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FRENCH FOOD SAFETY AGENCY

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Toxoplasma gondii

Nature and habitat

Main microbiological characteristics

Toxoplasma gondii is an obligate intracellular parasite. The parasite cycle consists of asexual multiplication, which occurs in the various tissues in homeotherms (mammals, birds), called intermediate hosts, and sexual multiplication, that occurs in the gut wall of cats and some other felidae (definitive hosts). Cats excrete oocysts in their faecal matter but these are not directly infectious when excreted, but become so after sporulation (1 to 5 days) and are then a potential source of contamination for intermediate hosts by ingestion. In the intermediate host, the oocysts are lysed in the intestine and release sporozoites, which are rapidly disseminated throughout the blood stream after conversion into tachyzoites. After the brief presence of the parasite in the blood for a few days, the parasites (in the form of bradyzoites) encyst in the tissues, particularly the striated muscles and the brain. Once ingested, the latter can contaminate the definitive host or a new intermediate host. Three main genotypes of *T. gondii* have been identified: all of them can infect humans, but there is a marked predominance of genotype II in mainland France.

Zoonotic character[1]

Toxoplasmosis is a zoonosis affecting cats and a few other felidae as definitive hosts and all homeotherms (mammals, birds) as intermediate hosts. The prevalence of toxoplasmosis is very variable depending on the species; however, it is always greater in sheep, goats and pigs from small-holdings than it is for other domestic animals: cattle, poultry, dogs and horses. Intensive farming helps reduce this prevalence, particularly in pigs.

Humans become contaminated by ingesting tissue cysts present in meat products from infected mammals (including game) and birds, or oocysts from the faecal matter of an infected cat and soiling vegetables, fruit and hands. Contamination due to ingestion of raw milk (containing tachyzoites) is possible but exceptional. The respective proportion of contamination from meat products (cysts) or vegetables (and water) is unknown.

Although cats play a major role in spreading the parasite, severe "case-control" studies have shown that having a cat is not a risk factor. This does not obviate the need to follow the hygiene measures outlined at the end of this document.

Reservoir

The parasite reservoir is both animal (cat and other felidae as definitive hosts, warm-blooded animals as intermediate hosts) and telluric, even hydric, due to the dispersion of oocysts in the environment.

Human disease

Symptomatic forms and asymptomatic infectious forms. Epidemic character

In humans, toxoplasmosis is usually a mild or asymptomatic infection. Severe forms are predominantly observed in the event of congenital infection, in immunocompromised patients and on the basis of the virulence of the infecting strains.

In the event of contamination occurring in a pregnant woman having previously tested negative for infection, there is a risk of mother-foetus transmission and congenital toxoplasmosis. The risk of transmission of the parasite increases with the age of the pregnancy at the time of maternal infection. The severity of foetal infection evolves in the opposite way. During the first three months of pregnancy, foetal infection occurs in less than 6% of cases but leads, in the majority of cases, to foetal loss or a severe form. Conversely, in the last 3 months of pregnancy, transplacental passage occurs in 80% of

(1) *Zoonosis: an infectious disease that can be transmitted from vertebrate animals to humans and vice-versa under natural conditions.*

cases and generally leads to sub-clinical infection. The clinical signs of congenital toxoplasmosis are very varied (neurological, ocular mainly) and of variable severity depending on the time of transmission: ocular lesions have an unpredictable potential to worsen throughout the individual's lifetime.

In immunocompromised patients (AIDS, bone marrow transplants, mainly) cerebral and ocular complications are the most common; these are usually due to reactivation of an infection acquired before the immunodepression.

In the absence of any immunodepression, severe forms can exceptionally be observed with strains with a specific genotype and virulence.

Toxoplasmosis is, above all, endemic, and sometimes epidemic. Twenty episodes of clustered cases of toxoplasmosis were recorded worldwide between 1965 and 2001. A foodborne source was established in 13 cases and a water source in 3. The number of individuals infected during these episodes is usually low (2 to 37). Two large epidemics attributed to drinking water occurred in Canada (5,000 cases in 1995) and Brazil (294 cases in 2002).

Human contamination methods other than by food and risk of secondary human-to-human transmission

There is no risk of human-to-human transmission of toxoplasmosis (apart from congenital toxoplasmosis). Accidental contamination in the laboratory is possible when handling parasites.

High-risk populations

Pregnant women testing negative to toxoplasmosis are exposed to a risk of contamination during pregnancy. Poor hand hygiene, the eating of undercooked meat and incorrectly washed raw vegetables are the main risk factors for acquiring toxoplasmosis.

The persistence of encysted parasites throughout the lifetime of the host maintains immunity against fresh infection.

Immunocompromised patients testing positive for toxoplasmosis are exposed to a risk of reactivation of their infection in the event of deficiency in cellular immunity (CD4 count < 100/mm^3).

Dose-effect and dose-response relationships

In humans, no dose-infection relationship study has been conducted and no ID50 or LD50 values have been determined. In animals, several studies have evaluated the infectiousness or virulence of different strains of *T. gondii*, but very few have done so with a sufficiently extensive inoculum range, permitting a good approximation of the dose-infection relationship. It is estimated that the infective dose is in the region of 1 oocyst, 1 cyst or 1 tachyzoite (for genotype I, the most virulent).

Diagnosis

Laboratory diagnosis of toxoplasmosis is conducted by serology and/or detection of the parasite or parasite DNA. Serological diagnosis combines detection of several antibody isotypes (IgG and IgM mainly). Measurement of the avidity of IgG can be used to exclude recent infection. In immunocompromised patients, serology is of little value for diagnosis but can be used to identify patients at risk of reactivation (positive serology). Testing for the presence of the parasite by mouse inoculation and testing for parasite DNA by PCR are recommended for the diagnosis of congenital infections and severe toxoplasmosis in immunocompromised patients.

Medical treatment and prevention

The different medicines available (sulphonamides combined with folic acid inhibitors, mainly) are only active on tachyzoites and not on cysts. Treatment is only warranted in congenital toxoplasmosis (antenatal treatment, then of the infant, the efficacy of which has not been formally demonstrated), symptomatic ocular toxoplasmosis or a central location in severe forms of toxoplasmosis occurring in immunocompromised patients or following infection with a very virulent strain. Medical prophylaxis with cotrimoxazole is recommended in all immunocompromised patients with a marked immune deficiency and testing positive for toxoplasmosis.

Prevalence and/or annual incidence of deaths, patients, healthy carriers (seroconversion, gastrointestinal carriage) and/or cases of hospitalisation. Comparison between France and other countries

Toxoplasmosis is a cosmopolitan parasitosis, with a seroprevalence that varies from one country to another (from 7 to 80%). Seroprevalences of less than 30% are observed mainly in North America, the United Kingdom, Scandinavia and South-East Asia. Prevalences of above 60% are seen mainly in Africa and Latin America. In France, the seroprevalence has been steadily decreasing for 40 years, reaching 54% in 1995 and 44% in 2003, with marked regional variations that have not as yet been clearly explained.

The incidence of toxoplasmosis in the general population is difficult to evaluate since infection is usually asymptomatic and is not declared. In France, the annual number of fresh

infections can be estimated by modelling at between 200,000 and 300,000 cases, with approximately 30-45,000 symptomatic cases. In AIDS patients, the number of cases of toxoplasmosis is approximately 200 per year, after having significantly fallen between 1992 (800 cases) and 1997 (250 cases).
The incidence of toxoplasmosis in seronegative pregnant women fell significantly between 1960 and 1995. The seroprevalence having fallen significantly over the same period, the number of infections related to all pregnancies remained at between 2.4 and 5.8 cases/1,000 pregnancies in 1995. For the year 2000, the number of seroconversions in pregnant women was estimated to be 2,700. Taking into account the risk of mother-foetus transmission, the number of live births of infants with congenital toxoplasmosis was estimated to be around 600 cases (including 175 with sequelae).

Role of foods

Food(s) involved

The main foods involved in contamination are meat from animals infected with *T. gondii* and eaten undercooked, and all vegetables that could be soiled with oocysts (telluric contamination). The risk of infection per portion is not known.
The consumption of seafood has been suggested as a possible source of infection. Several studies show that it is possible to experimentally contaminate shellfish with *T. gondii* oocysts. This contamination has never been proved in natural conditions.
The potential role of water as a source of contamination has been demonstrated on epidemiological bases, but the presence of oocysts in drinking water has only been demonstrated in an epidemic.

Conditions leading to contamination, development and survival of the microorganism in the foods involved

For foods of animal origin, these conditions are those of contamination of animals intended for human consumption. These conditions are not well known in natural environments. The development of industrial livestock farming has led to a reduction in the seroprevalence of toxoplasmosis in pigs. For foods of plant origin, any telluric contamination leads to a risk of contamination by oocysts.

Control measures in the food sector

Good hygiene practices

Washing raw vegetables potentially contaminated with soil is a measure for controlling contamination of foods with oocysts. Washing kitchen utensils after cutting meat is a measure for controlling individual or cross-contamination with any cysts present in meat.

Characteristics of physical, chemical and biological purification treatments

Cysts are killed by temperatures over 67°C and by freezing at –12°C for at least 3 days; applied to a piece of meat, this freezing duration may be inadequate if the piece is thick. They remain infective after several weeks at 4°C. Their infectiousness is maintained for 2 hours in highly acidic medium. Due to contradictory experimental results concerning the action of NaCl concentration, inactivation by saline concentrations of 2% to 3% for 48 hours cannot be considered to be certain.
Sporulated oocysts are killed by a temperature of 60°C applied for 1 minute; freezing, even at –20°C, is inadequate to completely deactivate oocysts. They withstand long periods in highly acidic medium and in alkaline medium and are very resistant to numerous disinfection agents, including bleach.
Tachyzoites are more fragile: they are destroyed by pure water, but can persist for several days in physiological liquids, such as milk at 4°C; they are destroyed by pasteurisation.
Of the other conditions that can be used to treat foods, only ionisation at a minimum dose of 0.5kGy is considered to be effective on the different parasite forms. Other treatment methods (microwaving, curing, smoking) have no certain efficacy.
To sum up, for foods that could contain cysts or be soiled with oocysts, cooking at a temperature of 67°C is effective. Freezing is an effective method to destroy cysts, but a core temperature of –12°C must be obtained, Ready meals or any other foodstuff of animal origin sold frozen (maximum temperature is –18°C) can be considered to be risk-free products in terms of *T. gondii*. However, the freezing of vegetables is ineffective on oocysts and home-freezing is very often inadequate to destroy cysts.

Monitoring in foods

Regulations in force applicable to foodstuffs identified as high-risk

None in France, Europe and the United States.

Principles of detection, counting and typing methods

No method for the detection of toxoplasmosis in water or food is standardised. Serological tests conducted in animals intended for human consumption can, if they are positive, provide an indirect indication of contamination

but without providing any indication of the degree and location of this contamination. In foodstuffs of animal origin, detection of parasites (cysts) is generally performed by mouse inoculation; this must be preceded by enzymatic digestion. The detection sensitivity varies depending on the quantity of meat treated. PCR has recently been suggested, but its sensitivity in comparison with biological tests has not been evaluated. Typing methods are based on different genetic markers studied by molecular biology; they do not generally have sufficient sensitivity to be directly applied to the food concerned.

Domestic hygiene

Basic hygiene rules must be applied to limit the risk of contamination of foods and hands by oocysts: handwashing with brushing of nails before and after handling foods, after gardening or touching objects contaminated by soil and after touching animals. Raw vegetables should be washed to eliminate all traces of soil. After handling food, it is necessary to wash hands, surfaces and used utensils.

Thorough cooking is required to destroy any cysts that could be present in meat: a "well done" meat loses its red colour and becomes pinkish-beige in the centre (temperature reached above 68°C).

If there is a cat in the home, the litter must be changed every day, wearing gloves.

Links

References

Afssa. Toxoplasmose: état des connaissances et évaluation du risque lié à l'alimentation – Report by Afssa's "*Toxoplasma gondii*" working group, 2006, 324 pp.

Contact details of reference laboratories (NRC, CRL, NRL)

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Web links

- CDC information on toxoplasmosis (description of the disease, prevention) and toxoplasma (cycle, epidemiology, biology), on-line references for articles concerning the impact of toxoplasmosis in the USA; for professionals and the general public
  http://www.cdc.gov/ncidod/dpd/parasites/toxoplasmosis/default.htm
- Various addresses for sites on toxoplasmosis prevention and treatment for AIDS patients (US recommendations)
  http://www.thebody.com/treat/toxo.html

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