

Toxoplasmosis

A comprehensive clinical guide

This authoritative and comprehensive account looks at the re-emergence of toxoplasmosis as a significant and potentially fatal infection. A team of acknowledged international experts reviews the latest diagnostic techniques, and the management of infection in pregnant women, neonates, the eye, transplant and other immunosuppressed patients and those with acquired immunodeficiency syndrome (AIDS). The contentious issue of the role of screening during pregnancy and in the newborn is covered in depth. The introductory chapters on biology, immunology and epidemiology of the infection provide an essential background to understanding the clinical disease. The full range of treatment strategies is presented in an easily accessible form.

Although the burden of this disease varies greatly from country to country, it remains a global public health problem which affects about one billion individuals. The natural history and life-cycle of the causative organism, *Toxoplasma gondii*, provide a fascinating insight into one of the most successful parasites on Earth.

This will be an essential source of reference for infectious disease specialists, microbiologists, parasitologists and obstetricians and gynaecologists.

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Edited by David H. M. Joynson and Tim G. Wreghitt
Frontmatter
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Preface

Exactly one hundred years ago, the first description of *Toxoplasma gondii* was recorded but a further 60 years were to elapse before the final identification of the cat family as the definitive host was made. The heteroxenous nature of the parasite, its ability to infect any warm-blooded creature, the territorial range of its hosts (especially birds) and the production of tissue cysts that can survive for many years have contributed to the world-wide dissemination of the infection. Indeed, it is reasonable to conclude that perhaps *T.gondii* is one of the most successful parasites on Earth. About one billion people throughout the world are infected though the prevalence of infection shows considerable geographical variation.

Transmission of infection is by ingestion of either oocysts as a result of environmental contamination or tissue cysts in raw or undercooked meat. It is probable that the favoured route of transmission varies in different parts of the world – the epidemiology of the infection is still not completely known. It is also possible that other vectors, for example water and aerosols, may be involved.

Toxoplasma infection can be acute, chronic, latent/quiescent or re-activated, while the clinical presentation, investigation and management can vary according to the specific patient group involved. Infection in the immunocompetent, though very common, is generally regarded as a trivial event though there are suggestions that it may in fact be a more debilitating illness than was previously supposed.

It has been known since the first quarter of the last century that toxoplasma can cause a devastating congenital infection but this was thought to be a relatively infrequent occurrence. However, there is now an increasing awareness that the effects of foetal infection are protean and may first present years or decades after birth. To try to reduce the risk of congenital infection, some countries have introduced prenatal or newborn screening. In other countries, the debate regarding the cost-benefit of screening is often controversial yet inconclusive due to lack of data and the failure to fund appropriate studies to address the issue.

The end of the twentieth century has witnessed a significant increase in the number of immunosuppressed and immunocompromised patients. This has occurred in the main as a corollary to advances in medical treatment and to the

xii **Preface**

advent of HIV infection and AIDS. Consequently, *T.gondii* has re-emerged as a significant cause of morbidity and mortality. This has spurred research and given new insights into the pathogenesis and immunology of the infection. These have revealed subtle inter-reactions with, for example, the host's immune system and HIV. This work may eventually lead to the development of an effective vaccine.

Fifty years ago, the diagnosis of toxoplasma infection took a huge step forward with the introduction of the Sabin and Feldman Dye Test. Remarkably, this has stood the test of time and is still regarded as the 'gold standard'. However, it is unwise to rely solely on one laboratory test. It is now usual practice to choose from a range of serological tests and methods of detection of the parasite by culture, nucleic acid detection or specific stains according to the specific patient group being investigated and the clinical questions that need to be addressed. Despite the plethora of tests now available, clinical acumen and awareness are still paramount.

Sadly, the mainstay of treatment is still a combination of ancient antibiotics that are not effective against the tissue cyst and can be both toxic and teratogenic. The apparent lack of interest in the pharmaceutical industry to develop new chemotherapeutic agents is to be regretted. A safe antibiotic that is effective against all forms of the parasite and crosses the placental and brain barriers is urgently required. The availability of such a drug and the prospect of a genuine cure would undoubtedly transform attitudes towards the infection.

Toxoplasma gondii has developed a complex biological relationship with humans. The manifestations of the infection that it causes are protean, unpredictable and subtle and can be difficult to diagnose, treat and prevent. The key factor in solving such problems is understanding based on knowledge and evidence. Thus, contributions have been invited from experts from a variety of scientific, epidemiological and medical fields so that a greater understanding of the disease as a whole is attained. The purpose of this book, therefore, is to be an easily accessible resource of information to clinicians, epidemiologists, microbiologists, midwives and nurses and others involved in caring for patients who are at risk or suffering from toxoplasmosis. It is hoped that this aim has been achieved.

D.H.M.J.

Historical perspective

- 1900 Laveran – detected the organism in the blood of a bobolink, a common American songbird.
- 1908 Nicholle & Manceaux – observed the causative agent in an African rodent *Ctenodactylus gondii* and gave it the name *Toxoplasma gondii*. ‘*Toxon*’ the Greek word for bow or arc and ‘*plasma*’ meaning form.
- 1908 Splendore – found the parasite in a rabbit.
- 1923 Janku – reported the first case of chorioretinitis in a child, found parasites in the eye and called them ‘sporozoa’.
- 1928 Levaditi – identified these ‘sporozoa’ as *Toxoplasma gondii*.
- 1938 Wolf & Cowan – identified toxoplasma as the cause of neonatal encephalitis; the first report of congenital transmission of *T. gondii*.
- 1940 Pinkerton & Weinman – reported a fatal case of disseminated toxoplasmosis in an adult.
- 1941 Sabin – described a triad of signs (retinochoroiditis, hydrocephalus and cerebral calcification) in an infant with congenital toxoplasmosis.
- 1948 Sabin & Feldman – development of the dye test, still the ‘gold standard’ half a century later.
- 1952 Slim – description of the ‘glandular’ form of acquired toxoplasma infection.
- 1954 Jacobs *et al.* – isolation of *T. gondii* from the eye of a patient with chorioretinitis.
- 1954 Weinman & Chandler – suggested that transmission of toxoplasma may be related to eating undercooked pork.
- 1960 Jacobs, Remington *et al.* – demonstration that tissue cysts were resistant to proteolytic enzymes.
- 1965, 1969 Hutchinson – discovered *T. gondii* in feline faeces and recognized that the cat was the definitive host.

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|-------|---|
| 1969 | Wallace – an epidemiological study of the population of some Pacific islands indicated the importance of the cat in the transmission of infection to humans. |
| 1970 | Dubey, Millar & Frenkel – the finding of sexual stages and the oocyst in the small intestine of the cat clarified the lifecycle of toxoplasma and indicated that it was a coccidian parasite. |
| 1970s | Increasing awareness of the risk to the foetus as a consequence of an acute toxoplasma infection in a pregnant woman. |
| 1980s | Emergence of <i>T. gondii</i> as a life-threatening infection in immunocompromised patients especially those with AIDS. |