Journal of the Uveitis Information Group | 2 £

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Deutsche Arbeitsgemeinschaft UVEITIS e.V.

INFLAM'OEIL

Ocular Toxoplasmosis

2/05

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Editorial

Let me start today's journal with some questions, dear reader:

What is the reason for most cases of posterior uveitis?
In what kind of uveitis may the visual acuity already be determined before birth?
Which kind of uveitis is a major problem for AIDS-patients?
In what type of uveitis would treatment with corticosteroids without antibiotics probably be a major mistake?

The answer to all these questions is „**Toxoplasmic uveitis**", caused by the parasite Toxoplasma gondii. This uveitis, known for thousands of years, is found worldwide. This is one of the reasons why today's journal is written by various experts and, for the first time, including authors outside Europe (Brazil and the USA). In the following articles they try to describe the initiating parasite, *Toxoplasma gondii*, and what role the beloved sweet cat plays in this infection. We will hear why Toxoplasmosis is so dangerous with possible severe consequences in pregnancy and why it may produce massive disease in people with defects of their immune system. Even if a few points remain controversial amongst experts, there is clear advice for a correct and successful treatment strategy for toxoplasmic uveitis, resulting in a quiet, non-inflamed eye.
Unfortunately the most important problem, reducing the number of recurrences, remains unsolved at the moment. So, my wish for the near future for patients with toxoplasmosis is to find a drug, which effectively can prevent new events.

All the people who participated in the preparation of this journal wish you informative reading.

Manfred Zierhut,
Professor of Ophthalmology, University Eye Clinic of Tübingen, Germany

Content

Cover Picture - Christine Riedel, Germany gcriedel@gmx.de

Portrait of *Toxoplasma gondii*

Toxoplasma gondii, the cause of the disease known as toxoplasmosis, is a parasite spread by cats that infects people all around the world. **Justine R. Smith, MBBS PhD**, *who is working at the Casey Eye Institute of Oregon Health & Science University, Portland (Oregon, USA), will begin our edition on toxoplasmosis of the eye by presenting some interesting facts about this parasite.*

What is *Toxoplasma gondii*?

Toxoplasma gondii (*T. gondii*), the cause of toxoplasmosis and a form of uveitis known as "toxoplasmic retinochoroiditis", is a parasitic microorganism that grows only inside the cells of humans and other mammals or the cells of birds. The genus name, *Toxoplasma*, derives from the Greek word, toxon or "bow", which refers to the fact that the infectious form of the parasite is shaped like a crescent. The species name, *gondii*, relates to the animal from which the parasite was first isolated, *Ctenodactylus gondii*, a rodent found in Northern Africa. *T. gondii* belongs to the Apicomplexa family of microbial parasites that also includes *Plasmodium*, responsible for malaria, and *Cryptosporidium*, a cause of diarrhea in humans. The parasite has a complicated life cycle that involves both a primary host (in which the parasite reproduces sexually) and secondary hosts (in which the parasite reproduces asexually, as described below).

Toxoplasmosis and cats

The cat is the primary host of *T. gondii*, contracting the disease by eating infected birds and rodents whose muscles harbor tissue cysts.

Fertilized eggs, or "oocytes", measuring about one hundredth of mm, are formed in the intestine of the cat and subsequently shed in the feces. Oocytes are extremely hardy and may survive in the environment for many months. Here they mature into an infectious form. When inhaled or ingested by another mammal or bird, which are secondary hosts, the oocyst passes to the intestine and hatches in the presence of digestive enzymes. In epithelial cells that line the intestine, "tachyzoites", the infectious form of the organism, are generated. Tachyzoites are able to replicate by simple division or so-called asexual reproduction. The tachyzoite is crescent shaped and considerably smaller than the egg, measuring just one five hundredth of mm in length. After replication, as the immune system brings the infection under control, tachyzoites transform

into dormant tissue cysts, or "bradyzoites", that are egg-sized or larger. However, for reasons that are not well understood, these cysts may, from time to time, convert back to tachyzoite form and a fresh cycle of infection and inflammation ensues. If ingested by a secondary host, tissue cysts will also yield tachyzoites into the intestine.

How *Toxoplasma gondii* enters our lives

T. gondii is a most successful parasite. It infects almost every mammal and bird. People become infected with *T. gondii* in several different ways: "eating" material that is contaminated by cat feces and contains oocytes; consuming undercooked meat that contains bradyzoites; or passage of tachyzoites across placenta from a pregnant woman to her unborn child. Although we previously believed that congenital infection was the most common way to contract *T. gondii*, recent epidemiological studies have revealed that infection is usually acquired in childhood through contact with cats or cat-contaminated material in the environment. Another reason that the parasite is so successful is its ability to form tissue cysts. As is the case for herpes simplex virus which causes cold sores, an infected person carries *T. gondii* for the rest of his/her life. Many different drugs have been used to treat patients with toxoplasmic retinochoroiditis. However, although these may control an attack, none completely rid the body of *T. gondii*. The pattern of infection with *T. gondii* in the human is illustrated in *Figure 1*.

Toxoplasma gondii and the eye

After leaving the intestine, tachyzoites spread throughout the body primarily via the blood stream. During this time, the parasite may cause a mild flu-like illness with enlargement of the lymph glands. This illness can be mistaken for glandular fever or even lymphoma. Persons with a compromised immune system, such as patients with AIDS, may develop more severe manifestations of infection. Once disseminated, the tachyzoite can infect many cell types. A tachyzoite multiples within a cell until the cell becomes swollen and bursts; newly released parasites, perhaps around 100, then infect neighboring cells. This is illustrated in *Figure 2*. In less than a minute the tachyzoite enters a cell, and some cells can become infected and be killed within the day. Depending on where the parasite lodges in the body, the infection has different manifestations. In the eye, *T. gondii* may cause retinochoroiditis, which is described in the following chapter. Parasites can produce discrete lesions in the brain, which may cause neurological symptoms depending on the area of brain that is involved. However, most children and their parents are never aware that an

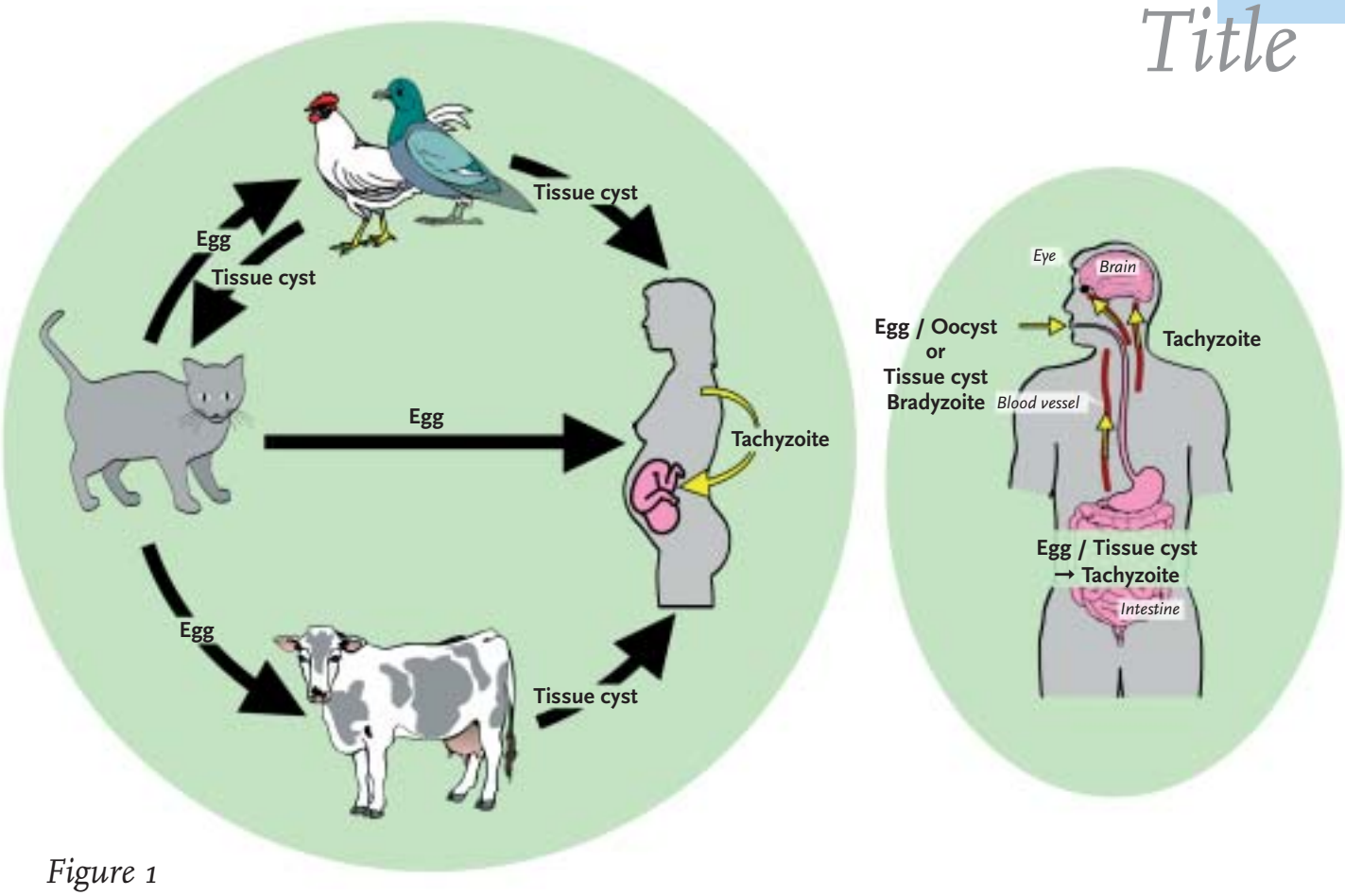

Figure 1
Pattern of infection with T. gondii. Humans may contract toxoplasmosis by ingesting oocysts, eating poorly cooked meat containing tissue cysts, or by tachyzoite crossing the placenta. Once inside the human body, tachyzoites disseminate via the blood stream and most often cause disease in the eye and the brain.

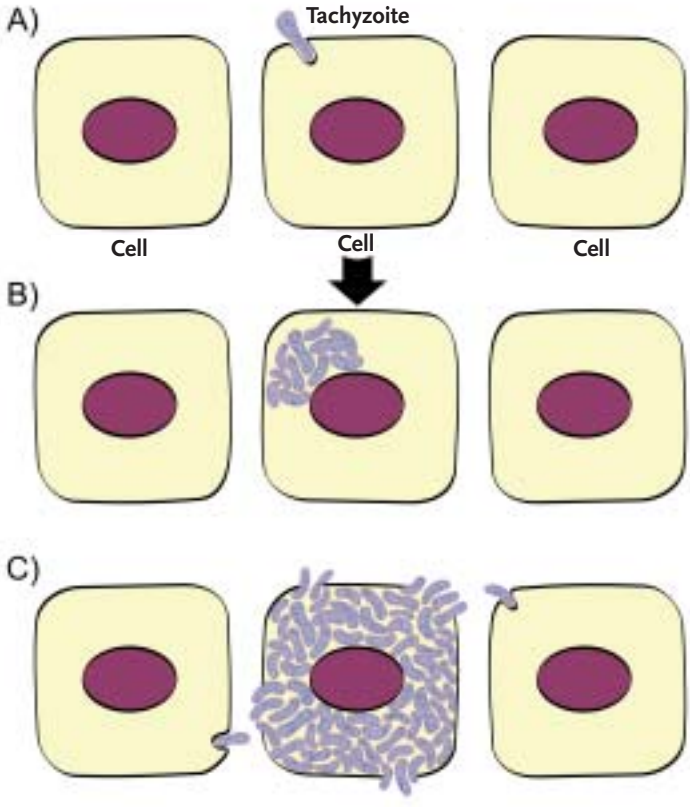

Figure 2
T. gondii infection of human cells.
(A) The T. gondii tachyzoite invades a cell, (B) divides within that cell, and (C) finally causes the cell to burst with release of many daughter tachyzoites that invade nearby cells.

infection with *T. gondii* has actually occurred. It is not until adulthood, when a tissue cyst breaks down and releases tachyzoites within the eye, that toxoplasmosis finally becomes symptomatic. We do not understand why the parasite

shows a preference to lodge in the eye and brain in humans. One possibility relates to the fact that both eye and brain are specialized to develop relatively weak inflammatory responses. This is important because inflammation can cause scarring that could be damaging to such vital organs. However, at the same time, this can make it difficult for these sites to eradicate infection. Another possibility is that tachyzoites penetrate into the eye and brain more easily than other organs of the body. Some research from our group suggests that the endothelial cells (cells that line blood vessels) in the retina may be particularly susceptible to infection with tachyzoites. We compared the susceptibility to *T. gondii* infection of retinal endothelium with endothelium from other parts of the body using a method called the [^{3}H]-uracil incorporation test. In these experiments, cells from a human being are infected with tachyzoites and grown in a dish with a chemical that the parasite needs (uracil). This chemical is attached to a radioactive label [^{3}H]. The radioactivity measurement from any given dish indicates how well *T. gondii* grew inside the cells in the dish. We observed that retinal endothelium yielded the highest radioactivity readings of all cell types tested. Presently we are focusing our research on understanding what causes this susceptibility to infection.

Toxoplasmosis: a longstanding global disease

Toxoplasmosis was first described in the medical literature in the twentieth century, but it is believed to have existed for thousands of years. Throughout Western countries and in developing nations, toxoplasmosis is a substantial health problem. Toxoplasmic retinochoroiditis is the most common retinal infection. Worldwide it is estimated that around one billion people are infected with *T. gondii*, and as many as 1 in 5 may develop retinal lesions. The most common time of life to contract the infection is early childhood, but new infections continue to occur through adult life. Cultures that favor eating undercooked meat and countries with poor public health care, demonstrate the highest levels of infection. Infections often occur as isolated cases, but large outbreaks have been reported, such as in 1995, when contamination of the local water reservoir by feral cats resulted in thousands of human infections in Victoria, Canada.

Conclusion

Understanding both the epidemiology of toxoplasmosis and the basic pathogenic mechanisms of *T. gondii* are important for development of preventive strategies to combat the infection. There is no effective vaccine against *T. gondii*.

Ocular Toxoplasmosis

In people with normal immunity, the involvement of the eye is the most common reason for concern in this systemic disease. **Prof. Carlos Pavesio, Consultant Ophthalmologist** *at Moorfields Eye Hospital in London, UK, describes the symptoms and signs found in ocular toxoplasmosis, which occur as a consequence of the inflammatory response triggered by the parasite which causes this disease, Toxoplasma gondii.*

What is inflammation?

Before going directly to the ocular disease, it is important to explain what inflammation means and what it can do. Inflammation is a reaction which involves activation of the immune system, in response to any aggression to the body, as is the case of the presence of an infectious agent. Our body is trying to eliminate an aggressor. So, inflammation is an important reaction which exists to protect the body against infections and cancer cells. But inflammation can also cause damage, especially if very intense, because many elements of this reaction can "attack" normal tissues which are nearby. The blood vessels become dilated, hence the redness seen in inflamed tissues, and allow the leakage of fluid into the surrounding tissues, which produces the swelling also present in inflammation. The vessels may be primarily involved in the inflammatory response, which means that the inflammation starts in the blood vessels themselves, but many times they are involved just because they are close to a focus of inflammation.

This attack to normal tissues produces damage and usually results in the formation of scar tissue, which will have more or less serious consequences to function depending on the tissue involved. A small scar in the finger will have no major consequences, but a small scar in the retina may produce significant visual loss.

How do I get Toxoplasmosis in my eye?

Until recently it was believed that most cases of ocular disease occurred as a consequence of congenital transmission (when the infection is acquired during pregnancy), but the evidence available now shows that many cases may probably result from infection acquired after birth. Eating undercooked meat, especially pork and lamb, and contact with cats represent well known risk factors for acquiring the disease. More recently it has been found that, in rural areas, the ingestion of contaminated water represents an important factor.

Once the parasite is in the body it will

reach the eye via the blood stream and will establish itself in the retina. There it will form cysts, which live inside your own cells, and do not elicit a response from the immune system. This is because the parasites are very smart in camouflaging themselves from your defences. They will only become visible to your defences when the cysts breakdown and release the parasites in the retina.

What are the symptoms?

The ocular disease will present in an acute form with sudden onset of floaters and/or blurring of vision, which are symptoms of disease occurring in the posterior part of the eye, and in some cases will also manifest symptoms of pain, redness and light sensitivity, typical of involvement of the anterior part of the eye.

This is all you will feel in a case of reactivation of the eye disease, but if you have just acquired the disease, the *Toxoplasma* will be going everywhere in your body and you may have variable symptoms, ranging from a very mild flu to a more severe widespread infection.

What is actually happening inside the eye?

In ocular toxoplasmosis the primary site of inflammation is the retina, where the cysts, mentioned above, containing many organisms lay dormant. It is the rupture of these cysts, which produce the inflammation called a retinitis. Depending on the location of the lesion the symptoms will vary. A lesion which is very close to the back of the eye (near the macula, which is the central area responsible for the details in your vision) will produce reduction of your central vision. If the very central area is involved the vision will drop to very low levels and this reduction of vision may be permanent (*Figure 1*).

A lesion which is close to the back of the eye, but not central, is likely to produce blurring of vision, which will be variable in intensity, and usually results in good recovery, many times to normal values. The reduction of vision in these cases is because of retinal swelling produced by the intense inflammation which is happening nearby. Once the inflammation settles down the swelling regresses and the vision improves, because the tissue was not permanently damaged (*Figure 2*).

Lesions which involve the very periphery of the retina will produce predominantly floaters, and the intensity of this will depend, predominantly, on the size of the lesion. Floaters represent debris shed into the vitreous by the inflammatory response, especially by leaky blood vessels.

As the inflammation settles down the amount of debris in the vitreous tends to reduce, but some degree of vitreous opacity always remains. These floaters may be sufficiently large and numerous

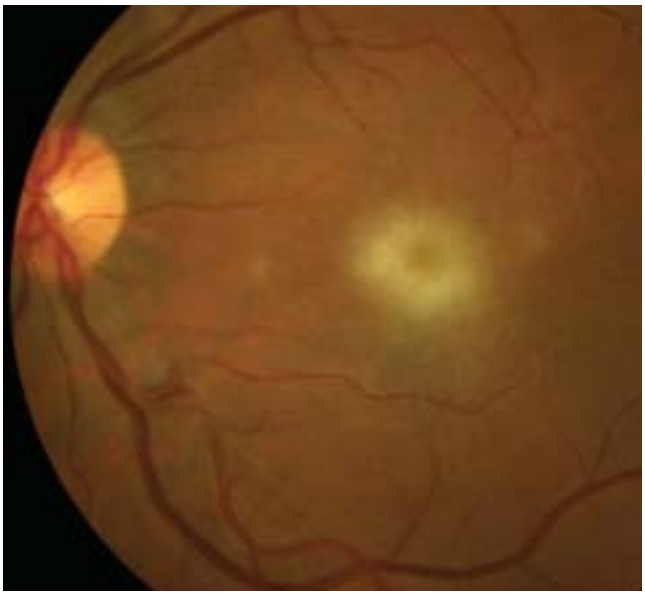

Figure 1:
This lesion is quite central (involving fixation) and will produce permanent visual loss.

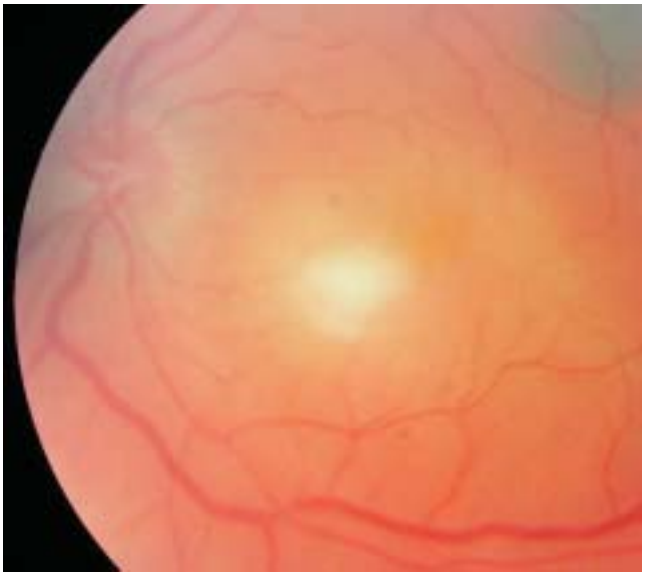

Figure 2:
Lesion very near fixation (but not involving it), with significant visual symptoms. It will result in a scar, but central vision may recover. The dark lesion seen superiorly is just a choroidal naevus (freckle).

to warrant treatment.
The inflammation affecting the front of the eye and producing the symptoms of redness, pain and light sensitivity, is a secondary phenomenon, occurring in association with the primary problem affecting the back of the eye. It will require specific treatment with eye drops and it tends to get better as the disease at the back of the eye gets under control.

What is the reason for reactivation and what can be done to prevent it?

One of the typical features of ocular toxoplasmosis is reactivation. As mentioned above this is likely to result from a break-down of a cyst of *Toxoplasma gondii* and for this reason occurs commonly near a previous scar, where cysts are more likely to be found. This lesion is referred to as a satellite lesion, and it is so typical that an ophthalmologist can make the diagnosis just by seeing it, without the need for any further tests (*Figure 3*).
In reality the reasons for reactivation are not clear. It is very possible that cyst break-down represents the normal life cycle of the cyst and the clinical manifestation will depend on the location inside the eye and intensity of the reaction of the organism against the parasite. There is nothing that you, as a patient, can do to change the risk of a reactivation, or in other words, no change in

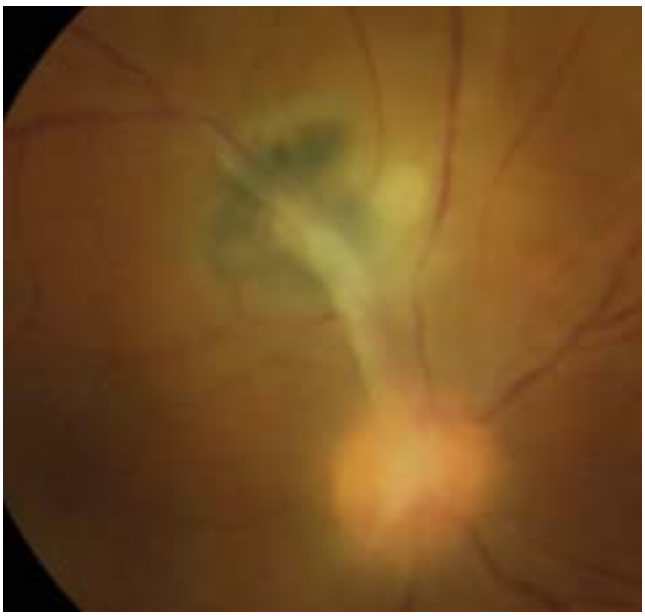

Figure 3:
Typical appearance of a reactivation with a new lesion (white) adjacent to a pigmented (black), old lesion.

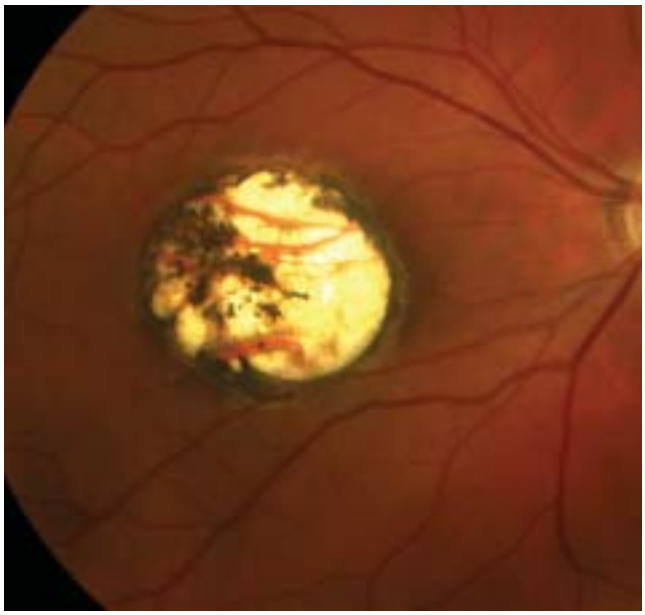

Figure 4:
Large central scar. The retina has been totally destroyed and the white seen is actually the sclera (outer coat of the eye).

your daily routine will modify it. There is some suggestion that a more prolonged course of treatment, given even without active disease, may reduce the risk of reactivation, but the reasons for this are also not clear and further confirmation is necessary.

What about visual loss?

When the retinal lesion involves the very central part of the retina (the macula), there is a good possibility that visual loss will result. Since the retinitis causes necrosis (destruction of the tissue), and the retina can not repair itself, there will be permanent loss of function. Children who acquire the disease during pregnancy may be born with large scars in the central retina (macula) and consequently with very poor vision (*Figure 4*). Unfortunately, in these cases, the disease usually involves both eyes. In the adult this occurrence of central lesions involving both eyes is rare, but visual loss in one eye can occur.

Apart from a central scar, vision may go down because of the appearance of abnormal vessels under the retina (choroidal neovascularisation). These vessels may appear in association with scars of any origin and produce visual loss also by generating more scar tissue. The appearance of these vessels is not associated with active retinal lesions, and the initial symptoms of visual disturbance will be different from a new recurrence of the disease. There will be

distortion of central vision initially, but without an increase in floaters.
The inflammation may also involve the optic nerve head (this is the part of the optic nerve which is visible inside the eye and is known as optic disc). That may happen when the retinal lesion occurs very near the nerve head and will usually result in loss of visual field (the part of your vision which is all you see around you).
Another way by which vision can be affected is by opacification of the vitreous body. This is a consequence of the inflammation and may be very mild, not generating many symptoms, or it may be dense enough resulting in a significant reduction in vision (*Figure 5*), which if not resolved after medical therapy is likely to require surgery to be corrected.
Another problem, which is also related to the changes to the vitreous induced by the inflammation, is retinal detachment. The vitreous body is attached to the retina and if the vitreous becomes inflamed and contracts it may pull the retina leading to a retinal detachment, which may require surgery.

Can visual loss be prevented?

As mentioned above, visual loss depends primarily on the location of the lesion in the retina, and to a certain extent on the intensity of the inflammatory response. Once the disease becomes active the doctor will decide if

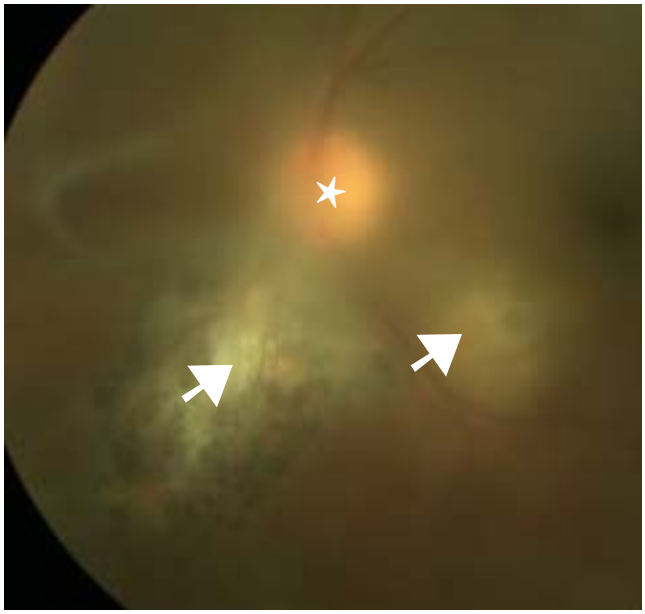

Figure 5:
Two inactive lesions (➘) near the optic disc (★), one of them larger with more pigmentation and the other one closer to the central retina. The vitreous body is not clear and is causing blurring of vision.

treatment is necessary or not, but for this he/she needs to see you as quickly as possible. Some lesions will be small and away from the centre, and for this reason may only be observed. Some lesions will be central and will result in vision loss regardless of the doctor's best efforts.
If you have a scar very near your central vision, the doctor will give you a grid (Amsler grid), which represents a good way of detecting distortion induced by the appearance of abnormal vessels under the retina or new macular edema (for more information see ***uveitis*** 1-05). The sooner they are recognised the

better since, depending on their location, different forms of therapy may be proposed.

How to prevent acquiring the disease?

Avoiding exposure to the known risk factors is the best way of not developing this disease. In the case of the cat it is important to wash your hands after handling the animal and especially after cleaning the litter box. Another tip is to clean the litter box daily, since the oocysts (eliminated in the cat's faeces) will take 48 hours to sporulate (become infective) – cleaning the box everyday means that even if you are exposed, the *Toxoplasma* is not ready to cause an infection. Avoid ingestion of poorly cooked meat and drink bottled water in areas where you may not be certain of the origin of the water.

Toxoplasmosis and AIDS

When the immune system is not in perfect shape as in patients with AIDS, ocular toxoplasmosis may result in very severe disease. **Professor Cristina Muccioli**, *working at the Department of Ophthalmology at the Federal University of São Paulo, Brazil, will explain why AIDS patients have a much higher risk for such an inflammation and what is different in the therapy.*

Toxoplasmosis in the immunocompromised patient

Toxoplasma gondii is an important opportunistic pathogen among immunocompromised patients (such as cancer patients or organ transplant recipients) and is a particularly severe problem in HIV-infected individuals. In contrast to the benign and self-limited course of infection in the general population, systemic and ocular toxoplasmosis in the immunocompromised and in patients with Acquired Immunodeficiency Syndrome (AIDS) is an aggressive and often fulminant disorder, causing central nervous system (CNS), visceral, and lymph node infection. Immunosuppression is associated with an increased risk of life-threatening toxoplasmosis as well as increase in the severity of ocular toxoplasmosis.

Toxoplasmosis is believed to be the most common non-viral infection of the brain in patients with AIDS. Clinical CNS toxoplasmosis is the most frequent cause of focal brain lesions in patients with AIDS. Toxoplasmic encephalitis may develop in 25% to 50% of AIDS patients. Although toxoplasmic encephalitis is common in AIDS, ocular involvement, in spite of being less frequent, is an important entity, because it is a treatable cause of severe visual loss in some patients. Ocular lesions may be the first manifestation of intracranial and disseminated toxoplasmosis or may occur without evidence of intracranial disease.

No consistently reliable and noninvasive means of diagnosing cerebral toxoplasmosis has been found. Histopathologic confirmation of the parasite in brain tissue obtained at biopsy yields definitive diagnosis, but false negative results have been reported. Serologic studies of sera from AIDS patients typically reveal anti-toxoplasma IgG antibodies, consistent with the high rates of seropositivity among the general adult population.

How do we diagnose Toxoplasmosis in AIDS patients?

The diagnosis of ocular toxoplasmosis in AIDS patients can be difficult to make,

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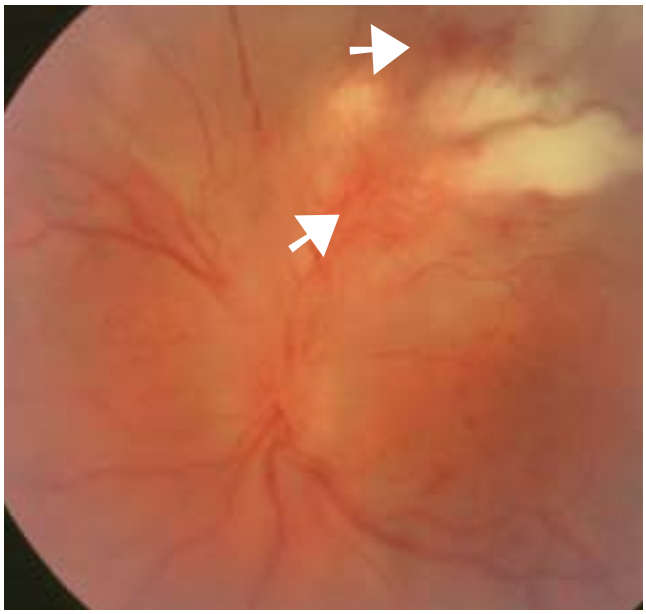

Figure 1:
Patient with AIDS and ocular toxoplasmosis that developed (neovascularization ➘).

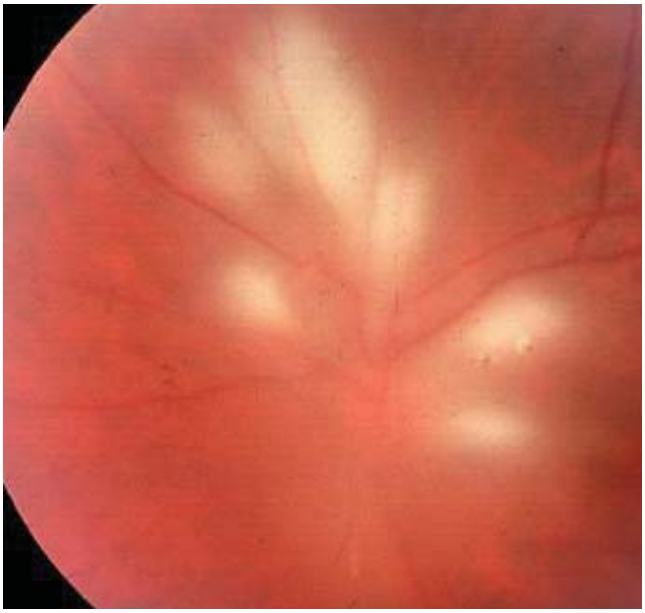

Figure 2:
Patient with AIDS and multiple active toxoplasmisc lesions.

because in some cases, the clinical picture of ocular toxoplasmosis in AIDS may be different and patients could develop an unusual presentation such as acute anterior uveitis due to iris infection with *Toxoplasma gondii*.

Ocular toxoplasmosis is the most common cause of retinal inflammation in immunocompetent patients and one of the most important causes of secondary ocular infection in HIV-infected patients. Ocular toxoplasmosis occurs in 1-2% of patients with AIDS in the US and in 8% of AIDS patients in Brazil. In HIV-infected patients, ocular toxoplasmosis can occur before the development of AIDS. The risk of life-threatening toxoplasmosis increases when CD4+ T-lymphocyte counts (a subtype of the white blood cells, which are extraordinary important for the control of infections) falls below 100/µl. These numbers are not sufficient for effective control of *Toxoplasma gondii*. Although the median CD4+ T-lymphocyte count specifically associated with toxoplasmic retinochoroiditis is not known, this infection can occur at higher counts than usually associated with cytomegalovirus (CMV) retinitis.

Although the majority of reported cases in HIV-infected patients have been unilateral, it is not uncommon to see bilateral cases. In HIV-infected patients, there can be single lesions, multifocal lesions in one or both eyes, and broad areas of retinal necrosis.

Such lesions can be more severe and aggressive than the ones observed in immunocompetent individuals. Lesions will continue to enlarge if left untreated, which probably explains the fact that most reported patients have had extensive areas of retinal necrosis by the time diagnosis is made. In most cases of ocular toxoplasmosis in immunosuppressed patients, there have not been pre-existing scars. Histopathologic examination of eyes from immunosuppressed patients with toxoplasmic retinochoroiditis reveals both tachyzoites and tissue cysts in areas of retinal necrosis and within retinal pigment epithelial cells. In immunosuppressed patients, including those with AIDS, parasites can occasionally be found in the choroid and vitreous, and the optic nerve may be infected (*Figure 1 and 2*).

How can we treat ocular Toxoplasmosis in AIDS patients?

The most typically used and successful regimen is the combination of sulfadiazine and pyrimethamine and folinic acid. Clindamycin can be used as an alternative option in patients intolerant to sulphonamide. Treatment is recommended for 4-6 weeks after resolution of all signs and symptoms (sometimes for several months or longer). Trimethoprim/sulfamethoxazole appears to be equivalent to sulfadiazine/pyrimethamine in HIV infected patients.

After treatment of the acute phase in AIDS patients, maintenance therapy should be started, usually with the same regimen that was used in the acute phase but at half the dose. Maintenance treatment should be continued until the patient recovers the immunity (CD4 count return to more than 200 cells/μl and HIV PCR viral load in the peripheral blood has been reasonably controlled for at least 6 months). Unfortunately, treatment does not prevent the recurrence of toxoplasmosis retinochoroiditis.

Conclusion

The AIDS epidemic has stimulated renewed interest in the medical therapy of toxoplasmosis because toxoplasma infection in these patients induces very severe inflammation. A goal of ongoing re-search is to identify treatment regimens that will be able to kill the cysts.

Title

Congenital ocular Toxoplasmosis

Congenital toxoplasmosis (CT) is the most frequently encountered congenital infection. Here, **Prof. Justus G. Garweg**, *Department of Ophthalmology, Inselspital, University of Bern, Switzerland,* **PD Laurent Kodjikian** *and* **Prof. Francois Peyron**, *at the Departments of Parasitology and Ophthalmology, Croix-Rousse Hospital, University of Lyon I, Claude Bernard, Lyon, France report about the long-term outcome of functional and morphological manifestations with specific focus on ocular disease according to personal experience and published evidence.*

Toxoplasmosis and Pregnancy

Toxoplasma gondii is presumably the most frequent infectious cause of posterior uveitis (inflammation of the posterior parts of the eye, which can not be seen from outside) throughout the world. In the majority of cases this infection has been acquired long ago and the parasites lay dormant in the healthy retinal tissue prior to inducing ocular disease. There exists evidence that 2/3 of cases are congenital in origin (which means the infection has been acquired prior to birth), and only 1/3 may be attributed to infection during life after birth.

The incidence of congenital toxoplasmosis is estimated for German speaking countries to 0.5 – 4 infected individuals per 1000 births, and in French speaking countries the incidence may be as much as 7 per 1000 births. Approximately 40% of German women of childbearing age have acquired immunity against the infection prior to their first pregnancy, which means they harbour antibodies against the parasites in their sera, which protect them widely against transmission during pregnancy. The remaining women have a risk of 0.5 – 1.5% of acquiring toxoplasmosis during pregnancy. If this happens, the parasite is distributed through the blood vessels and throughout all tissues of the body. The infection normally evolves in healthy individuals without signs of disease.

For the unborn child, in contrast, there is a significant risk of congenital infection and eventually severe disease. This risk at the beginning of pregnancy is pretty low, but continuously increases to 90% at the time of delivery. Vice versa the likelihood of severe organ damage for the child decreases from

90% at the beginning of pregnancy to less than 10% at birth (*Figure 1*). If toxoplasmosis is acquired during pregnancy the child has an overall risk of 30 – 40% of developing congenital toxoplasmosis. The individual risk of organ damage is related to the time of fetal infection. Very early in pregnancy it is likely to lead to death of the fetus or to produce still birth. An infection acquired during early pregnancy harbours a risk especially of severe neurological disease. Therefore, cord blood analysis and ultrasonography, particularly focussing on head and brain, should be performed. In contrast, ocular involvement may occur independently of the time of infection with the greatest risk when the infection is acquired around the 28th week of pregnancy.

The outcome of disease in congenital Toxoplasmosis

Information regarding the outcome of disease in congenital toxoplasmosis is confusing and inconsistent. A French

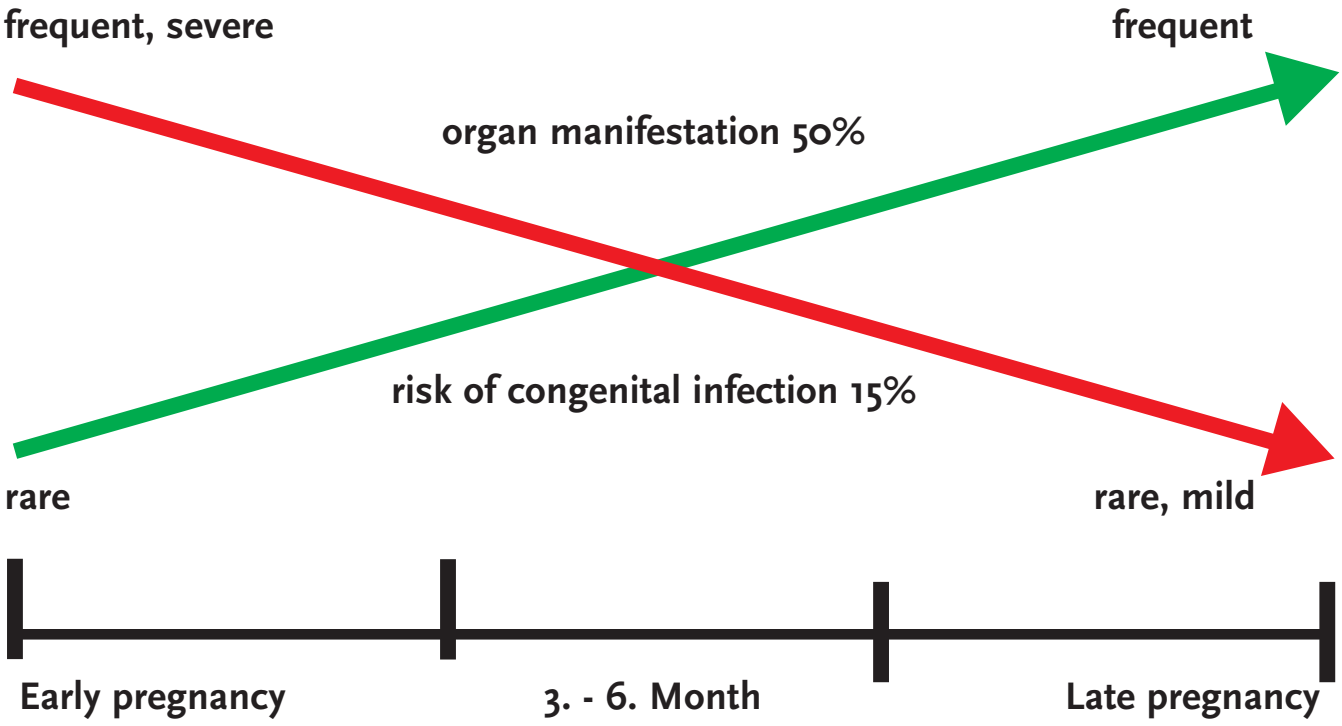

Figure 1:
Congenital Toxoplasmosis: Time of maternal infection and risk of transmission to the child

group of scientists reported a few years ago, that, after treatment during the first year of life, 24% of children developed ocular lesions due to toxoplasmosis in the later course of their lives, but information regarding the visual function is not available. Our own group has recently published the functional and morphological outcomes of a great cohort of children with congenital toxoplasmosis who had also been treated during the first year of their life.

After more than 6 years of follow-up after diagnosis 71% of these children had no clinical manifestation of their congenital infection, and 5% manifested neurological signs (i.e., hydrocephalus, cerebral calcifications and cramps), but no ocular disease. Twentyfour percent of the children developed ocular lesions as a consequence of their congenital disease; in every fifth casetogether with other manifestations. Only 6% of children had ocular lesions at birth, the remaining ones developed these in the later course of their life. Ocular involvement was observed in many cases long after the first year, sometimes up to 10 years after birth. In 66 children with ocular involvement we were able to assess the visual function. Eighty-five percent of the children with chorioretinitis (*Figure 2*) had normal visual acuity, despite of their ocular lesions. In 15% of the cases visual acuity of one eye was reduced, with 12% being mild, and in only one instance there was servere visual loss. In approximately 28% of children both eyes were involved, but a moderate bilateral reduction in visual acuity was present in only 3 instances. In summary, the visual outcome of congenital ocular toxoplasmosis seems to be much better for children who receive treatment during the first year of life.

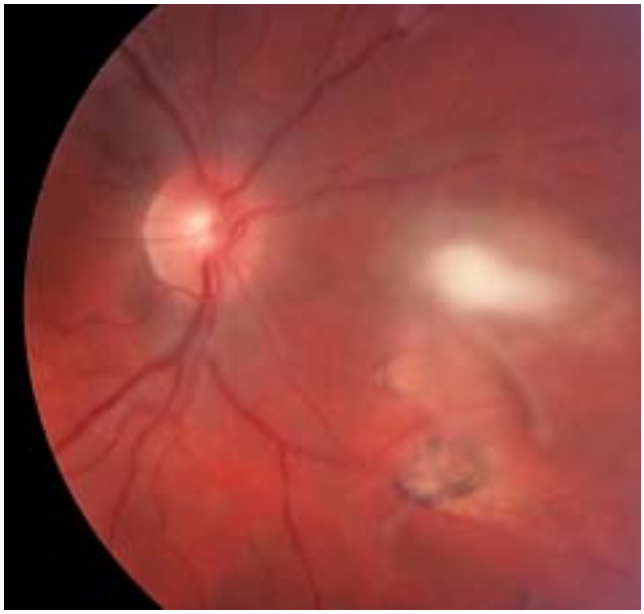

Figure 2:
Congenital ocular toxoplasmosis in a 27 years old healthy male individual: As is typical for congenital ocular toxoplasmosis, there is an old chorioretinal scar (white centre and pigmented sharply delineated rim) which is usually asymptomatic. The patient visited us with an increasing number of floaters on this eye over the last 2 weeks, but without any additional functional impairment. The view to the retina shows reactivation with a new whitish lesion and surrounding tissue swelling.

Diagnostics in congenital Toxoplasmosis

If a congenital toxoplasmosis is suspected, it is strongly recommended to obtain not only mother blood but also umbilical vein blood from the child in order to have baseline values for the development of immunity of the child against the parasite. After birth, a detailed clinical examination of the posterior parts of the eye and a skull x-ray or ultrasonography is performed depending on the clinical findings at birth. Blood examinations are performed to follow the development of *Toxoplasma* antibodies during the first year of life.

The therapy of congenital Toxoplasmosis

Until now there is no evidence that early (i.e. during pregnancy) therapy is able to reduce the risk of congenital infection or to prevent severe organ manifestations. However, therapy of children with congenital infection during the first year of their lives has generally been found to be beneficial and therefore has been widely accepted.

Conclusion

One might conclude that every fourth mother who acquires toxoplasmosis during pregnancy will give birth to a child with congenital toxoplasmosis. Amongst these children with congenital toxoplasmosis, only one in ten will show ocular involvement at birth. But up to the age of 10 years, 30% of children will manifest the disease in the eyes. Therefore we would suggest regular eye examinations for children with congenital toxoplasmosis. The relevance of early diagnostics and treatment in cases of suspected congenital toxoplasmosis during pregnancy has not been established and a decision is usually made on the individually estimated risk of complications.

Title

Therapy of ocular Toxoplasmosis

Treatment of ocular toxoplasmosis is not always necessary, but when indicated several good drugs are available. **Prof. Dr. Aniki Rothova** *from the Uveitis Center at the FC Donders Institute of Ophthalmology, University Medical Center Utrecht, the Netherlands, describes the rules for treatment and possible drugs.*

Who needs treatment of ocular Toxoplasmosis?

Not everybody who has ocular toxoplasmosis (OT) needs treatment. An episode of active OT usually quietens down spontaneously within several weeks. Moreover, the drugs used for toxoplasmosis may cause adverse effects. In addition, the treatment has limited effect: it only stops the multiplication of parasites during the active attack, but does not destroy the silent "sleeping form" of the parasite, the bradyzoite. The bradyzoite remains in the retina throughout the patient's life and may cause flare-ups. Unfortunately, the currently available drugs do not eliminate this silent form of *Toxoplasma* from the eye and therefore treatment does not protect patients against possible future attacks. The most important complication of OT is a permanent loss of visual acuity through the formation of scars in the central part of the retina (macula). During an active attack of OT, the inflammation causes a cloudy vision and patients might see moving black shadows, but these problems usually disappear during several weeks. What is more, during the attacks the scars in the retina are formed, but fortunately not all patients develop scars in the central part of the retina. If the scar is situated in the peripheral (not seeing) part of the retina, the visual prognosis is excellent. However, if the lesion is situated in the centre of the retina (macula) or near the optic nerve, permanent loss of central visual acuity may occur and these patients require aggressive treatment (*Figure 1*).

Antibiotics are important

The standard treatment includes a combination of diverse anti-parasitic drugs, of which the most powerful is pyrimethamine (Daraprim). The treatment is usually given for four to six weeks during an active attack, but may be longer; the duration of treatment differs with the individual and (largely) depends on the severity of the attack. Additional drugs, such as sulfonamides or various antibiotics (clindamycin or

azithromycin) improve the effectiveness of the treatment. Sulfonamides add to the anti-parasitic effect of pyrimethamine, but frequently cause allergic reactions, such as severe skin rash. Moreover, pyrimethamine and sulfonamides may also severely reduce the growth of blood cells in the bone marrow and may cause a temporary drop in white blood cells and platelets. Therefore, regular control of blood counts is necessary. *Toxoplasma* parasites and young blood cells need folic acid for their growth. Pyrimethamine and sulfonamides prevent the formation of folic acid in the human body. However, contrary to *Toxoplasma*, human cells in bone marrow can use folinic acid given in tablets (folinic acid works like folic acid in human body). Therefore folinic acid (Ledervorin) is usually added to the treatment to prevent side effects of pyrimethamine and sulfonamides. Folic acid should not be used during the treatment, since it makes the treatment ineffective. The antibiotics clindamycin and azithromycin have a weaker effect on *Toxoplasma* than pyrimethamine, but luckily both have relatively few side effects. In laboratory experiments the expensive drug atovaquone was also effective on the latent forms of parasite and a hope has arisen that atovaquone could destroy all the parasites in human body. Unfortunately, the eradication and the cure with atovaquone do not occur in humans and even despite this treatment, the recurrent form of the disease develops frequently. Treatment with steroid eye drops may further reduce the inflammation. Additional eye drops may be needed to reduce elevated intraocular pressure.

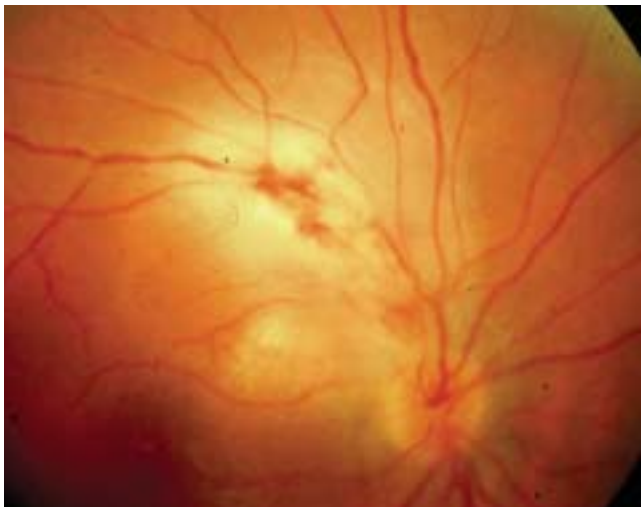

Figure 1:
Toxoplasmic lesion in the retina before the treatment

Should Corticosteroids be part of the medication?

Corticosteroids are drugs, which can strongly reduce the eye inflammation, but unfortunately they might also stimulate *Toxoplasma* growth. It is sometimes necessary to use prednisone with the purpose to reduce inflammation during the course of OT. However, it is essential never to use corticostroids alone, but always together with anti-parasitic drugs. Typically corticosteroids are added to treatment 1-3 days after commencement of the antiparasitic drugs.

Title

Problem: the pregnant women and ocular Toxoplasmosis

Pregnant women who have a flare-up of OT are normally not treated unless they have dangerous or severe symptoms. This is because the medications might be of considerable risk to the fetus, especially in the early stages of the pregnancy. The cooperation of gynecologist and ophthalmologist is required in these cases. The antibiotic spiramycin is given to pregnant women with systemic toxoplasmosis to prevent the infection of the fetus; this drug is in high concentration in the placenta and can form a barrier between infected mother and not (yet) infected child. Spiramycin does not penetrate into the eye and is not used for ocular disease.

Treatment of patients with low immunity

(AIDS patients, patients on anti-cancer treatments and patients following organ transplantations):

In general, the same drugs are used for as in patients with full immunity; however, continued treatment with at least one anti-parasitic drug is necessary to maintain disease quiescence (see also page 17).

Prevention of future attacks

The eye problems in OT are likely to recur and it takes constant watchfulness to notice new flare-ups early and to prevent deterioration of eyesight. Reliable medical prevention of future attacks is not yet possible. Prolonged treatment with at least one of the anti-parasitic drugs minimizes the frequency of recurrences, but the experiences with this long-term treatment are not abundant and the optimal regimens for continued treatment are not yet established. Nevertheless, for patients at risk of losing visual acuity in their better eye, continued treatment with anti-toxoplasmic drugs might be the only option.

Congenital disease

Pregnant woman with systemic toxoplasmosis should always be evaluated by an experienced gynecologist. The treatment possibilities depend on the stage of the pregnancy and on evidence of infection of the fetus. Newborns infected by *Toxoplasma* should be evaluated and treated by an experienced pediatrician eventually together with an ophthalmologist and if necessary, a neurologist. Infected newborns are usually treated with a combination of pyrimethamine and sulfonamides during one year (see also page 21).

Prevention of Toxoplasmosis

Since a vaccine is not yet available, it is important to prevent toxoplasmosis in pregnant women and people with decreased immunity. The crucial factor is adequate information how to avoid

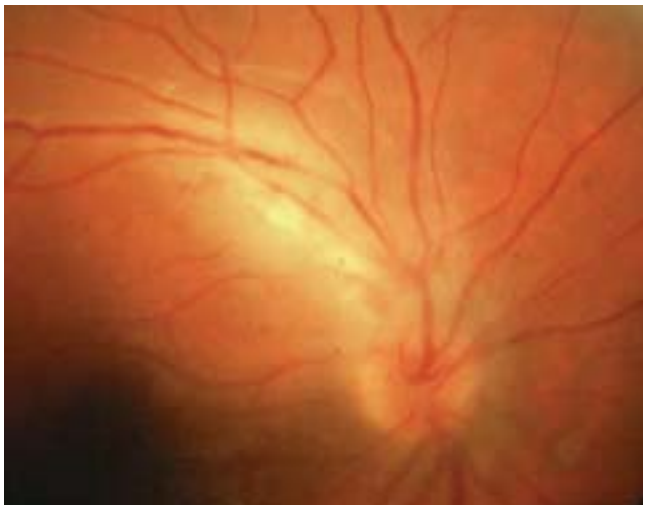

Figure 2:
Same lesion, 3 weeks after the onset of treatment

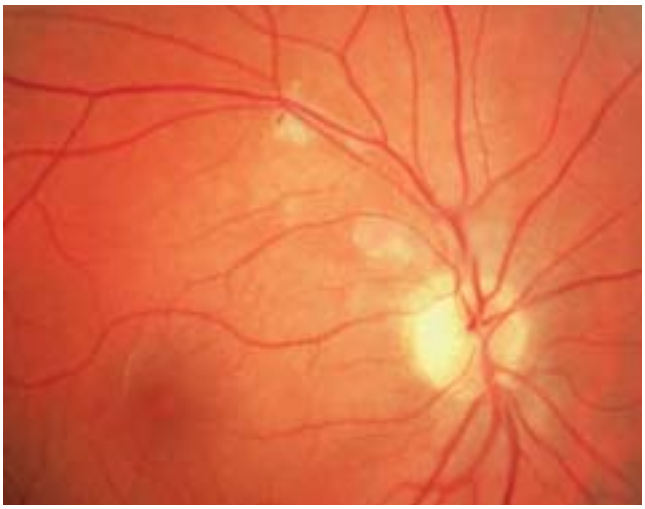

Figure 3:
Same lesion, 6 weeks after the onset of treatment

infection (e.g. cook meat until it is well done and do not taste on beforehand, wash fruit and vegetables, wear gloves when working in the garden and avoid cat litter). There are several examples in Europe, France and Austria in particular, where *Toxoplasma* infection is assessed in the course of general programs for all women at childbearing age. At present, a special European Toxoplasmosis Working Group of experts investigates the efficacy of these strategies and evaluates the best regimens for prevention and treatment possibilities for pregnant women and their newborn children infected with toxoplasmosis.

Conclusion

There are multiple drugs available for the reduction of inflammation in ocular toxoplasmosis. Unfortunately none of these drugs seems to reduce the rate of recurrences. So, the future research has to concentrate on this issue.

Toxoplasmosis in Uveitis

Patient Report from France

Narrative from a mother confronted with congenital Toxoplasmosis.

I was 26 years old when pregnant with my first child. At the first consultation the gynecological examination revealed no antibodies to toxoplasmosis. The gynecologist warned me of the risks of contracting toxoplasmosis during pregnancy and gave me dietary and hygiene advices to prevent contracting the disease. I followed this advice avoiding eating red meat and cooking vegetables and fruits, except for those with rind. In spite of this, at the monthly serological testing in my 6th month of pregnancy, the gynecologist told me I had just seroconverted. My antibodies were positive; I had caught toxoplasmosis. I was extremely anxious, knowing the risks of fetal infection and did not understand, how I possibly had acquired it, since I had adhered rigorously to the diet and had had no contact with cats. I later learned that other means of contamination had been discovered: tap water or by breathing in contaminated dust. I was immediately treated with the antibiotic Rovamycin while awaiting sampling of amniotic fluid to know if the baby was contaminated. The day of the scheduled sampling, the gynecologist could not perform the puncture due to the stage of pregnancy; the baby took up too much space, so there was not enough fluid accessible. Since sampling was too risky, they decided to treat me as if the baby was contaminated. I therefore took two antibiotics, Adiazine and Malocide, until the end of my pregnancy.

I delivered early, at the 36th week of pregnancy. The baby was hospitalized for cord blood sampling and serology for antibodies, a cerebral echography, a spinal tap, an ophthalmological examination and an overall biological workup. I was at his side throughout the tests. I was worried, imagining that he might be contaminated and have ocular and cerebral complications.

Happily, he was in good health. However, he was contaminated and the pediatrician recommended a one-year treatment with antibiotics (Adiazine and Amlocide in alternation with Rovamycine) and cortisone. It was very hard to have him take the medicine. Indeed, these antibiotics do not exist in pediatric

formulas. Therefore we had to use pills destined for adults, to adapt the doses to his weight, crush the pills and make him swallow them mixed with milk. He then associated milk with medication, which had to be taken absolutely. He developed anorexia and was very difficult to feed. He also had to undergo a blood test once a month to keep track of his antibodies and secondary effects of the treatment. This was a particularly difficult period for both him and us.

The ophthalmological examinations were normal and the infant developed normally, save for his nutritional disorders, which persisted until he was 6 years old.

I thought I could relax, but when he was 11 years old, his school called us. My son complained of a black spot in front of his right eye. I urgently consulted an ophthalmologist and the doctor confirmed the presence of a burst of ocular toxoplasmosis centered beside the optic nerve and a large black spot in the visual field linked to the focus. My son was hospitalized for 3 days in a pediatric unit to be treated with antibiotics, as usual Adiazine and Malocide, and cortisone perfusions. After 3 weeks, there was a cutaneous allergic reaction to Adiazine, which was replaced with Zithromax. But this treatment was effective and the focus rapidly healed and each day my son could see a reduction of his black spot until it disappeared completely.

Today, my son is 13 years old. He is very well. However, I know that a relapse can occur in 50% of the cases within 3 years. I have therefore warned him and asked him to alert me to any ocular anomalies. I am also well aware that there is no definitive cure. For him, it is a source of anxiety and he constantly asks me questions about toxoplasmosis. If he has another recurrence, he knows he will have to be treated again. There is a maintenance therapy, which greatly reduces the frequency of recurrences. One only has to take a Bactrim pill once every three days for at least 2 years. This only applies to multi-relapse cases. Since my son had an allergic reaction to Adiazine, he cannot take advantage of this treatment, which is otherwise efficacious.

We must live with the risk of a recurrence and remain vigilant without worrying too much. My son has asked all the questions and all the answers provided have been frank. This has finally allowed us to reassure him. I hope that this narrative will be useful to other women confronted with the problem of congenital toxoplasmosis. I confess I initially felt very guilty because I passed on this disease to my son. But in retrospect, I realize that I did what was necessary to avoid contracting toxoplasmosis. Fate did the rest.

C. V.

Ocular Toxoplasmosis in a German Patient

With the exception of wearing glasses, which is usually quite normal as one grows older, I have never had any eye problems. Therefore it was very frightening to experience what became a major problem with my left eye, almost overnight. I remember quite well that my eye felt strange. It was like suddenly having the sensation of something being in it. Furthermore an opaque coating had formed over the eye. There was no pain and I felt perfectly fine otherwise.

As it is often the case, this happened at a weekend. By Monday I was very much aware that something was wrong, as the symptoms had not disappeared. I immediately went to my eye doctor, who was most concerned, as the pressure in my eye was very high. Consequently I was given a tablet to relieve this. My doctor admitted that he was not entirely sure what was wrong, however he had a feeling that it may be uveitis caused by toxoplasmosis. He recommended that I go to my doctor to have blood tests done and that I should see an eye specialist as soon as possible. The situation was very worrying and all I could think about was that I may be going blind.

After initial visits to the local hospital my husband and I decided to seek specialist advice. Having seen the specialist it was then confirmed that I did indeed have toxoplasmosis induced uveitis. When the treatment began, it was at the time a great relief as finally a name had been put to the problem and it was now being treated.

Treatment consisted of a barrage of pills including antibiotics and cortisone in high doses. This did not help my self-confidence, as I gained weight with the cortisone and had to counter act other unwanted side affects which could have affected other parts of my body.

I learned that the kidneys needed help so I had to take medicine for that. Also bone problems can arise in the long term hence more pills to counteract this, not to mention the numerous eye drops which have to be fitted in between. Suffice it to say I had to make a daily plan of what and when to take. However at the time I would have taken anything, if it would have helped to solve the problem.

After many visits to the specialist it seemed that things were improving. Unfortunately, it was not to be and after complications it became necessary to have a delicate surgery (vitreous membrane had formed in front of the macula) which was also done successfully.

Gradually, after more than two years, things have stabilised and although the sight in my left eye will never be as it was due to macular atrophy, I'm thankful that at least the inflammation seems to be quiet.

S. S.

Patient Report from the USA

I feel extremely lucky to have been born with very good (20/15) vision, so it was quite the shock when I woke up one day with cloudy vision in my left eye. It was very subtle the first day and part of me wondered if I was just imagining it. Fortunately I happen to work in an ophthalmology clinic, so the next day a doctor looked at my eye. He saw swelling on the cornea and white blood cells accumulating in the front of my eye. I was diagnosed with iritis. I began using steroid drops four times a day and followed up with my doctor three days later. He told me that my eye looked much better, which I didn't understand because my vision was getting worse. The cloudiness increased significantly, to the point that everyone and everything looked as if it were a "Glamour Shot" photo. I was seeing debris in the form of little specks and lines, as well as experiencing occasional flashes of light. I was also having a lot of difficulty driving at night, because the cloudiness made headlight glare so bad. My doctor referred me to an uveitis specialist, who diagnosed me with toxoplasmosis. I was happy to taper off the steroid drops, but I had to start taking large antibiotic pills for six weeks. For the first few weeks I saw no improvement in my vision, and when it did start improving, it was a slow process. It is now three months since my diagnosis. While the cloudiness and flashes of light are gone, I can still see debris when I'm in bright rooms or looking at white surfaces and it will likely be a while before that debris absorbs into my body. I am grateful, however, to have been in such good hands throughout this experience.

S. F.

Patient Report from Brazil

I am a 24 year old lady from Brazil. When I first woke up with one of my eyes completely blurred, not seeing anything, I started to feel desperate. I went to a hospital to be examined by a doctor that referred me to a uveitis specialist. I talked to some friends and made a web search to try to identify a specialist and I found the one who really took good care of my eyes and me. She (the uveitis specialist) examined my eyes and answered all my questions regarding what uveitis and toxoplasmic uveitis are and how my treatment will be. After a while I was a little calmer but I felt very anxious and very scared about what could happen to my vision. I started my treatment with the combined specific therapy comprised of sulphadiazine, pyrimethamine and folinic acid as well as with oral corticosteroids and topical eye drops.

After 2 weeks my vision was not good enough and my doctor requested another ophthalmological examination (called OCT) that revealed macular edema as a complication. I started to feel very scared with the possibility of having my vision decreased or with the possibility of losing my vision. My doctor again was very professional and asked me to maintain the treatment and to stay calm waiting for the improvement in my vision. According to my doctor, my vision has a good chance to recover because the toxoplasmic lesion was not in a very important location at the retina.

After 6 weeks of therapy I recovered, reaching my previous visual acuity and started taper the drugs.

After this period, I stopped all medications and I am having now regular eye examinations every 6 months. So far, I have not developed any new ocular lesions, which I know may happen.

What I want to say in my report is that during the period that I developed blurred vision, I could not stop thinking on how important vision is, especially for someone like me who is still doing a University course and working in a laboratory where I must have very good vision to perform my work. I do realize how important it was to be helped and examined by a good specialist that was able to offer me good ocular treatment as well as a good psychological support.

CFM

News from Science

*In each edition "**uveitis**" will present a service for ophthalmologists informing about aspects from pathogenesis, diagnostics and therapy of uveitis. This time* **Professor Bahram Bodaghi**, *University of Paris VI, Paris, France, reports from the Meeting of the ARVO (Association for Research in Vision and Ophthalmology) which took place in May 2005 in Fort Lauderdale, USA, when 10 presentations were dedicated to toxoplasmic retinochoroiditis.*

Experimental models

Development of an acute ocular Toxoplasmosis Model in Mice.
I.Blader, E.Charles.
Microbiology and Immunology, University of Oklahoma Health Sciences Center, Oklahoma City, OK., USA

The pathogenesis of ocular toxoplasmosis needs to be better defined. It is still important to develop different experimental models in order to understand the pathophysiology of toxoplasmic retinochoroiditis but also to develop diagnostic tools and to evaluate different therapeutic strategies before clinical trials. Interestingly, a new model of acute ocular toxoplasmosis in mice was presented by Blader and Charles from the University of Oklahoma. Different concentrations of *Toxoplasma gondii* were injected into the vitreous of C57BL/6 mice and inflammation was assessed at 2, 4 and 6 days after injection. In the comparison with eyes injected with 1,000 tachyzoites, which showed very slight inflammatory reaction, those injected with 10,000 tachyzoites and examined at day 6 after injection displayed severe retinochoroiditis, vitritis, destruction of retinal architecture and retinal detachment. High numbers of parasites could be detected in all layers of the retina as well as the optic nerve. This murine model will allow the authors to address different issues such as how ocular immune responses are activated and which parasite proteins are important for the development of ocular lesions.

Analysis of immunomodulatory Genes of human Müller Cells infected with *Toxoplasma gondii*.
Knight et al., Rayne Institute, London, United Kingdom

Human Müller cells, one of the retinal components, have been used to study molecular interactions with the parasite (two different strains of *T. gondii*). Nucleic acids and supernatants were collected from infected and non-infected

Physicians and Uveitis

cells at different time intervals and compared using DNA microarray technology. This method allowed the authors to evaluate upregulation of different pro-inflammatory proteins such as MCP-1, IL-6 and IL-8 after infection. Interestingly, upregulation of these molecules plays an important role in recruiting inflammatory cells to clear infection. The cytokines IL-4 and IL-6 may play a role in the promotion and maintenance of parasite encystment.

Interaction between *Toxoplasma gondii* Tachyzoites and retinal microvascular Endothelium.
Chipps et al., Casey Eye Institute, Oregon Health & Science University, Portland, OR, USA

Endothelial cells are another major cell type for parasitic replication and an important target for the pathogenesis of this agent. Susceptibility to ocular toxoplasmosis may be related to preferential binding between tachyzoite and endothelial cells. By using a recombinant yellow fluorescent protein-expressing RH strain *T. gondii* tachyzoites to infect sections of unfixed human retina, Chipps et al. quantified the number of parasites overlying endothelium compared with non-endothelial retina. The distribution of binding was different for endothelial and non-endothelial regions in two independent donors. Obviously, the ability of tachyzoites to bind to retinal endothelium is an important factor influencing susceptibility to parasitic infection. This interaction may be a critical factor for infection and disease progression.

Epidemiology

Epidemiology of secondary Uveitis in Germany.
Leuchtenberger et al., Interdisciplinary Uveitis Center, University of Heidelberg, Heidelberg, Germany

In order to evaluate distribution of the disease and determine the efficacy of antiparasitic strategies epidemiological data on ocular toxoplasmosis are still lacking in the general population but also during immunodeficiency.
Data on secondary uveitis in Germany have been reported by Leuchtenberger et al. 1022 patients were included in this retrospective study, performed between 2001 and 2004. More than 58% of patients presented with a secondary uveitis. An infectious condition was determined in 18% of patients, the most frequent types being herpetic infections (37%) followed by toxoplasmosis (34%). In AIDS patients, the prevalence of toxoplasmic retinochoroiditis seems to change since the introduction of highly active antiretroviral therapy. Cytomegalovirus retinitis remains the major vision-threatening condition even though its incidence has significantly decreased.

Physicians and Uveitis

Prevalence of Posterior Ophthalmic Disease in Patients seen in a collaborative Infectious Disease/ Ophthalmology Clinic Setting. Gill et al., Ophthalmology, Mount Sinai Medical Center, New York, NY, USA

Ophthalmic Manifestations in HIV positive Patients: Evaluation of 286 consecutive Patients in one Year. Modorati et al., Departement of Ophthalmology, University Hospital San Raffaele, Milan, Italy.

Two studies, one from the USA and one from Italy have determined the incidence of ocular complications in HIV-patients followed between 2002 and 2004 or 2003 and 2004, respectively. Interestingly, results seem to be similar in both series. Toxoplasmosis was identified in nearly 6% of patients in New York (USA). Frequency of toxoplasmosis, syphilis, candidiasis and tuberculosis was 12.2% in Milan (Italy).

Diagnosis

Recurrent ocular Toxoplasmosis Evaluation: Findings from Fluorescein Angiography and Indocyanine Green Angiography. M.H. Amaro and C.Muccioli, Ophthamology, Federal University of São Paulo, São Paulo, Brazil.

Fluorescein and indocyanine green angiography (ICG) are two diagnostic methods used for the management of posterior uveitis. Fluorescein angiographic patterns have been previously well-described, showing the presence of a necrotic lesion within the retina. Angiographic findings observed in 23 cases with recurrent toxoplasmosis have been reported. Toxoplasmic regions display initial hypofluorescence in the centre of the active recurrent lesion and hyperfluorescence in the margin in the later phases in all cases. ICG showed initial hypofluorescence in the active recurrent lesions, but also multiple hypofluorescent spots surrounding the active lesion in more than 2/3 of cases, multiple hypofluorescent spots far away from the active lesion in normal areas in the funduscopy and fluorescein angiography (25% of cases) and finally hyperfluorescent spots in the region of active lesion in less than 10% of cases. ICG gave evidence of more widespread disease or adjacent inflammatory effects due to the infectious agent.

Physicians and Uveitis

Interestingly, these results show that the disease may involve more areas than what was expected.

Immunoblot and Witmer's Coefficient Comparison in ocular Toxoplasmosis
Galland et al., Ophtalmologie, CHU Timone, Marseille, France.

Role of PCR in Diagnosis and Management of infectious Uveitis.
Vasseneix et al., Ophthalmology, La Pitié Salpêtrière Hospital, Paris, France

Diagnostic management of infectious uveitis remains a major challenge for ophthalmologists. PCR and serologic analysis of ocular fluids may be proposed in atypical forms of severe, chronic and sight-threatening uveitis, in order to avoid the use of aggressive or non conventional immunosuppressants and to propose a specific therapeutic strategy. The diagnosis of ocular toxoplasmosis is based on clinical examination, especially funduscopy. However, in atypical cases, analysis of ocular fluids (aqueous humor or vitreous) is mandatory in order to confirm a parasitic infection. Three different presentations were dedicated to the molecular diagnosis of infectious uveitis, including toxoplasmic retinochoroiditis.
T. gondii proteins (immunoblot) and specific anti-parasite antibody production may be identified in the aqueous humor. In a retrospective study performed between 2001 and 2004, results of anterior chamber tap performed in 40 cases of putative and severe toxoplasmic retinochoroiditis were reported. Sensitivity of the immunoblot technique was 63.6% and that of the Witmer coefficient 45.5%. Combined sensitivity of both techniques together was 77.3%. For the authors, this type of examination appears to be indicated in atypical cases of ocular toxoplasmosis when diagnosis is not made after two weeks of evolution.

Vasseneix et al. have reported the serological and molecular analysis of aqueous humor in patients referred for an infectious condition with an atypical clinical presentation. Among 671 patients managed during 2001, an infectious condition was identified in 188 cases (28%). Toxoplasmosis was the most frequent etiology (67 cases) followed by herpetic infections (51 cases), bacterial infections (53 cases) and candidiasis (6 cases). Analysis of ocular fluids was contributory in 87% of parasitic uveitis, 45% of viral anterior uveitis and 83% of viral retinal necrosis. PCR seemed to be more informative in patients with viral infection, whereas evaluation of specific intraocular antibody production was more sensitive in patients with toxoplasmosis.

Therapeutic options

Verteporfin Photodynamic Therapy (PDT) of CNV Associated With Toxoplasma Retinochoroiditis.
Leys et al., Ophthalmology, University Hospitals Leuven, Leuven, Belgium

Conventional treatment of ocular toxoplasmosis is based on antiparasitic drugs. Different molecules are now available and different associations may be used in order to control parasite replication. Choroidal neovascularization remains one of the complications of toxoplasmic lesions. Secondary hemorrhage may induce severe visual loss. As for age-related macular degeneration, photodynamic therapy with verteporfin may be proposed in complicated lesions of ocular toxoplasmosis. Leys et al. report a series of 8 patients, treated for choroidal neovascularization. Mean visual acuity increased from 20/225 to 20/123 during a mean follow-up of 2 years. Persistent closure of neovascular lesions was achieved in 7 out of 8 patients with a mean number of 1.8 treatments and without any significant adverse event. However, a longer follow-up is recommended before further conclusions.

Cultural Corner

Everything You Always Wanted to Know About Rennes

Rennes is the capital of Brittany. It is connected to Paris by train (2 hours 15 with the TGV). The names "Rennes" stems from "Riedones", a tribe that inhabited this part of Gaul in the 2nd century BC. The Romans named it "Condate". Attacked in 275 AD, the city is later fortified, and the wall reinforced still during the XIVth and XVth centuries.

King Charles VIII's engagement ceremony to the duchess Anne de Bretagne was held in the Notre Dame de Bonne Nouvelle chapel in 1491. Brittany then belonged to France, as ascertained in 1532 by the Union treaty.

Today there are more than 200,000 inhabitants in Rennes. The city buzzes with activity in fields such as teaching (60,000 students), research (3,500 researchers), and music (in particular the renowned "Transmusicales").

Public transportation allow blind or handicapped to discover the city.

You will be able to walk at leisure in the old districts. Around the Cathedral, century-old streets remain in spite of the terrible fires of December 29, 1720 during which 33 streets and 900 houses were burnt to the ground. Explore the lovely narrow streets of "Saint-Sauveur", "de la Psalette", "du Chapitre", "Saint-Yves" and "Saint-Michel", with colourful wooden houses dating back to the XVth century.

The city hall was built in the XVIIth century by Gabriel. It looks upon the National Theatre of Brittany by the architects Joly and Carly. The square is exceptionally pretty. Nearby the Parliament of Brittany, designed by Salomon de Brousse in the XVIIth century deserves your admiration.

On Saturday mornings you can discover the public market on the Place des Lices, whose name comes from the tournaments of the Middle Ages. This market is one of the best-known and richest in France.

A few miles away are famous places from ancient legends such as the “Val sans retour” (Vale whence none is coming back), the fountain of Barenton or Merlin’s tomb. A bit further away are Saint-Malo, Dinard, Lorient, Quiberon and Belle-Île en Mer.

Enjoy your stay!

Marie-Jo Ménager-Joulain

Image:
Porte Mordelaise

Uveitis Information Group

A patient led information and support group.

Activities

- Provision of information and support by letter, phone and email.
- Public meetings around the UK.
- Web site

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