



## Ocular toxoplasmosis past, present and new aspects of an old disease



M. Maenz<sup>a,1</sup>, D. Schlüter<sup>b,1</sup>, O. Liesenfeld<sup>c,1</sup>, G. Schares<sup>d,1</sup>, U. Gross<sup>e,1</sup>, U. Pleyer<sup>a,\*,1</sup>

<sup>a</sup> Eye Clinic – Charité Universitätsmedizin-Berlin, Augustenburger Platz 1, 13353 Berlin, Germany

<sup>b</sup> Institute of Medical Microbiology, Otto-von-Guericke-University Magdeburg, Germany

<sup>c</sup> Institute for Microbiology and Hygiene, Charité Universitätsmedizin-Berlin, Germany

<sup>d</sup> Institute of Epidemiology – Friedrich-Loeffler-Institute – Greifswald-Insel Riems, Germany

<sup>e</sup> Institute for Medical Microbiology and German Consulting Laboratory for Toxoplasmosis, University Medical Center Goettingen, Germany

### ARTICLE INFO

#### Article history:

Available online 9 January 2014

#### Keywords:

Ocular toxoplasmosis

Uveitis

*Toxoplasma gondii*

Retinochoroiditis

### ABSTRACT

Ocular toxoplasmosis (OT) is considered the most frequent form of infectious posterior uveitis and is caused by the protozoan parasite *Toxoplasma gondii*. The resulting vision loss frequently incapacitates patients and places a considerable socio-economic burden on societies in particular in developing countries. Although, toxoplasmic retinochoroiditis is a world-wide phenomenon stark regional differences with regard to prevalence and presumably route of infection exist. This review will discuss our current clinical understanding of OT including typical and atypical manifestations, patient characteristics which influence the course of disease and treatment options. Even though, congenital and acquired OT are not regarded as separate entities, certain differences exist, which will be assessed and evaluated in detail. A strong focus is laid on the disease causing parasite *T. gondii*, since solving the mystery of OT aetiology and the development of improved therapies will not be possibly with clinical science alone, but rather requires a precise understanding of parasitological and immunological pathomechanisms. Additionally, the biology and genetics of *T. gondii* form the foundation for novel and sophisticated diagnostic methods. Scientific advances in the recent years have shed some light on the different role of *T. gondii* strains with regard to OT manifestation and severity of disease. Genetic and environmental factors influencing OT will be presented and commonalities between OT and toxoplasmic encephalitis will be briefly discussed. Furthermore, the laboratory tools to study OT are crucial in our understanding of OT. *In vivo* and *in vitro* experimental approaches will be summarised and evaluated extensively. Finally, a brief outlook is given in which direction OT research should be headed in the future.

© 2014 Elsevier Ltd. All rights reserved.

### Contents

1. Introduction .....	78
1.1. Historical background .....	78
1.2. Introduction to <i>T. gondii</i> biology .....	79
1.3. Prevalence of <i>T. gondii</i> infections and ocular toxoplasmosis .....	79
2. Ocular toxoplasmosis – clinical aspects .....	81
2.1. Spectrum of clinical presentations .....	81
2.1.1. Retinochoroiditis .....	81
2.1.2. Punctate outer retinal toxoplasmosis .....	81
2.1.3. Neuroretinitis .....	82
2.1.4. Scleritis .....	82
2.1.5. Complications .....	82
2.2. Congenital vs. acquired infection .....	83

\* Corresponding author. Tel.: +49 30 450 554202; fax: +49 30 450 554900.

E-mail address: [uwe.pleyer@charite.de](mailto:uwe.pleyer@charite.de) (U. Pleyer).

<sup>1</sup> Percentage of work contributed by each author in the production of the manuscript is as follows: Maenz: 30%; Schlüter: 15%; Liesenfeld: 10%; Schares: 7.5%; Gross: 7.5%; Pleyer: 30%.

2.3.	Patient factors related to susceptibility and severity in ocular toxoplasmosis	84
2.3.1.	Genetic host factors	84
2.3.2.	Patients' age	85
2.3.3.	Patient immune status – disease in immunocompromised individuals	86
2.3.4.	Other factors	86
2.4.	Diagnosis – serology and intraocular investigations	86
2.4.1.	Differential diagnosis	86
2.4.2.	Serological findings	86
2.4.3.	Analysis of intraocular specimen	88
2.5.	Treatment	88
2.5.1.	Treatment goals and general considerations	88
2.5.2.	Current treatment indications	89
2.5.3.	Clinical studies	89
2.5.4.	Alternative treatment approaches	90
2.5.5.	Future therapies	91
3.	Epidemiology, parasitology and neuro-immunology of <i>Toxoplasma gondii</i>	91
3.1.	Parasitological considerations	91
3.1.1.	Route of infection, environmental and parasite related factors contributing to infection and disease	91
3.1.2.	Classical clonotypes vs. emergence of atypical strains	92
3.2.	Immunology of <i>T. gondii</i> infection	93
3.3.	Pathomechanisms and neuro-immunology of <i>T. gondii</i>	93
4.	Experimental approaches to study ocular toxoplasmosis	94
4.1.	Animal models	94
4.1.1.	Parasite entry/methods of infection	95
4.1.2.	Onset of disease and manifestation	95
4.1.3.	Self-limitation of disease and recurrence	95
4.1.4.	Pathogen strains	95
4.1.5.	Experimental manipulation of disease course	95
4.1.6.	Immunomodulation & immunosuppression	95
4.1.7.	Conclusions	97
4.2.	<i>In vitro</i> experimental models	98
4.2.1.	Host cell response to parasite entry	98
4.2.2.	Parasite replication and infectious capabilities	98
5.	Future directions	98
5.1.	Epidemiology	98
5.2.	Prevention	98
5.3.	Pathophysiology	99
5.4.	New diagnostic and detection options	99
5.5.	Treatment	99
	Funding	99
	Acknowledgements	99
	References	99

## 1. Introduction

### 1.1. Historical background

To this day ocular toxoplasmosis (OT) remains a challenging ocular disease with many open questions with regard to disease manifestation, pathophysiology and its management. Our current understanding of OT evolved over the course of more than a century through careful clinical observation, epidemiological and parasitological studies.

Retinochoroidal scars – a clinical hallmark of OT – were probably already depicted in the mid 19th century (Fig. 1). Toxoplasmic retinochoroiditis as part of the disease manifestation of congenital toxoplasmosis in a newborn was first described by the Czech ophthalmologist *Janku* in 1923, and was considered an established medical fact almost two decades later (*Janku, 1923; Wolf et al., 1939*). After discovery of the parasite by *Nicolle* in 1907 (*Nicolle, 1907; Nicolle and Manceaux, 2009*), OT was recognised as an ocular pathology in adults by *Wilder* as late as 1952 (*Wilder, 1952b, a*). The seminal work of *Hogan* sparked and defined research on OT for the better part of the next two decades (*Hogan, 1950, 1956, 1958a, b; Hogan et al., 1957, 1964, 1958*). Most notably, already at

this time the first treatment regimes were introduced in the shape of the antimalarial drug pyrimethamine in combination with sulphonamides and corticosteroids, which are still the most frequently prescribed agents until today (*Perkins et al., 1956; Ryan et al., 1954*) [see Section 2.5]. Whereas in the past – and with very limited success – clinical researchers attempted to subcategorise OT based on clinical parameters such as localisation of lesions, severity of inflammation, age of first manifestation, mode of infection and type of complications, OT today is understood as a disease with a broad spectrum of manifestations. Regardless of whether toxoplasmic retinochoroiditis occurs in immunocompromised and immunocompetent patients respectively, or whether OT is acquired congenitally or postnatally, no clear distinction between disease entities can be observed. The dogma that OT is an exclusive congenital disease eroded in the 1980s and today it is well recognised that postnatally acquired infection and subsequent ocular inflammation is the most frequent form of OT (*Gilbert and Stanford, 2000*). Based on advances in the recent decades, we know that OT is the most frequent form of infectious posterior uveitis representing up to 85% of all cases (*Talabani et al., 2010*). Where data are available pronounced geographical differences in disease prevalence can be observed. Particularly high prevalences are reported for

Download English Version:

<https://daneshyari.com/en/article/4031955>

Download Persian Version:

<https://daneshyari.com/article/4031955>

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