which would need to be included in any risk assessment. Further data on seroprevalence in farm animals would also be useful in monitoring the effectiveness of control measures in animal husbandry. Testing of a larger range of meat samples would also be useful in identifying the main sources of risk.

11.34 There is no standardised method for detecting oocysts on or in foods, nor is there a molecular method for detecting viable organisms in foods. Reports of the detection of viable cysts are based on *in vivo* studies.

11.35 *Toxoplasma* has been found in a wide variety of meats. However based on the available, limited evidence, beef and housed chicken appear less commonly infected, than other meat. This may broadly mirror the findings of studies of a range of live animals (see Section 7).

11.36 Tachyzoites and bradyzoites are relatively fragile whereas oocysts and tissue cysts are relatively resistant to food preparation and processing. Thus washing of salads and vegetables may remove some surface contamination of oocysts, whereas inactivation of the more resistant tissue cyst requires adequate cooking. Curing of meats may be effective in removing viability, depending on the process used. The effect of novel food preparation methods is not established.

11.37 The source of infection cannot be determined from disease manifestations.

11.38 Standard laboratory tests cannot distinguish an infection due to oocysts from one due to tissue cysts. Assays developed more recently may help to address this issue.

11.39 Consumption of undercooked meat is likely to be an important risk factor for pregnant women and immune-compromised groups.

11.40 Oocyst contamination of the environment is an important risk factor in infection.

11.41 There is variation in the consumer advice given by different countries.

## **Recommendations**

11.42 We note that the current data on prevalence and burden of disease are incomplete and we recommend that consideration is given as to how the existing data gaps regarding both the prevalence and burden of disease can be addressed.

11.43 A number of risk assessments or risk profiles have been produced but all highlight a number of data gaps and the difficulty in filling them. There is, however, general agreement that the costs of the relatively small proportion of cases with severe disease make toxoplasmosis one of the most costly of gastro-intestinal infections. Whilst there are not enough data to carry out a full assessment of the burden of disease in the UK, it seems reasonable to proceed on the basis of the assessments made in the USA and Netherlands. This would justify further work to assess the importance of the foodborne route, to identify the most important risks and appropriate risk management measures, and to refine the burden of disease assessment.

11.44 The disease burden associated with toxoplasmosis in the UK mainly reflects infection of immune-compromised individuals including the unborn child. Consequently, risk management strategies could be focused on relevant sub-populations. However, as healthy individuals may go on to become immune-compromised later in life it is also important to consider the potential burden of latent infection of the immune-competent population.

11.45 Further studies are required to establish seroprevalence in UK livestock species. This data would be useful in the assessment of different husbandry practices on the likelihood of infection and also to inform risk management measures.

11.46 It is recommended that methods are developed to assess the number and distribution of viable tissue cysts in a range of edible tissues.

11.47 Further studies are needed to enable us to relate the outcomes of seroprevalence studies to prevalence and levels of viable tissue cysts in edible tissues (or to determine that this is not practical or possible).

11.48 Notwithstanding the inherent difficulties, it would significantly assist risk assessment if further studies were undertaken to determine the prevalence and/or concentration of toxoplasma contamination in meat and other foods in the UK (see also 7.60 on method development).

11.49 Studies to assess the effect of a number of microbiological reduction/destruction processes e.g. salad washing, milk fermentation and various meat curing methods on toxoplasma would assist risk assessment. Similarly the effect of novel food preparation methods on the viability of toxoplasma should be assessed.

11.50 None of the case control studies has involved cases in the UK. Given the variability in seroprevalence across Europe, differences in food handling and consumption, and in climate, a case control study in the UK should be considered. However, it is worth noting that none of the case control studies provides evidence of environmental sources being more important than food as a source of human infection.

11.51 Studies that seek to exploit recently reported methods that can distinguish sporocysts from tissue cysts as source of infection should be considered.

11.52 If a case control or other studies confirm food as an important source of infection and control measures are identified, better data are required on the incidence of human infection and its complications in the UK as a baseline for subsequent comparison.

11.53 The current UK advice to pregnant women should be reviewed in the light of current knowledge, and the advice given by other countries.

11.54 In reviewing the advice to pregnant women, the need for similar advice for other immune-compromised groups should also be considered. Advice to the immune-competent population should not be ignored.

**Ad Hoc Group on Vulnerable Groups: Membership**

**Chair:**

Professor Tom Humphrey (to February 2011)

Dr Richard Holliman (from February 2011)

**Members:**

Mr John Bassett

Professor John Coia

Mr Alec Kyriakides (to March 2011)

Dr Richard Holliman

Professor Paul Hunter (to March 2011)

Mrs Jenny Morris

**Co-opted Members:**

Dr Edward Guy (Public Health Wales)

Mr Paul Hutchinson (AHVLA)

**Assessor:**

Mr Stephen Wyllie (Defra)

**Secretariat**

Mr Adekunle Adeoye

Ms Sarah Butler

Dr Darren Cutts (to June 2010)

Dr Sophie Rollinson (from September 2010)

**Acknowledgements**

The Group wishes to thank Dr Judith Hilton for her original report and Miss Jodie Crabb (Defra) for her assistance in producing Table 6.

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Table 6: Summary of advice to consumers on toxoplasmosis and other foodborne pathogens

**Examples of advice to consumers on toxoplasmosis  
Annex III**

Country	Vulnerable Group	Advice	Website
Austria	Pregnant women	<p><b>Home cooking hygiene and general hygiene rules:</b></p> <ul style="list-style-type: none"> <li>• regular, thorough hand washing before and after preparing food, after animal contact and after visiting the toilet</li> <li>• use of clean towels, possibly single use towels, for drying hands</li> <li>• preparation of meat, raw eggs and raw vegetables on different, preferably smooth working surfaces; thorough cleaning of the work area immediately after use</li> <li>• avoid cross-contamination in the refrigerator. Store raw foods separately from ready to eat foods</li> <li>• Clean the refrigerator 1 x week</li> <li>• Don't break the cold chain and check refrigerator and freezer temperatures regularly</li> <li>• Do not consume food beyond its expiration or consumption date</li> <li>• Throw away mouldy food</li> <li>• Generally keep pets away from the kitchen area</li> </ul> <p><b>Take special care with certain foods:</b></p> <ul style="list-style-type: none"> <li>• No raw or incompletely-cooked meat (such as carpaccio, beef tartare, medium steak)</li> <li>• No raw milk or raw milk products and otherwise boil it before consumption</li> <li>• no food that contains raw eggs, like homemade tiramisu</li> <li>• no soft or lubricated cheese, otherwise remove the rind before consumption</li> <li>• No Mettwürste and fermented sausages (salami)</li> <li>• no sliced sausage packaged in foil</li> <li>• No cold smoked/fermented fish (marinated salmon)</li> <li>• No raw seafood (oysters, sushi)</li> <li>• Thoroughly wash fruit, vegetables and salads</li> </ul>	<a href="http://www.ages.at/">http://www.ages.at/</a>

Finland	Risk groups include pregnant women or those whose immunity is impaired because of illness.	<ul style="list-style-type: none"> <li>• Wild and domestic animal access to growing areas, as well as contamination of surface water contamination, must be prevented.</li> <li>• Irrigation water quality has to be perfect.</li> <li>• Root vegetables should be washed thoroughly with clean water.</li> <li>• Meat should be carefully cooked until done.</li> <li>• In particular take care of good hand hygiene, for example, after touching a cat.</li> </ul>	<a href="http://www.evira.fi">http://www.evira.fi</a>
France		<p>Some basic rules of hygiene must be applied to limit the risk of food and hand contamination. These include:</p> <ul style="list-style-type: none"> <li>• washing of hands with brushing under nails before and after handling food, after gardening or touching objects spattered with soil</li> <li>• washing of raw vegetables to eliminate all traces of soil</li> <li>• careful washing of worktops and utensils used after handling of foodstuffs</li> <li>• sufficient cooking of (red or white) meat before consumption: for red meat, this means that it turns a beige-pink colour in the internal part (temperature exceeds 68°C). Microwaving food does not guarantee that the parasite has</li> </ul>	<a href="http://www.afssa.fr">http://www.afssa.fr</a>

		<p>been destroyed effectively.</p> <p>In case there is a cat at home, have its litter washed daily with boiling water, preferably by someone else than the pregnant woman, or wearing gloves. Bleach does not provide an extra guarantee when cleaning the cat litter. Cat scratches are not at-risk.</p>	
Germany	Individuals with a weakened immune system and pregnant women who have no antibodies to toxoplasmins:	<ul style="list-style-type: none"> <li>• Do not eat any raw sausage or meat products (minced meat, carpaccio, smoked sausage, smooth textured sausage, salami); thoroughly cook meat dishes.</li> <li>• Carefully rinse, peel and/or cook raw fruit and vegetables prior to consumption.</li> <li>• Store food with clumps of earth attached, like potatoes and carrots, separately</li> </ul>	<a href="http://www.bfr.bund.de">http://www.bfr.bund.de</a>

		<p>y from other foods.</p> <ul style="list-style-type: none"> <li>• Avoid contact with cat faeces.</li> <li>• Wash hands frequently.</li> </ul>	
Luxembourg	Advice to pregnant women on listeriosis and toxoplasmosis	<p><b>Good hygiene practices:</b></p> <p><b>1. Clean</b></p> <ul style="list-style-type: none"> <li>• Wash fruits and raw vegetables well.</li> <li>• Wash hands and utensils after handling food.</li> </ul> <p><b>2. Separate</b></p> <ul style="list-style-type: none"> <li>• Separate raw foods from cooked foods.</li> <li>• Prepare raw meats separately from fruit and vegetables.</li> <li>• Do not use the same utensils with raw foods and cooked foods.</li> <li>• Keep pets, flies and other insects, and rodents off food.</li> </ul> <p><b>3. Cook</b></p> <ul style="list-style-type: none"> <li>• Cook well right through raw foods of animal origin (meat, eggs, offal ...).</li> <li>• Eat prepared food and leftovers as soon as possible and preferably after cooking (&gt; 60°C throughout).</li> </ul> <p><b>4. Cool</b></p> <ul style="list-style-type: none"> <li>• Keep food out of the danger zone, &lt;4°C or &gt; 60°C.</li> <li>• Refrigerate food promptly.</li> <li>• Clean the fridge regularly.</li> <li>• Respect consumption deadlines.</li> </ul> <p><b>What can I do to prevent toxoplasmosis?</b></p>	<a href="http://www.securite-alimentaire.public.lu">http://www.securite-alimentaire.public.lu</a>

		<ul style="list-style-type: none"> <li>• Observe the same good hygiene practices as those set for listeriosis. [above]</li> <li>• Avoid changing cat litter and gardening or at least, wear gloves.</li> <li>• Wash hands after contact (petting ...) with cats and dogs.</li> <li>• Do not feed the cat with raw meat.</li> </ul>	
Ireland	<p>General advice for avoiding disease from farm animals:- Many of the diseases listed below do not usually cause serious illness in healthy adults, however, they can be extremely serious in certain groups of people including:</p> <ul style="list-style-type: none"> <li>• very young and elderly people</li> <li>• people with suppressed immune systems</li> <li>• pregnant women.</li> </ul> <p>Common diseases that can be transferred from animals to humans include:</p> <ul style="list-style-type: none"> <li>• <i>Salmonella</i></li> <li>• <i>Campylobacter</i></li> <li>• Verocytotoxigenic <i>E. coli</i> (VTEC), including <i>E.coli</i> O157</li> <li>• Listeria</li> <li>• Toxoplasmosis, Leptospirosis, Q Fever, Brucellosis, Cryptosporidiosis, Tuberculosis</li> </ul>	<p><b>Personal Hygiene</b> Hands should always be washed thoroughly with soap and water:</p> <ul style="list-style-type: none"> <li>• after contact with animals</li> <li>• after going to the toilet</li> <li>• after handling raw meat</li> <li>• before food preparation.</li> </ul> <p><b>Good Food Practices</b></p> <ul style="list-style-type: none"> <li>• Food should be cooked thoroughly.</li> <li>• Uneaten cooked food should be stored in the fridge.</li> <li>• Raw and cooked foods should be kept separate when refrigerated.</li> <li>• Stored cooked food should be reheated thoroughly before eating.</li> <li>• Raw fruit and vegetables should be washed before eating.</li> <li>• Milk should be pasteurised.</li> <li>• Do not drink raw milk.</li> </ul>	<a href="http://www.fsai.ie">http://www.fsai.ie</a>

Sweden	(TB). Pregnant women Advice to reduce the risk of being infected by <i>listeria</i> and toxoplasma:	<ul style="list-style-type: none"> <li>• Keep chilled foods cold, preferably at +4°C in the refrigerator.</li> <li>• Gravad, smoked fish and sushi: eat newly made or newly packaged products. Check the packaging date.</li> <li>• Do not eat raw meat. Mincemeat, poultry, lamb, pork and game should be well done.</li> <li>• Avoid sliced sandwich fillings and cold ready-made food towards the end of their best-before date.</li> <li>• If you want to eat dried, cold-smoked or gravat meat, such as parma ham or salami – freeze it for three days before you eat it.</li> <li>• Avoid cheese made from unpasteurised milk. Also avoid mould- ripened or washed rind cheese even if it is made of pasteurised milk, for example brie, gorgonzola, chèvre, vacherol and taleggio. Cheese used in cooking that has been heated until it is bubbling is quite safe to eat.</li> <li>• Wash your hands before starting to</li> </ul>	<a href="http://www.sva.se">http://www.sva.se</a> .
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		<p>prepare food, between different raw materials and after working in the garden. Wash the cutting board and cooking utensils between different foods.</p> <ul style="list-style-type: none"> <li>• Wash fruit and vegetables.</li> </ul> <p>The toxoplasma parasite can also be spread through cat faeces.</p>	
Switzerland	Pregnant women	<p>For safety reasons pregnant women should give up consumption of raw (eg Tartarbrötchen) or insufficiently cooked/fried (bloody) meat (especially beef, lamb, poultry or game). Similarly, hands and utensils should always be thoroughly washed after handling raw meat or offal. Cat handlers should pay attention to good hand hygiene, particularly during pregnancy. Since neither a drug able to prevent transmission to the child nor symptoms in children is available, a diagnosis or treatment of infection during pregnancy is not helpful.</p>	<a href="http://www.bag.admin.ch">http://www.bag.admin.ch</a>
UK	General advice but highlighting the need for pregnant women and those with immune deficiencies to take extra precautions	<ul style="list-style-type: none"> <li>• <b>Wear gloves when gardening, particularly when handling soil.</b> Also, be sure to wash your hands thoroughly afterwards with soap and hot water.</li> </ul>	<a href="http://www.nhs.uk/Conditions/Toxoplasmosis/Pages/Prevention.aspx">http://www.nhs.uk/Conditions/Toxoplasmosis/Pages/Prevention.aspx</a>

		<ul style="list-style-type: none"> <li>• <b>Do not eat raw, or undercooked, meat</b>, particularly lamb, pork, and venison, including any ready-prepared chilled meals. Cook all red meat until no trace of pinkness remains and the juices run clear, and do not taste meat before it is fully cooked. Wash your hands thoroughly after handling raw meat.</li> <li>• <b>Avoid sheep and their newborns</b> during the lambing season if you are at extra risk. Although unlikely, an infected sheep or its newborn lamb could pass the infection to you at this time.</li> <li>• <b>Wash all kitchenware thoroughly</b> after preparing raw meat.</li> <li>• <b>Wash all fruits and vegetables</b> before cooking and eating, including ready-prepared salads.</li> <li>• <b>Avoid unpasteurised goat's milk</b> or products that are made from it.</li> <li>• <b>Do not handle or adopt stray cats.</b></li> <li>• <b>Avoid cat faeces in cat litter or soil.</b> Wear gloves if</li> </ul>	
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		<p>you are changing a cat litter tray, and if you are pregnant, or immune deficient, ask someone else to do this for you. Wash your hands thoroughly afterwards.</p> <ul style="list-style-type: none"> <li>• <b>Feed your cat dried, or canned, cat food</b>, rather than raw meat.</li> </ul>	
US	Pregnant women	<p>You and your family should:</p> <ul style="list-style-type: none"> <li>• Wash your hands with soap and warm water <i>after</i> touching soil, sand, raw meat, cat litter, or unwashed vegetables.</li> <li>• Wash all cutting boards and knives thoroughly with soap and hot water <i>after</i> each use.</li> <li>• Thoroughly wash and/or peel all fruits and vegetables before eating them.</li> <li>• Separate raw meat from other foods in your grocery shopping cart, refrigerator, and while preparing and handling foods at home.</li> <li>• Cook meat thoroughly. The internal temperature of the meat should reach 160°F (71°C). Use a food thermometer to</li> </ul>	<a href="http://www.fda.gov/food">http://www.fda.gov/food</a>

		<p>check.</p> <ul style="list-style-type: none"> <li>• Don't sample meat until it's cooked.</li> <li>• Avoid drinking untreated water, particularly when travelling in less-developed countries.</li> </ul> <p><b>Cats</b></p> <ul style="list-style-type: none"> <li>• If possible, have someone else change the litter box. If you have to clean it, wear disposable gloves and wash your hands thoroughly with soap and warm water afterwards.</li> <li>• Change the litter box daily. The parasite doesn't become infectious until one to five days after it's shed in the feces.</li> <li>• Wear gloves when gardening in a garden or handling sand from a sandbox because cats may have excreted feces in them. Be sure to wash your hands with soap and warm water afterwards.</li> <li>• Cover outdoor sandboxes to prevent cats from using them as litter boxes.</li> <li>• Feed your cat commercial dry or canned food. <i>Never</i> feed your cat raw meat because it can be a source of the</li> <li>• <i>T. gondii</i></li> </ul>	
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		<p>parasite.</p> <ul style="list-style-type: none"><li>• Keep indoor cats indoors. Be especially cautious if you bring outdoor cats indoors.</li><li>• Avoid stray cats, especially kittens.</li><li>• Don't get a new cat while you're pregnant.</li></ul>	
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**Glossary**

Aetiology	The cause or origin of a disease
Asymptomatic	Without symptoms
Atoxoplasma	A genus of protozoa
Bradyzoites	The crescent-shaped stage of toxoplasma found in tissues
Chorioretinitis	An inflammatory condition of the choroid and retina of the eye, usually as a result of parasitic or bacterial infection.
Congenital	Existing at or before birth
Definitive host	An organism in which a parasite develops to an adult or sexually mature stage
Encephalitis	Inflammation of the brain
Enzyme	A protein that acts as a catalyst
Epithelial	Pertaining to or involving the outer layer of the skin
Gamete	A sexual reproductive cell
Geophagy	Ingestion of soil
Hepatocyte	A liver cell
Hodgkin's disease	A type of cancer involving enlargement of the lymph nodes, spleen, and liver
Hydrocephalus	An abnormal accumulation of cerebrospinal fluid within the skull
Immunocompetent	Being able to resist infection
Immunocompromised	Used to describe someone who has an impaired immune system – usually due to treatment or underlying illness.
Intracranial	Within or on the surface of the brain
Intrauterine	Within the womb

Lymphadenopathy	Chronic abnormal enlargement of the lymph nodes
Mustelids	Of the mammal family <i>Mustelidae</i> which includes stoats, weasels, otters and badgers
Odds Ratio	A statistical calculation used to assess the risk of a particular disease if a certain exposure is present
Oocyst	The structure in which sporozoites are formed
Parasite	An organism that lives in or on another organism
Pathogen	Organism able to cause disease/illness
Parasitaemia	The presence of parasites in the blood
Pepsin	An enzyme which breaks down proteins in acid solution to form peptides
Pneumonitis	Inflammation of the lungs
Prophylaxis	Treatment to prevent or control the spread of disease
Proteolytic enzyme	An enzyme that aids the breakdown and assimilation of proteins
Protozoan	A class of one-celled organisms
Population Attributable Fraction	A statistical calculation used to represent the contribution of a risk factor to a disease
Retinochoroiditis	Inflammation of the eye (the retina and choroid)
Sabin-Feldman dye test	A blood test used to detect antibodies to <i>Toxoplasma gondii</i>
Sarcocystis	A genus of parasitic protozoa
Sequelae	Condition resulting from a former illness
Seroconversion	The development of antibodies in the blood in response to immunization or infection
Seroprevalence	A measure of the occurrence of a disease within a defined population, measured by

	blood testing
Seropositivity	Having a positive reaction to a blood test showing the presence of disease
Sporozoites	Cells which form the infective stage of certain protozoa following reproduction
Sporulation	The formation of spores or sporozoites
Tachyzoites	The stage of toxoplasma present within host tissues
Toxoplasmosis	Disease caused by the parasite <i>Toxoplasma gondii</i>
Viscera	The internal organs of the body

### Abbreviations

AFSSA	Agence Française de Sécurité Sanitaire des Aliments
CD4	Cluster of differentiation 4. (A receptor for HIV, enabling the virus to gain entry into its host)
CI	Cumulative Incidence (a measure of disease frequency during a period of time)
CNS	Central Nervous System
EFSA	European Food Safety Authority
FIV	Feline immunodeficiency virus
FeLV	Feline leukemia virus.
HAART	Highly Active Antiretroviral Therapy
IgG	Immunoglobulin G (A group of antibodies against certain viral infections that circulate in the blood)
NaCl	Sodium chloride
NaOH	Sodium hydroxide
OR	Odds ratio

PAF

Population attributable fraction

PCR

Polymerase Chain Reaction