Clinica Chimica Acta 461 (2016) 83–89

Contents lists available at ScienceDirect

Clinica Chimica Acta

journal homepage: www.elsevier.com/locate/clinchim

Review

Serological diagnosis of toxoplasmosis and standardization

Kuo Zhang, Guigao Lin, Yanxi Han, Jinming Li *

National Center for Clinical Laboratories, Beijing Hospital, Beijing, People's Republic of China

ARTICLE INFO

Article history:
Received 21 April 2016
Received in revised form 19 July 2016
Accepted 23 July 2016
Available online 25 July 2016

Keywords:
Toxoplasma gondii
Serological diagnosis
Standardization

ABSTRACT

Humans can be infected by the intracellular parasite *Toxoplasma gondii*, which causes toxoplasmosis, a common parasitic disease. Although the infection is generally asymptomatic for most adults, severe complications may occur in some individuals, especially women in early pregnancy. Serologic diagnosis is used as a routine practice to determine the immune status for infection by *T. gondii*. In this review, we attempt to provide an overview of the serological diagnosis of toxoplasmosis, including diagnostic strategy, current problems in detection with specific antibodies, and the standardization of *T. gondii* serological detection.

Contents

1. Introduction

Toxoplasma gondii is an intracellular parasite. Many species of warm-blooded animals, including humans, can be infected by the protozoan *T. gondii*, and infection may cause the common parasitic disease toxoplasmosis [1]. It has been estimated that the global seroprevalence of *T. gondii* in the general population is between 10 and 70% [2,3]. Although the infection is generally asymptomatic for most adults and the clinical disease is generally not recognized, severe complications may occur in some individuals, including immunocompromised patients, transplant recipients, and patients with AIDS [4]. In addition, primary infections of pregnant women are associated with potential congenital infections and abortions, as *T. gondii* may cross the placenta barrier [1]. Therefore, in several countries, especially France and Austria, prenatal screening of women is performed with the goals of early recognition, diagnosis, and treatment of *T. gondii* infections [5]. Serologic diagnosis is routinely used to determine the immune status with regard to *T. gondii* infection [6].

Several serological testing methods, as well as many kinds of commercial kits and automated platforms, are available for *T. gondii* detection; however, it should be noted that there is large variability in the assay results of different clinical laboratories using different commercial kits [7]. Inaccurate or inaccurately interpreted results using antibodies

* Corresponding author at: National Center for Clinical Laboratories, Beijing Hospital, No.1 Dahua Road, Dongdan, Beijing 100730, People's Republic of China.
E-mail address: jmli@nccl.org.cn (J. Li).

http://dx.doi.org/10.1016/j.cca.2016.07.018
0009-8981/

may influence a patient's decision, especially in regards to a pregnancy [8]. In this review, we provide an overview of data on toxoplasmosis, with focus on strategies for serological diagnosis of toxoplasmosis, current problems in clinical *T. gondii* serological detection, a discussion of the need for clinical laboratories to participate in external quality assessment (EQA) schemes and the standardization of *T. gondii* serological detection.

2. How *T. gondii* is transmitted to humans

Humans and other warm-blooded animals are intermediate hosts of *T. gondii*, and members of the family Felidae, such as domestic cats, are the definitive hosts. The life cycle of *T. gondii* includes a sexual cycle in definitive hosts and an asexual cycle in intermediate hosts. There are three infective stages in the life cycle of *T. gondii*: rapidly multiplying tachyzoites (or endozoites), bradyzoites contained in tissue cysts, and sporozoites in sporulated oocysts. Within intermediate hosts, *T. gondii* undergoes two asexual phases including rapid tachyzoite multiplication and the formation of tissue cysts. The termination of asexual multiplication initiates sexual reproduction, which occurs only in definitive hosts. Unsporulated oocysts in the feces are released into the external environment. These three stages are all infectious to humans, with *T. gondii* infection acquired through the following routes: 1) vertical transmission of tachyzoites through the placenta; 2) horizontal transmission by ingestion of food and water contaminated by oocysts or through gardening; 3) horizontal transmission by ingestion of raw or uncooked meat containing tissue cysts [7,9,10]. The life cycle of *T. gondii* is shown in Fig. 1.

3. Prevalence of *T. gondii* infections in humans

It has been assumed that approximately 10 to 70% of the global human population has been exposed to *T. gondii* [2,3]. In fact, the seroprevalence varies widely among different countries and different regions in the same country. Generally, countries in Latin America and Southeast Africa with warm and humid climates were found to have high seroprevalences, moderate seroprevalences were found in Central and Southern Europe, and lower seroprevalences were reported in North America, North Europe, Southeast Asia, China, and Korea. A previous review retrieved literature published before 2009 for seroprevalence data in pregnant and childbearing women, and mapped the global status of *T. gondii* seroprevalence [11]. We retrieved literature published after 2009 [12–32], and the data for some countries are shown in Table 1. Though a trend of decreased prevalence over time was found in some countries, for example the Netherlands with 26.0% in 2006/2007 [95% confidence interval (CI) 24.0–28.0] compared to 40.5% (95% CI 37.5–43.4) in 1995/1996 [21], the overall *T. gondii* seroprevalence is still high throughout the world.

4. Immune response to *T. gondii* infection and serological diagnostic strategy

Following infection with *T. gondii*, immunoglobulins (Ig) are produced successively and the kinetics of antibody production may help to define the stage of infection. IgA and IgM are first produced 1 week after infection, and titers reach a plateau within a month and then decrease after 1 to 6 months. In some individuals, IgM can be detected for a long time after acute infection; therefore, a true-positive IgM result could indicate acute, recent, or past infections [33–36]. Adjunctive tests are now available, such as specific IgA detection, IgG titers analysis, or IgG avidity detection, which allow a better determination of the stage of infection. However, specific IgA could not be used as a surrogate marker to identify an acute infection. Specific IgG reaches a plateau within 2 to 3 months after the onset of infection and then decreases and persists with residual titers for life [7]. A true-positive IgG result indicates a past infection, but it cannot accurately determine the timing of the infection [37]. In the clinic, the serological detection of IgM and IgG antibodies levels are the basis for identifying infection and the most commonly used methods [7].

The diagnostic strategies for toxoplasmosis have been reviewed by previous publications [7,33,34] according to the patients' immune background and the clinical settings, including immunocompetent subjects, immunocompromised individuals, pregnancy and newborns. The diagnostic strategies are summarized in Fig. 2. Prenatal diagnosis of pregnancy and congenital toxoplasmosis are the most challenging situations and the interpretation of results is the most problematic in these cases. Sensini [34] has illustrated the different serological patterns in pregnancy and newborns. These serological patterns include IgG- and

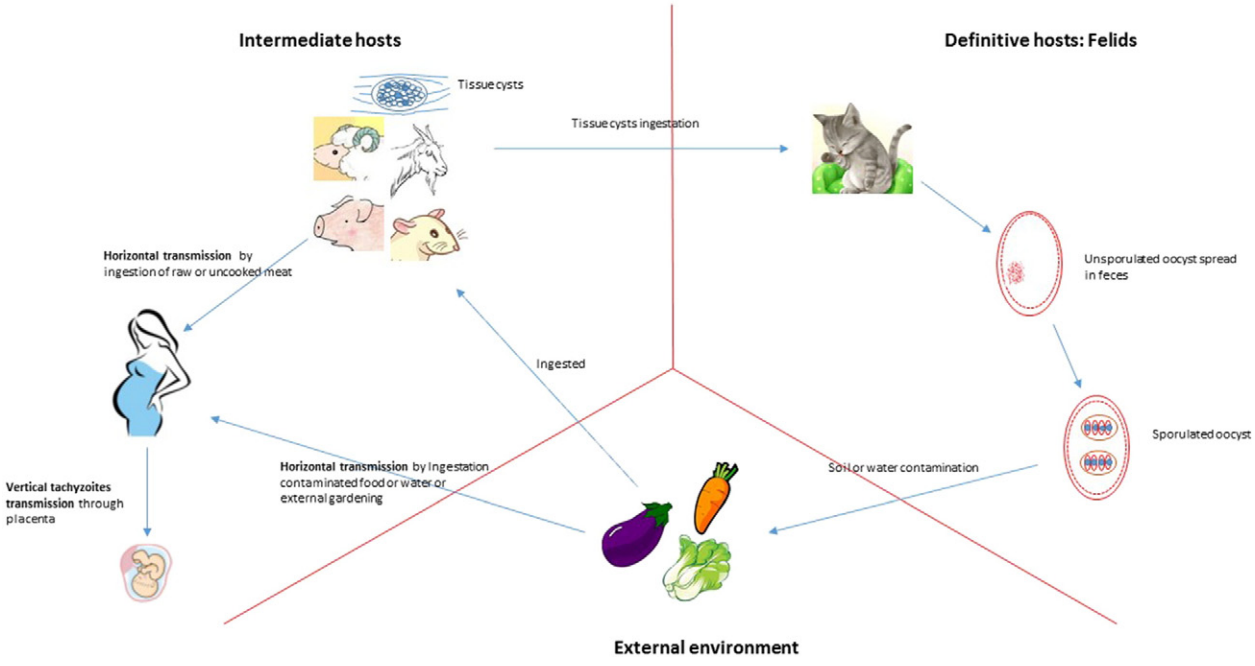

Fig. 1. Life cycle of *T. gondii* and its transmission to humans.