FIRST INTERNATIONAL IUIS-FAIS-IMMUNO-ETHIOPIA COURSE

University of Gondar, Gondar, Ethiopia, February 26-March 5, 2017

"**New developments in the immunology, diagnosis and treatment of cutaneous and visceral leishmaniasis, schistosomiasis and helminth infections in an area of high tuberculosis prevalence"**

Supported by a grant to IUIS from the Bill & Melinda Gates Foundation, the IUIS Education Committee, the University of Gondar, the Foundation of Research in Biochemistry, Epalinges, Switzerland and by WHO-IRTC, University of Lausanne, Switzerland.

Report prepared by Dr Michelle Letarte with contributions from Drs Pascale Kropf, Fabienne Tacchini-Cottier, Clive Gray, Reto Guler & Asrat Hailu and from the course student rapporteurs, Donald Severin Kamdem, Sergey Yegorov, Beak-San Choi, Hasnaa Maksouri, Uwagie-Ero Edwin Aihanuwa and Edward Cruz Cervera.

Organizers:

Dr Pascale Kropf (Department of Medicine, Imperial College London and University of Gondar)
Yegnasew Takele (Wellcome Trust Fellow, University of Gondar and Imperial College London, UK)
Dr Michelle Letarte (Chair, IUIS Education Committee, Department of Immunology and Hospital for Sick Children, University of Toronto, Canada)
Dr Fabienne Tacchini-Cottier (University of Lausanne, Department of Biochemistry, WHO-Immunology Research and Training Center)
Dr Ingrid Müller (Imperial College London, UK)
Dr Clive Gray (Institute of Infectious Disease and Molecular Medicine, University of Cape Town, South Africa)

Facilitators:

Dr Martin Olivier (Infectious Diseases and Immunology in Global Health Program, Research Institute of the McGill University Health Centre, Montreal, Canada)
Dr Reto Guler (International Centre for Genetic Engineering & Biotechnology & Division of Immunology, University of Cape Town, Cape Town, South Africa)
Dr David Sacks (Intracellular Parasite Biology Section, NIH/NIAID, Bethesda, MD, USA)
Professor Asrat Hailu (Microbiology, Immunology &Parasitology Department, University of Addis Ababa, Addis Ababa, Ethiopia)
Dr Abraham Aseffa (Armauer Hansen Research Institute, Addis Ababa, Ethiopia)
Dr Alain Dessein (Immunology and Genetics of Parasitic diseases, INSERM-Aix-Marseille University, Marseille, France)
Dr Severine Blesson (DNDi, Geneva, Switzerland)
Dr Zewdu Hurissa Dadi (University of Gondar, Ethiopia)

Introduction:

The IUIS-FAIS-IMMUNO-ETHIOPIA Course was the first international course ever held at the University of Gondar. Excellent facilities were provided at the Gondar College of Medical Sciences and transport of participants to and from hotel to hospital were generously provided by our host, the University of Gondar, as well as the accommodation costs of all facilitators. Forty students were present at the course, representing 16 countries: 13 from Ethiopia, 4 each from Morocco & Sudan, 3 from Kenya, 2 each from Burkina-Faso, Nigeria, Zimbabwe & England, and one each from Cameroon, Uganda, Mali, South Africa, Tunisia, India, Peru and Canada. Most expenses were supported by the BMGF grant to IUIS except for support for the four Sudanese students, which was provided by the Foundation of Research in Biochemistry, Epalinges, Switzerland, the WHO-IRTC, University of Lausanne, and the IUIS.

The final program of the course is attached as a separate file. All preparatory material for the course, the references and the lectures can be found in the IMMUNO-ETHIOPIA COURSE module on the Immunopaedia site (www.immunopaedia.org.za). All students had to study the preparatory online material prior to coming to the course in Gondar. This was to insure that they all had similar background knowledge in the area and could benefit optimally from the face-to-face course. The on-line material was prepared from a combined effort between the invited facilitators and substantial input from Drs Kropf on Leishmaniasis. The Immunopaedia team also provided input into several sections and created multiple-choice questions for student interaction and self-assessment. This material was made available to all registered students 6 weeks prior to the course and was designed to "prime" the students on the basics of the immune system before coming to the course. The ImmunoEthiopia content is to be moved to the full open access part of the site under "special focus areas" so that all users of Immunopaedia can gain benefit from the material covered on the course.

Day 1: Official Opening

In his opening remarks, in the afternoon of *February 26*, the Academic Vice-President of the University of Gondar, *Dr Asrat Atsedewoyen,* informed us that the University has 40,000 students and 7,000 staff and that the hospital is known for its experience with Neglected Tropical Diseases. He officially opened the course and wished us a productive week. Dr Pascale Kropf welcomed everyone to Gondar and thanked Professor Asrat Hailu for his enormous contribution to leishmaniasis in Ethiopia and the establishment of BSc and MSc programs in Immunology. Yegnasew Takele, the first Ethiopian to obtain a Welcome Trust Fellowship for his MSc and currently for his PhD on the immunology of *Leishmania*-HIV coinfections, was the main local organizer and welcomed everyone to his country and gave us essential information throughout the week. Yegnasew also introduced the Leishmaniasis Research and Treatment Center (LRTC); an outstanding ward and laboratory facility that treat patients with leishmaniasis; Yegnasew contributed to the set up of the diagnostic laboratory in this center and was the head of the diagnostic laboratory for over a decade.

Professor Asrat Hailu gave a fascinating *overview of leishmaniasis as a major public health issue in Ethiopia* and described *the various forms of cutaneous leishmaniasis*, stressing that it is the most neglected form of this disease. He discussed the complexity of both cutaneous and visceral leishmaniasis and their devastating impact at the global level and told us that a vaccine should work. Professor Hailu established the first Leishmaniasis Research and Treatment Center (LRTC) in Gondar in 2004 and another center in Arbaminch. The Gondar center now provides training for 12 centers throughout Ethiopia and collaborates with East African countries.

Professor Alain Dessein, described *how whole genome analysis will delineate factors responsible for disease pathogenesis that will lead to better treatment for Leishmania and Schistosoma infections*. He gave an overview of genetic host factors playing important roles in progression and treatment of these diseases, using several examples from his own research in several African countries. Dr. Dessein also emphasized that recent technological advances have made genome wide association studies affordable as integral parts of large clinical studies and can contribute valuable information towards developing immunological therapies. A reception on the roof of the Florida Hotel concluded the day and allowed the participants to get acquainted with one another, warmed by an open fire and with great views of the city lights and the gazing stars.

Day 2: Cutaneous Leishmaniasis (CL): experimental and human

February 27 was devoted to ***Cutaneous Leishmaniasis (CL)*** and Drs Fabienne Tacchini-Cottier and Ingrid Müller described the current state of knowledge concerning *the mechanisms of innate and adaptive immune responses in experimental and human CL.* Neutrophils, NK cells, and monocytes play an important role in the susceptibility / resistance to CL and further investigation is needed to understand innate cell interactions at the site of infection and in the persistent lesions. In terms of adaptive immunity in experimental models of CL, a $CD4^{+}$Th1 response is generally associated with healing while a Th2 response is associated with non-healing lesions. The Th1 cells produce IFN-γ that activates macrophages, upregulating iNOS and therefore NO production that is toxic to the parasites. Th2 cells via production of IL-4 and IL-13 activate macrophages and upregulate arginase, producing polyamines that stimulate the growth of parasites. Depletion of the substrate arginine also leads to suppression of T cell responses. The importance of developing and maintaining memory T cells after *Leishmania* infection was also discussed.

Dr Abraham Aseffa summarized *the diagnosis of CL*. He described the major forms of disease affecting Ethiopians: localized (LCL), mucocutaneous (MCL), mucosal (ML) and diffuse (DCL) and their respective clinical features with illustrations that stressed the diversity and severity of disease. He also mentioned how complex the differential diagnosis of skin lesions associated with the various forms of CL was versus that of other skin infections. He also talked about how pregnancy and HIV infections can modify CL presentation. There are numerous diagnostic tests with variable accuracy but the gold standard is the demonstration of parasites by microscopy, histopathology, culture and/or PCR (for species identification).

Professor Asrat Hailu discussed *the treatment of CL.* It is difficult to treat CL as it represents a group of complex disease entities. The treatment depends on the species of parasites, types of CL, stage of the lesions, spontaneous cure rate, characteristics of the interventions (pharmacokinetics of the drugs in terms of skin penetration and predilection for tissue) and the immune status of the patients. Systemic chemotherapy may consist of oral treatment with miltefosine (FDA approved in 2014) while local chemotherapy may use topical paromomycin. Pentavalent antimonial (SbV) compounds have been used traditionally to treat leishmaniasis in the Old World. Local heat therapy, photodynamic therapy and cryotherapy are also practiced with mitigated results. Overall, it is extremely difficult to treat CL and much remains to be done to ameliorate the outcome for patients affected with the multiple forms of this most neglected tropical disease.

Day 2: Introduction to grant writing

Research grant writing and its principles were discussed by Dr Clive Gray in a very interactive way that challenged the students to answer questions pertinent to what would constitute a successful application. A series of slides on grant writing were presented that can be found in the IMMUNO-ETHIOPIA COURSE module on the Immunopaedia site (www.immunopaedia.org.za).

The students were then divided into 7 groups according to their interests and started thinking of a pertinent, innovative theme that could be developed into a grant application. The said grants, consisting essentially of 6 slides or more, would then be presented by each group on the last day of the course to a mock panel that would then offer critique and rank the applicants. One or two facilitators per group guided the initial discussion on potential grant topics.

Day 3: Visceral Leishmaniasis (VL): experimental and human

Dr David Sacks gave a comprehensive lecture *on the immunology of leishmaniasis, acquired through experimentation with animal models.* Several species have been used as models. Mouse findings do not readily extrapolate to human. Hamsters, which can be infected during the bloodmeal of infected sandflies, represent a better model although lacking the necessary reagents for characterization of immune response; hamster studies have shown that therapies combined with antibiotics increase survival rate. Dogs are currently used for field vaccine trials. Some unresolved questions remain: Is CD8 T cell exhaustion in mice a consequence of host modulation or is it genetically determined? In which skin cell type does the sandfly take its greatest parasite load?

Dr Pascale Kropf discussed innate immunity and *the role of neutrophils and monocytes in human VL.* Neutrophils can actually kill *Leishmania* parasites intracellularly. NETs may contribute to containment of promastigotes at sites of inoculation, facilitating their intake by macrophages. An increased number of immature neutrophils was observed in blood of VL patients, with increased expression of CD63 and CD15 and decreased expression of CD62 and CD10. Higher levels of arginase were also observed in a subpopulation of neutrophils in VL patients and were associated with arginase-induced immunosuppression. The release of NETs by neutrophils was also lower in VL patients, possibly allowing for more efficient dissemination of the parasites. Questions emerging from this talk are that human VL patients show impaired neutrophil activity and yet most patients are treated with pentavalent antimony drugs that reduce neutrophil activity. Are there better treatments? Is the physiological neutropenia observed in most Africans associated with enhanced susceptibility to *Leishmania*?

Dr David Sacks then presented a talk on *T cell responses in human VL*. T cell activation is a hallmark of VL but should we rely on whole blood or plasma in examining the immune system of VL patients? Can we expect cytokines to be present in the skin of patients with active VL? If IL-10 is a candidate for future immunotherapy, how does one balance the inflammation that may follow blocking this cytokine?

Professor Asrat Hailu gave a lecture on *Diagnosis of VL* and raised a series of questions. What is the gold standard for VL diagnosis? Can peripheral blood be used instead of a bone marrow puncture? What about the development of non-invasive tests, such as one that uses saliva? If patients present at a chronic phase of disease, can one rely on serological test for diagnosis in endemic areas? There is no quality control in laboratory diagnosis of VL in Ethiopia; are there some in other countries?

Drs Severine Blesson and Zewdu Hurissa Dadi discussed *the treatment of VL*. According to DNDi, the efficacy of treatment of VL in Africa is lower than in any other part of the world; furthermore, strains are different in various regions. Pharmacovigilance safety outcomes show a significant difference with patient age. *The treatment of VL in special populations* indicate that Miltefosin should be avoided in all cases of pregnancy but that Amphotericin B is compatible with breast feeding. Conditions such as cardiac and renal dysfunction and old age may affect the outcome due to certain drug-associated toxicities. Questions arising are: What is the efficacy of Amphotericin B/Paramomycin combinations? Any plan for a clinical drug trial in Ethiopia? Do children require adjusted therapy doses and are babies born to VL positive mothers being followed?

Dr Martin Olivier discussed the *mechanisms of VL Immune Evasion: Role of Parasite extracellular vesicles. Leishmania* parasites have been shown to release exosomes that affect host immune responses. *Leishmania major* and *donavani* exosomes promote IL-8 production by macrophages, which is responsible for recruitment of neutrophils to the site of infection. *Leishmania* exosomes have been shown to alter human monocyte responses to IFN-γ, by reducing TNF-α production and increasing immunosuppressive IL-10. In mice, these exosomes exacerbate disease, resulting in a Th2 skewing of the immune response. *Leishmania* parasites constitutively secrete exosomes into the sandfly midgut, and these are co-injected together with the parasite during the blood meal of the insect vector into the host. Leishmanial sandfly "nanobiome" exacerbates CL pathology by overinducing inflammatory cytokines, such as IL17α. Targeting leishmanial exosomes may lead to new ways of protecting from or decreasing CL development. Exosome-based therapeutic delivery was also discussed briefly.

The meeting was also an opportunity for young researchers to present their exciting new work on leishmaniasis, schistosomiasis and co-infections with HIV and TB. The poster sessions took place over two afternoons (on Days 3 & 5). Participants presented a total of 28 posters on leishmaniasis. These covered a wide range of aspects of this neglected tropical disease, including its epidemiology, diagnosis, treatment, parasite vectors and co-infection with other pathogens.

The changing epidemiology of leishmaniasis was an issue raised by a number of participants. Mouad Ait Kbaich from the University of Hassan II Casablanca, Morocco, presented his research into the distribution of the cutaneous form in southern Morocco, demonstrating important changes in the epidemiological pattern of the disease and showing that some areas have cutaneous leishmaniasis (CL) caused by up to 3 different *Leishmania* species.

Woyneshet Gelaye from Bahir Dar Regional Health Research Laboratory Center, Ethiopia, presented data showing the emergence of new CL foci in the northern Amhara region of Ethiopia. These data raise the question of which factors are contributing to such changes in disease distribution – these may include environmental changes, changes in vector populations and host population migration.

Diagnosis of visceral leishmaniasis (VL) is most commonly carried out by analysis of spleen aspirates, an invasive and painful procedure that carries a certain level of risk. Salah Boshara, from the University of Khartoum, Sudan, investigated a novel, non-invasive diagnostic tool for VL – an ELISA urine test. His study showed promising results, and with an increase in sensitivity, the test could become a realistic alternative to current diagnostic techniques.

A number of posters looked at host immune responses to the parasite, and at the immune state of the patients suffering from leishmaniasis. Endalew Yizengaw, in work carried out at the University of Gondar, Ethiopia, showed that VL patients had impaired neutrophil function. This is likely to be important not only in terms of VL disease progression, but also regarding the risk of secondary infections such as pneumonia in VL patients.

All in all, these poster sessions highlighted the importance of bringing together researchers from different parts of the world, working on different aspects of leishmaniasis. This enabled the sharing of both results and ideas, and the formation of new collaborations, which will be key for tackling leishmaniasis in the future.

Day 4: Immunity to Schistosomiasis/helminths/HIV and the impact of co-infections on VL

Professor Alain Dessein gave us a lecture on the *Immunology of human schistosomiasis.* This disease is caused by parasitic flat worms, which inhabit the blood vessels mainly in the gut and urogenital organs. While the adult parasitic worms have an immune quiescent phenotype, the eggs secreted by the worms tend to induce granuloma formation in the gut, liver and other internal organs, leading to enlargement of the organs and tissue fibrosis. Not every individual living in an endemic setting will develop a pathological condition and some people are less susceptible than others. Dr. Dessein's research has uncovered a strong genetic predisposition to pathological sequelae of schistosomiasis. One such example is the association between IFN-gamma (IFN-γ) and IFN-γ receptor (R1) polymorphisms in *Schistosoma mansoni*-induced hepatic fibrosis. These polymorphisms control the expression of IFN-γ and its receptor in the liver and modulate the host immune response. Polymorphisms that lead to reduced IFN-γ signaling turn out to be protective against parasite-induced pathology. More recently, IL-13 polymorphisms have been associated with regulation of eosinophil recruitment and control of response to schistosomiasis. Dr Dessein concluded that genetic polymorphism studies are indispensable in delineating the factors responsible for disease pathogenesis and can contribute valuable information toward developing immunological therapies.

Professor Asrat Hailu delivered a lecture on the *impact of helminth-induced immunity on visceral leishmaniasis*. Prof. Hailu drew our attention to a basic and yet very important concept of parasite localization (e.g. tissue or gut dwelling) and its effects on immune response generation and overlap with concomitant infections. Despite the paucity of knowledge about helminth-leishmania co-infections, it appears that leishmaniasis is exacerbated by helminth co-infections in experimental models and human patients. Ironically, there is also evidence that infections with visceral leishmaniasis could possibly protect from re-infections with helminth due to parasite-modulated immune responses.

Immunology of *Leishmania / HIV co-infections* was divided in three parts. Dr Clive Gray gave a review on the innate and adaptive immune response with a particular focus on bridging the communication between innate and adaptive cells within lymphoid organs. He also talked about the link between microbial translocation and the extent of the pro-inflammatory response and HIV infection. While ART works in the majority of cases, 10-25% of patients develop Immune Response Inflammatory Syndrome (IRIS) within 12 weeks of treatment. The excess of pro-inflammatory cytokines lead to localised tissue oedema and focal inflammation, which can eventually cause systemic inflammatory response. There are very few systematic studies of HIV/VL co-infections but it is likely that the status of the patients is hyper-inflammatory and immune-compromised.

Dr Severine Blesson talked about treatment modalities in the case of HIV/VL co-infections, reporting on trials with combinations of ambisome and miltefosine and the use of pentamidine as prophylaxis. She stressed the need for better treatment strategies. She detailed the hopes for the LEAP HIV-VL 0511 clinical trial currently ongoing at The University Hospital Gondar, in shedding some light on initial treatments, extended treatments and prophylaxis.

Professor Asrat Hailu shared with us his experience over the years in Ethiopia and the complexities of cases with relapse, a common theme in HIV-VL patients. He indicated that while only 3% of HIV- patients relapse at 1 year, 100% of HIV+ VL+ patients relapse at 3 years, whether on ART or not. This appears to be due to superimposed immune suppression, reduced CD4 T cells, and pancytopenia. Overall, the life expectancy of co-infected HIV/VL patients on ART is decreased by several years. Thus co-infected patients have a chronic carrier state, highly immune-compromised and hyper-inflammatory, and current treatments are not very effective.

In poster format, Mr. Tibila Kientega presented a study conducted in Burkina-Faso that identified high prevalence of soil-transmitted helminths in school children. In addition, this poster presented a pilot study on the use of RT-PCR to diagnose *Giardia intestinalis*, a protozoan parasite, which was found to be highly prevalent in this school setting.

Ms. Seble Worku presented a study describing an association between major helminth infections and anemia in school children from Northwest Ethiopia. This epidemiological study has important implications: anemia is a serious public health problem globally, and in Ethiopia prevalence of anemia among school children can be high. Treatment of helminths is relatively inexpensive and could lead to a significant improvement in the children's health.

Maritha Kasambala from Zimbabwe investigated the inflammatory markers involved in *S. haematobium* protective immunity and susceptibility to infection. She found that the IFN-γ A/T genotype produced a low level of IFN-γ leading to susceptibility to infection while the IFN-γ A/A genotype produced a high level of IFN-γ leading to resistance to infection.

Ruth Kerubo Nyakundi from Nairobi, Kenya studied the effect of prenatal exposure to *Schistosomiasis* co-infections on fetal immune responses. Her findings are that the type of co-infection in the mother influences the children's immune response.

Thabo Rantata Victor Mpotje from South Africa showed that BATF2 is necessary for the development of regulatory type-1 immune responses during experimental Schistosomiasis. His findings are that the absence of BATF2 decreases Immune Response type 1 and increases the Th2 response, leading to fibrosis.

Moses Egesa from Uganda works on circulating immune mediators to *Schistosoma mansoni* skin-stage vaccine candidate antigens. He found that a skin antigen produced a predominant Th1 pro-inflammatory response.

Donald Severin Kamdem from Cameroon studied host-regulated pathology during *Schistosomiasis* and found that *S. haematobium* driven urinary tract pathology is host-dependent in diseased school children.

A poster relating to co-infections was presented by Dr Samson Muuo Nzou, from the Kenyan Medical Research Institute (KEMRI). He detailed his success in diagnosing VL and TB in patients using a multiplex system. He has set up a trial to test VL-TB co-infection in over 3000 patients. With this information, Dr Nzou hopes to advise the Kenyan healthcare sector into refining its practices when diagnosing patients with more complex infections.

Other co-infection studies raised new ideas and unexpected results. Ms Emilia Tariro Choto from the University of Zimbabwe is studying the immune response into male genital schistosomiasi*s* and HIV co-infection, which led her to look into the genetic polymorphisms involving two key cytokines generated by the infected host during the co-infection; single nucleotide polymorphisms (SNP) for the promoter sites of IL-10 and TNFa. It appears that a polymorphism into the TNFa AA allele may be one link driving the transmission and progression of co-infection.

Another novel finding was presented by Mr Sergey Yegorov (University of Toronto), who showed results of a clinical trial conducted in Entebbe, Uganda focusing on the effects of *Schistosoma mansoni* infection on HIV susceptibility. In this study, treatment of *S. mansoni* infection was shown to reduce HIV entry into endocervical and blood CD4+ T cells. This result suggests that *S. mansoni* treatment and/or prevention may offer a novel strategy to reduce HIV transmission in regions with high disease burden, and provide a rationale for strengthening schistosomiasis eradication programs in HIV-affected regions.

The afternoon was devoted to the visit of the Leishmaniasis Research and Treatment Centre in small groups, and to grant writing sessions.

Day 5: Immunity, vaccines and treatments for tuberculosis

Dr Reto Guler gave an overview of TB immunology before reporting on current cutting edge TB research. He explained that the fate of infected macrophages determines host resistance and that versatile myeloid cell subsets within granulomas contribute to tuberculosis-associated inflammation. The pattern recognition receptors, TLRs, sense *Mycobacterium tuberculosis* on the surface of macrophages while NLRP3 and AIM2 act as intracellular sensors that activate the inflammasome. Dr. Guler explained the central dogma of cell-mediated immunity to tuberculosis where IFN-γ produced by TH1 cells and TNF-α (produced by T cells and macrophages) activate the anti-microbial activity of macrophages killing *M. tuberculosis* through nitric oxide production and phagosome-lysosome fusion, which acidifies the phagosome and delivers lysosomal enzymes. He expanded on this dogma and showed that different T cell subsets and antibodies contribute to protective immunity to TB. Dr. Guler further explained that the balance in lipid mediators (prostaglandin E2, lipoxins) and type 1 interferon regulate inflammation and pathology during *M. tuberculosis* infection.

In his second lecture, Dr Guler spoke about host-directed drug therapies (HDT) for TB and how *M. tuberculosis* evades protective host immune effector functions. An early literature study suggested that statins decreased mortality in patients with bacteremia (Liappis et al. Clin Infect Dis. 2001). Statins target the mevalonate pathway involved in the synthesis of cholesterol. More recent findings by Dr Guler, showed that statin therapy was able to reduce *M. tuberculosis* burden in human macrophages and in mice by enhancing autophagy and phagosome maturation (Parihar and Guler et al. Journal of Infectious Diseases 2014). Other research groups have reported that the use of statins and the length of statin therapy were associated with protective effect against active TB in humans (Lai C-C et al. Thorax 2016). Further findings published by Dr. Guler showed that systemic and topical treatment enhanced host protection against cutaneous *Leishmaniasis* by increasing macrophage phagosome maturation and killing effector functions. The statin treatment reduced CL lesion size and parasite load, through the induction of H_2O_2, which is an important effector function of classically activated macrophages (Parihar et al. Sci Rep. 2016). Dr. Guler ended the presentation by describing literature results for Vitamin D and Metformin as other HDT examples for TB.

An interesting poster relating to co-infections was presented by Dr Samson Muuo Nzou, from the Kenyan Medical Research Institute (KEMRI). He detailed his success in diagnosing VL and TB in patients using a multiplex system. He has set up a trial to test VL-TB co-infection in over 3000 patients. With this information, Dr Nzou hopes to advise the Kenyan healthcare sector into refining its practices when diagnosing patients with more complex infections.

Another poster stressed the need to identify external factors involved in the spread of infections, for example the vectors. In the Marrakech-Safi region of Morocco, Mr Mohamed Daoudi from Cadi Ayyad University in Morocco is monitoring the spread and species of sandflies potentially carrying the *Leishmania* parasite in order to correlate with epidemiological studies. Such an approach could be used to monitor the potential rise in HIV, VL and HIV-VL co-infection rates, and determine if the vector influences co-infections.

Other co-infection studies raised new ideas and unexpected results. Ms Emilia Tariro Choto from the University of Zimbabwe is studying the immune response into male genital schistosomiasis and HIV co-infection, which led her to look into the genetic polymorphisms involving two key cytokines generated by the infected host during the co-infection; single nucleotide polymorphisms (SNP) for the promoter sites of IL-10 and TNFa. It appears that a polymorphism into the TNFa AA allele may be one link driving the transmission and progression of co-infection.

Dr Amelia Ngozi Odo from Nigeria's University in Nsukkas, has been fighting to be heard for help in bringing knowledge and education into the Enugu state of Nigeria. Implementing the basic measures needed to practice public hygiene has been a particular challenge. In the future with the support she needs, Dr Odo anticipates to provide a strategy for the practice of WASH; **WA**ter, **S**anitation and **H**ygiene. With the provision of a good water supply, waste management and education in practicing hygiene, offers a barrier into the spread of infection, in particular helminth infections in patients with tuberculosis in Nigeria.

Day 6: Grant presentation and panel discussion

One major focus of the course was on grant writing; how to stand out, how to be specific, how to be creative, given the tools at hand. Grant writing, during which trainees were asked to form teams and compile an abbreviated grant proposal, was probably by far the least familiar and most challenging part of the conference. Despite some heated discussions, this was a rewarding team building experience that brought everyone together in the spirit of collaboration. Despite challenges with power cuts and sporadic contention with a wi-fi connection, the students conceived seven brand new ideas for mock grant submission:

1) Evaluation of a new urine based *Leishmania* antigen test for diagnosis and monitoring treatment outcome in visceral leishmaniasis in Ethiopia

2) The international innate immunity consortium in localized cutaneous leishmaniasis

3) Gut Microbiota Signature of Resistance to *Schistosoma mansoni* Reinfection

4) Linkage analysis in Sudanese families to identify genes associated with increased relapse of PKDL

5) Impact of mother HIV status on infant neutrophil G alpha 1 GPCR signaling pathway

6) Effects of maternal parasite co-infections on infant immune responses to vaccination

7) Do parasite factors contribute to the diverse cutaneous disease spectrum caused by *Leishmania aethiopica*?

The proposals were all presented first and then the mock panel offered their comments and in fact allocated mock funding to the first two proposals, due to limited funding. The winners were so happy despite the fact that this was just a mock exercise.

Day 7: Round-table Discussions / Course evaluation / Closing Remarks / Visit to Fasil Ghebbi

Student rapporteurs summarized the major findings of the course that led to an animated discussion. They really appreciated the interactive nature of the course and the grant writing exercise. Comments were made on the fact that Immunopaedia was a one-way street, and students would like to have a site where discussions could take place. We should also offer sessions on how to write a good CV, how to prepare a study design, how to develop grant proposals. What they appreciated the most in the course, was to meet colleague students from different countries and to realize that they share a lot in terms of work situation, future career, and that they can and should work together on larger projects on basic research in endemic countries. Evaluations of the face-to-face course by the students agreed with these conclusions and there was a general feeling of having accomplished a lot and having learned a great deal in a week in a friendly atmosphere.

The Immunopaedia preparatory material was also evaluated by the students, who were overall very positive about this learning website. Seventy percent (70%) of the registered students completed all modules of the pre-course material and those unable to finish cited time as the main issue. Most (60%) completed the on-line quizzes and downloaded the resources available for extra reading. Of the recorded short talks that were posted on Immunopaedia, T cell subsets, HIV and viruses were the most popular. Over 90% of respondents thought the Immunopaedia site was easy to navigate and visually appealing.

Certificates were distributed to all participants and the 4 winners of the poster competition were announced (prizes provided by IUIS).

We then had the visit of *Dr Desalegn Mengesha*, President of the University of Gondar and *Dr Asrat Atsedewoyen* the Academic Vice-President of the University of Gondar. We were able to thank them for hosting a very successful course. The President thanked us for having initiated and delivered the first international course at his University and officially called the course to a close.

After a brief lunch, we went as a group to visit Fasil Ghebbi, the fabulous remains of a fortress-city that includes Fasilides' castle, Iyasu I's palace, Dawit III's Hall, a banqueting hall, stables, and the Empress Mentewab's castle. Everyone enjoyed this social time together. This concluded an intense, dynamic and interactive 7 days.

Thank you to the Bill and Melinda Gates Foundation without whom this course would not have been possible.


Welcome to


IUIS-FAIS Immuno-Ethiopia 2017
BILL & MELINDA GATES foundation
IUIS


University of Gondar
SERVING THE COUNTRY SINCE 1954