

## **7<sup>th</sup> Tropical Dermatology Course of the German Dermatological Society (DDG) and the International Society for Dermatology in the Tropics (ISDT) with DDA-Certificate, Manaus, Brazil, October 2019**

Andrea Vanegas, Isaak Effendy and Helmut Schöfer

The 7<sup>th</sup> Course in Tropical Dermatology of the German Dermatological Society (DDG) and the International Society for Dermatology in the Tropics (ISDT) took place from 17 to 22 October 2019 in Manaus, Brazil, the capital of the fascinating Amazon rainforest. In cooperation with Brazilian colleagues of the Fundação de Dermatologia Tropical e Venereologia Alfredo da Matta, Manaus (FUAM, Tropical Dermatology) and the Fundação de Medicina Tropical Heitor Vieira Dourado, Manaus (FMT-HVD, Tropical Medicine), the dermatologists and tropical dermatology and tropical diseases specialist Major Dr. Andrea Vanegas (Hamburg) and Colonel Dr. Marcellus Fischer (Hamburg) as well as Prof. Dr. Isaak Effendy (Bielefeld) and Prof. Dr. Helmut Schöfer (Wiesbaden) prepared a three-day course program and a DDA-certified basic seminar for tropical dermatology of the ISDT.

A total of 21 lecturers, partly from Brazil, partly from Germany, opened a very broad spectrum of tropical dermatoses with special emphasis on the local conditions in the Amazon region, in Brazil and other South American countries for the 95 course participants (37 dermatologists and dermatologists in training from Germany, Austria, Switzerland, as well as 58 dermatologists from Brazil, Spain and Portugal).

The FUAM is the dermatological reference center of the Amazonas State in Brazil and cooperation partner of the WHO for leprosy and sexually transmitted diseases (STI). Patients suffering from tropical diseases in the Amazonas State are referred to the FMT-HVD (hospital and academic institution). Both institutions offer physicians worldwide the opportunity to learn of endemic tropical diseases and tropical dermatology in Amazonas.

On October 17<sup>th</sup>, after a welcome by the course coordinators Dr. Andrea Vanegas and Prof. Helmut Schöfer, lectures were held. Major Dr. Claus Richter, specialist in dermatology at the German Military Hospital (Bundeswehr) in Ulm, spoke about the history of tropical dermatology (first tropical institutes in Europe: Liverpool 1821, London School for Hygiene and Tropical Medicine 1899 and the Bernhard-Nocht-Institute for Tropical Medicine in Hamburg 1900).

Prof. Sinesio Talhari (Professor of Dermatology, Federal University and Nilton Lins University in Amazonas and currently consultant of dermatology at the FUAM) researched the fascinating tropical dermatoses in the huge Amazon region for decades. The focus was on infections such as endemic treponematoses, cutaneous leishmaniasis and leprosy, but also histoplasmosis, prurigo, scabies, folliculitis, Kaposi's sarcoma and the effect of HIV infection and immune reconstitution inflammatory syndrome on tropical dermatoses. Likely, in the Amazonas State STIs are increasing again, the differential diagnosis e.g. to cutaneous leishmaniasis may be difficult.

Prof. Isaak Effendy, Head of Dermatology at the Municipal Hospital of Bielefeld and co-coordinator of the course spoke about the WHO concept of Neglected Tropical Skin Diseases (Skin -NTDs), with currently 10 neglected dermatological tropical diseases. The fight against NTGs (about 1 billion people are affected worldwide) is made considerably more difficult by influences such as poverty, migration, difficulties in accessing health services, climatic influences and a lack of medicines and vaccines. With the skin NTDs now being propagated, the WHO is yet trying to make it easier and quicker to identify general NTDs so that they can be treated promptly and effectively.

Worldwide there are about 0.7-1.2 million new cases of cutaneous leishmaniasis every year. With the migration of people from endemic regions in the Middle East, but also from North Africa, which has been continuing for years, the number of patients with "Old World leishmaniasis" in European dermatological practices and clinics has increased considerably. Assistant Professor Dr. Sibylle Schliemann, specialist for dermatology from the University of Jena, reported on the most frequent *Leishmania species* diagnosed here such as *L. major* (from Syria and Afghanistan) and *L. infantum* (from Mallorca, Spain) but also on a cutaneous leishmaniasis outbreak in the Ethiopian highlands, the importance of preventive measures and the difficulty of treating complex lesions.

Interesting oncological questions were the focus of the lecture of Prof. Michael Tronnier, chief physician of the department of dermatology of the Helios Clinic in Hildesheim. His focus was on clinical-histopathological relation of paraneoplastic skin diseases and cutaneous side effects of new system therapies in dermato-oncology. Prof. Tronnier spoke among others about diagnoses such as the erythema gyratum repens, the acanthosis nigricans maligna and the erythema necrolyticum migrans as well as about papules, keratoses, itching and vitiligo in connection with malignancies and their system therapies.

In the mycological laboratory of the FMT-HVD, Dr. Katia Cruz, public health specialist and mycologist, examines smear and tissue material from about 2000 patients with mycoses per year. Of the total of 10,000 samples sent to the fungal laboratory, 50% come from skin and nails. Her current focus is the investigation of fungal diseases in HIV-patients, especially infections caused by Dermatophytes and *Cryptococcus spp.*. The most common pathogens are *Candida spp.*, *Malassezia spp.*, various Dermatophytes and *Cryptococcus sp.*, but also the causative agents of chromomycoses, histoplasmosis and lobomycosis.

The causative agent of cutaneous leishmaniasis in Brazil is mainly *L. braziliensis*. Dr. Paulo Machado from Salvador, Bahia State, works there in the field of immunodermatology and heads the Department of Immunology at the Edgar Santos University Hospital of the Federal University of Bahia. He reported on several clinical studies on cutaneous leishmaniasis that were conducted under his supervision in the rural area of Corte de Pedra, Bahia. In about 1000 infections per year caused by *L. braziliensis*, 90% of the patients became ill cutaneously, 5% disseminated, 3% at the mucous membranes and 2% with atypical symptoms. After a single administration of antimony or pentamidine (the first choice drugs approved in Brazil for cutaneous leishmaniasis) a cure rate of 50-60% is achieved depending on the immune response. Clinical trials are currently underway with GM-CSF in combination with conventional drugs against *L. braziliensis* as well as miltefosine and amphotericin.

Professor Carolina Talhari works at the University of the State of Amazonas in Manaus and as a consulting and research dermatologist in Manaus with focus on leprosy, HIV, leishmaniasis and bullous dermatoses. In her lecture she concentrated on the endemic pemphigus foliaceus or "Fogo selvagem" known in Brazil since 1903, explained the role of desmoglein 1 as target antigen of acantholysis in this blistering disease and the disease variants reported in Colombia and other countries of South America but also in Tunisia.

Jacqueline Sachett, Professor at the University of the State of Amazonas and researcher at FUAM, together with PhD student Pedro Ferreira Bisneto, presented the topic of snakes in Brazil and the consequences of their bites in the last lecture of the day. Among the 405 known snake species in Amazonas region, *Bothrops* (also known as Jararaca) and *Lachesis muta* (a Surucucu genus of pit vipers) are of medical importance. These two species are responsible for about 90% of all snake bites in Amazonas. The course participants had the opportunity to get to know different snake species (in preserved form).

On the second day of the course, October 18<sup>th</sup>, Dr. Virginia Vilasboas, chief of the dermatology residence program at the FMT-HVD and Dr Katia Cruz coordinated clinical rounds for the European

participants to visit around 30 patients with various endemic skin diseases at the outpatient clinic and on the wards. The patients who suffered from endemic tropical dermatoses such as leprosy, pemphigus foliaceus (Fogo selvagem), cutaneous leishmaniasis, chromoblastomycoses or lobomycoses were of particular interest. But also for the classical dermatoses and skin tumors many new aspects (climatic influences, diseases on strongly pigmented skin etc.) resulted from the case presentations which could be discussed directly with the accompanying Brazilian colleagues (Fig. 1).

Dr. Katia Cruz led the course participants, who were divided into small groups, through the laboratories (mycology, histopathology) and described the special problems of laboratory diagnostics under tropical conditions (Fig. 2).

In the following scientific session in the lecture hall of the FMT-HVD very interesting clinical-histopathological case demonstrations of lobomycosis, sporotrichosis, tuberculoid leprosy, atypical mycobacterioses of the skin, disseminated cutaneous leishmaniasis, chromoblastomycosis and pemphigus foliaceus were presented by the colleagues of the dermatology department.

After a joint lunch typical for the Amazonas near the FMT-HVDC, Fabio Francesconi, Professor of Dermatology at the Federal University of Amazonia, started the scientific afternoon program with a comprehensive lecture on "Histoplasmosis in the Amazon Region". About 10% of all AIDS patients in Brazil die of this systemic mycosis (third most frequent cause of death in AIDS). Ten different manifestation patterns of the skin changes complicate the clinical differential diagnosis (molluscum contagiosum-like, acne-like, ecthyma-like ulcerative, plaque-like, follicularly bound, vasculitic, etc.) The diagnosis is usually confirmed by skin biopsies.

The next speaker was Dr. Marcellus Fischer, head of the Clinic for Dermatology at the German Military Hospital (Bundeswehr) in Hamburg and co-founder of the tropical Dermatology consultation at the Bernhard-Nocht Institute for Tropical Medicine in Hamburg. Dr. Fischer was one of the first German dermatologists who came to Manaus 20 years ago to complete a tropical medicine course at the FMT-HVD. Since then he has officially participated in several international missions in Asia and Africa as a dermatologist and a high-ranking officer of the German Federal Armed Forces (Bundeswehr). Dr. Fischer talked about the most important filarioses in tropical medicine such as onchocerciasis and lymphatic filariasis, explained the challenges of drug mass treatment with DEC and albendazole and the difficulties of successfully eliminating these pathogens.

The fact that cutaneous leishmaniasis in the Amazon is quite different from leishmaniasis in the Old World in terms of pathogen species, vectors and clinical picture was excellently presented by Dr. Jorge Guerra, specialist for infectious diseases and head of the Leishmaniasis Consultation in Manaus for more than 30 years. He also addressed the special risk factors for leishmaniasis in the Amazonas, such as environmental changes, deforestation, depletion of natural resources and agricultural activities. About one third of all cases of cutaneous leishmaniasis caused by *L. guyanensis* develop mucosal involvement after many years. Early, professional therapy can prevent this dangerous development. Furthermore, co-infections with HIV, secondary infections, genital lesions and atypical lesions during pregnancy are particular challenges in the treatment of leishmaniasis in the Amazonas.

After a coffee break, we continued with the topic "Kaposi's sarcoma". Professor Helmut Schöfer, coordinator of the course, with over 40 years of clinical experience in infectious skin diseases and sexually transmitted infections at the Department of Dermatology of the University Hospital in Frankfurt am Main, explained the different forms of this HHV-8 associated vascular tumor. Using clinical examples, epidemic, endemic, iatrogenic and Kaposi sarcomas associated with the immune reconstitution inflammatory syndrome were presented. Antiretroviral combination therapy plays a prominent role in HIV-associated Kaposi sarcomas. It reduces the occurrence of tumors in HIV-infected patients by about 90%.

Travel medical advice is of great importance for private or professional travel to the tropics. Assistant Professor Dr. Silja Bühler, head of the travel outpatient clinic at the Bernhard-Nocht Institute for Tropical Medicine in Hamburg explained how this is sensibly carried out. As an example, she used her own vaccination book to explain how she had prepared her trip to Manaus. It became clear that a travel medical consultation must include both general and very individual recommendations. Current disease outbreaks and endemic factors of the travel region that promote tropical diseases (e.g. the vectors of pathogens, climate change, etc.) must be taken into account.

One of the most fascinating topics for tropical dermatologists is lobomycosis, which was discovered in the Brazilian Amazon region and is primarily found only in Central and South America. Dr. Alex Panizza, consultant in dermatology at the FMT-HVD, shared his experience with this rare mycosis with us. About 500 cases have been documented in Brazil so far. This tropical skin disease caused by *Lacazia loboi* occurs in humans and dolphins in the western Amazon river (known as Solimões in Brazil). Early diagnosis can reduce the complications and consequences of treatment of choice (surgical removal of all lesions). For oral treatment, itraconazole or posaconazole are used in combination with clofazimine.

Dr. Bartosz Malisiewicz, consultant at the Department of Dermatology of the university hospital in Frankfurt am Main, presented interesting clinical pictures on the subject of "Pigment disorders in tropical countries". These include various hypo- and depigmentation disorders, e.g. hypochromic lesions in Mycosis fungoides, Post Kala-azar dermal leishmaniasis (PKDL), Progressive Macular Hypomelanosis, Leucoderma syphiliticum, Onchocerciasis and endemic Treponematoses. Dr. Malisiewicz also reported on the use (and misuse) of traditional and toxic bleaches on more pigmented skin and their consequences.

The afternoon's academic session was concluded by Lieutenant Dr. Juliano Cezar Silva Mota of the Department of Dermatology at the Military Hospital in São Paulo, Brazil with a brilliant presentation on a case of cutaneous tuberculosis.

Afterwards the participants visited the FMT-HVD snake center. There a whole range of preserved snakes from the Brazilian rainforest were presented up close with their most important characteristics.

During the weekend all participants had the opportunity to visit the tourist attractions of the 2-million-city of Manaus. During the city tour, the famous opera house (Amazonas Theater) built in 1884 and the historic Adolpho Lisboa market on the banks of the Rio Negro were among the attractions visited. Directly on the outskirts of the city, the Adolpho Duque nature reserve, which covers more than 100 square kilometers, there is a first contact feasibility for the European participants with the tropical rainforest. After a short hike and climbing a 42-meter-high observation tower, one could enjoy a wonderful view of the different levels of the rainforest. More information about fauna and flora was then given in the adjacent Open-Air Amazon Museum (MUSA). The next day the course group went by boat to interesting places in the surroundings of Manaus and to the impressive confluence of the Rio Negro and Rio Solimões: Encontro das Águas, which together form the Amazon up to its entry.

On the last day of the international course, the agenda included a visit to the FUAM with a focus on leprosy. Over a total of three hours in rotation in seven examination rooms, patients with the various forms and complications of leprosy, but also with chromomycosis and severe Darier's disease, were presented. Dr. Monica Souza, consultant of dermatology and head of the department for medical education at the FUAM, had carefully prepared and coordinated this clinical visit. The course participants examined the patients in small groups of 4-5 doctors and were instructed by the colleagues there, among other things, in the sampling techniques of leprosy diagnostics (Bacteria Index).

After a lunch break, Prof. Christoph Bendick, dermatologist with 27 years of professional experience in tropical dermatology in developing countries, reported on his experiences with leprosy in Cambodia

("The Faces of Leprosy in South East Asia"). In the social context of this country, he described not only the medical problems but also the challenges of a demanding leprosy program. In 2018 a total of 150 new cases of leprosy was discovered and treated in Cambodia.

Dr. Larissa Goes, consultant of dermatology at the FUAM, presented a case of an atypical type II leprosy reaction with painful lesions that clinically mimicked a Kaposi sarcoma.

A leprosy control program is also in place in Brazil. Both Professors Carolina and Sinesio Talhari presented this project, for which the FUAM is the WHO reference and cooperation center for the Amazonas. Once again, it became clear that, in addition to diagnostics and therapy of leprosy and its skin reactions, questions of identifying contacts, preventive therapies and compliance are of decisive importance.

The international course continued with a presentation by Prof. Sinesio Talhari on the endemic treponematoses (Pinta) caused by the spirochaete *Treponema carateum*. This non-venereal tropical treponematoses was first described in Manaus in 1973. It is transmitted by contact with diseased skin, which remains the only organ affected. After an incubation period of 2-3 weeks, a primary, slow-growing papule develops. This papule disseminates and the now confluent papules become dark livid. They heal with residual hypopigmentation and atrophy. Penicillin and azithromycin are suitable for therapy.

Similar to Europe, the development of resistance in gonococcal infections in Brazil is an important issue. Dr. Jose Carlos Sardinha, Director of the Department of Venereology at the FUAM and Prof. Sinesio Talhari reported on the current epidemiological STI data from Manaus. In the case of persistent genital ulcers, skin biopsy plays a greater role in Amazonas to rule out infections with *Haemophilus ducreyi* (ulcer molle). Important STI differential diagnoses here are also histoplasmosis and mycobacteriosis of the skin including leprosy. No cases of granuloma inguinale or lymphogranuloma venereum have been reported in Manaus at present.

At the end of the international course, Dr. Claudia Reber, pediatrician with experience in Sierra Leone, India and French Guiana, reported on skin diseases in children in Sierra Leone. In this African country 70% of the population lives in extreme poverty. The shown cases of severe skin reactions like Stevens-Johnson syndrome, massive exanthema, deep skin infections in case of malnutrition (Kwashiorkor) and HIV infection lead to often unsolvable problems under conditions of limited medical resources.

On the day after the International Course, the German-speaking participants were offered a 4-hour basic curricular seminar in tropical dermatology to obtain the DDA-Certificate in Tropical Dermatology. Prof. Isaak Effendy, Bielefeld, lectured on "Travel-related Infections", Assistant Professor Dr. Sibylle Schliemann, Jena, on "Non-tropical dermatoses in tropical countries", Dr. Bartosz Malisiewicz, Frankfurt/M, on "Indicator symptoms in tropical dermatology", Dr. Marcellus Fischer, Hamburg on "Safari in Africa: Skin symptoms leading to the diagnosis of infectious diseases", Prof. Helmut Schöfer, Wiesbaden, on "STIs in the tropics", and Dr. Alexander Sumenko, Hamburg on "The role of the mission dermatologist of Bundeswehr in the tropics".

This last part of the 7<sup>th</sup> course in tropical dermatology also ended with a joint lunch of all seminar participants in a typical local restaurant.

Tropical dermatology has shown Brazil from its best side! The course participants had a lot of experiences, valuable collegial encounters and a big bundle of new knowledge in tropical dermatology in their luggage on departure.



Fig.1: Brazilian and international participants after the exercise units of the second day of the course at the FMT-HVD (7<sup>th</sup> Tropical Dermatology Course of the German Dermatological Society (DDG) and the International Society for Dermatology in the Tropics (ISDT) in Manaus, Brazil, October 2019



Fig.2: Visit to the mycological laboratory of the FMT-HVD (Head: Dr. Katia Cruz)



Fig. 3: Rio Negro at the Ponta Negra in Manaus, Amazonas State, Brazil