REVIEW

TOXOPLASMOSIS AS A PUBLIC HEALTH HAZARD

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Recent advances in the epidemiology and life cycle of toxoplasmosis are reviewed. Cats play a kev role. *Toxoplasma* has a coccidian-type entero-epithelial cycle with oocyst production in the feline host. An extra-intestinal cycle occurs in both feline and non-feline hosts. The worldwide distribution and the public health significance of toxoplasmosis as a zoonosis is discussed, with particular reference to available data regarding Southern Africa.

INTRODUCTION

The aetiological agent of toxoplasmosis, *Toxoplasma gondii*, is a protozoan parasite belonging to the Order Eucoccida. *T. gondii* was first reported simultaneously in 1908 by Nicolle and Manceaux in a North African rodent, *Ctenodactylus gondii*, and by Splendore in São Paulo in the rabbit. *T. gondii* has since been isolated in the tissue of many species of mammals and birds, and the parasite is known to have a world-wide distribution with the exception of Antarctica.

The first description of a possible congenital infection in man was in 1923, when Dr Joseph Janku, an ophthalmologist in Prague, described parasitic cysts which he found in the retina of an eleven month old child with congenital hydrocephalus and microphthalmus. Transplacental transmission was first described by Cowen, Wolf and Paige in 1939.

Human toxoplasmosis is divided into two main forms: Congenital and Acquired Congenital infection, the first form to be described, has various clinical manifestations including the following: Hydrocephaly; microcephaly; icterus; convulsions; chorioretinitis; cerebral calcification; blindness; mental retardation; epilepsy; deafness and various other neurological abnormalities.

The acquired form also covers a wide clinical spectrum including: Lymphadenopathy; ocular lesions; fatal acute fulminating pneumonitis; myocarditis and encephalomyelitis. The lymphoglandular form is a frequent manifestation of an acquired infection. There is also a high incidence of asymptomatic infections in man.

In animals toxoplasma infections are also known to cause various symptoms, for example, abortion storms in sheep; ocular lesions in cats; myelomalacia in horses. Asymptomatic infections also occur.

With regard to human toxoplasmosis, congenital toxoplasmosis continues to be of the utmost importance and concern as a zoonosis and clinical entity. For example, in the United States, an estimated 3 000 babies are born with the disease each year. It has been calculated that of these babies, 5 to 15% die, 8 to 10% have marked brain and ocular lesions, 10 to 13% have moderate to marked visual damage and 58 to 72% are clinically normal at birth but some of these develop active retinocorticoiditis in childhood or young adulthood. The total annual cost of neonatal toxoplasmosis in the United States has been estimated at approximately forty million dollars - including hospitalisation, institutionalisation and special education.

It is now well established that toxoplasmosis is a true zoonosis manifesting itself sporadically in humans and with cats playing a key role in the epidemiology of toxoplasmosis in mammals, including man, and birds.

In order to evaluate the epidemiology and public health significance of toxoplasmosis it is necessary to have a clear understanding of the life cycle of *T. gondii*.

LIFE CYCLE

The most recent advance in the study of toxoplasmosis was when *T. gondii* was shown to have coccidian affinities with an entero-epithelial cycle and oocyst production in cats and other felines. Only domestic cats and certain other members of the family Felidae have been shown to produce *Toxoplasma* oocysts. In addition, *Toxoplasma* has highly successful tissue-invasive (extra-intestinal) forms which are capable of proliferation in many hosts.

Two cycles in separate biotypes and three stages of *Toxoplasma* are known and can now be linked into a life-cycle. In cats, the entero-epithelial stage is generally similar to that in other coccidia, and leads to gametogony and oocyst production with sporogony. Two additional stages occur in the extra-intestinal tissues: Tachyzoite-forming groups (“trophozoites”) occur during the acute infection and bradyzoites within the tissue cysts are found during chronic infection.

The three known stages of *Toxoplasma* are bradyzoites (tissue cyst stage), tachyzoites (proliferative forms in tissue during acute infection) and sporozoites (in sporulated oocysts).
Sporulated oocysts originating from feline faeces.

The appearance of these stages, together with the nature of the oocysts, indicates that Toxoplasma gondii is a coccidian parasite related to the genus Isospora. The oocyst of Toxoplasma (b) is much smaller than the oocysts of I. felis (a) (Fig 1).

**Fig. 1:** Oocysts of *Isospora felis* (a) and *Toxoplasma gondii* (b) × 1 500
(Kind permission J W Plant et al)

**Extra-intestinal (tissue) cycle:**

These stages, which also occur in cats, appear to constitute the entire cycle in non-felines. In non-feline hosts infection is usually from the ingestion of sporulated oocysts of feline origin or the ingestion of tissue cysts containing bradyzoites or transplacental infection of the foetus with tachyzoites after ingestion of encysted bradyzoites or sporulated oocysts by the pregnant female. Tachyzoites then spread from cell to cell and are disseminated to various organs in macrophages, lymphocytes, granulocytes and in free forms in the circulation.

In the acute visceral infection, as seen in many hosts, the tachyzoites develop within a vacuole in a multitude of cell types. From about 8 to 16 or more organisms accumulate in the host cell before it disintegrates and new cells are infected. These are the "tachyzoite-forming groups" of the acute infection in which rapid replication occurs.

The severity of the infection is determined by the degree of cellular necrosis caused either directly by the number of proliferating tachyzoites or indirectly by hyper-sensitivity, or by both. Cyst formation then begins and appears to coincide with the development of immunity.

Tissue-cysts are characteristic of the chronic infection and occur mainly in the brain, heart and skeletal muscle. Cysts may persist for months and it appears that they may persist for the life of the host.

**Epidemiology**

Serological surveys carried out in various parts of the world confirm the high prevalence of *Toxoplasma* infection in man and animals. More than a third of the population in most parts of the world have antibodies indicating past infection with *T. gondii*.

It has been noted that *Toxoplasma* antibodies in humans tend to vary in different parts of the world, with positive dye test percentages in human groups varying from 0% in Eskimos to 83% in parts of Nigeria. Of 806 samples of human sera collected in South Africa 37% were positive for *Toxoplasma* antibody.

Age groups have repeatedly shown a classic distribution of incidence in serological surveys, the number of positive reactions being low in the first decade of life and increasing with age.

Based on the new concept of the life cycle, an extensive transmission scheme for *T. gondii* can now be drawn up. Basically the three modes of transmission are carnivorous, faecal contamination and transplacental.

Oocysts are the key to understanding the epidemiology of *Toxoplasma* infections in nature, since they can infect mammals and birds. The oocysts are non-infective when unsporulated, with sporulation taking 1 to 5 days. Millions of oocysts may be shed in a single stool.

It has been shown that oocysts excreted in cat faeces may remain infective for a year in warm, moist climates and longer in cooler climates. Oocysts have been isolated from naturally contaminated soil. It is therefore likely that yards and gardens around the house provide good sites for the persistence of oocysts.

**Transmission of Toxoplasmosis**

*Toxoplasma* oocysts are found to be resistant to most common detergents, acids and alkalis, but are...
killed by boiling water, dry heat (66°C), 10% ammonia and by incineration.\textsuperscript{10, 11, 12, 16, 20, 23, 28}

Serological surveys have indicated that Toxoplasma infection is prevalent in livestock throughout the world. Approximate seropositives for each species on a worldwide basis are: Cattle 22%, sheep 39%, goats 22%, horses 19% and dogs 33\%\textsuperscript{33}. Toxoplasma cysts have been isolated from consumer cuts and diaphragm muscle specimens of lamb, pork and beef\textsuperscript{32}.

The mode of transmission of T. gondii in herbivorous animals remains largely unexplained. There are, however, indications that faecal contamination of pasture and concentrates by infected cats may play an important role in infecting herbivores.

It is generally accepted that freezing is not a reliable way of killing Toxoplasma tissue-cysts\textsuperscript{12, 19, 23}. Tissue-cysts in meat are killed by heating the meat throughout to 60°C\textsuperscript{33}. Cats can become infected with T. gondii by eating infected birds, small mammals (eg rodents), raw or undercooked meat or offal or by faecal contamination from cats that are excreting Toxoplasma oocysts\textsuperscript{10, 16, 33}.

Data collected indicates that common species of domestic rats (eg Rattus rattus and R. norvegicus) are chronic carriers of the tissue form of the parasite and probably serve as a reservoir of infection for the cat\textsuperscript{29}. It has also been shown that mice can acquire Toxoplasma infection from ingesting oocysts from cat faeces\textsuperscript{3}.

Immunity to the intestinal stages in cats is apparently not absolute. When the antibody titre related to a first infection had fallen, cats could successfully be re-infected, with renewed oocyst production. Some cats with antibody will pass oocysts under experimental conditions, and not all cats that shed oocysts develop antibody\textsuperscript{9-14}. Cats usually have lower titres of antibody than dogs, mice or humans. For these reasons, serological data are diagnostically less useful in cats\textsuperscript{18}.

Numerous Toxoplasma antibody surveys in cats have been performed throughout the world. The prevalence of antibody has been found to range from 5 to 85\%\textsuperscript{34}. Cats younger than a year of age have been shown to already have a high antibody titre\textsuperscript{32}. The prevalence of Toxoplasma was higher in stray cats than in domiciled cats, strays probably having more opportunities to become infected by feeding on garbage (eg scraps of raw meat) and hunting rodents and birds\textsuperscript{3}.

Infected raw or undercooked meat can serve as the source of human toxoplasmosis\textsuperscript{4, 12, 21, 31, 33}. It is thought that most of the infections in man result from the accidental ingestion of oocysts originating from cat faeces\textsuperscript{14}. Oocysts in cat faeces are usually buried superficially in soil, often close to human habitations. From 10 000 to 100 000 oocysts have been isolated from a gram of contaminated soil. After digging in contaminated soil, between 7 and 13 mg of soil can be removed from under the fingernails, which might contain 10 to 100 oocysts. Thus infected garden soil, children's sandpits, cat litter pans etc. can be a source of human infection\textsuperscript{10, 13}.

Laboratory workers appear to be at risk when working with faeces of infected cats\textsuperscript{8, 16, 24}. Being the owner of a cat appears to increase the risk of infection\textsuperscript{1, 20, 22, 25}. In serological surveys, no significant difference was however noted between veterinarians and the normal population controls\textsuperscript{18}.

In certain instances human infection appears to have been related to the handling or consumption of raw or undercooked meat\textsuperscript{10, 19, 21, 28, 33}. The most widely quoted example is an epidemic of acute lymphoglandular toxoplasmosis involving five medical students. The students all ate rare hamburger at the same place on the same night, and evidence indicated that this was the way in which the infection was acquired\textsuperscript{34}. T. gondii has frequently been isolated in hares and rabbit in all parts of the world. Rabbit handlers and hare trappers have been shown to have a high prevalence of antibodies\textsuperscript{13}.

It is conceivable that some cases of human toxoplasmosis result from the ingestion of infected raw eggs or infected chickens. Toxoplasma has been isolated from chicken eggs and various organs and tissues of the chicken\textsuperscript{16, 17, 23}.

It is also possible that coprophagic arthropods such as flies, cockroaches, certain snails and slugs which normally feed on faeces are involved as transport hosts of the parasite. Viable oocysts have been isolated from these transport hosts\textsuperscript{13, 19, 34}. The mechanical transmission of oocysts by filth flies from cat faeces to milk has been demonstrated experimentally\textsuperscript{39}.

T. gondii has also been isolated from the milk of cows, goats, sheep, pigs, dogs, cats, rabbits, guinea-pigs and mice with naturally occurring or experimentally induced infections\textsuperscript{21, 28}.

The possibility of the transmission of Toxoplasma by blood transfusions must not be ignored. An asymptomatic infection in a donor with a late parasitaemia can play a role here\textsuperscript{19}.

It seems clear, from the present data, that the cat is a necessary link in the maintenance of Toxoplasma infection as a zoonosis\textsuperscript{35}. However, the question still remains as to the relative importance of other routes of infection to man.

Increasing numbers of cases of toxoplasmosis in the compromised host are being recorded. This is in patients undergoing therapy for malignancies, in patients on immunosuppressive agents and in people suffering from an immunodeficient disease. Reactivation of a dormant acquired latent infection or a primary generalised infection may occur\textsuperscript{12, 28}.

The occurrence of habitual abortion in women due to Toxoplasma infection is rather contentious. The foetus is generally only infected during primary infection of the mother. Premunition appears to be of practical importance in preventing infection of the foetus during successive pregnancies in women\textsuperscript{12}. From the majority of the literature it appears that there is no valid evidence to indicate that abortion in two successive pregnancies is either common or habitual\textsuperscript{12, 16, 19}.

A mother with a positive titre to Toxoplasma at conception should not be in danger of infecting the foetus in utero with T. gondii\textsuperscript{16, 19}. However, occasional cases of congenital toxoplasmosis have occurred in lambs of ewes that had high antibody levels of Toxoplasma at mating\textsuperscript{14}.

Te Groen\textsuperscript{31} mentions that Langer succeeded in isolating Toxoplasma in 23 of 70 women with habitual abortions, repeated miscarriages, premature births and stillbirths, or from their foetuses in whom other causes had been excluded. He also described a number of cases, where patients with poor obstetrical histories plus positive Toxoplasma sera delivered healthy infants after being treated solely for Toxoplasmosis.
THE PUBLIC HEALTH HAZARD

In spite of the fact that toxoplasmosis is a relatively uncommon clinical disease, it continues to be a significant public health problem in terms of the severity of the disease. This is confirmed by the reported cases of toxoplasmosis in human foetuses and neonates, children, adults, cancer patients, transplant and transfusion patients, and ophthalmic patients. The world-wide distribution of this zoonosis, together with the recent knowledge of the role played by oocysts shed by felines and tissue-cysts in slaughter animals as a source of human infection, makes Toxoplasma infection a potential hazard for any seronegative human. Jacobs sums up the problem by saying "The man going blind from progressive toxoplasmic retinochoroiditis is not compensated for by the fact that his condition occurs less frequently than other causes of loss of vision."

The danger of Toxoplasma infection in the young seronegative pregnant woman should always be of great concern. As a rule toxoplasmosis does not manifest itself in the form of an epidemic. Observations from France record that about 40% of women who contract toxoplasmosis while pregnant will produce infected offspring.

The recent revelations concerning the life cycle of T. gondii and the clearer understanding of the epidemiology of toxoplasmosis should be of great interest to the veterinarian, gynaecologist, paediatrician, neurologist, ophthalmologist and the public health official. It now seems clear that Toxoplasma infection can be traced directly to man's use of animals as pets or for food.

The cat shedding oocysts appears to play the main role in the epidemiology of human toxoplasmosis. The ingestion of tissue-cysts and the other routes of infection may not be as common a source of infection. People coming in contact with contaminated soil, cat litter pans, children's sandboxes etc. can expose themselves to infection. From the occupational aspects, those at greatest risk appear to be cat owners, laboratory workers, slaughtermen, butchers and housewives. Cultural patterns concerning meat preparation and eating habits may play a role here as well.

REFERENCES


On this basis, a scheme for the prevention of toxoplasmosis in humans, especially pregnant women, and in cats could include the following:

1. Heat meat throughout to 60°C before eating.
2. Wash hands after handling raw meat.
3. Feed cats only dry, canned or boiled food.
4. Flush cat faeces down the toilet; scale litter pans daily; incinerate disposable litter trays daily.
5. It is imperative that cat faeces be disposed of daily, whether in the home, hospital, kennels or in the zoo that keeps Felidae.
6. Cover children's sandboxes when not in use.
7. Wear gloves when handling litter pans and potentially contaminated soil.
8. Avoid newly acquired cats to the household of a pregnant woman.
9. In the laboratory avoid contamination of hands, centrifuge, microscope, benches etc. with cat faeces. Gloves should be worn at all times by those handling cat faeces.
10. The periodic faecal examination and serological surveillance of cats is not all that effective. The short duration of excretion of oocysts and the uncertainty of differentiating the oocysts from those of Isospora may add to the frustration of the practitioner trying to make a diagnosis.

Serological data can be misleading in cats. Presence of antibody to Toxoplasma in cats indicates previous exposure to Toxoplasma and are thus less likely to be excretors of Toxoplasma at the time of examination and in the future. However, this is not necessarily true in each case. Thus basically a seropositive cat is a safer cat to have in the household.

Daily contact with pet cats during clinical practice does not necessarily increase the risk of exposure to infection. The veterinarian is more likely to become infected from contaminated laboratory apparatus, litter pans in the small animal hospital or from handling material infected with tissue-cysts.

We live in a "sea" of Toxoplasma and in the future the wide Toxoplasma infection rate in both man and animals may have to be reduced by the introduction of legislation to possibly prevent the feeding of raw meat or offal to cats, the control of feral and stray cats, the development of a Toxoplasma coccidiotat, and the development of an effective vaccine for young children and animals.
34. WALLACE G.D. 1972 Experimental transmission of Toxoplasma gondii by cockroaches. Journal of Infectious Diseases 126:545.

INFORMATION

EFFECT OF PESTICIDES ON HOST DEFENCES

Although a significant quantity of information is available concerning the toxicological properties of pesticides, there is a dearth of information about their potential effects on host defences, the mechanisms which assist humans in resisting a wide variety of infectious diseases. Hypersensitivity reactions occasionally develop as a result of the activation of these host defence mechanisms through exposure to a number of substances, including pesticides; since little is known, there is a need for data especially in regard to the effects of exposure to low dosages of pesticides such as might be encountered from residues in foods. Accordingly, researchers of Pennsylvania State University's Agricultural Experiment Station initiated studies aimed at determining the effects of varying acute and chronic oral doses of five common pesticides, using experimental mice selected on the basis of uniformity. The pesticides tested were ametryne, carbaryl, chlorothiram, DDT and parathion.

The experiments entailed the use of "sensitive and specific techniques", and the testing of two components of host defences by means of what are described as "the most modern and sensitive procedures available". The defences tested were: the ability of an animal to form antibodies, and to form activated white blood cells.

Results thus far indicate that administration of relatively high acute doses of the five pesticides can cause a marked depression in antibody and activated white blood cell production ability. Lower acute doses did not cause any significant effects. These results would be comparable to cases of accidental acute pesticide poisoning, suggesting a probable reduction in the human's host defences.

The chronic administration of small quantities of the various pesticides revealed no significant effects except in the case of parathion, which resulted in a significant depression of the above host defence components. The effects of small doses of pesticides over long periods of time still remain to be determined.

The researchers plan to do this and also to test the effects of exposure to pesticides in aerosol containers, as humans frequently encounter this type of exposure. They say that complete and systematic evaluation of the consequences of pesticide exposure on all host defences appears to be warranted, and that an added incentive for investigation would be the possibility of discovering chemicals which may be used to manipulate host defences to advantage.

("Can Pesticides Alter Host Defences?", Science in Agriculture, Vol. XXIII, No. 2, Winter, 1976, p. 16: Pennsylvania Agricultural Experiment Station, Agricultural Administration Building, University Park, Pennsylvania 16802.)