June 28 (Friday) 13:40-17:10 Room 1 (Auditorium)

6th International Workshop on Ocular Tuberculosis

Chairs / Moderators: Soumyava Basu *(India)*
Daniel Vitor Vasconcelos-Santos *(Brazil)*
Annabelle A. Okada *(Japan)*

13:40-13:50	**Introduction to the session and its objectives** Soumyava Basu *(India)*
13:50-13:57	**WHO recommended treatment for extrapulmonary tuberculosis** Annabelle A. Okada *(Japan)*
13:57-14:04	**Treatment of intraocular tuberculosis and its duration in India** Parthopratim Dutta Majumder *(India)*
14:04-14:11	**Treatment of Intraocular tuberculosis and its duration in Myanmar** May Zun Aung Win *(Myanmar)*
14:11-14:18	**Diagnosis and treatment of intraocular tuberculosis in South Africa** Derrick P Smit *(South Africa)*
14:18-14:25	**Treatment of intraocular tuberculosis and its duration in South America** Daniel Vitor Vasconcelos-Santos *(Brazil)*
14:25-14:32	**Management of Immune-Mediated Complications in Ocular Tuberculosis: A North American Perspective** John Gonzales *(USA)*
14:32-14:39	**Treatment of Intraocular tuberculosis and its duration in Europe** Edoardo Baglivo *(Switzerland)*
14:39-14:50	**Short Break**
14:50-15:00	**Summary of gaps in the knowledge- Management:** Daniel Vitor Vasconcelos-Santos *(Brazil)*
15:00-15:10	**Summary of gaps in the knowledge- Current study designs:** Soumyava Basu *(India)*
15:10-16:30	**Panel Discussion**
16:30-17:10	**Presentation of prospective study design and conclusion:** Annabelle A. Okada *(Japan)*

Panelists: Narsing Rao *(USA)*
John Gonzales *(USA)*
Wesley Ribeiro Campos *(Brazil)*
Carlos Pavesio *(United Kingdom)*
Padmamalini Mahendradas *(India)*
Shelina Oli Mohamed *(Malaysia)*
Hassan Al-Dhibi *(Saudi Arabia)*
Rina La Distia Nora *(Indonesia)*
Yong Tao *(China)*
Jessica Marie Abano *(Philippines)*
Somsiri Sukhavatcharin *(Thailand)*

Ocular tuberculosis (TB) is being increasingly recognized as a cause of intraocular inflammation in both TB-endemic and non-endemic countries. In previous years, the International Workshops of Ocular Tuberculosis have discussed diagnostic criteria, imaging characteristics and prognostic factors of this condition. The theme for this year's workshop is the treatment of ocular TB. In general, treatment of extrapulmonary TB (EPTB) has not been addressed with the same rigor as pulmonary TB, in scientific literature. The WHO guidelines have little information on treatment of EPTB. Thus, it becomes the responsibility of specialists of different organ systems to develop guidelines for their respective fields. These guidelines are expected to include not only dosage and duration of anti-TB therapy, but also different forms of adjunctive therapy, that are specific to the organ.

In this year's workshop, speakers from different countries will describe the patterns of ocular TB and its treatment in their respective countries. This will be followed by a panel discussion to evaluate the currently available evidence on treatment of ocular TB. Specifically, we would address the dose and duration of anti-TB drugs, determinants of treatment end-points, approach to treatment failure, and the role of various forms of adjunctive therapy, specifically anti-inflammatory therapy. It is expected that the discussion would lead to development of a prospective study design to evaluate the optimal treatment duration for ocular TB.

WHO recommended treatment for extrapulmonary tuberculosis

Annabelle A. Okada
Kyorin University School of Medicine, Tokyo, Japan

The WHO TB Treatment Guidelines 4th Edition published in 2010 was the last comprehensive general guidelines produced by the WHO. In it, there was only 1 full page on the treatment of extrapulmonary tuberculosis (EPTB). The major summary points were that of specific forms of EPTB, lymphatic, pleural, and bone/joint disease are the most common, while pericardial, meningeal and disseminated (miliary) forms are the most fatal. Furthermore, the Guidelines stated that the frequency of extrapulmonary involvement increases with HIV disease. Finally, treatment regimens recommended in the Guidelines for EPTB were the same as for pulmonary disease, with the exception of longer treatment for TB meningitis (9-12 months) and for bone/joint disease (9 months), and the consideration of adjuvant corticosteroid treatment for TB meningitis and TB pericarditis. An additional recommendation was that ethambutol should be replaced by streptomycin in cases of TB meningitis, presumably because of possible neurotoxicity.

Extrapulmonary tuberculosis is thus a common condition with real morbidity and real mortality. Moreover, recent studies suggest that the proportion of EPTB out of all TB patients has increased over the past couple of decades. As with pulmonary TB, efforts to eradicate EPTB require resources for data collection, analysis, guidelines and policies. In the absence of leadership by the WHO on EPTB, various investigators have attempted to fill the void. This talk will present the WHO guidelines as well as an overview of a few pertinent studies on ocular tuberculosis.

Treatment of intraocular tuberculosis and its duration in India

Parthopratim Dutta Majumder
Sankara Nethralaya, Chennai, India

With 2.2million new cases every year, more than 300,000 deaths, and economic losses of $23 billion, tuberculosis remains India's biggest health crisis. Ocular tuberculosis presents a complex clinical problem due to a wide spectrum of presentations and difficulty in diagnosis. Though there has not been a standard guideline for the treatment of intraocular tuberculosis, a broad consensus does exist-mainly extrapolated from the treatment of pulmonary tuberculosis. In addition to showing its beneficial effect, treatment with multi-drug anti-tubercular chemotherapy in intraocular tuberculosis has been found to show significant reduction in recurrences of uveitis. Like in other forms of extrapulmonary tuberculosis, use of low-dose corticosteroids, concomitant with multidrug anti-tuberculosis treatment has been reported to exert a protective effect against tissue damage from delayed type of hypersensitivity. The emergence and spread of antimicrobial resistance against Mycobacterium tuberculosis, is a major concern in a tuberculosis-endemic country like India and has been reported in patients with intraocular tuberculosis. More recently, Indian extrapulmonary guidelines were developed to provide guidance on uniform, evidence-informed practices for suspecting, diagnosing and managing patients of extrapulmonary tuberculosis under the auspices of central government initiative. This presentation aims to discuss the brief review of literature on the treatment of intraocular tuberculosis published from India, overview of anti-tubercular chemotherapy in India.

Treatment of Intraocular tuberculosis and its duration in Myanmar

May Zun Aung Win[1,2]
[1]*Yangon Eye Hospital, Yangon, Myanmar,* [2]*Ophthalmology Department, University of Medicine (1), Yangon, Myanmar*

With 190,000 new turberculosis cases every year, the global TB report published by the World Health Organization lists Myanmar as one of the highly tuberculosis-burdened countries in the world. The retrospective study of a tertiary eye center in Myanmar estimates 32.4% of Intraocular TB patients in 139 uveitis cases, anterior uveitis 12/ 139, intermediate uveitis 8/ 139, posterior uveitis 13/ 139, and panuveitis 12/ 139.
The current treatment of ocular tuberculosis includes the schemes of isoniazid, rifampicin, pyrazinamide and ethambutol for 2 months, followed by the 7-month prescription of isoniazid and rifampicin and systemic immunosuppression in sight threatening cases. The diagnosis of intraocular TB varies and the practice pattern is based upon the reports of patient history with pulmonary TB, experience of contacts with TB-infected patients, the presence of suggested ocular findings, the exclusion of other known causes of uveitis, a positive mantoux test, the positive QuantiFERON TB Gold test and a positive response to anti-TB treatments without recurrence. However, QuantiFERON Gold test is expensive in Myanmar and as a result, active and latent TB patients with financial problems do not have adequate access to initial diagnosis. It is therefore expected that national TB program would scale up its diagnosis system and provides it accessible to active and latent TB patients in Myanmar in the future.

Diagnosis and treatment of intraocular tuberculosis in South Africa

Derrick P Smit
Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

South Africa has the second highest incidence of both tuberculosis and TB/HIV co-infection worldwide and yet we remain unable to diagnose intraocular tuberculosis (IOTB) with conviction. With no gold standard available for the diagnosis of IOTB we used the 2014 classification by Gupta et al to calculate the prevalence as 33.0% in a prospective study in Cape Town. HIV infection occurred in 31.4% of these patients of whom 65.7% had possible IOTB and 34.3% probable IOTB. No confirmed IOTB cases were recorded due to the poor sensitivity of current confirmatory tests.
In our endemic setting we confirmed that QuantiFERON-TB Gold (QFT) testing was not superior to tuberculin skin testing (TST) in diagnosing IOTB. We noted that both TST and QFT were likely to return negative results when CD4+ counts were <100 cells/mL. Chest X-ray had a sensitivity of 14.7%, specificity of 94.3%, positive predictive value of 55.6% and negative predictive value of 69.5% for IOTB. We identified cases that responded extremely well to anti-TB treatment despite not meeting the proposed criteria for a diagnosis of IOTB. These included HIV- patients with sclerokeratouveitis and HIV+ patients with subretinal abscesses. We recommend an 8 week trial of treatment with 4 anti-TB drugs (isoniazid, pyrazinamide, rifampicin and ethambutol) in cases where we are: 1) unable to exclude underlying IOTB or 2) where immunosuppression alone cannot completely resolve ocular inflammation and we suspect that latent TB might play a role.
We believe biomarkers may play an important future role in diagnosing IOTB.

Treatment of intraocular tuberculosis and its duration in South America

Daniel Vitor Vasconcelos-Santos
Faculty of Medicine, Universidade Federal de Minas Gerais, Belo Horizonte, Brazil

Tuberculosis (Tb) remains an important cause of morbidity and mortality in South America. The largest absolute numbers are concentrated in Brazil, where around 91,000 new cases are estimated annually, 10% of them involving HIV-coinfected individuals. In contrast, intraocular Tb has been documented as a rare etiology of intraocular inflammation in Brazil, representing 0.7-5.2% of all cases of uveitis in the two largest recent epidemiological reports from uveitis referral centers in the Southeast part of the country.
Current therapeutic recommendations of Brazilian health authorities for extrapulmonary (including intraocular) Tb preconize observed therapy for 6 months, employing an intensive RHZE (rifampicin + isoniazid + pyrazinamide + ethambutol) scheme for 2 months, followed by RH (rifampicin + isoniazid) for 4 months. Even though systemic steroids are primarily recommended for Tb meningoencephalitis (also with extension of RH for 1-3 months), they have also been employed for sight-threatening intraocular Tb in most referral centers in Brazil.
Significant variation is still seen in diagnostic/practice patterns of intraocular Tb in Brazil. Main challenges include presumption/definition of Tb in the absence of extraocular involvement, as well as paradoxical reactions and long-term management of these cases.

Treatment of Intraocular tuberculosis and its duration in Europe

Edoardo Baglivo
Clinique de l'Oeil, Geneva, Switzerland

Tuberculosis is a contagious disease that spreads when a person breathes in bacteria exhaled and aerosolized by an infected person. One third of the world's population is infected with the latent form of the disease, and one tenth of infected people become ill with active TB during their lifetime. Tb can usually be cured with six months of antibiotic therapy.
Europe's burden is among the lowest in the world, but the number of new multi Drug resistant TB (MDR TB) cases is the highest.
TB is strongly associated with social determinants of health such as poverty, imprisonment, and migration. People living with HIV or suffering from diabetes are at increased risk. The region has the highest proportion of new and retreated cases of MDR TB.
For active TB, antibiotics are recommended for at least six to nine months. Molecules and length of treatment will depend on age, overall health, drug resistance and organ (s) affected. The most common medications used include Isoniazid, Rifampicin, Ethambutol, Pyrazinamid. In latent TB it is advised to take only one or two types of TB drug. Active TB will require several drugs at once. In drug-resistant TB, a combination of fluoroquinolones and injectable medications, such as amikacin or capreomycin, are used for 20 to 30 months.
Ocular involvement has been reported in I, IV% of the patients with active pulmonary TB. VI, VIII% of patients with pulmonary TB were found to have ocular inflammation. Mycobacterium tuberculosis may affect any structure of the eye masquerading as several infective and non infective entities.

Management of Immune-Mediated Complications in Ocular Tuberculosis: A North American Perspective

John Gonzales
Francis I. Proctor Foundation, University of California, San Francisco, CA, USA

Many cases of ocular tuberculosis are diagnosed without demonstration of acid-fast bacilli. Instead, the diagnosis of ocular tuberculosis is invoked when a patient is positive for past exposure to tuberculosis with ocular inflammatory features that are compatible with tuberculosis, though it has myriad manifestations.
The mainstay of therapy for ocular tuberculosis is anti-tuberculosis therapy, but it is clear that ocular tuberculosis may not entirely be related to *Mycobacterium tuberculosis* directly infecting ocular tissues. Indeed, some cases of ocular tuberculosis may require immunosuppression to manage its immune-mediated component. And, unlike some autoimmune conditions where systemic immunosuppression may be delayed until completion of anti-tuberculous therapy, ocular inflammation in tuberculosis frequently requires expeditious use.
Systemic corticosteroids remain a mainstay of therapy for immune-mediated complications. However, when ocular inflammation exhibits chronicity and steroid-dependency, an approach reminiscent of the treatment paradigms used in non-infectious uveitis can be considered. Antimetabolite therapy may be used as some agents, including methotrexate, have antimicrobial properties. Calcineurin inhibitors may be considered for those exhibiting refractoriness to antimetabolite therapy alone. Biologic anti-tumor necrosis factor inhibitors can be cautiously considered in especially recalcitrant, sight-threatening situations though coordination with infectious disease specialists is mandatory.