LMU LUDWIG-MAXIMILIANS-UNIVERSITÄT MÜNCHEN

Conference on Tropical Medicine and Global Health

Book of Abstracts

April 4 - 6, 2019
University of Munich

Jahrestagung der
Deutschen Gesellschaft für Tropenmedizin und Internationale Gesundheit (DTG)

Österreichischen Gesellschaft für Tropenmedizin, Parasitologie und Migrationsmedizin (ÖGTPM)

Including Special Track Symposium
„Humanitarian Aid and Development Cooperation“

www.dtg-jahrestagung2019.de

Greeting

Dear Colleagues,

a warm welcome to the **Conference on Tropical Medicine and Global Health** in Munich! This year the interdisciplinary conference has a new format and will run once more as a joint annual meeting between the German Society for Tropical Medicine and International Health (Deutsche Gesellschaft für Tropenmedizin und Internationale Gesundheit, DTG) and the Austrian Society for Tropical Medicine, Parasitology and Migration Medicine (Österreichische Gesellschaft für Tropenmedizin, Parasitologie und Migrationsmedizin, ÖGTPM). We are also honoured to have the following societies taking part

- **The Society for Dermatology in the Tropics e.V.**
- **The Committee for Women's Health Issues in Development Cooperation (AG FIDE)**
- **The Society for Paediatrics in the Tropics (GTP)**
- **The German Society for Surgery in the Tropics (DTC)**
- **The German Center for Infec on Research (DZIF)**

Another new feature is that the **Symposium for Humanitarian Aid and Development Cooperation** will be held as a parallel track on April 5th. For the first time, this conference will officially be held in English as well as German, to enable wider international participation. In addition, for the first me we are featuring a partner country, Tanzania, which will be at the focus of our attention. We are very much looking forward to welcoming colleagues from Tanzania and other parts of the tropical world.

Sustainable solutions to Global Health challenges require novel and ever more comprehensive and multidisciplinary approaches. We therefore aim to bring together different fields of expertise as well as numerous stakeholders in order to broaden perspectives, facilitate interdisciplinary exchange and promote innovation.

Parallel tracks at this conference will address important issues in clinical care of travelers and migrants, novel diagnos cs, highlights in basic research and testing of new clinical interventions, as well as their efficient use in improving health care in developing countries. Under the track **„Partner Country Tanzania"** we recognize that solutions can only be found in cooperation with partners in the developing world and highlight the importance of research driven by our partners.

We will also invite presentations of successful examples of research and development cooperation. Finally, it is a great honour for us that the Bavarian Government Executive (Bayerische Staats-kanzlei) will host an official reception for the congress participants in the classical building of the Munich Residenz. An event you should not miss!

We hope you'll enjoy the conference!

Prof. Dr. Michael Hoelscher
Conference Chair

Dr. Camilla Rothe
Chair Scientific Committee

Prof. Dr. Herwig Kollaritsch
Chairman ÖGTPM

Dr. Dr. Carsten Köhler
Chairman DTG

Scientific Program at a Glance

Thursday, April 4, 2019

	Plenary Hall	Room B101	Room B139	Room B138
11.00-13.00	CIH Pre-Meeting / 10 Years CIH (Room C112)			
13.00-13.45	Lunch Break			
13.45-14.00	Congress Opening			
14.00-15.00	PL1 Plenary „Tanzania – Europe“			
15.00-15.30	Coffee Break			
15.30-17.00	**S1:** Novel Diagnostics/ Digital Health	**S2:** Partner Country Tanzania	**S3:** One Health/ Emerging Infections	**S4:** Global Health 1
from 18.30	Get-together at the Munich Residence			

Friday, April 5, 2019

	Plenary Hall	Room B101	Room B139	Room B138
08.00-08.45		**S5:** Meet the DTM & H Course Director	**S6:** Klinisches Quiz	Symposium Humanitarian Aid and Development Cooperation
09.00-10.00	PL2 Plenary: Poverty & Health			
10.00-10.30	Coffee Break /Presentation Body Map Exhibition			
10.30-12.00	**S7:** Tuberculosis & Antimicrobial Resistance	**S8:** Preventive Medicine & Occupational Health	**FG1:** Tropen-gynäkologie	Symposium Humanitarian Aid and Development Cooperation
12.00-13.30	Lunch Break	**WS I**: Pictorial Seminar-Ultrasound in Tropical Diseases (Room C112)	Lunch-Symposium Merck	**WS II**: Feldlabor in der Tropenmedizin (Room C111)
13.30-15.00	**S9:** Blood-borne Infections: HIV & Hepatitis	**S10:** Climate Change and Health/ Environ-mental Health	**FG2:** Tropen-pädiatrie	Symposium Humanitarian Aid and Development Cooperation
15.00-16.00	Coffee Break and Poster Viewing			
16.00-17.30	**S11:** Malaria and other Vector-borne Diseases	**S12:** Non-communicable Diseases & Health System	**FG3:** Tropen-dermatologie	Symposium Humanitarian Aid and Development Cooperation
17.30-17.45	Coffee Break			
17.45-18.15	Verleihung des DTG Preises			
18.15-19.15	DTG-Mitgliederversammlung			
From 19.30	Bavarian Evening at „Der Pschorr"			

Scientific Program at a Glance

Saturday, April 6, 2019

	Plenary Hall	Room B101	Room B139	Room B138
09.00-10.30	**S13:** Neglected Tropical Diseases	**FG4:** Junge DTG/ Junge Parasitologen	**FG5:** Tropen-chirurgie	**S14:** Global Health 2
10.30-11.00	Coffee Break / Presentation Body Map Exhibition			
11.00-12.00	PL3 Plenary: Vaccines/Novel Diagnostics			
12.00-12.45	PL4 Plenary: 2 Jahre in der Tropenmedizin			
12.45-13.00	Closing			
13.00-13.15	Lunch Break			
13.15-15.15			Tropenmedizin Update (Room B139)	
15.15-15.30	Coffee Break			
15.30-17.00			Reisemedizin Update (Room B139)	

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S9: Blood-borne Infections: HIV & Hepatits

S10: Climate Change and Health /Environmental Health

S11: Malaria and other Vector-borne Diseases

S12: Non communicable Diseases & Health Systems

S13: Neglected Tropical Diseases

FG 4: Junge DTG/Junge Parasitologen

FG 5: Tropenchirurgie

S14: Global Health 2

Poster

S1: Novel Diagnostics/Digital Health

S1-1

Application of matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry in diagnostic helminthology: a proof-of-concept study

M. Feucherolles[1], S. Poppert[2, 3], Y. Endriss[2, 3], C. Hermosilla[4], B. Lundström-Stadelmann[5], J. Utzinger[2, 3], S. L. Becker[1, 2, 3]
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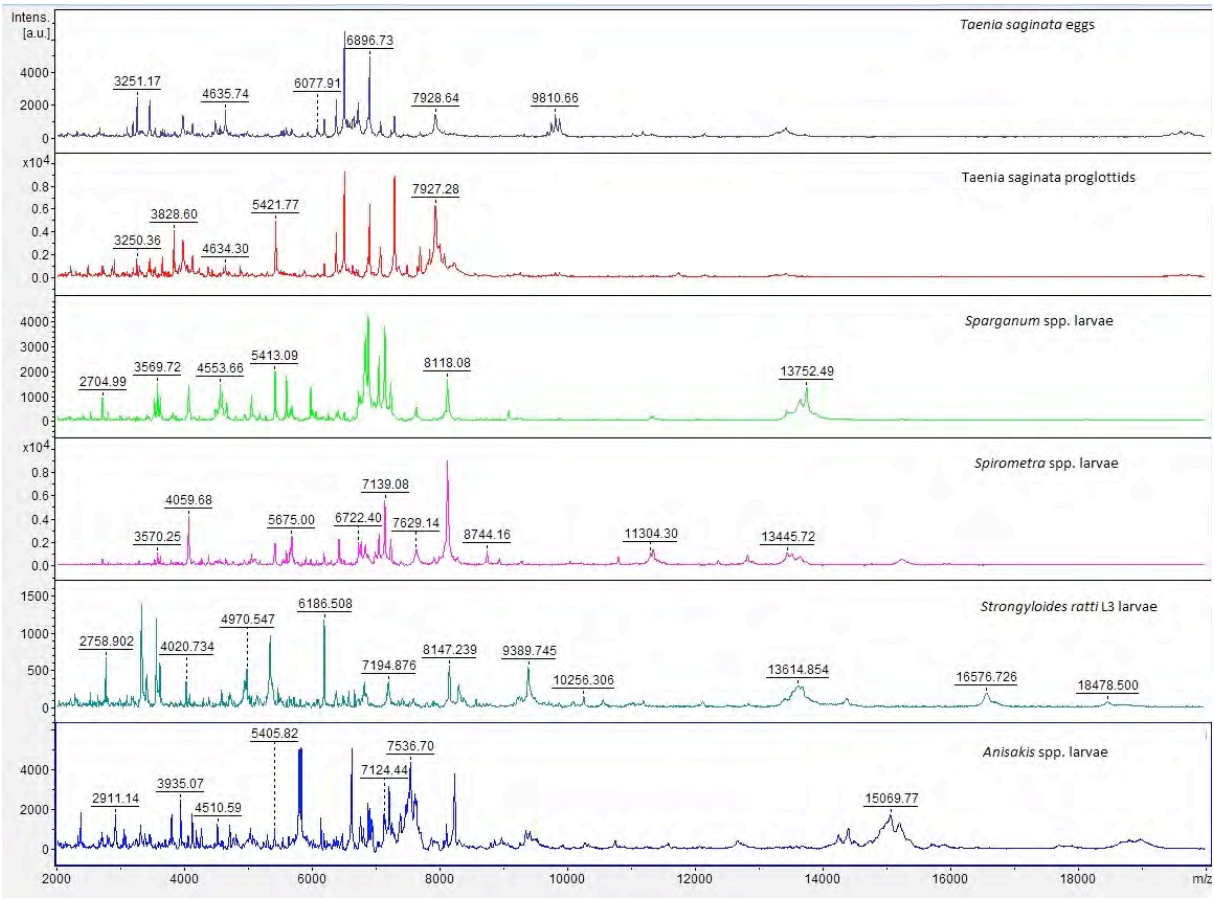
Background:
Helminth infections are major neglected tropical diseases and pose a great burden on human and animal health. The diagnosis of most helminth species relies on the microscopic examination of e.g. stool, blood or tissue samples. Yet, the sensitivity of microscopy is low,some species cannot reliably be distinguished by microscopy alone (e.g. *Taenia* spp. eggs) and the required expertise for accurate species identification is waning in many laboratories. Matrix assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrometry is a relatively new technique that is now routinely employed in diagnostic centers as a rapid and reliable technique for identification of bacteria and yeasts. In parasitology, only a few studies have assessed this method on protozoa and ectoparasites. We carried out a proof-of-concept study to evaluate MALDI-TOF mass spectrometry as diagnostic tool for pathogenic helminths.

Methods:
Eggs, larvae and adults of different helminth species (*Anisakis* spp., *Schistosoma* spp., *Sparganum* spp., *Spirometra* spp., *Strongyloides* spp., *Taenia* spp.) were subjected to an acid formic/acetonitrile-based protein extraction. Each sample was spotted eight times using α-cyano 4-hydroxy cinnamic acid matrix (HCCA) before subsequent MALDI-TOF analysis on a MicroFlex LT mass spectrometer (Bruker Daltonics; Bremen, Germany). Four spectra (m/z 2 to 20 kDa) were acquired from each spot, resulting in 32 spectra per species. A specific software was used to clean the spectra (outlines, flatlines, baseline subtraction and smoothed) and create a Main Spectra (MSP) in-house database. Repeatability and reproducibility were also evaluated. The in-house database was tested in combination with the commercially available Bruker database to identify the raw mass spectra generated during the MALDI-TOF analysis.

Results:
The protein spectra obtained from different helminths showed characteristic patterns with specifics peaks, allowing for an accurate differentiation between different genera.



MALDI-TOF mass spectrometry spectra obtained for different helminth species. Spectra were zoomed on a range of 2-20 kDa.

Protein spectra of eggs and proglottids stemming from *T. saginata* could also be distinguished based on specific protein peaks. The in-house database was able to accurately identify the generated raw mass spectra without matching any bacterial spectra from the commercially available database.

Conclusion: Our study provides the proof-of-concept that MALDI-TOF mass spectrometry can be successfully employed to detect and identify helminths of medical and veterinary importance. There is a need for further studies that employ the technique on helminth eggs, larvae and adults to develop comprehensive MALDI-TOF protein spectra databases that will subsequently enable a reliable species identification.

Keywords: Diagnosis, Helminthology, Matrix-assisted laser desorption/ionization time-of flight, MALDI-TOF MS, Neglected tropical diseases

S1-2

RLEP LAMP for the diagnosis of leprosy

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Leprosy caused by M. leprae is a neglected, chronic infectious disease predominantly affecting skin and peripheral nerves which is transmitted through the aerial route. The disease is spectral and categorized according to the Ridley-Jopling classification based on type of lesions and bacterial load into tuberculoid, lepromatous and borderline forms. Alternatively a simplified, field-based classification introduced by the WHO distinguishes paucibacillary (PB, up to five lesions and/or impaired nerves) and multibacillary (MB, more than five lesions and/or impaired nerves) forms. In the absence of bacteriological evidence misclassification and misdiagnosis leading to inappropriate treatment occurs. To bring back the laboratory diagnostic component into routine practice, beyond AFB microscopy with its own limitations regarding sensitivity and specificity, a range of PCR-based molecular diagnostic tests targeting various gene markers has been applied to the diagnosis of leprosy from skin biopsies and slit skin smears with a positivity rate approaching 50% in PB and 80% in MB cases. Our own group developed a RLEP qPCR on nasal swabs constituting a less invasive sampling technique which facilitates early diagnosis of leprosy cases as well as laboratory assessment of contact persons. Although recognizing the superiority of PCR compared to other diagnostic techniques, WHO currently does not recommend PCR for diagnosis nor screening of contact persons as PCR would be difficult to perform in most field settings, PCR assays lack standardization, currently no PCR tests are commercially available, and PCR requires technical and laboratory expertise. Loop-mediated isothermal amplification (LAMP), a promising nucleic acid based candidate point-of-care technology applicable for decentralized diagnosis at primary health care level without the need for sophisticated laboratory equipment, has the potential to change that situation. Based on own experience with the development of a dry-reagent based (DRB) IS2404 LAMP for decentralized diagnosis of Buruli ulcer in cooperation with the Foundation for Innovative Diagnostics (FIND) which currently awaits clinical validation in Togo, our group designed and validated a DRB RLEP LAMP assay for the diagnosis of leprosy from nasal swabs. Using a set of four lyophilized primers (RLEP F3, RLEP B3, RLEP FIP, RLEP BIP) and lyophilized isothermal mastermix ISO-DR-004 (OptiGene, Horsham, UK), the assay was validated on a Genie III portable real-time fluorimeter (OptiGene). The limit of detection was 1.000 RLEP copies as determined with serial dilutions of a RLEP plasmid standard. Testing of 30 RLEP qPCR confirmed “must detect” samples showed a sensitivity of 92%, testing of 40 “must not detect samples” derived from RLEP qPCR negative patients with other conditions and a set of mycobacterial cultures resulted in a specificity of 100%.

S1-3

The digitalization of health networks in sub-Saharan Africa: report of CYSTINET-Africa, a multidisciplinary research consortium for Taenia solium taeniosis/cysticercosis

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In CYSTINET-Africa, a multidisciplinary One Health network with a focus on Taenia solium taeniosis/cysticercosis, capacity building represents a key success indicator for the project outcome. Data sharing is mandatory and is best done digitally but can be challenging in large health networks. Here we share our own experience within CYSTINET-Africa highlighting key aspects of network digitalization in remote rural areas of sub-Saharan Africa with respect to sustainability of the systems setup.

Firstly, we compare different providers of data collection tools (EpiCollect [1], KoboToolbox [2], MagPi [3]) with an emphasis on data privacy regulations (DSVGO). Secondly, during data collection we follow a re-designed medical workflow for our epidemiological studies in which we use a so called “patient pass”. Thirdly, hardware and software procurement concerns are highlighted in addition to potential infrastructure challenges.

The new DSVGO [4] impacts decisions of data storage locations, its software to be used and data exchange agreements to be specified if data is transferred between multiple countries. We compare different existing software solutions for offline data collection, based on their features, such as creation of questionnaires, ease of use, storage and backup, data privacy concerns, license models and costs.

	MagPi	EpiCollect 5	KoBo Toolbox
Open Source	No	No	Yes
License	Not stated	Not stated	BSD 2-clause "Simplified"
Data Ownership	Data Creator	Data Creator	Data Creator
Costs	500 Dollar per month	Free	Free
Data Security	Magpi uses the most advanced tools and engineering practices available to build and maintain the system. In fact: Not a single specification or naming of any type of encryption.	Chat with developer revealed the following: "We don't want to give up our data sink" This why hosting on other servers than ours is not allowed.	Storing all personal and medical data on facility owned server infrastructure Not encrypted in database, but database is in own hands.
Backups	Automatic backups made	Automatic backups made	Backups need to be created
Active Development	Yes, private company	Yes, university project	Yes, public domain
API connectivity	Yes	Yes	Yes
HTTPS (SSL)	Yes	Yes	Yes
Data encrypted	Not specified, server location seems to be USA.	Not specified, server location seems to be UK.	Form encryption, RSA encrypted locally ODK Briefcase
Secure data synchronization	Yes, via HTTPs	Yes, via HTTPs	Yes, via HTTPs
Questionnaire creation	Questionnaire Builder via website (basic program only allows primitive inputs)	Questionnaire Builder via website (allows barcodes etc.)	Questionnaire Builder via website (allows barcodes etc.)
Deployment			
Hosting	MagPi, stores all personal and medical data	EpiCollect 5, stores all personal and medical data	Either storing all personal and medical data on self owned server infrastructures, or using Amazon Web Services (AWS)
Others			
Database format	Unknown	Unknown	PostgreSQL for Data MongoDB for preparing output
Support	Email, Skype (payed ~125 Dollar Per Hour)	User groups	User groups, email
Mobile devices	IOS/Android	IOS/Android	Android

Table Abbreviations:
API: Application Programming Interface – Interface to connect to application and services
HTTPS: Hypertext Transfer Protocol Secure – Secure data transfer via websites
RSA: Encryption algorithm of Rivest, Shamir, Adleman from MIT – de facto standard
ODK: OpenDataKit – Document standard for remote data collection
AWS: Amazon Web Services

Comparison of different data collection tools

Since data collection tools typically do not offer workflow support for epidemiological studies, standard operation procedures (SOPs) need to be adapted to integrate seamlessly. The use of barcode labeling techniques helped to provide the needed traceability. In our scenario, blood and stool samples are mapped to a unique patient barcode to be traceable but still anonymous. To support such an approach, the “patient pass” shall minimize errors in data sample collection and handling.

To assure data access, server availability tests are established to assure server uptime [5]. Based on results of different tests, backup servers are put in place using synchronization techniques to mirror existing data to additional remote locations. Concerning hardware and software procurement, we advise for international single source procurement for hardware with limited availability, while strengthening local industry for procurement of commonly available goods like printers, computer monitors and consumable supplies.

In summary, to digitalize medical data in multi-country studies 5 important steps can be highlighted: (1) assessment of local conditions for data storage by using existing tools, (2) assurance that data exchange agreements are in place, (3) customization of workflows for traceability and anonymity reasons, (4) selection of a data collection tool that adheres data privacy regulations of all involved countries, and (5) mixed procurement of hardware and software - national and international.

[1] https://goo.gl/rxT4zf
[2] https://goo.gl/egMjHn
[3] https://goo.gl/RSdVhd
[4] https://goo.gl/Wixekv
[5] https://goo.gl/GevAqD

S1-4

Mobile instant messaging (WhatsApp®) for pharmacovigilance of pellagra during Isoniazid preventive therapy (IPT) implementation

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Background
Isoniazid preventive therapy (IPT) is recommended to prevent tuberculosis in HIV-positive patients in high prevalence settings as in various African countries (1). Isoniazid has long been described to cause pellagra in patients with borderline-low niacin levels (2). Malawi's population is vulnerable to micronutrient deficiencies (3) due to often non-fortified maize-based diet and food shortages.

Objective
To improve pharmacovigilance for pellagra-like changes using WhatsApp® in a large antiretroviral treatment (ART) cohort after implementation of IPT.

Methods
Lighthouse clinics in Malawi serve more than 90,000 ART patients in three large and multiple smaller sites; clinicians had not reported pellagra previously. After implementation of IPT in all clinics in September 2017, a description of pellagra with photographs of characteristic skin manifestations and a request to report suspected cases was posted to all Lighthouse clinicians using WhatsApp®

Results
33 cases (79% female) with pellagra-like symptoms were reported within three months (Jan-Mar 2018). All patients had characteristic skin changes; four reported additional diarrhea. All patients had started IPT 1-4 months (mean 2.7) prior to onset of symptoms and had been taking ART for 10-120 months (mean 68) without complications prior to the skin changes. Pictures of skin conditions were shared for all cases, allowing verification of the typical rash and increasing awareness amongst clinicians.

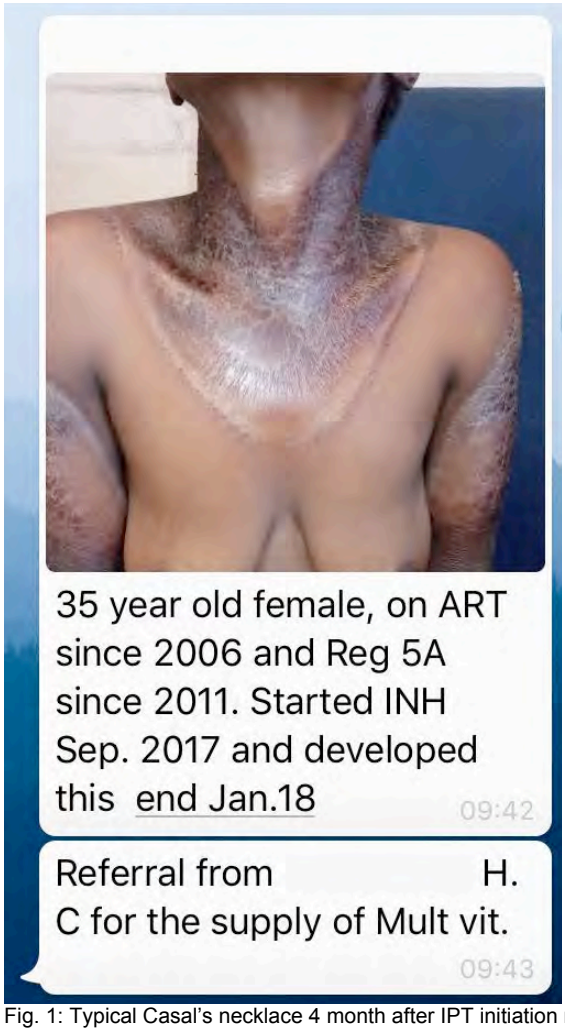

Fig. 1: Typical Casal's necklace 4 month after IPT initiation reported on Whatsapp®

All patients stopped IPT and received vitamin B3.

Conclusion

An unexpectedly high number of cases with pellagra were seen, which does not necessarily prove a causal association with IPT as increased awareness may have biased reporting. Nevertheless, the accumulation of cases during a short period, the onset after 2-3 months of IPT and the established biological pathway suggest causality and the number of cases itself raised concern of drug safety in our patient population. Our report shows that WhatsApp® can be useful in epidemiological surveillance and pharmacovigilance, as it allows timely identification of cases by multiple clinicians in different locations. The possibility of sharing images without endangering patient confidentiality improves case identification; real-time comments allow immediate treatment advice. ART programs implementing IPT in malnourished populations should be aware of pellagra as a potential side effect and provide for vitamin substitution.

1) WHO: Recommendation on 36 months isoniazid preventive therapy to adults and adolescents living with HIV in resource-constrained and high TB- and HIV-prevalence settings – 2015 update.
2) Harrison RJ et al: Pellagra caused by isoniazid. BMJ 1956;2.4997: 852.
3) Matapandeu GS et al: An Outbreak of Pellagra in the Kasese Catchment Area, Dowa, Malawi. AJTMH 2017; 96:1244-1247.

S2: Partner Country Tanzania

S2-1

Screening of 1003 whole blood samples from febrile patients in Mbeya, Tanzania for the presence of Relapsing Fever Borrelia using real-time PCR

C. Luetke-Daltrup[1, 2], V. Fingerle[3], A.-C. Neumann[1, 2, 4], N. E. Ntinginya[5], C. Manyama[5], L. Sudi[5], G. Margos[3], G. Dobler[4, 6], M. Hoelscher[1, 4], N. Heinrich[1, 4], A. Wieser[1, 2, 4]
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Relapsing fevers are vector borne diseases caused by bacteria of the genus *Borrelia*. The clinical course is characterized by recurrent episodes of fever. Epidemiologically relapsing fevers are more common in resource limited settings and rarely occur in central Europe. There are two main relapsing fever groups, Louse borne relapsing fever (LBRF) caused by *Borrelia recurrentis* is transmitted by the body louse and is characterized by high mortality rates and epidemic occurrences. Tick borne relapsing fever (TBRF) is transmitted mainly by soft ticks and caused by different related *Borrelia* species. TBRF can be found in certain geographical areas epidemically and occurs sporadically in patients. The clinical course is most often less severe, lethality is low [1, 2]. Reports about the prevalence of TBRF vary considerably in the literature. It is generally assumed that the burden of disease is underestimated due to the lack of sensitive detection in patient material.
In this study, 1003 blood samples from the Mbeya region (Tanzania), which were collected during the HOMA trial were investigated for the prevalence of *Borrelia* DNA. Therefore, freshly frozen whole blood samples of acute febrile patients were extracted using a robotic platform and investigated for the presence of *Borrelia* DNA with two different and newly validated real-time PCR protocols. The protocols were validated with enumerated *Borrelia* cultures, as well as extracted positive blood samples to have a sensitivity of 10^2-10^1 DNA copies/5µl. Controls included T/L-BRF strains *B. miyamatoi*, *B. hermsii* and *B. recurrentis*. Lyme group *Borrelia* were also detected. One protocol was based on SYBR green, the second on TaqMan probes, both using a different set of primers. Similar studies used this approach successfully to detect *Borrelia* in the blood of patients [3]. Within this study however, no *Borrelia* could be detected. This may be due to regional peculiarities. It may be a highly unlikely sporadically occurring disease which is of less importance given the overall disease burden. The patient cohort was selected to be regionally as well as socio-economically diverse. A significant proportion of the study participants were rural inhabitants with livestock keeping.
This is the first cohort of acute febrile patients in the Mbeya region, which has been screened for relapsing fever *Borrelia*. Within the sample, no relapsing fever cases could be found. Thus, the disease seems to be absent or present only in very small numbers in the population.
1. Melkert, P., et al., RELAPSING FEVER, A DISAPPEARING CAUSE OF FEVER AND MATERNAL DEATH IN SENGEREMA, TANZANIA, EAST AFRICA. East Afr Med J, 2013. 90(4): p. 137-41.
2. Elbir, H., D. Raoult, and M. Drancourt, Relapsing fever borreliae in Africa. The American journal of tropical medicine and hygiene, 2013. 89(2): p. 288-292.
3. Cutler, S.J., et al., Ornithodoros savignyi, the Tick Vector of "Candidatus Borrelia kalaharica" in Nigeria. J Clin Microbiol, 2018. 56(9).

S2-2

Prevalence of (pre)-cancerous cervical lesions and cervical cancer awareness in Kilimanjaro Region, Tanzania

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Kilimanjaro Christian Medical Center, Moshi, Tanzania, United Republic of

Background
In Tanzania, cervical cancer (CC) is the leading cancer in women with an annual incidence of 9770 cases and 6695 deaths per year [1]. Mortality rate could be reduced through a comprehensive approach including HPV vaccination, timely diagnosis, screening and treatment programmes as recommended by the Tanzanian National Guidelines[2]. However, the number of screenings programs remains low, especially in rural areas due to lack of equipment and trained staff.
Majority of women in rural areas have limited knowledge about CC when compared to urban areas [3], leading to limited attendance rates in screening services. Kilimanjaro Region belongs to the rural areas with a population of 2 million. Screening programs are sparse and data about CC awareness and knowledge are lacking.
The Cancer Care Centre at Kilimanjaro Christian Medical Center implemented a Prevention and Awareness Campaign (PrevACamp) to offer mass screening of cervical cancer and to gain data about knowledge in this region.

Methods
From October 2017 to November 2018, 1914 women attending PrevACamp, answered questionnaires about CC knowledge. 1884 women district have been screened using VIA (visual inspection of the cervix after acetic acid application).

Results
63 out of 1884 women were VIA positive (3,3%).

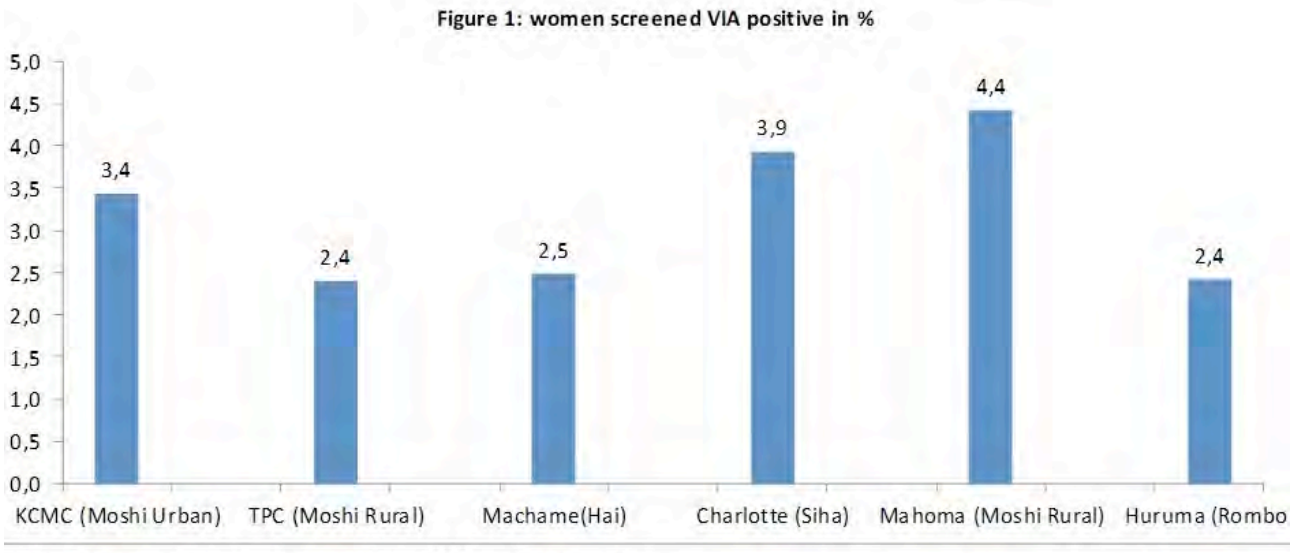

Figure 1: Percentage of women screened VIA positive by site
Figure 1 women screened VIA positive in %

37% of women in urban and 31% in rural districts never heard about CC (p=0,014). Awareness of HPV vaccination was higher in rural (36%) than in urban (16%) areas (p=0,000). Education level influence knowledge about HPV vaccination (primary education 25%, secondary education 32%, p=0,002). General awareness about risks factors is low, ranging from 0,8% in non-educated women to 8,9% in all women below 35 years.

Variable	N	Ever heard about CC	Awareness about prevention vaccine	Awareness about risks of CC	Awareness about at least one symptom of CC
Place					
Moshi Urban	916	580(63.3%)	146(15.9%)	58(6.3%)	324(35.4%)
Rural Area	998	685(68.6%)	358(35.9%)	50(5.0%)	502(50.0%)
All	1914	1265(66.1%)	504(26.3%)	108(5.6%)	826(43.2%)
Education					
Never been in school	121	63(52.1%)	19(15.7%)	1(0.8%)	48(39.7%)
Primary education	1290	845(65.5%)	323(25.0%)	68(5.3%)	548(42.5%)
secondary level and higher	503	357(71.0%)	162(32.2%)	39(7.8%)	230(45.7%)
Age					
<35	563	378(67.1%)	140(24.9%)	50(8.9%)	214(38.0%)
35-44	497	346(69.6%)	143(28.8%)	23(4.6%)	221(44.5%)
45-54	402	280(69.7%)	117(29.1%)	20(5.0%)	195(48.5%)
55+	452	261(57.7%)	104(23.0)	15(3.3%)	196(43.4%)

Table 1: Knowledge on prevention vaccine, risks and symptoms of cervical cancer by education level, age and place of residence (n=1914)

Table 1: Knowledge on prevention vaccine, risks and symptoms of cervical cancer by education level, age and place of residence (n=1914)

Discussion

VIA positivity was found to be surprisingly low compared to previous studies [4] in East Africa. These findings need further investigation and sub-group analysis. Overall knowledge and awareness were considerably low in all Districts, but higher in educated women and in rural areas. While the first finding is reasonable, the latter was unexpected. A possible explanation might be the long tradition of faith-based health services throughout the Region with a focus on rural areas.

The limited knowledge about HPV vaccination is alarming and needs to be addressed by further education and information campaigns in schools and in communities at social and religious gatherings and through media.

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S2-3

The quality and the composition of Albendazole, Mebendazole and Praziquantel available in Northern Tanzania

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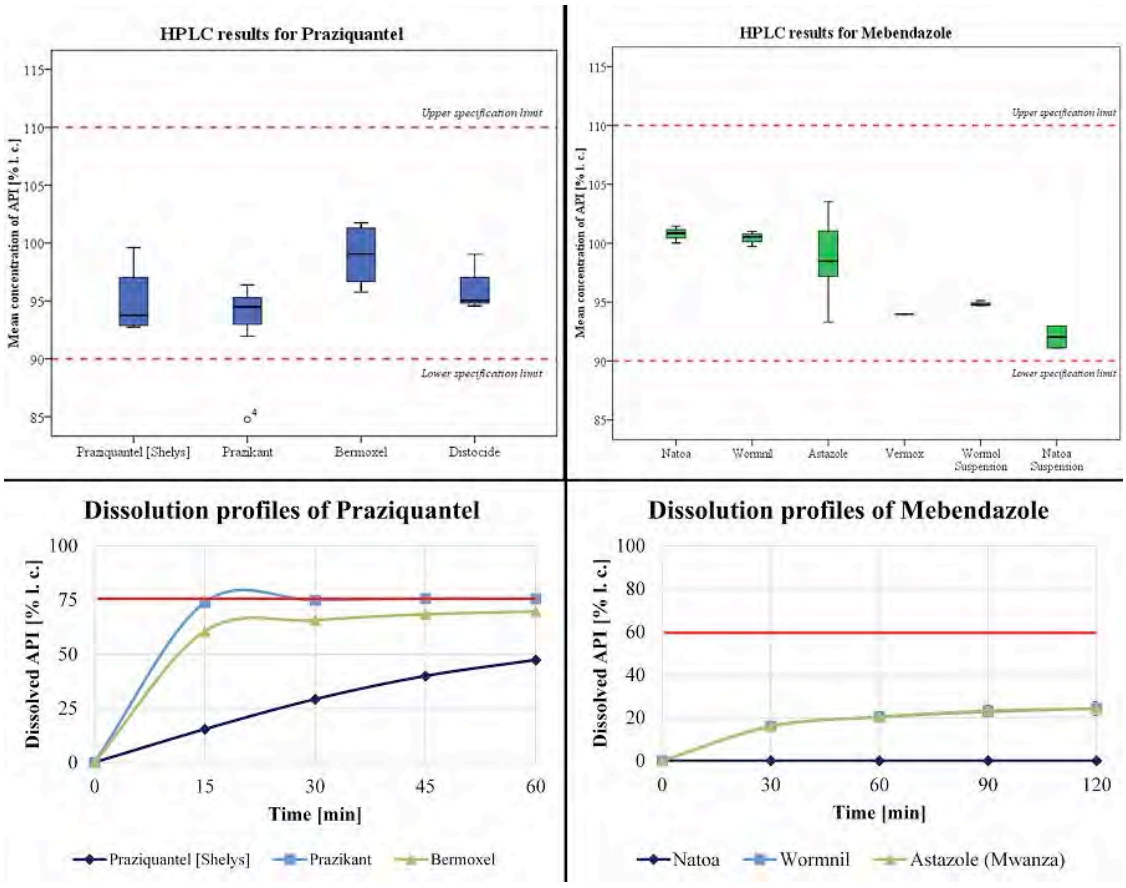
Background
An estimated 1.7 billion of people worldwide suffer from soil-transmitted[1)] and water-borne[2)] helminthiases, with high prevalences given in Africa. The main control strategy is mass drug administration of anthelminthic drugs. Despite frequent reports of substandard and falsified products, little information is available about the quality of anthelminthic medicines.

Methods
43 batches of the anthelminthic drugs Albendazole (ABZ), Mebendazole (MBZ) and Praziquantel (PZQ) were collected in the northwest of Tanzania from 27 randomly selected local suppliers, with focus on the city of Mwanza. The tablets and their packages were visually examined and afterwards assessed by two different methods. Mass uniformity, disintegration times and thin-layer chromatography (TLC) were performed applying the GPHF Minilab®. In addition, dissolution profiles and high-performance liquid chromatography (HPLC) were used to assess quality and composition.

Results



Physical characteristics of all but 7 batches fully complied with the WHO checklist despite 4 out of the 28 different products not being registered in Tanzania (by 12/2018). Mass uniformity of each tablet per batch was checked against WHO criteria: 87.0 % (20/23) of the brands passed the tests, 13.0 % failed to meet the limits. Disintegration times revealed 3 out of 23 products not meeting the Minilab® requirements at all, 2 partly failing. 78.3 % of the batches fully passed, ranging between 0.75 and 23.75 minutes. The dissolution profiles of 3 MBZ brands tested so far revealed severe deficiency: in accordance to WHO standards, no product released a minimum of 60 % of a reference sample. 3 PZQ batches assayed resulted in just one passing the requirements of the US Pharmacopeia of 75 %. The quality of active pharmaceutical ingredient (API) of the 39 different batches of tablets was determined by means of TLC. Not a single sample fell below the Minilab® specifications between 80 % and 100 % label claim (l. c.) of an adequate reference sample. In comparison to the TLC findings, HPLC results confirmed the appropriate concentration of active pharmaceutical ingredient in all samples tested so far (between 90 % and 110 % l. c.).

Conclusions

Sufficient concentration of API in a sample of antihelminthic medicine does not inevitably correlate with its galenic features. The samples tested were of varying quality, as only 1 PZQ batch met international dissolution standards. Further *in vivo* evaluation (for instance by therapeutical drug monitoring or egg reduction / cure rates) is required though before seriously questioning distinctive drug batches.

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S2-4

Free access to digital health information in Iringa, Tanzania: Development, provision and testing the effect of digital health messages to rural communities

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Background/ Introduction
The spread of digital technologies and global interconnectedness has a significant potential to accelerate progress towards achieving the health-related Sustainable Development Goal 3 at a global level, which includes access to free health education. The Non-discriminating access for Digital Inclusion (DigI) project aims to establish pilots for the InfoInternet access in Tanzania.

Objective
To increase health knowledge regarding HIV/AIDS, tuberculosis (TB) and Taenia solium cysticercosis/taeniosis (TSCT) by a digital health promotion intervention in the population of Izazi and Migoli villages (the intervention villages) in rural Iringa, Tanzania, in order to promote early access of health care services and the application of preventative strategies. Specifically, the project aims to:
1) Develop digital health messages related to HIV / AIDS, TB and TSCT.
2) Promote use of the digital health messages in the intervention villages
3) Assess the effect of the digital health messages related to health knowledge

Materials & Methods
1) Digital health messages (currently in the last stage of development), addressing prevalence, transmission, symptoms, treatment and prevention for HIV / AIDS, TB and TSCT.
2) A digital platform, providing the communities with free access to digital health messages, via own mobile phones and devices, and tablets and screens available in the local information kiosk.
3) A two-armed cluster controlled trial is planned to measure health knowledge on HIV/AIDS, TB and TSCT. Baseline knowledge scores will be calculated in both groups. After implementation of the digital health intervention, knowledge uptake and retention will be assessed by a questionnaire, in both arms, immediately after, 3-, 6- and 12-months after the intervention rollout.

Outlook
We anticipate that providing health message in a digital format will increase health related knowledge, which ultimately will lead to an adaptation of health seeking behaviour. The digitalisation of health information may contribute to the strengthening of health systems, especially in resource poor settings.

S3: One Health/Emerging Infections

S3-1

Transmission networks of Cryptosporidium spp. in rural sub-Saharan Africa: a multi-country study

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Introduction. High prevalence and mortality from Cryptosporidiosis among children in sub-Saharan Africa has been shown in recent years, however transmission dynamics and reservoirs are yet to be investigated. This multicentre study traces back Cryptosporidium positive children to their close human and animal contacts in order to identify transmission networks and reservoirs.

Methods. Stool samples from children below 5 years with diarrhoea were collected at hospitals in Gabon, Ghana, Madagascar and Tanzania. Cryptosporidium positive and negative initial children were followed to the community, where stool samples from all household members, neighbouring children (<5 years) and animal contacts (cows, sheep, goats and dogs) were obtained. Samples were screened for Cryptosporidium spp. by PCR-RFLP analysis of the small subunit rRNA gene and sequence analysis of the 60 kDa glycoprotein gene for C. hominis and C. parvum. Contact networks were identified and rate ratios (RR) calculated.

Results. Among 1,363 initial children 44 (20%), 47 (11%), 25 (11%) and 68 (14%) were diagnosed with Cryptosporidium spp. in Gabon, Ghana, Madagascar and Tanzania, respectively. The following species were diagnosed: 144 (79%) C. hominis, 26 (14%) C. parvum, 10 (5%) C. meleagridis, 2 (1%) C. felis and 1 (1%) C. xiaoi/bovis. Across the countries the proportion of infections ranged from 8% to 20% in household members (N=350), from 20% to 36% in neighbouring children (N=245) and from 11% to 15% in animals (N=338). Among 108 contact networks gp60 subtyping established 37 clusters, which contained 49% and 54% of Cryptosporidium positive household members and neighbours, respectively, but only 18% of Cryptosporidium positive animals. In comparison to Cryptosporidium negative initial children, positive initial children had an increased risk of having positive household members (RR = 2.5; 95%-Confidence Interval (CI): 1.5–5.2) or positive neighbouring children (RR = 2.7; 95%-CI: 1.6–4.8), but no risk of having positive animals (RR = 1.3; 95%-CI: 0.8–2.1) in their contact network.

Conclusions. Cryptosporidiosis in rural sub-Saharan Africa is characterized by clusters among human contacts, to which zoonotic transmission, despite close human-livestock contacts, seems to contribute only marginally. Shared sanitation facilities or water sources may be responsible for anthroponotic neighbourhood transmission. Public health programmes need to focus on improving hygiene and sanitation practices, particularly in the context of infant and childcare.

S3-2

Cross-reactive Antibody Responses Induced by Zika Virus in the Absence of Detectable Neutralizing Activity Enhances Dengue Virus Infection in Rhesus Macaques

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Dengue (DENV) and Zika virus (ZIKV) are Flaviviruses that induce highly cross-reactive antibody responses. Earlier studies have extensively reported that antibody responses induced by one serotype of DENV leads to antibody dependent enhancement (ADE) of Dengue infection with a heterologous serotype. We hypothesized that DENV cross-reactive antibodies induced by ZIKV could similarly enhance subsequent infection with DENV. We tested our hypothesis in the rhesus macaque model by infecting either ZIKV naïve or ZIKV immune animals with DENV-2 and examined the kinetics of plasma viremia, binding and neutralizing antibody responses, cumulative blood counts, body weight and temperature, and cytokine levels. Our results demonstrated that ZIKV immune animals experienced a significant increase in acute plasma DENV-2 viremia as compared to ZIKV naïve animals. This enhancement of acute viremia was accompanied by increased body temperature, loss of body weight, neutropenia, lymphocytosis, hyperglycemia, high reticulocyte counts, and release of pro-inflammatory cytokines, symptoms usually associated with severe dengue. Prior exposure to ZIKV infection induced higher levels of DENV cross-reactive binding antibodies with little or no neutralizing activity. Interestingly, cross-neutralizing antibody titres induced by ZIKV remained at sub-neutralizing levels (<1:10) during the 1st week after DENV-2 infection when DENV-2 viral loads peaked suggesting that DENV failed to boost anamnestic responses induced by ZIKV immediately after DENV challenge. Interestingly, serum from ZIKV immune animals was found to enhance infection of all 4 serotypes *in vitro*. These results suggest that enhancing antibodies in the absence of detectable neutralizing activity induced by previous ZIKV likely contributed to the ADE of DENV in ZIKV immune animals. To test this hypothesis, we co-infected rhesus macaques simultaneously with ZIKV and DENV-2. Our results showed that co-infection induced significantly high levels of neutralizing antibody responses against both ZIKV and DENV that was associated with delayed ADE responses *in vitro* compared to ZIKV naive animals. These findings raise the prospect that simultaneous vaccination against both ZIKV and DENV could overcome the potential complications associated with ZIKV immune responses and enhancement of DENV infection. In conclusion, our studies for the first time reveal a critical interplay between ZIKV and DENV immune responses that have implications for DENV pathogenesis and the development of effective vaccination strategies against ZIKV.

S3-3

First reported case of fetal microcephaly associated with Zika virus infection in a German traveler returning from Thailand

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Background
Zika virus (ZIKV), primarily transmitted by Aedes mosquitoes, belongs to the *Flaviviridae*. Since the ZIKV epidemic outbreak in Brazil in 2015-16, it has been established that ZIKV infections during pregnancy can cause congenital Zika syndrome including microcephaly. Several studies support the WHO's and national recommendations for pregnant women to avoid travelling to ZIKV endemic countries.

Case report
A 27-year-old pregnant woman from Germany spent a two-week vacation in Thailand, from November 22 to December 5, 2017 (week 9+5 to 11+4 of gestation). At the end of her stay, she complained of fevers, headache and a rash for two days. Back in Germany, she presented to an emergency unit with painful photosensitivity, nausea and increasing headache. Vital parameters, temperature and the physical examination were unremarkable at that time. The patient denied a cerebrospinal puncture and a head MRI. No fetal ultrasound or ZIKV-specific diagnostics were performed. Symptoms subsided within five days.
Cranial malformations and microcephaly of the fetus were diagnosed at gestational week 32. After intensive counseling, the patient opted for an elective termination of pregnancy at week 34+2.

Diagnostic findings
An ultrasound at week 32+1 revealed a fetal microcephaly, ventriculomegaly and abnormal gyrification. A fetal MRI at week 33+1 confirmed the cerebral anomalies. The amniotic fluid was negative for CMV-DNA, Parvovirus-B19-DNA and ZIKV-RNA at that time. The karyotype of the fetus was normal (46, XX). The mother´s serum was positive for anti-ZIKV-IgG and negative for IgM.
The autopsy revealed a female fetus with weight 2000 g and length 45 cm with regularly developed inner organs. The head circumference was 25 cm, corresponding to a value below the 3rd percentile. The fetal brain tissue was positive for ZIKV-RNA. An immunohistochemical analysis showed intense staining of multiple cerebral cells, but no cerebellar or pontine staining.

Conclusion
To our knowledge this is the first ZIKV-associated case of microcephaly worldwide in a traveler returning from Thailand. A stay in Thailand during the first trimester of pregnancy in non-immune women should be considered a risk-factor for microcephaly.

S3-4

Rabies, dog-bites & critical care in Queen Elizabeth Central Hospital and south Malawi (2012-18).

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Introduction: 95% of 20-50,000 worldwide deaths from rabies occur in Africa and Asia with 40% children affected. WHO estimates that in 99% of cases dog-bites are responsible. Conservative estimations surpass reported cases 20-40 fold. Queens Hospital in Blantyre and Zomba Hospital are housing the icus for the 13 hospitals in the southern Malawi (catchment area 7 million).
Objective: To deliver data on rabies for the largest Malawian Hospital and to estimate the impact of rabies on the southern region´s critical care.

Methods: Data were retrieved on critical care, from the Malawian Health Information Management System and through interviews with icu-responsible physicians and clinical officers.
Results: Queens treated 1870 patients suffering from dog-bites during six years (2012: 490, 2013: 449, 2014: 351, 2015: 234, 2016: 85, 2017: 261; Mean: 311,7/year) with a drastic decline from 2012 to 2016, which did not continue in 2017.
We admitted 48 patients suffering from rabies (2.6 % of our dog bite patients with a wide variety between 0.85% in 2015 and 7.06% in 2016).
Forty paediatric patients (83.3%) were seen and eight adults (16.7%). The percentage of rabies under our dog-bite patients in adults was constantly between 0% and 2.3 %. Children varied between 0.4% and 4.7%. (2012: 1a/10 p, 2013: 1a/17p, 2014: 3a/5p, 2015: 1a/1p, 2016: 2a/4p, 2017: 0a/3p). No continouus development in the prevalence of rabies in children or adults in connection with dog-bites could be detected.
No patient (0%) was admitted to Queens two critical care units. All patients were admitted to wards without ventilation facilities. Zomba hospital did not admit a patient suffering from rabies between 2015 and February 2018 (no ICU in Zomba before). We are not aware of any surviving patient (loss of follow up for all discharged patients).
As limitations we see the rare occurence of bites from other rabies infested animals, the challenges of a mainly clinical diagnosis (despite experienced specialists), the difficult diagnosis of paralytic rabies and the facts that a few clear cut cases might have been send home immediately without admission procedure and that rabies is for any medical person a quite impressive diagnosis whereas the number of minor dog-bite injuries might be underdocumented due to neglect.
We saw a (counted) prevalence of 0.1/100,000 for the southern region only through patients of our hospital. Following WHO´s estimations mean that for southern Malawi´s prevalence is 2-4/100.000 only through Queens Hospital.

Conclusion: Rabies cases are still very frequent and probably higher than assumed even by non-conservative estimations. Paediatrics is grossly overrepresented and rabies does not use our critical care ressources to a significant degree.

Lit.: Risk factors for enteric perforations in patients with typhoid fever Am J Epidemiol (2004) 160 46-50

S4: Global Health 1

S4-1

Global Health – A Concept Not Yet Fully Embraced By The New European Research And Innovation Framework

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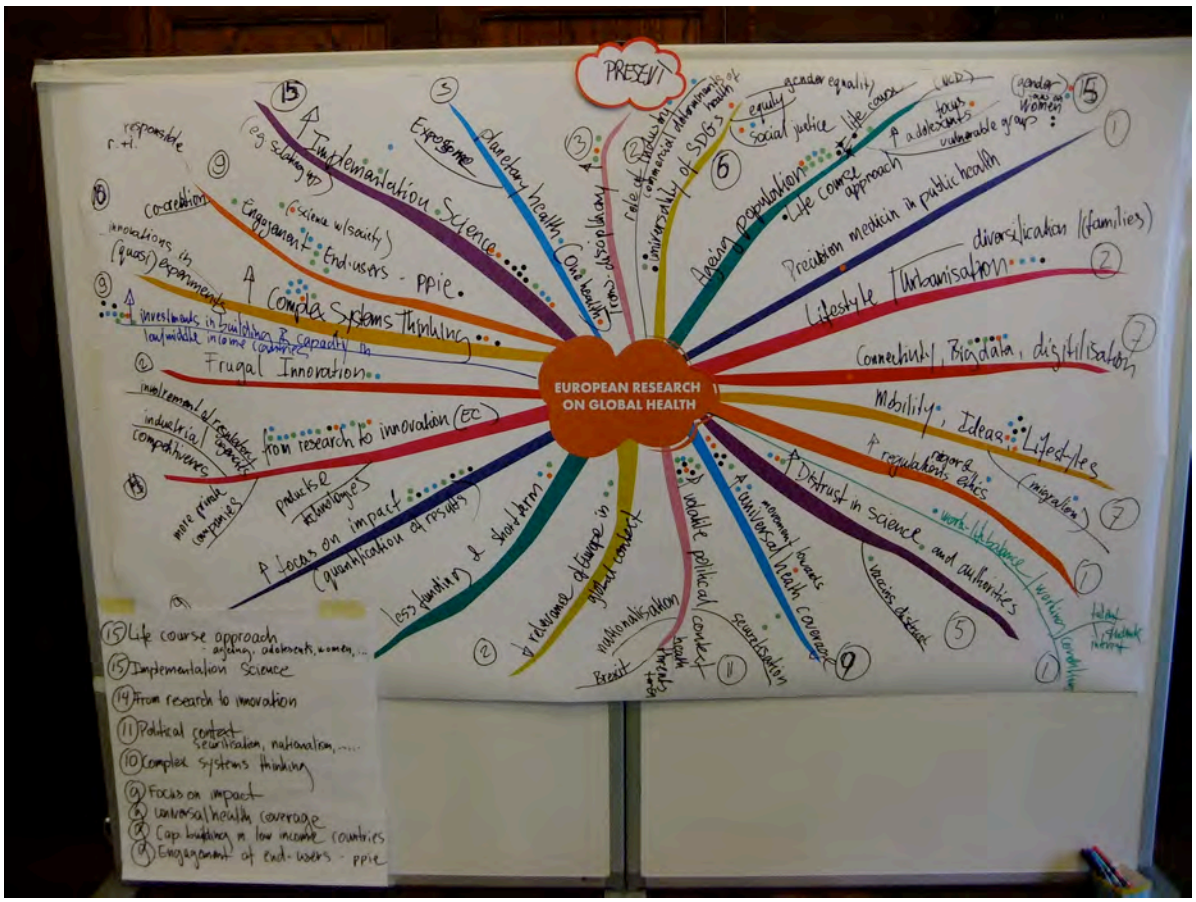
The Horizon Europe (HE) Research and Innovation (R&I) Agenda for the time-frame 2021-2027 constitutes an important framework and funding instrument for R&I for Global Health (GH). This poster addresses the main components of GH(1), offers a critique of HE, and makes recommendations for improving the framework by applying a global outlook on health. The critique is based on a meeting of researchers from 14 European GH institutes in Brussels in July 2018 which used a Future Search Conference methodology(2).
While the importance of this framework for health research and innovation was acknowledged, the analysis of the documents showed that HE has not yet embraced the concept of Global Health(3) and provided an inadequate budget allocation for health R&I. Informed by the 2030 Agenda and a Global Health concept, additional emphasis on the global interconnectedness of health and commitment to Global Health in the entire HE Framework is necessary. The inclusion of Low and Middle Income Countries (LMICs) in all components of this framework is essential to ensure access to all EU R&I initiatives and equitable collaboration with European institutes. This would contribute towards providing sustainable and affordable GH solutions such as frugal innovations(4) from which countries worldwide could benefit.



Trends in Global Health Research

Participatory approaches at the Brussels consensus meeting proved useful for assessing R&I health needs, intensifying the institutes' health advocacy in relation to the EU and developing a global vision. One concrete outcome was the creation of a new network of European GH research institutes, which needs to engage with global partners as well as civil society and government representatives. In order to devise global solutions to global problems, global networking and transdisciplinarity(5) must be strengthened so that key stakeholders have a voice in the R&I agenda. An enhanced EU strategy on GH could help invigorate world-class health research and promote the implementation of needed innovations globally.

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S4-2

A cross-sectional mixed-methods study of sexual and reproductive health needs, knowledge and access to services among refugee adolescent girls in the Nakivale refugee settlement, Uganda

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Background: Humanitarian crises and migration make girls and women more vulnerable to poor sexual and reproductive health (SRH) outcomes. Nevertheless, there is still a dearth of information on SRH outcomes and access to SRH services among refugee girls and young women in Africa. We conducted a mixed-methods study to assess SRH needs, experiences and knowledge of refugee girls in the Nakivale settlement, Uganda.

Methods: A cross-sectional survey among 260 adolescent girls 13-19 years old was conducted between March and May 2018. Concurrently, in-depth interviews were conducted among a subset of 28 adolescents. For both methods, information was collected regarding SRH knowledge, experiences and access to services and commodities. The questionnaire was entered directly on the tablets using the Magpi® app. Descriptive statistical analysis was performed. Qualitative data was transcribed and analysed using thematic content analysis.

Results: A total of 260 participants were interviewed, with a median age of 15.9 years. The majority of girls were born in DR Congo and Burundi. Of the 93% of girls who had experienced menstruation, 43% had ever missed school due to menstruation. Regarding SRH knowledge, a total of 11.7% were not aware of how HIV is prevented, 15.7% did not know any STI and 13.8% were not familiar with any method to prevent pregnancy. A total of 30 girls from 260 were sexually active, of which 11 had experienced forced sexual intercourse. The latter occurred during conflict, in transit or within the camp. A total of 27 of 260 participants had undergone female genital mutilation (FGM). The most preferred sources for SRH information was parents or guardians, although participants expressed that they were afraid or shy to discuss other sexuality topics apart from menstruation with parents. A total of 30% of the female adolescents had ever visited a SRH service centre, mostly to test for HIV and to seek medical aid for menstrual problems.

Conclusions: Adolescent refugee girls lack adequate SRH information, experience poor SRH outcomes including school absence due to menstruation, sexual violence and FGM. Comprehensive SRH services including sexuality education, barrier-free access to SRH services and parental involvement are recommended.

S4-3

Teaching Global Health: Developing a transdisciplinary global health curriculum for Germany, Austria and Switzerland

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Background: In the past decade, the importance of Germany in the lobal ealth landscape as well as the interest in global health challenges within Germany both considerably increased. Various stakeholders stressed the need to expand and improve global health education in Germany and German speaking countries; and several courses, seminaries or summer schools were introduced at medical faculties and beyond. Despite the rise of global health education, to date no broadly accepted or used catalogue of learning objectives exists. The diverging and conflicting concepts of global health are a key barrier. Taking advantage of this window of opportunity, this project seeks to develop a catalogue of global health learning objectives for and in collaboration with stakeholders from Germany, Austria and Switzerland.

Methods: The project consists of three project phases: First, (I) we are going to conduct scoping review on definition and conceptualizations of global health, followed by a concept analysis to identify key commonalities and differences. Based on these, distinct global health concepts defined through a set of specific global health characteristics (e.g. on the role of medicine/public health) will be developed. This will provide a basis for discussion and selecting a global health concept on which the catalogue will be based on. In a second phase, (II) we will identify essential learning objectives and global health content through (II.a) a scoping review of the scientific literature, (II.b) assessing the curricula of curses and seminaries currently offered in medical faculties in the three countries, as well as (III.c) an open-question online survey of global health experts. Those experts will be approached through (a) existing global health networks and organizations, as well as through (b) direct contact of experts in universities, think tanks and NGOs, who would not necessarily define their work as global health, but who can provide valuable contribution to global health issues (e.g. development economics). In a final step, (III) the research team will assess, sort and categorize the content provided in phase II based on the definition developed in phase I. The output of this process will be a catalogue of learning objectives, which we will be revised based on two rounds of critical review provided by willing participants of phase II.c. Key-decisions will be discussed in a project advisory group, consisting of experts from different disciplines and professional backgrounds to reflect the transdisciplinary nature of global health.

Conclusion: One output will be a tool to classify the ways global health can be understood, which can be used to facilitate discussion and to visualize those differences. The main output will be a systematically developed catalogue of learning objectives developed for and together with stakeholders from Germany, Austria and Switzerland. An evaluation is planned as a follow-on project.

S4-4

The destructive power of creation - Growth and innovation as underlying principles leading to human mass dying and potential extinction

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Percentage growth looks harmless if numbers are low however percentage growth is (counter intuitively) not linear, but exponential.
With a rule of thumb one can calculate the doubling time as 70/ growth in % (70 arises from ln 2 *100). A population that grows by 2% per year will double after 70/2=35 years.
Growth, of populations or economies, leads to depletion of resources with potentially violent global and local competition for remaining resources.
The discovery of fossil fuels as energy resource around 250 years ago has allowed for tremendous growth and progress in a very short time span. If the current CO2 emissions continue, the atmospheric CO2 concentrations will reach concentrations that negatively affect cognitive functions within the lifetime of our children and reach lethal concentrations within a few generations. Methane is a 25 times more potent greenhouse gas than CO2 and might apart from human economic activities be released in large amounts from melting permafrost areas of the earth.
With melting of polar ice shields global warming will accelerate as sun energy that previously was reflected through the albedo effect gets saved in the oceans.
With “depletion of resources" we think of resources to keep up our civilisation such as oil and gas. However we also have to consider the depletion of resources essential for the pure survival of human beings, such as water. While human populations grow exponentially, ground water levels shrink nearly everywhere. It won’t be long before the first mega city runs dry.
Where cities rise, natural habitats must go. The currently on-going mass extinction of animal species is caused by Homo sapiens. Despite its current large population, Homo sapiens may also go extinct if the biosphere becomes incompatible with human survival as some post nuclear-war or runaway climate change scenarios suggest.
If we are not facing near term human extinction we will at least face enormous challenges in the coming years with potential mass dying in some regions of the world, most of them probably in poor developing countries of the tropics.

Source: Norbert Georg Schwarz. Das Pandora Prinzip. Die zerstörerische Kraft der Schöpfung. ISBN 9783748158110. BoD ,Books on Demand, Hamburg-Norderstedt. 2019. (Englische Ausgabe für April 2019 geplant).

S7: Tuberculosis and Antimicrobial Resistance

S7-1

Novel point-of-care LAM assay for the detection of tuberculosis in people living with HIV with superior sensitivity

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Background

Most tuberculosis-related deaths in HIV patients could be prevented with earlier diagnosis and treatment. The only commercially available tuberculosis point-of-care (POC) test (Alere LAM assay) has insufficient sensitivity. A next-generation urinary POC assay (Fuji LAM assay), developed for superior diagnostic accuracy, was assessed.

Methods

Independent, blinded assessment of the Fuji assay was performed according to manufacturer's guidelines on urine samples from three independent inpatient cohort studies conducted at two South African district hospitals. Diagnostic accuracy, against both microbiological (MRS) and composite reference standards (CRS), and in comparison with the Alere assay, was analysed.

Results

A total of 968 newly admitted patients living with HIV were included, with a microbiologically-confirmed tuberculosis prevalence of 62% and a mean CD4 count of 149 cells/µl. Against the MRS, the pooled sensitivity of the Fuji assay (75.8% (95%CI 72.3-79.1)) was 31% higher compared to the Alere assay (44.7% (95%CI 40.7-48.7)). Specificities were 96.0% (95% CI 93.0-97.8) and 98.2% (95%CI 95.8-99.2) against a CRS, respectively. In the subgroup of patients with CD4≤100cells/µl, the Fuji assay had a sensitivity of 87.1% (95%CI 83.4-90.1) versus 58% (95%CI 53.0-62.9) with the Alere assay. The yield of sputum-based diagnostics was substantially limited by the proportion of patients able to produce sputum (on day1 of admission only 153 of 420 (36.4%) patients whereas 418 (99.5%) provided urine). This resulted in only 26.6% of patients being diagnosed with TB on day1 using sputum Xpert MTB/RIF (G4) in the one cohort with systematic screening regardless of symptoms. In contrast, Alere diagnosed 43.3% and Fuji yielded 64.5% of diagnoses.

	Microbiological Reference Standard (MRS)[1] N=968		Composite Reference Standard (CRS)[2] N=968	
	Sensitivity [95% CI]	Specificity [95% CI]	Sensitivity [95% CI]	Specificity [95% CI]
Fuji LAM	75.8% [72.3-79.1]	91.0% [87.7-93.5]	69.0% [65.5-72.4]	96.0% [93.0-97.8]
Alere LAM	44.7% [40.7-48.7]	95.1% [92.4-96.9]	40.7% [37.1-44.4]	98.2% [95.8-99.2]
Difference (Fuji LAM - Alere LAM)	31.2% [22.6-39.3] significant	-4.1% [-17.9-9.8] not significant	28.4% [20.7-35.7] significant	-2.2% [-18.4-14.1] not significant

Diagnostic accuracy of the novel Fuji LAM assay compared to the Alere LAM

Conclusions

The Fuji LAM assay offers markedly superior diagnostic sensitivity, while maintaining specificity, in comparison to the Alere LAM assay. Given the superior diagnostic yield on day one of admission, this assay could transform tuberculosis diagnosis for people living with HIV who require hospitalisation.

S7-2

First in human clinical and non-clinical development of the antitubercular benzothiazinone BTZ-043

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BTZ-043 is the first member of nitrobenzothiazinones, which are among the most potent antimicrobials against Mycobacterium tuberculosis (Mtb). BTZ-043 undergoes a highly selective reductive prodrug-activation with a subsequent covalent binding and inhibition of decaprenylphosphoryl-β-D-ribose 2'- epimerase (DprE1), an essential enzyme for the cell wall synthesis in mycobacteria. Remarkably, benzothiazinones are highly active against recent MDR and XDR strains while intrinsic resistance was not found in any current patient isolate of Mtb. The active ingredient BTZ-043 is synthetically available in high quality on a kilogram scale. Development of a preliminary oral formulation finally enabled the GMP production of a study medication suitable for human use. After compilation of a preclinical data package for BTZ-043, approval for a first in human study was obtained and the trial was successfully performed. The objectives of this single ascending dose study comprised the investigation of safety and tolerability of BTZ-043 of supposedly active doses as well as the pharmacokinetic parameters of the study medication, differences in exposure between sexes and assessment of the proarrhythmic risk. BTZ-043 showed a good safety and tolerability profile and very good plasma levels in supposedly therapeutic ranges as extrapolated from preclinical PK/PD studies. Data from a recently completed 6 month toxicology study in rats confirmed the high tolerability of BTZ-043 over the presumed therapeutic time. Off target candidates identified in a previous screening study were further characterized in vitro. We also investigated the metabolism of BTZ-043 in rats, minipigs and humans and found no human specific metabolites. In analogy to preclinical studies in rats and minipigs, a significant proportion of BTZ-043 is readily transformed to an oxygen-sensitive hydride Meisenheimer Complex (M2) in the human circulation, which posed a challenge for bioanalytics. Recently, the successful synthesis of radiolabeled BTZ-043 facilitated the quantitative assessment of the distribution of drug related material as well as mass balance studies in rats. Dosimetry calculations for a future human radiolabeled mass balance and Met-ID study were performed. Development of a tablet formulation for further clinical development is currently ongoing. A phase 1b/2a study including in-vivo drug-drug interaction and food effect sub-studies are scheduled for late 2019.

The drug candidate BTZ-043 is currently being developed within a joint project of the German Centre of Infection Research (DZIF), InfectControl 2020, BMBF and the Free State of Thuringia. The Phase 1b/2a study will be funded by the EDCTP and BMBF.

S7-3

Urinary tract infections in outpatients at a referral hospital in Central Ethiopia: Microbiological surveillance of pathogens and antimicrobial resistance

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Background
Urinary tract infection (UTI) is the most common infection worldwide and the most common indication for antimicrobial treatment, thereby making it to one of the major drivers for development of antimicrobial resistance (AMR), particularly in Enterobacteriaceae. The geographical distribution of causing pathogens and antibiotic resistance patterns differs globally. The objective of this study is to assess the spectrum of pathogens and their AMR patterns at the Asella Teaching and Referral Hospital (ATRH), Ethiopia. It is aimed to provide surveillance data for empirical treatment decisions at the ATRH. The data is part of a larger research network with study centers in six countries in sub-Saharan Africa, together with partners from four other German institutions established within the ESTHER (Ensemble pour une Solidarité Therapeutique en Reseau) program.

Methods
In this ongoing study, outpatients with clinical signs of UTI who attend to the ATHR since July 2018 are included. Demographic data and clinical information are collected using a standardized questionnaire. Midstream urine samples are examined by urine dipstick analysis (Siemens Multistix 10 SG). In patients fulfilling diagnostic criteria for UTI (symptoms of UTI and positive urine dipstick) urine cultures and subsequent disc diffusion test are performed for species identification and antimicrobial susceptibility testing.

Results
Until December 2018 a total of 392 participants were included. Urine culture was positive in 39.8% (n=156) of cases. 89.1% (n=144/162) of all isolated bacteria were Gram-negative. Among those, 58.3% were E. coli, 36.8% Klebsiella spp., 2.1% Acinetobacter spp. and 1.4% Pseudomonas spp. Resistance rates were 41.7% for amoxicillin/clavulanic acid, 50.75% for piperacillin, 55% for 3rd generation cephalosporines, 66.7% for ciprofloxacin and 11.1% for meropenem. The nitrofurantoin resistance rate was rather low (25.7%), probably due to its rare application. Overall, there were 27.1% of Gram-negative isolates fulfilling criteria for 3MRGN (multi resistant Gram-negative) and 3.5% for 4MRGN, respectively.

Discussion and Conclusion
Most common isolates for pathogens causing UTIs were E. coli and Klebsiella spp. AMR rates were high among all antibiotics commonly available and used in Ethiopia. We found a considerably high rate of carbapenem resistance, even though those are rarely used in the country. To date, systematic survey of bacterial isolates and common resistance patterns are lacking. High rates of AMR are jeopardizing treatment success with empiric antibiotic treatment choices available in the hospital and its surroundings. Ongoing surveillance of AMR and strengthening of antimicrobial stewardships programs and a One Health approach are needed to tackle the challenges resulting from antimicrobial resistance.

S7-4

Emergence of phylogenetically diverse and fluoroquinolone resistant Salmonella Enteritidis as a cause of invasive nontyphoidal Salmonella disease in Ghana

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Background. *Salmonella enterica* serovar Enteritidis is both a prominent cause of zoonotic enterocolitis globally, in association with the industrial production of eggs and poultry, and of bloodstream-invasive nontyphoidal Salmonella (iNTS) disease in sub-Saharan Africa (sSA). Distinct, multi-drug resistant genotypes associated with iNTS disease in sSA have recently been described, often requiring treatment with fluoroquinolone antibiotics, which have now become key agents in reducing iNTS-associated morbidity and mortality in sSA. Conversely, in industrialised countries, antimicrobial use in poultry production has led to frequent fluoroquinolone resistance amongst globally prevalent enterocolitis-associated lineages.

Methodology. 27 *S*. Enteritidis isolates from patients with iNTS disease and two poultry isolates, collected between 2007 and 2015 in the Ashanti region of Ghana and notable for a high rate of diminished ciprofloxacin susceptibility (DCS), were whole-genome sequenced. These isolates were placed in the phyletic context of 1,067 sequences from the Public Health England (PHE) *S*. Enteritidis genome database. Single linkage SNP clustering was used to derive maximum likelihood phylogenies, in order to understand whether emerging fluoroquinolone resistance is associated with African or globally-circulating clades of *S*. Enteritidis, as treatment and control measures are likely to be different.

Results. Four major *S*. Enteritidis clades were represented, two global and two African. All 13 DCS isolates, containing a single gyrA mutation at codon 87, belonged to a global PT4-like clade responsible for epidemics of poultry-associated enterocolitis (see Table 1). The majority (11/13) of DCS isolates, including one poultry isolate, belonged to two monophyletic clusters in which gyrA 87 mutations appear to have developed within the region. The remaining two DCS isolates clustered with PHE isolates associated with travel to Spain and Brazil.

Table 1. Phylogenetic clades and antimicrobial resistance determinants of human iNTS disease-associated and poultry *S.* Enteritidis isolates collected in rural Ghana (n = 29)

	'global epidemic clade'	'North American Lineage' [1]	'West African Clade'	'Central/ East African Clade'	Outliers	Total
Total	**15**	**6**	**5**	**1**	**2**	**29**
Human bloodstream isolates	14	5	5	1	2	**27**
DCS[2]	7	0	0	0	0	**7**
MDR[3]	1	0	4	0	0	**5**
DCS and MDR	5	0	0	0	0	**5**
Fully susceptible	1	5	1	1	2	**10**
Poultry meat isolates	1 (local)	1 (imported)	0	0	0	**2**
DCS	0	0	0	0	0	**0**
MDR	0	0	0	0	0	**0**
DCS and MDR	1	0	0	0	0	**1**
Fully susceptible	0	1	0	0	0	**1**

[1] 'North American Lineage' of a second global clade.
[2] Diminished ciprofloxacin susceptibility (DCS). Conferred in all 13 DCS isolates in this study by a single nucleotide polymorphism at codon 87 of *gyrA*.
[3] Multidrug resistance (MDR). Defined in this study as resistant to ≥3 antimicrobial classes.

Conclusions. Extensive phylogenetic diversity is evident amongst iNTS disease-associated *S.* Enteritidis in rural Ghana. Antimicrobial resistance profiles differed by clade, highlighting the challenges of devising empirical antibiotic guidelines in the absence of diagnostic microbiology facilities and resistance monitoring. Fluoroquinolone resistance appears to have predominantly emerged locally, although a lesser role for importation of resistance may also exist. The detection of fluoroquinolone resistance in phyletically-related poultry and human isolates is of major concern and surveillance and control measures within the region's burgeoning poultry industry are needed to protect a human population at high risk of iNTS disease.

S8: Preventive Medicine & Occupational Health

S8-1

Long-term immunogenicity after yellow fever vaccination in immunosuppressed and healthy individuals

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Background The vaccine against yellow fever (YFV) is generally contraindicated in immunosuppressed patients. Nevertheless, an increasing number of immunosuppressed travellers wish to visit yellow fever-endemic regions. In this study we were interested to see if the vaccination's long-term protection against yellow fever (YF) is impaired in patients who had received the YFV prior to the start of their immunosuppressive therapy. We felt this study was especially relevant in the light of the recent statement by the World Health Organisation (WHO) that a single YFV confers lifelong immunity and a revaccination of immunocompetent individuals after 10 years is not necessary.

Methods Our study examined 35 healthy individuals and 40 immunosuppressed patients who had received the YFV prior to the onset of their immunosuppression. We analysed the long-term influence of the immunosuppressive therapy on the protection acquired by the YFV by measuring the neutralising antibodies (NA) with the Plaque Reduction Neutralisation Test (PRNT) with a median interval of 20.6 years after the YFV. We assessed risk factors for a seronegative result (PRNT of 1:< 10) and their influence on the magnitude of the NA.

Results 87% (n=35) of immunosuppressed patients showed a PRNT of 1: >10 and thus NA at a protective level compared to a percentage of 89% (n=31) in the control group. The geometric mean titre of NA did not differ between the groups. The duration of an underlying rheumatic disease was the only risk factor found for a lower magnitude of NA.

Conclusion No evidence was found that the use of an immunosuppressive medication started after the administration of the YFV had an influence on the long-term preservation of neutralising antibodies. But since we only measured NA, the question remains as to whether patients with an altered immune system due to the immunosuppressive therapy would be fully protected against the wild-type YF virus.

S8-2

Implementing cost-effective multimodal interventions to improve hand hygiene compliance in Ayder Hospital, Ethiopia

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Introduction: Healthcare associated infections (HAI) pose an emerging burden on Global Health while developing countries are 2-20 times more affected than developed. In Ethiopia, the prevalence of HAI in tertiary care hospitals reaches 19.41%. Hand hygiene (HH) is known to be the most effective measure to reduce HAI. However, scarcity of safe water, hand sanitizer and dispensers as well as insufficient facilities challenge endeavours to increase HH compliance.

Intervention: In a "Clinic Partnerships" project funded by the German Federal Ministry for Economic Cooperation and Development (BMZ) and the Else Kröner-Fresenius Foundation, improvement of HH practices and compliance at Ayder Hospital, Mekelle, Northern Ethiopia was targeted. A bundle strategy consisting of in-house production of hand sanitizer and dispensers for every patient bed, staff education and motivation, and implementation of a multidisciplinary infection prevention committee was followed in close cooperation with the Hygiene Department of Katholisches Klinikum, Bochum, Germany. Efforts focussed on exchange of knowledge and experience and required high involvement of the Ethiopian partner.

Results: HH-compliance observations were performed before and after 7 months of the ongoing intervention. Starting from a baseline of 4.83%, HH-rate was increased by 8-times to 38.6%. HH before touching and after touching a patient were considerably improved (2.2% to 24.65% and 4% to 50.55% respectively). Hand rub is accepted as the main disinfection method. Infection prevention has become a hospital-wide emphasized topic.

Conclusions: HH campaigns in developing settings profit from multimodal strategies and exchange of knowledge. Utilization of local resources should be further emphasized.

S8-3

The EFFO Project: Supporting Rwanda's Ebola Preparedness by a Train-the-Trainer Approach

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Introduction:
EFFO stands for *Efficiency by Edification* and is a transcultural Train-the-Trainer (TTT) programme managed by the Robert Koch Institute. The project was initiated in 2014 during the outbreak of Ebola Virus Disease (EVD) in West Africa and jointly developed by experts from Germany, Burkina Faso and Senegal. The main target group of EFFO trainings are frontline health care workers (HCWs), preparing them for a possible outbreak of High Consequence Infectious Diseases. As an associated partner of the ESTHER Hospital Partnership between the University Teaching Hospital of Butare (CHUB) and the Institute of Tropical Medicine and International Health, Charité, EFFO began training activities in Rwanda in 2018. They were gradually intensified due to the two EVD outbreaks in neighbouring Democratic Republic of Congo (DRC).

Methods:
In cooperation with the Rwanda Biomedical Centre (RBC), EFFO conducted two TTT events. Each comprised two parts: A 5-day trainer workshop on EVD transmission prevention, mitigation measures and teaching methods, followed by a 3-day EFFO training for frontline HCWs, organised and conducted by the new trainers under supervision of the EFFO team. The interactive and participatory trainings include various methods, such as sociometry, practical and transfer exercises along with presentations. A simulation exercise, the third part of the TTT, was conducted at CHUB.

Results:
Since June 2018, EFFO has trained 19 Rwandan trainers, who have trained 30 HCWs from facilities near the border to DRC. Motivation among trainers and participants alike has been exceptionally high. Great satisfaction among participants and an increase in knowledge measured by pre- and post-tests (from 73% to 87%) show that trainings have been successful in terms of knowledge and skills transfer. RBC and EFFO are currently planning the roll-out of trainings for HCWs by the pool of EFFO trainers, and a second simulation.

Conclusion:
As the course of the EVD epidemic in DRC remains unpredictable, EFFO continues to support Rwanda's preparedness activities in work force development. In light of the positive results from the trainings to date, partners are in the process of formalising the collaboration beyond the current outbreak. Next steps in the project include the consolidation of a regional trainer network to provide a platform for exchange and mutual support in epidemic prevention and response. The experience from Rwanda confirmed that the EFFO training concept is transferrable to different contexts.

S8-4

IPAMU – a Madagascar-Germany partnership project aiming to investigate Health Care Worker Infections during the 2017 Pneumonic Plague Outbreak

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This poster/presentation gives an overview of the IPAMU project, first impression of the findings and faced challenges.
A pneumonic plague (PP) outbreak occurred in Madagascar from August to November 2017, leading to 2417 cases including 209 deaths. The majority of cases (77%) were clinically identified as PP. 81 Health care workers (HCWs) had symptoms compatible with plague, none of them died [WHO 2017]. So far only historical/ anecdotal reports describe possible transmission and burden of PP within the group of HCW. [Kool 2005]. HCW PP infections can have a great impact as HCW can pass on PP further in nosocomial settings, and regular medical care is affected due to absent HCW and patients fear of contracting PP within a hospital setting. In order to better understand HCW infections with PP, the IPAMU project was founded by Malagasy and German partners, funded by the Global Health Protection Program of the German Federal Ministry of Health. The overall objective is to obtain the serological status, characteristics and knowledge, attitude and practices (KAP) of cases (HCW who had symptoms compatible with PP during the epidemic according to the Malagasy surveillance authority, DVSSE), compared with KAP of HCW who are non-cases.
This study was structured in three parts: serology, KAP survey and in-depth qualitative interviews. In June 2018, serology of cases was obtained by Malagasy partners. A four-week field trip with data collection took place in September 2018. Quantitative data collection was guided by structured interviews using a KAP questionnaire. The KAP survey was conducted in two major cities; Antananarivo (four hospitals) and Toamasina (two hospitals and a mobile clinic). All available cases who underwent serology were included. HCW who were non-cases from the same departments were randomly selected and added to the KAP survey as a comparative group. Non-structured qualitative interviews were performed with cases and key informants (e.g. head of department). Using information from the KAP, we compared risk behavior, e.g. usage of personal protective equipment of cases and non-cases.
Out of 81 HCW who had symptoms compatible with plague according to WHO, 36 cases were located in the two cities and recruited for serology. One participant (3%) was anti-Yersinia pestis – IgG positive. Sixteen symptomatic HCWs could be included in the KAP survey, as well as 53 non-symptomatic HCWs. Data analysis is ongoing. Upcoming results will be presented.
Challenges included the complexity of case definitions of pneumonic plague and its application in an outbreak setting as well as difficulties in identifying a sufficient number of HCW cases. Transmission and infection patterns of PP among HCW remain a complex and understudied concern.

[Kool 2005] Kool JL. Risk of person-to-person transmission of pneumonic plague. Clin Infect Dis. 2005.
[WHO 2017] http://www.afro.who.int/health-topics/plague/plague-outbreak-situation-reports, accessed 11 Jan 2019.

S9: Blood-borne Infections: HIV & Hepatits

S9-1

Tonsil Vaccination with MVA encoding SIV genes is Associated with Better Anamnestic Control of Acute Viremia after Low Dose Rectal Challenge with SIVmac251

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Mucosal tissues are the major entry sites for Human immunodeficiency virus (HIV). Induction of strong immune responses in these tissues is critical to prevent entry and viral replication in these tissues. Given the highly compartmentalized nature of the mucosal immune system, we hypothesized that vaccines that target the organized mucosal lymphoid tissues such as the tonsils in the oral cavity or Peyers pathches in the small intestine will lead to better protection from acquisition and viral dissemination. We tested out hypothesis using the rhesus macaque model combined with a low dose rectal challenge. A total of 28 rhesus macaques of Indian origin that were negative for Mamu-A*01 and B17 were used in the study. Animals were vaccinated with plasmid DNA encoding SIV-env, gag and pol by intramuscular electroporation followed by MVA encoding the same genes given either via the tonsils (n = 7), enteric capsules (n = 7), or intramuscularly (n = 7) and compared to unvaccinated controls (n = 6). All animals were challenged intrarectally with a repeated low dose of SIVmac251. Our results showed that 43% of animals that received tonsil MVA resisted infection by the 10th challenge as compared to 14% for IM and 0% for enteric vaccinated animals. Tonsil MVA was accompanied by a significant anamnestic control of acute viremia by 2-logs at 4 week PI. Though there was no significant induction of neutralizing antibody responses against SIVmac251 challenge stock, we observed significant level of neutralizing activity against teir1 isolates in tonsil vaccinated animals as compared to other groups that was accompanied by higher mean ADCC responses. Anamnestic increase in V1V2 responses at 2 weeks post-challenge was significantly higher in animals that received the tonsil MVA vaccine as compared to IM vaccinated animals suggesting that tonsil vaccination was associated with induction better memory B cell recall responses compared to other vaccination approaches. Taken together, our results suggest that combining oral lymphoid tissue vaccination with IM vaccination using MVA based vaccine vectors will aid in better control of HIV infection.

S9-2

Novel concepts for early infant HIV test & treat and infant HIV prevention strategies

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Elimination of infant HIV is targeted by the 2030 United Nations Sustainable Development Goals, however, in 2017 an estimated 180,000 infants still were newly HIV-infected. Prevention of mother-to-child transmission (PMTCT) includes life-long antiretroviral treatment (ART) for all pregnant or breastfeeding women, and ART coverage in this population is meanwhile reported around 90% in most high HIV endemic African countries. Early infant diagnosis (EID) around 6 weeks post-partum has improved infant enrolment in care and contributed to improved outcomes for many children with HIV. All HIV exposed uninfected infants (HEU) should receive at least 4 weeks of nevirapine infant prophylactic treatment (IPT) after birth, infants born from mothers with a high MTCT risk (high viral load, late or no ART initiation) should receive 12 weeks of a dual enhanced prophylactic (eIPT) regimen.
Infant HIV mortality peaks at 3 months of life, and early infant ART initiation is expected to reduce infant mortality/morbidity and the establishment of HIV reservoirs, leading to potential advantages for sustained HIV remission or treatment durability. EID birth testing, and especially the availability of novel point-of care (PoC) nucleic acid tests providing results within 2 hours as a bed-side intervention, enables antiretroviral test & treat procedures, likely impacting infant health outcomes. In addition, PoC VL testing in mothers around delivery enables the immediate identification of MTCT high risk criteria, leading to eIPT and potentially lesser MTCT rates.
Furthermore, the development of HIV specific broadly neutralizing antibodies (bnAbs) opens the perspective of preventive passive immunization concepts in HEU, or treatment intensification in addition to ART in HIV-infected infants. BnAbs, like the VRC01 (monthly applications) or VRC01_LS (3-monthly applications) have shown good safety profiles in neonates, the VRC01 is currently tested for prevention in African high risk adult populations (AMP Study).
In Mbeya, Tanzania, we have recently evaluated the accuracy and operation feasibility of EID PoC and VL PoC testing from birth in HIV-infected mothers and their infants. We found an excellent HIV PoC test performance and high acceptability among health care worker and mothers. In the soon starting LIFE Study, performed in Tanzania and Mozambique, we will further evaluate the clinical impact of birth EID-PoC testing and immediate ART initiation in a cluster randomized design. We will further evaluate the impact of PoC VL testing at delivery on MTCT rates. We further received funding to perform a preventive bnAb study (Neo bnAb) conducted in Tanzania and Mozambique to evaluate the impact on HIV infants transmission during the peripartum and breastfeeding period. We expect that these key studies will further consolidate MTCT guideline and introduce HIV specific passive immunization strategies that could significantly alter the infant HIV epidemic.

S9-3

Approximation of the genotype distribution within global chronic hepatitis B virus infections

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Hepatitis B Virus (HBV) is genetically diverse and divided into nine genotypes, A to I, that differ in their primary transmission route, chronicity rate, development of liver cirrhosis and hepatocellular carcinoma and treatment response to Interferon-α. So far, it is not known how many of the 250 million chronic HBV infections are caused by which genotype. This knowledge, however, could assist to specify the HBV disease burden, plan health policies, optimize diagnostic tests, and develop new broadly active antiviral therapies. We performed a comprehensive literature research on studies reporting HBV genotyping data throughout the world. Over 900 publications were assessed and genotyping data extracted from 213 sources covering 125 countries. Using previously published HBsAg country-estimates and UN population data, we estimated the number of infections with each HBV genotype per country and world-region and the genotype distribution within global chronic HBV infections.
Distinct differences in the genotype distribution between world regions were confirmed in our study which often correlated with geographical boundaries or the dissemination of ethnical groups. The drastic differences in the number of HBV infections between world-regions strongly influenced the world-wide genotype distribution. We estimated that approximately 96% of global HBV infections are caused by only five (A-E) of the nine genotypes: Genotype C was found to cause most infections (26%), followed by genotype D (22%), E (18%), A (17%) and B (14%). The four remaining genotypes F-I were estimated to cause together less than 2% of global HBV infections. While alluding to major biases inherent in such studies, our work provides an up to date review of world-wide genotyping results and an initial approach to estimate the genotype distribution within global HBV infections. It furthermore reveals world areas with poor genotyping data which should be addressed in future studies. Besides clinical implications of the HBV genotype distribution, our study highlights the need to expand HBV cell culture and animal models to at least include genotypes A-E to represent the fast majority of global HBV infections.

S9-4

Supporting HIV care for inpatients in a government referral hospital in Malawi: One year results from a systematic care program for advanced HIV Disease

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Background: HIV positive patients admitted to hospital often have advanced HIV disease and carry a high risk of mortality. Common causes of death are undiagnosed or late diagnosed tuberculosis (TB), other pulmonary infections and infections of the central nervous system. The World Health Organization (WHO) published guidelines for care of advanced HIV disease in 20171, but implementation of these guidelines requires availability of significant resources. However, hospitals, caring for the sickest proportion of HIV patients, rarely receive additional funds. HIV programs like the Lighthouse (LH) HIV clinics receive external vertical funding in Malawi.

Objective: To implement an externally funded program of care for inpatients with advanced HIV disease in the medical wards of Kamuzu Central Hospital, a tertiary referral hospital in Malawi.

Methods: The care program comprised a room on the medical ward, identified as inpatient “HIV care room”, a full-time nurse, and a ~25% equivalent of a clinical officer (seconded by LH). Point-of-care CD4 tests were provided for all newly diagnosed HIV patients and for patients on ART upon medical request. Serum cryptococcal antigen (CrAg) tests and urine-lipoarabinomannan (LAM) tests for disseminated TB were performed for all patients found with CD4 counts below 100 cells/mm3. For patients diagnosed with cryptococcal meningitis (CM) amphotericin and fluconazole were provided, which are not regularly available in the public sector. TB drugs were available on-site; treatment could be started on the day of diagnosis. Anti-retroviral drugs were available on site for patients newly requiring ART, who ran out of ART during their hospital stay or who needed switching to 2nd line ART.

Results: In 2017, 274 inpatients initiated ART (54% female); 39% of those were classified as WHO stage III or IV. 306 patients started TB treatment (43% female) through the service; 79% of the TB patients were HIV co-infected. Table 1 shows numbers and test results for CD4, CrAg and LAM tests. 39.4% of all inpatients tested had a CD4 count below 100 cells/mm3, underlining the high proportion of severe immunosuppression. The yield of positive CrAg and LAM tests was 10.8% and 23.1% respectively. 75 patients were treated for CM with amphotericin/fluconazole with an average of 8.7 doses of amphotericin per patient. CM in-hospital mortality was 28%. The total incremental cost of the advanced HIV care program within the medical ward was 27,555 US$/year or 2,296 US$/month.

Test	Total		
		<100	>100
CD4	583	230 (39.4%)	353 (60.6%)
		pos	neg
CrAg*	185	20 (10.8%)	165 (89.2%)
LAM*	298	69 (23.1%)	229 (76.8%)
		>1000	<1000
POC-VL	90	37 (41.1%)	53 (58.9%)

*tested in patients with CD4<100/µl

Table: HIV-disease related tests provided for KCH inpatients

Conclusion: As our model shows implementation of the WHO guidelines for advanced HIV is feasible but comes at a substantial cost for hospitals. Through successful cooperation of the kind described, improved HIV care for patients with advanced disease is possible.

1World Health Organization. Guidelines for managing advanced HIV disease and rapid initiation of antiretroviral therapy, 2017.

S10: Climate Change and Health /Environmental Health

S10-1

Climate change - one of the biggest health threats of our century

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The Paris-Climate-Agreement of December 2015 has boosted hopes to curb the warming of the globe below 2°C and thus avoid the real bad consequences resulting from climate change. However the gap between good-will declarations and their implementation will require to overcome many obstacles. To protect health is one of the important reasons to stop climate change - emphasized once more at the "2nd International Conference on Climate Change and Health" in July 2016 and recently again at COP 24 in Poland in 2018.
The "north" with its industrialization originally was the main culprit causing the problem. The poorest countries, however, will suffer the main burden of disease and death resulting from climate change. The industrialized countries have long started to protect themselves by introducing "adaptation" measures yet low income countries hardly have the means to finance such interventions.
"Climate change is the biggest global health threat of the 21st century" is a claim supported widely by health professionals in Great Britain – while in Germany there is no such attitude. Although the evidence base for the potentially dramatic health consequences of climate change is strong – and growing – this aspect is neither sufficiently addressed in the international climate change negotiations nor in the German discourse on the topic.
An additional reason to curb climate change has been researched only recently: many mitigation interventions have direct and important positive "co-effects" on health. They do not result from a reduction of the classic "greenhouse gases" – which by themselves are not toxic - but from a decrease of "short lived climate pollutants" which are emitted together with the classic gases. At the same time many activities promoted by health professionals for preventive reasons have "co-benefits" for mitigation because they reduce emissions of long as well as short lived climate pollutants.
The health sector and health professionals have a special responsibility to be informed about these relations and to educate the public about it.

S10-2

The association of Buruli ulcer disease endemicity with major climatic, epidemiological and socio-environmental factors: a geospatial analysis from southern Nigeria.

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Introduction:
Nigeria is a Buruli ulcer (BU) endemic country; however the dramatic increase of new cases observed recently, suggests that dimensions of BU endemicity are yet not fully understood. BU is characterized by small yet highly clustered incidence and transmission from contaminated environments to humans. Thus, given the low prioritization and the limited resources available for combating BU, identification of climatic, epidemiological and socio-environmental factors predictive of BU endemicity is crucial.
Thus, we analyzed the association of the 164 BU cases, reported between 2012 and 2015, in 4 Nigerian States with a series of climatic, socio-environmental and epidemiological factors at the level of the respective Local Government Areas (LGAs).

Methodology:
All BU cases reported between 2012 and 2015 were visited and geocoded. Prevalence (Pr) per 100,000 has been calculated for every different LGA reporting BU cases, which served as our outcome variable. Data on relevant climatic, socio-environmental and epidemiological parameters, which served as independent variables, were obtained from services based on remote Earth Observation data, OpenStreetMap, online mapping tools, literature review and geocoding of data in the field. In a first step of our analysis we developed geospatial illustrations of the reported BU cases. Secondly we performed a Spearman rank correlation between the outcome and the independent variables. Finally, a regression analysis was performed using a generalized linear model in order to assess the most accurate predictive model for the BU Pr at the LGA level.

Results:
Proximity of BU cases towards different types of water bodies was evident in the geospatial illustration. The correlation analysis revealed an inverse correlation between BU Pr and median land slope, average annual rainfall as well as to distance to ponds, lakes and all kinds of waterbodies (composite variable comprising ponds, lakes, rice fields and rivers). With respect to the prediction quality, the best performing model included two independent variables, i.e. distance to rivers and to all kinds of waterbodies, yielding a Root Mean Square Deviance of 3.8.

Discusssion:
In accordance with existing evidence, our data are suggestive of an association of BU Pr with proximity to water bodies and level landscapes. Models taking into account distance to water body related variables had the best prediction quality for the presence of BU. As systematic active case finding activities need to be intensified, geospatial analysis could serve as an important prioritization tool in planning cost-efficient BU-interventions at the subnational level. A larger-scale project encompassing regions with wider climatic, sociodemographic and epidemiological diversity and higher number of BU cases is recommended, in order to verify our results and better assess the predictive quality of a series of further factors, such as the degree of water flow and water temperature.

S10-3

Fighting against permethrin resistant and non-resistant strains of bed bugs (Cimex lectularius) with the use of a special fogger and a combination of H2O2 fluid and permethrin – a light at the end of the tunnel

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Bed bugs (Cimex lectularius) are an increasing pest all over the world. One of the major reasons therefore are the traveling habits of the people and transportation of goods, which enabled bed bugs a massive and fast distribution to hotels, hostels and cabins of any standard and without limitation to poverty. Bed bugs feed on humans at night and may cause wheals, redness and pruritus and as consequence of the nightly visits insomnia and anxiety state. Until now there is no confirmed vector role for the bed bugs, but experimentally the can transmit some pathogens e.g. Trypanosoma cruzi.
Countermeasures in the past led to selection for resistant bugs, including resistant against pyrethroids.
We therefore tested the viability of resistant and non-resistant strains of bed bugs (15 individuals per group) after they were exposed to a mixture of permethrin and H2O2, permethrin alone and H2O2 alone by the use of a modified fogger (droplet size ~ 1 μm). On the molecular level we investigated the expression of mRNA of several detoxification enzymes from the groups cytochrome P450 monooxygenases, glutathione-S-transferases and carboxylesterases by the use of RT-qPCR.
The mixture (permethrin and H2O2) performed best during the viability study as well as during the detoxification studies. This might be due to a synergetic effect of the compounds. After exposure to permethrin the oxidative stress increases and additionally O2 radicals are applied.
This are first promising results, but other strains of bed bugs have to be tested to confirm the success of this treatment.

S10-4

Vibrio harveyi wound infection after motorboat propeller amputation injury in Mallorca, Spain

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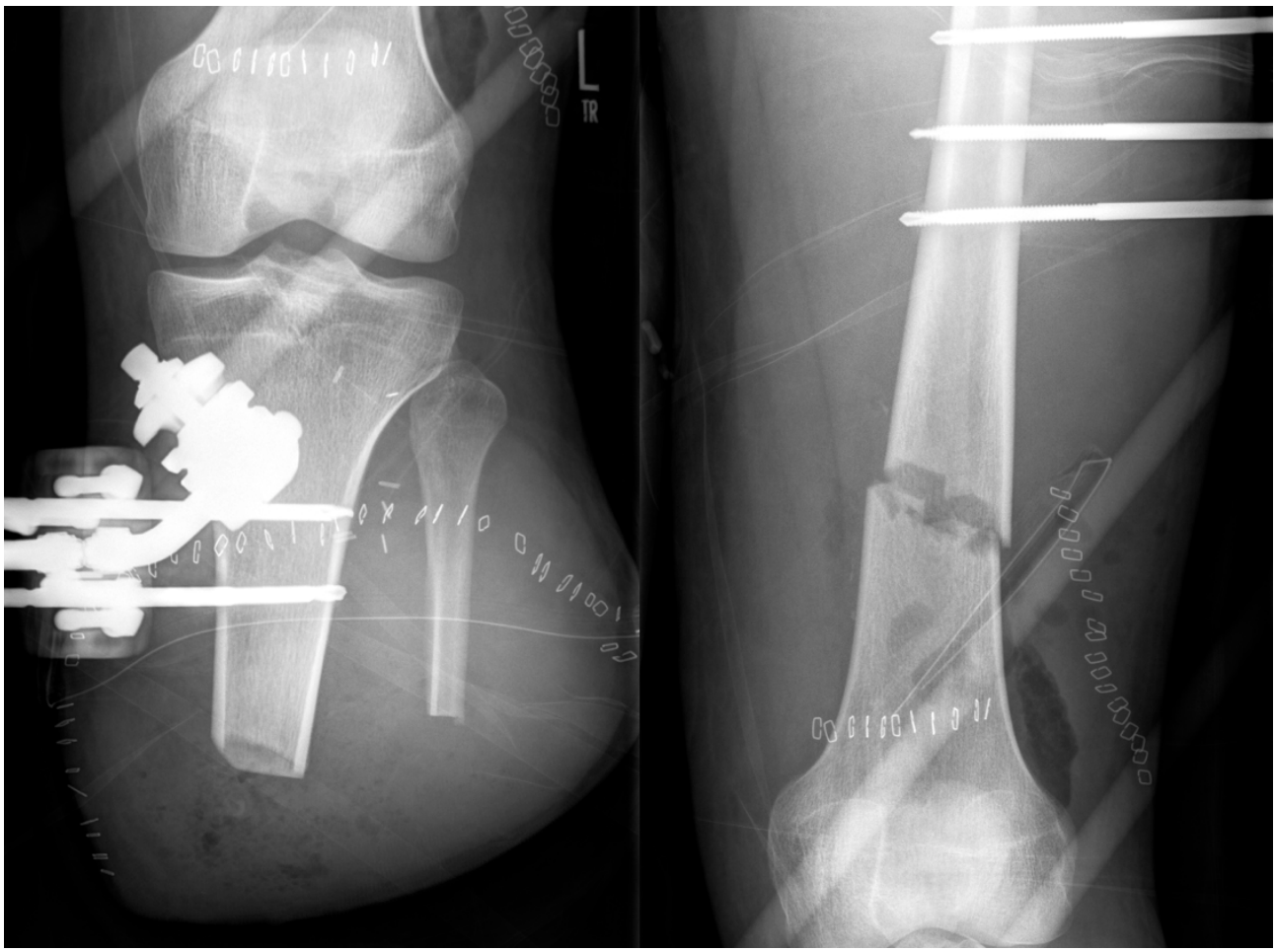
A 26-year old male patient was admitted to our hospital by air transport from Mallorca, Spain. While snorkeling in the sea he had been struck by the propeller of a passing motorboat and had suffered complete amputation injury of his lower leg and contracted distal femur fracture which had been stabilized with joint-spanning external fixation (Figure 1). On admission he was found to have fever of 38.5°C and elevated CRP of 256 mg/dl. Surgical revision showed wound infection with severe skin and muscle necrosis. Tissue cultures subsequently grew Vibrio harveyi and antibiotic treatment with Ceftriaxone and Ciprofloxacine was initiated. The patient repeatedly had to undergo surgical debridement, but could later be discharged from the hospital.



Vibrio spp. are gram-negative halophilic bacteria. Non-Cholera Vibrio spp. infections are most often associated with consumption of raw shellfish or traumatic exposure to sea or brackish water and can cause gastroenteritis, wound infections and septicemia. At least 12 Vibrio spp. are pathogenic for humans with most infections caused by V. vulnificus, V. parahaemolyticus, V. alginolyticus and V.cholerae (non-O1/non-O139). Vibrio spp. thrive in warm climates, so infections are most

commonly reported in tropical and subtropical regions. However, due to global warming, there is growing concern that Vibrio spp. may represent an increasing clinical problem in Europe. Only five human infections with V. harveyi have been reported so far. One girl developed wound infection after a shark bite in the USA (1), another girl with lymphoma developed sepsis after swimming in the sea in France with a central line (2) and three patients acquired wound infections in the Dominican Republic (3) and Australia (4, 5) respectively.
We report the second case of V. harveyi acquired in Europe and the first one acquired in Spain. The long-lasting hot summer period of 2018 may have led to an abundance of Vibrio spp. in the coastal water and thus have favored infection in the patient.

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S11: Malaria and other Vector-borne Diseases

S11-1

Mosquitos are mixing vessels for interspecies viral microbiome

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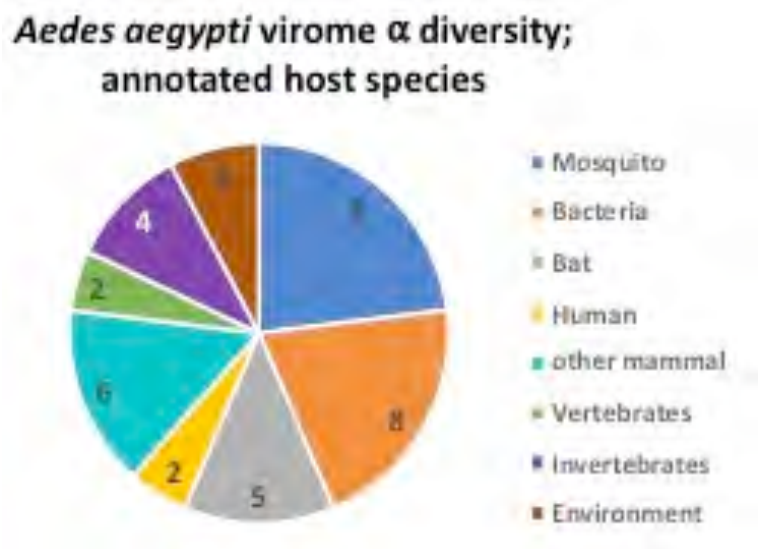
Background: Infectious viral pathogens such as Dengue virus are highly adapted to their arthropod vector. Nevertheless, mosquitos do carry also other mosquito- specific viruses, allowing genetic recombination of diverse viruses that turns mosquitos into potential virologic mixing vessels. Advances in NGS have expanded our knowledge on the richness of viruses harbored by arthropods. Yet, little is known about the actual composition and sources of the mosquito virome as in most of previously conducted studies only 1-5% of metagenomic reads were of viral origin.

Materials/methods: In this study, we tested a pool of Aedes aegypti mosquitos from a tropical region (Barbados) and compared their virome profile to pools of Culex spp. mosquitos from the same and from a distinctively other habitat (Austria) by applying our previously developed virus purification and enrichment protocol (VIPEP), combined to a metagenomic NGS based approach. Bioinformatic sequence analysis was done on nucleotide and protein level with subsequent molecular validation by specific qPCR assays.

Results: Throughout all 4 mosquito pools, an average of 70% of reads matched viral database sequences of 111 virus taxa from 18 phylogenetic families with nucleotide sequence similarities from 64% - 99%. We detected a great diversity of viruses infecting human, animal and plant hosts as well as marginally described viruses previously found in environmental samples only. Viral species of the families of Genomoviridae, Circoviridae and Microviridae were among the most abundant.



Aedes aegypti virome alpha diversity

Conclusions: We traced back the sources of the mosquito virome by individual phylogenetic sequence analysis, identifying four big reservoirs of viral infection and colonization of mosquitos: (i) known mosquito specific viruses (ii) viruses of animals or humans that mosquitoes feed on (iii) viruses isolated from feces of animals, feeding on mosquitoes (iv) environmental viruses colonizing mosquito surfaces. Beside sequences with high similarity to database entries we also report several novel sequences with low identity rates to conserved viral marker genes. This study characterizes the virome of field caught Aedes aegypti and Culex spp. mosquitos at unseen sensitivity, contributing to a better understanding of arbovirus evolution that may act as prediction tool for human disease epidemics at early stage.

S11-2

Detecting histidine-rich protein 2 gene deleted malaria parasites

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Malaria parasites that undergo detection by rapid diagnostic tests (RDT) are a threat to patient care and to malaria elimination and eradication activities (1,2). RDTs that rely on the detection of Plasmodium falciparum histidine-rich protein 2 (HRP2) in an infected person´s blood are in widespread use in malaria endemic regions including Africa (3). In 2010, malaria parasites have been identified in South America that lack the gene for HRP2 (and HRP3) and since then reports are accumulating from all over the globe – although it remains difficult to estimate the true prevalence of these hrp2 deleted parasites in a certain country (4,5). Relevant studies investigate the locus of hrp2 and hrp3 by PCR and report a respective deletion if no amplicon could be detected after PCR amplification. In order to increase the sensitivity for hrp2 detection and to reduce the likelihood of false hrp2 deletion reporting, we have developed the first probe-based, quantitative PCR protocol that allows simultaneous detection of 4 genes. In addition we validated our protocol with clinical samples from Gabon. This novel methodology allows sample throughput at economic costs and provides an important tool for ongoing RDT studies driven by WHO

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S11-3

Capillary blood and malaria diagnostics

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Background:
Traditionally, malaria is diagnosed in samples of peripheral blood. However, it is uncertain whether diagnostic performance characteristics of capillary (CAP) and venous (VEN) blood samples are equally favourable for detection of malaria parasites. Therefore, we assessed a potential difference in the parasite density of paired CAP and VEN blood samples and further investigated the diagnostic performance characteristics of CAP and VEN samples in a prospective observational study.

Methods:
Patient recruitment took place between September 2015 and February 2016 in Gabon. CAP and VEN blood was sampled from finger pricks and venipunctures, respectively. Subsequently, paired CAP and VEN samples were prepared in a standardised way and parasitological analysis was performed with light microscopy and qPCR. Performance characteristics of CAP and VEN samples using microscopy were evaluated against a qPCR gold standard.

Results:
376 patients were recruited. Median (IQR) age was 14 (5 to 39) years and m/f ratio was 0.98. Microscopy revealed a median (IQR) parasites/microlitre of 495 (85 to 3,243) in CAP and 429 (52 to 4,074) in VEN samples manifesting in an on average +16.6% (p=0.04) higher CAP parasitaemia compared with VEN parasitaemia. Concordantly, qPCR demonstrated that on average -0.278 (p=0.006) cycles were required to detect parasite DNA in CAP samples. CAP sensitivity of microscopy relative to the gold standard was 81.5% versus VEN sensitivity of 73.4%, while specificities were 91%. CAP and VEN sensitivities decreased to 63.3% and 45.9%, respectively, for a subpopulation of patients with low parasite densities (below 250 parasites/microlitre), whereas specificities were 92%. The odds to detect gametocytes in CAP blood were 4.2-fold (95% CI: 1.54 to 14.26) higher compared with VEN blood.

Conclusions:
Measurement of malaria parasitaemia yields higher results in capillary blood samples than in venous samples. Further, it was shown that capillary blood sampling improves diagnostic sensitivity of malaria parasite detection by light microscopy and molecular methods. These findings may have important implications for routine diagnostics, patient management, as well as, for research and elimination campaigns of malaria.

S11-4

Causes of Fever in Gabonese Children: A Cross-Sectional Hospital-Based Study

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BACKGROUND:
The epidemiology of febrile pediatric infectious diseases is very dynamic in the tropics. The commonly-known causes and their frequency may change or evolve over time. In this study, we assessed the current spectrum of pathogen causes of febrile diseases leading to pediatric hospitalization in Lambaréné, Gabon.

METHODS:
We recruited children below 16 years of age, ill enough to require hospitalization, with body temperature ≥ 38°C, in a provincial secondary level of care hospital in Gabon. A comprehensive past medical history-taking and a full physical examination were performed prior to blood sampling. Additionally, saliva, urine, stool or pus collections, radiographs or echography was performed, depending on lead signs and symptoms present on admission. Routine diagnostic laboratory tests were performed on site whilst advanced analyses were conducted later in specialist laboratories.

RESULTATS:
A total of 600 patients was included. The overall median of the body temperature was 39°C [38° - 41.5°C].
Pathogens isolated were 314/510 (61.6%) parasites, bacteria 107/510 (20.9%) and viruses 89/510 (17.4%): Malaria was diagnosed in 311/600 (51.8%) patients; Septicemia was found in 17/600 (3%) patients, and typhoid fever in 4/600 (0.7%); a broad spectrum of both bacteria and viruses have been isolated from the throat, urine, stool and blood samples. Overall, 377/600 (63%) patients had multiple diagnoses. Noninfectious diagnoses associated with infections were nutrition disorders, anemia, and gastrointestinal disorder. In 35/600 (6%) patients, no diagnosis was established. At the end of the hospitalization, 596/600 (99.3%) were discharged cured, whilst 2/600 (0.3%) had a fatal outcome.

CONCLUSION:
Besides malaria; in many patients, non-parasitical, non-bacterial infectious agents were identified as causative agents of febrile disease, calling for an adjustment of both diagnosis and treatment protocols in our setting in Lambaréné and possibly beyond.

S12: Non communicable Diseases & Health Systems

S12-1

Global burden of atherosclerotic cardiovascular disease in people living with the hepatitis C virus. A systematic review, meta-analysis and modelling study.

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Background: It is estimated that over 70 million people worldwide are living with hepatitis C virus infection. Emerging evidence now points towards an association between hepatitis C infection and atherosclerotic cardiovascular disease.

Purpose: To determine the association between hepatitis C and cardiovascular disease, and estimate the national, regional and global burden of cardiovascular disease attributable to hepatitis C.

Data Sources: Medline, Embase, Global Health and Web of Science from inception to 9th May 2018.

Study Selection: Longitudinal studies that evaluated the risk ratio of cardiovascular disease in people with hepatitis C compared to those without. We did not impose any language restriction.

Data Extraction: Two investigators independently extracted data and assessed risk of bias for each eligible study. Any disagreements were adjudicated by a third reviewer.

Data Synthesis: The random-effects meta-analysis across 36 studies, including 341,739 people living with HCV, demonstrated that the pooled risk ratio of cardiovascular disease in people living with hepatitis C was 1.28 (95% confidence interval 1.18–1.39, Figure 1). Globally, 1.5 million DALYs per annum were lost due to hepatitis C associated cardiovascular disease. Low- and middle-income nations bore the most burden with the South Asian, Eastern European, North African and Middle Eastern regions accounting for two thirds of all hepatitis C associated cardiovascular DALYs (Figure 2).

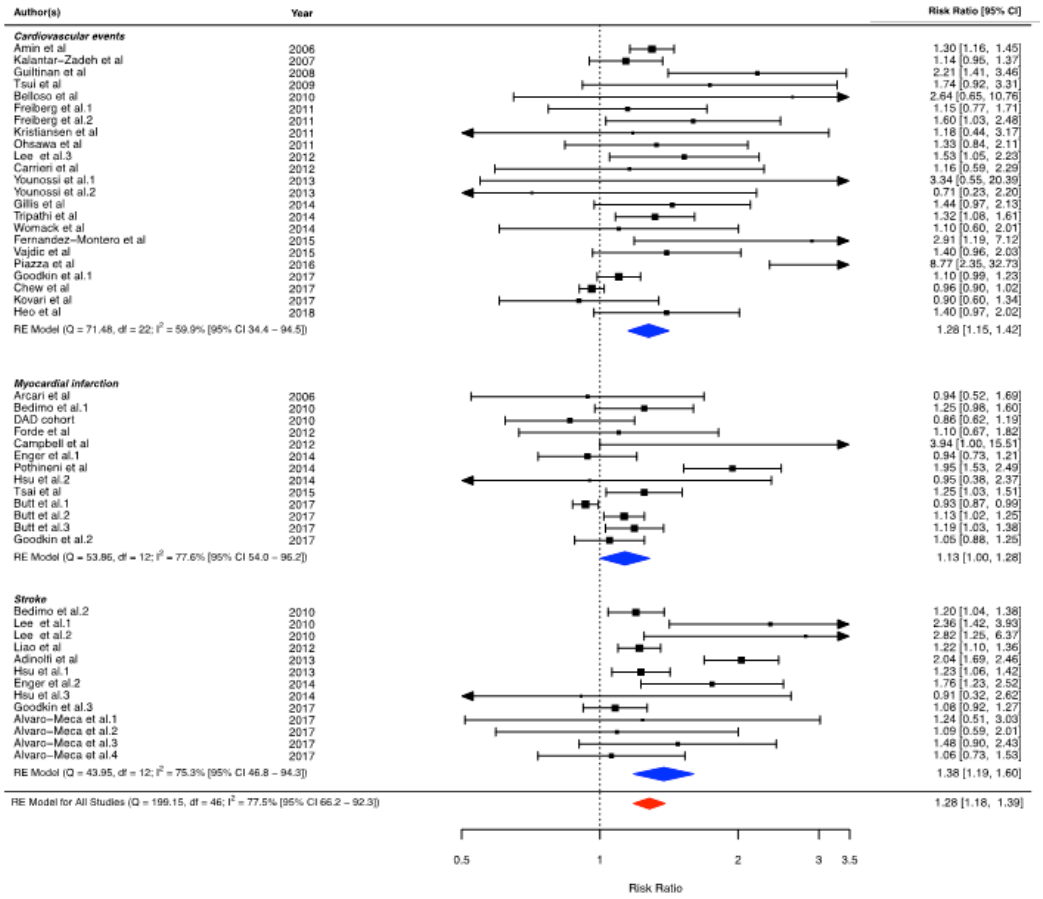

Figure 1. Pooled risk ratio for cardiovascular disease in people living with hepatitis C virus infection versus those without.

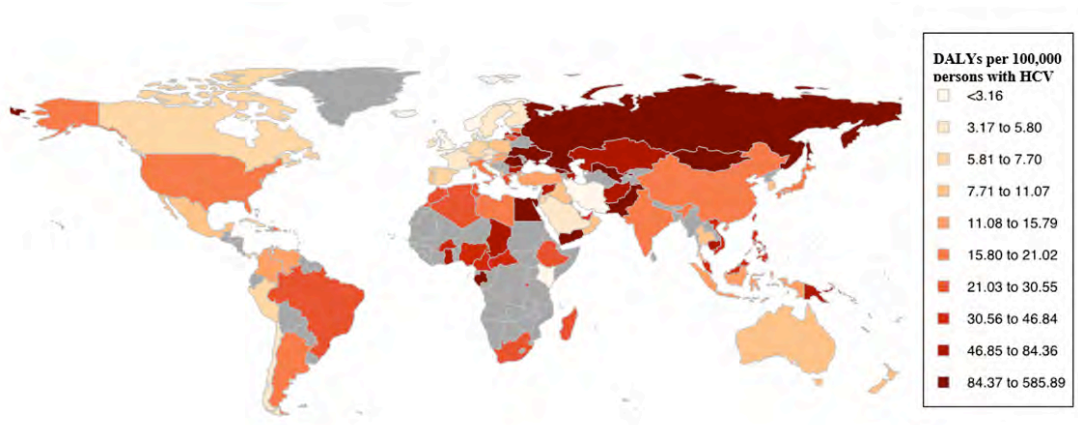

Figure 2. Cartogram showing disability-adjusted life years per 100,000 persons for cardiovascular disease attributable to hepatitis C virus infection.

Limitations: Most studies originated from high-income countries even though the burden of disease is highest in low- and middle-income countries.

Conclusions: Hepatitis C virus infection is associated with an increased risk of cardiovascular disease. The global burden of cardiovascular disease associated with hepatitis C infection was responsible for over one and a half million disability-adjusted life years with the highest burden in low- and middle-income countries.

PROSPERO registration: CRD42018091857

S12-2

Cervical cancer in HIV-infected and non-infected women from Mbeya, Tanzania

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Background: Cervical cancer (CC) is one of the leading malignancy in women from sub-Saharan Africa. In Tanzania CC screening is scaled out, however, women diagnosed with CC often present late and have limited access to cancer treatment or palliative care. Currently, only 2 hospitals provide CC radio-chemotherapy in the country (Ocean Road Cancer Institute, Dar es Salaam; Bugando Medical Center, Mwanza).
Methods: In the ongoing 2H Study, conducted in Mbeya, women received CC screening, including visual inspection with acetic acid (VIA), cyto-histopathology and HPV subtyping. Since 2013 we screened 2008 women (45% HIV+). Women diagnosed with CC were referred to the META gynaecology hospital in Mbeya for disease staging (FIGO) and management planning.
Outcomes: So far we identified 234 cancer cases (6.4% adenocarcinoma), N=99 in HIV+ and N=135 in HIV- women, however, distributions are not representative due to sampling bias. HIV+ women were significantly younger than HIV- women at the time of cancer diagnosis (median age 45 (range 21 to 76) vs 56 (range 31 to 87), p<0.001). The median CD4 count in HIV+ women with cancer diagnosis was significantly lower than in HIV+ women with no or low grade lesions (352 vs 452 cells/μL), no associations was found in respect to the ART status or VL suppression. HPV analysis was performed in 192 cases, and HPV16 or 18 detected in 76% of HIV+ versus 64% of HIV- women (p=0.076), followed by HPV45 (15%), HPV35 (9%) and HPV52 (9%). FIGO staging, treatment and outcome information are available for 124 cases and shown in table 1.

Cancer stage	N	1 year survival	3 years survival	Surgery/ hysterectomy	Radio/chemo therapy	Palliative or not known
Early Stage (FIGO I)	13	92%	63%	7 (54%)	1 (8%)	5 (38%)
Advanced Stage (FIGO II or IIIA)	54	75%	30%	1 (2%)	23 (43%)	30 (55%)
End Stage (FIGO IIIB or IVA)	57	35%	1%		17 (30%)	40 (70%)

Survival rates and interventions performed in women diagnosed with cervical cancer stratified by cancer stages

The majority of women presented with advanced or end stage disease, and although substantial numbers received treatment, survival rates were low and most women did not receive and or attended interventions.
Conclusion: HIV+ women seem to more rapidly progress to CC and most cancer cases are associated with a potential vaccine preventable HPV 16 and 18 infection. Scale-up of cancer treatment in Tanzania is notable, however, palliative management is often not provided and women are lost for health management due to infrastructural and financial challenges, but also distrust in their public health system.

S12-3

Breast cancer diagnosis, treatment and survival in Mali

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Background
Breast cancer is the most prevalent cancer in sub-Saharan Africa, with a high mortality rate and a steady increase in incidence. Since the majority of breast cancer cases are diagnosed at a late stage when treatment is less effective, early detection approaches have gained prominence in the international debate on how to improve survival from the disease in sub-Saharan Africa. This pilot study in Mali, Western Africa, is to our knowledge the first that analysesd the entire patient pathway from first symptom recognition to beginning of treatment, following-up patients at least 18 months after diagnosis. Our study considered patient, disease specific and healthcare system related factors and analysed their association with time to first healthcare visit, diagnosis and treatment and their impact on overall survival.

Method
A prospective hospital cohort study was conducted at the only pathology department in Mali, at the University Hospital in Bamako. All the female patients with a breast cancer diagnosis between January and April 2016 were interviewed with a structured questionnaire (N = 64) to gather information about breast symptom recognition and first healthcare visit. Information on beginning of treatment and survival were collected at 18-months follow-up. Simple Cox regression analyses were performed.

Results
The median time to first healthcare visit was 4.8 months, from first healthcare visit to diagnosis was 0.9 months and for the patients who started treatment (N = 46) the time from diagnosis to treatment was 1.3 months.

Time Interval	Study	Country	Time in month		
			mean	median	
First Symptom recognition to First health care visit					**%<3 months**
	Benbakhta 2015 [15]	Morocco	3,2		
	Elzawawy 2008 [22]	Egypt	1		77
	Ermiah 2012 [23]	Libya		4	45,5
	Ibrahim 2012 [24]	Nigeria	12,2		18.4
	Moodley 2016 [11]	South Africa	5,5		
	Moodley 2018 [16]	South Africa		0,8	40,0
	Mousa 2011 [25]	Egypt	6,2	2,3	57
	Odongo 2015 [26]	Uganda	22,6	13	11
	Olajdje 2014 [27]	Nigeria	17		
	Pace 2015 [28]	Rwuanda		5	
	This study	Mali	13,4	4,8	42,6
					%<1 month
First health care visit to Diagnosis	Benbakhta 2015 [15]	Morocco	1,1		
	Ermiah 2012 [23]	Libya			84,5
	Moodley 2016 [11]	South Africa	3		
	Moodley 2018 [16]	South Africa		0,9	
	Mousa 2011 [25]	Egypt	1,7	0,6	
	Pace 2015 [28]	Rwuanda		5	
	This study	Mali	6,4	0,9	50
					%<1 month
Diagnosis to Treatment	Benbakhta 2015 [15]	Morocco	1,1		
	Dedey 2016 [29]	Ghana	1,1		46,1
	Moodley 2018 [16]	South Africa		1,2	
	This study	Mali	2,5	1,3	40,7

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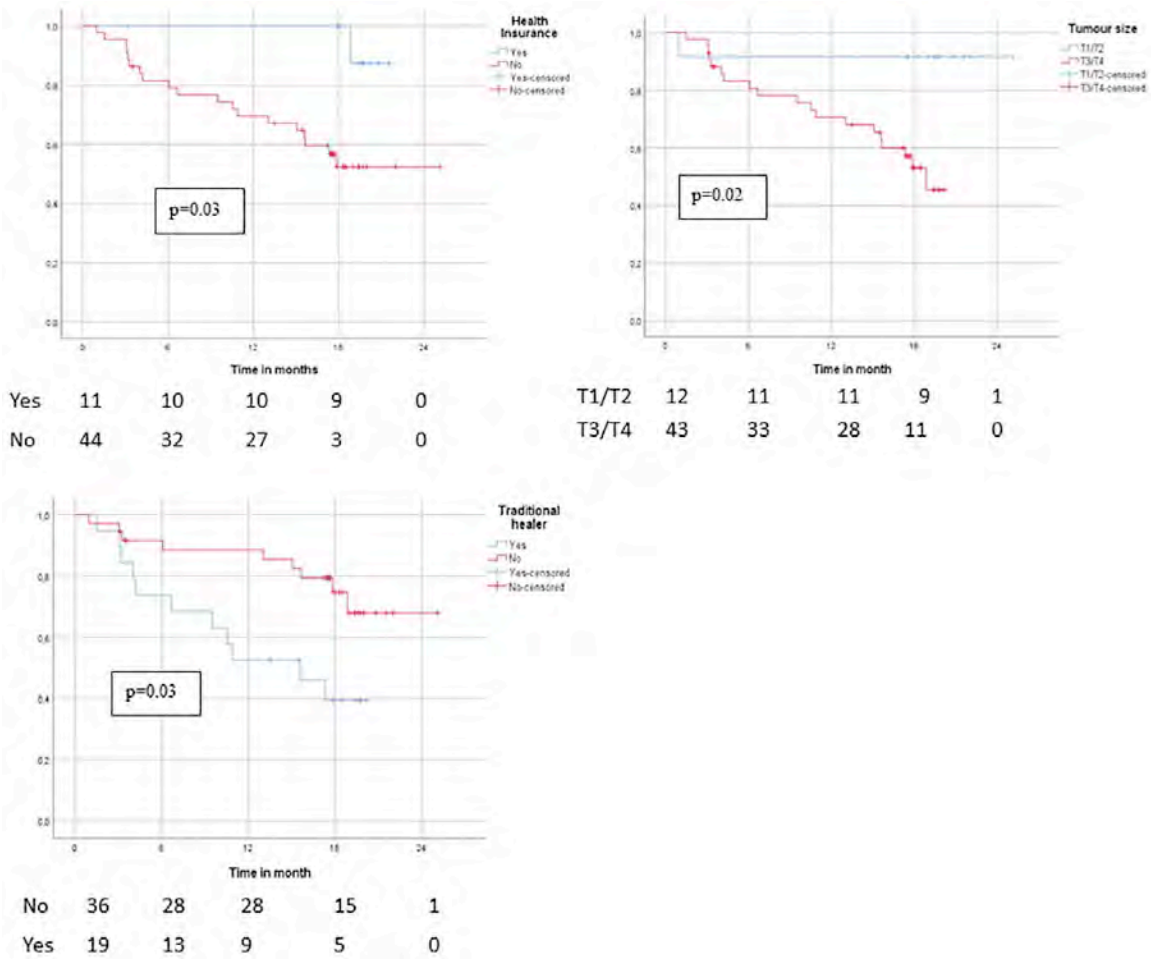
Time intervals

Knowledge of breast-self-examination and correct symptom interpretation increased the chance of an earlier healthcare visit. Prolonged time to diagnosis was found for working women compared to housewives and for those living within Bamako. Living outside Bamako and smaller tumour size (T1/T2) prolonged time to treatment. Visit of a traditional healer, larger tumour size (T3/T4)and having no health insurance shortened survival time.



Survival curves

Time to first healthcare visit and subsequent time to diagnosis had no influence on survival.

Conclusions

The results show that a continuum of breast cancer care is currently not given for the majority of patients in Mali, but has to be considered to fully benefit from any early detection programs and to improve survival of breast cancer patients. Focus should be on financial barriers at the patient level but also on barriers in providing adequate diagnostic and treatment services, including the needed medical work force. International efforts in providing standard diagnostic and treatment options, palliative care at low cost and training for medical doctors should be prioritised to improve breast cancer survival in Mali and other sub-Saharan countries.

Publication

Grosse Frie K et al. (2018) Factors associated with time to first healthcare visit, diagnosis and treatment, and their impact on survival among breast cancer patients in Mali. PLoS ONE 13(11):e0207928.

S12-4

Health Facility Readiness in a remote Karnali Province of Nepal

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Introduction: Health facility readiness refers to the ability and capacity of health facilities to offer a health services, measured through selected tracer items that include trained staff, guidelines, equipment, diagnostic capacity and medicines and commodities.

Objectives and Methods: The objectives of the Health Facility Readiness survey were to measure i) current availability of services and staff, basic equipment, standard precautionary practices, laboratory services, drugs and other commodities, ii) client satisfaction on priority services and iii) service delivery and performance gaps. The survey included hospitals (10), primary health care centers (13), health posts (81) and clients (140) from 10 districts of Karnali Province of Nepal. Data collection was done based on the WHO's Service Availability and Readiness Assessment tool by trained enumerators and analyzed using Stata software.

Findings: Availability of all five modern FP methods was not optimal (36%), but antenatal, delivery, postnatal and childhood treatment services were satisfactory. Around four-fifths of the health facilities lacked readiness in terms of standard precautions for infection prevention and medicine and commodities. Only 60 percent of the sanctioned positions for medical doctors were filled, but only one-third were present on the day of visit. Training on delivery, long acting reversible contraception and treatment of childhood illnesses was quite good (>60%). Though treatment guidelines are important to offer standard and precise instructions on managing care and to maintain quality, the survey results showed a wide variation in the availability of guidelines. Counseling is often neglected during health care provision (e.g. only 37% receiving information on postnatal danger signs). Nearly 1/5th health facilities didn't maintain audio and visual privacy.

Conclusion: The survey showed concerns on quality of services delivered by health facilities and identified areas of improvements. Improving in service availability and quality would result better uptake of health services as well as better health outcomes. Mechanisms to monitor the readiness of health facilities should be institutionalized.

Disclaimer: The Survey was carried out by the United States Agency for International Development (USAID) funded Strengthening Systems for Better Health Project. The contents of this abstract are the sole responsibility of authors and do not necessarily reflect the views of USAID or the United States Government.

S13: Neglected Tropical Diseases

S13-1

A novel cell-free method to culture *Schistosoma mansoni* from cercariae to juvenile worm stages for *in vitro* drug testing

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The anthelminthic treatment against schistosomiasis is limited and relies almost exclusively on a single drug, praziquantel (PZQ). Even though PZQ is potent in killing adult worms it has been shown to have limited activity against earlier developmental stages. Current *in vitro* drug screening strategies depend on newly transformed schistosomula for initial hit identification, thereby limiting sensitivity to new compounds predominantly active on later developmental stages. This study aimed to establish a highly standardized, straightforward and reliable culture method to generate and maintain advanced larval stages in vitro. We present here how this method can be a valuable tool to test drug efficacy at each intermediate larval stage, reducing the reliance on animal use (3Rs). Cercariae were mechanically transformed into skin stage schistosomula and successfully cultured under cell- and serum-free conditions for up to four weeks. Under these conditions, larval development halted at the lung stage. Addition of human serum propelled further development into juvenile worms within eight weeks. Skin and lung stages, as well as juvenile worms (late liver stage), were tested with known anti-schistosomal compounds such as PZQ, oxamniquine, mefloquine and artemether. Our findings showed stage-dependent differences in larval susceptibility to the tested drugs. The phenotype of juvenile worms, when exposed to reference drugs, was comparable to previously published works for ex vivo harvested adult worms. This *in vitro* assay can help reduce reliance on animal experiments in the search for new anti-schistosomal drugs and provide a platform for the investigation of the host protein- or cell-mediated effects on the parasite's development.

S13-2

Impact of helminth infections during pregnancy on humoral vaccine immunogenicity in Gabonese infants

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In times of Expanded Programs on Immunization (EPI) for infants worldwide, the incidence of vaccine-preventable disease decreased notably. However, the protective efficacy of those vaccines is highly variable in different populations. Several reports found that children in low- and middle-income countries are less responsive to vaccines than children from high income countries, which is likely not only to be associated with malnutrition and bacterial co- infections but also with parasitic co-infections.
Helminths actively modulate immune responses of their host towards TH2 and regulatory immune responses which may affect immune responses to vaccines. *In utero* exposure through parasite-derived products crossing the placenta has been hypothesized to impact the development of the neonate's immune system. Therefore, we conducted a study to assess the impact of maternal helminth infection during pregnancy on the humoral vaccine immunogenicity of their offspring in Lambaréné and surroundings, Gabon.
Pregnant women in their last trimester were screened for helminths and assigned to groups based on their helminth status. Infection was diagnosed microscopically by the Kato-Katz, copro-culture, urine filtration and blood saponin staining methods. After birth, the infants received the vaccines given within the EPI at birth, 6, 10 and 14 weeks, as well as measles vaccination at 9 months and were followed-up until 1 year of age. Antibody titers to measles, diphtheria, pertussis, tetanus, poliomyelitis, hepatitis B and *Haemophilus influenza* type B (HiB) vaccines were measured from mother and cord blood at delivery and from children at 9 and 12 months of age using commercial and validated ELISA Kits.
A total of 123 mother-child pairs were available for analysis. 42.3 % of the mothers were infected with helminths; *Schistosoma haematobium* being the most prevalent. We found significant lower IgG levels against HiB antigens in the infected mothers' group and corresponding cord blood and lower levels of IgG against tetanus toxoid in the cord blood of infants born to helminth-infected mothers.
However, there was no difference in IgG in infants from helminth-infected versus non-infected mothers at month 9 and 12 following completion of childhood vaccinations.
Our data show that infection with helminths is still common in pregnant women in Gabon but has only subtle, presumably not clinically significant effects on infants´ immune responses to vaccines given as part of the EPI.

S13-3

A Burden of Disease assessment of Loa loa infection in Gabon: preliminary data

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Loiasis is a parasitic infection highly endemic in west and central Africa. Previously often considered as a benign infection, the true impact of loiasis on affected communities is unknown. Burden of disease studies including calculation of disability adjusted life years are a well proven tool to assess objectively the impact of a disease on an affected population. However, in-depth studies on disease impact in endemic populations have never been performed for L. loa. This cross-sectional study was performed in rural Gabon to establish the burden of disease caused by loiasis. Inclusion criteria were local residency for at least two years and an age above two years. Participants were interrogated a standardized questionnaire covering loiasis specific symptoms, history of eye worm and health care seeking behavior. At the same time L. loa microfilaria diagnostics were performed including thick blood smear preparation and concentration techniques. For data analysis case definition for Loa positivity was set as reported history of eyeworm or detectable microfilariae, while Loa negativity was defined as no history of eyeworm nor detectable microfilariae nor history of Calabar swelling. To avoid an overestimation of Symptom frequency, incidence in the L. loa negative population was subtracted from incidence in the L. loa positive population. Appropriate Disability weights were chosen from the Global Burden of Disease Study 2010. Incidence was extrapolated to the population of Gabon and DALYs for the year 2017 were estimated using the DALY calculator Application in R. 1232 participants were recruited, of which 54% were female and were aged between 2 to 98 years. The odds for L. loa positivity rose by 2.5 in the older age group ($p<0.0001$), whereas sex was not associated with L. loa positivity ($p=0.606$). L. loa microfilariae were detectable in 301 participants. Microfilariae densities ranged from 1 to 76 250 Mf/mL. Using these data, a burden of disease analysis was performed, revealing a relevant amount of disability adjusted life years lost within affected communities in Gabon.

S13-4

Immune activation profile in Wuchereria bancrofti infected individuals in Upper East Region, Ghana

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Background: Susceptibility to HIV has been linked to systemic CD4+ T cell activation in cohorts of seronegative individuals with high HIV-exposure risk. We recently described an increased risk of HIV transmission in individuals infected with *Wuchereria bancrofti*, the causative agent of lymphatic filariasis, and aim to evaluate the underlying reasons for this phenomenon.

Approximately 68 million individuals are infected and more than 850 million people worldwide remain at risk of becoming infected with *W. bancrofti*, a filarial parasite which can infect humans through mosquitos. While there are both adult and microfilariae life cycles of the parasite in humans, it is the adult worm which cause the pathology of lymphangitis, lymphedema and hydrocele. Infections are chronic and persist over many years. The majority of infected individuals remain asymptomatic, however ~ 30% develop filarial pathology. Different clinical outcomes of a filarial infection are associated with distinct immunological phenotypes.

During the previous research, *W. bancrofti* infection was diagnosed by measuring circulating filarial antigen in plasma. During the ongoing study “Risk of HIV Infection through Nematode Organisms” (RHINO) participants will be recruited and characterized by the presence of microfilariae in the night blood, testing for filarial antigen, and a clinical description of the disease status.

First participants were recruited in the Upper East Region of Ghana. This area is remote and therefore not equipped with flow cytometry devices.

Methods: Several technical points first needed addressing:
• Development of a flow cytometry method that uses small blood volumes.
• Development of a method with intermittent storage of the sample.

First Results: We improved upon a whole blood staining flow cytometry protocol using 100 µl of anticoagulated blood and stained with extracellular antibodies (CD3, CD4, CD8, CD25, CD27, CD38, CD45, Beta 7, CCR-5, HLADR) before lysing and freezing the cells in liquid nitrogen. In a second step, thawed cells were stained for intracellular domains (FoxP3, Eomes, Tbet) and visualized using a CytoFlex cytometer.

We plan to compare 50 individuals of each of the following groups:
• *W. bancrofti* infected with microfilariae in the night blood
• *W. bancrofti* infected without microfilariae in the night blood
• Participants with filarial lymphedema (all negative for circulating filarial antigen)
• Control persons without *W. bancrofti* infection living in the same area

Samples from approximately 200 patients have been collected and 50 thus far processed, demonstrating the robustness of the method. We plan to process more samples in the upcoming weeks to describe potential differences regarding the immune profile among the four different groups. These data will then be used to evaluate which of the distinct outcomes of a filarial infection might be associated with an increased risk for HIV acquisition.

FG 4: Junge DTG/Junge Parasitologen

FG4-1

Trichomonas vaginalis lysosomes - a study on a protist stomach

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Trichomonas vaginalis is the most common non-viral sexually transmitted pathogen, although its prevalence has been underestimated and the mechanisms of pathogenesis are still poorly understood. In the female urogenital tract, *T. vaginalis* feeds on bacteria occurring in the vaginal fluid, but also on vaginal epithelial cells and erythrocytes. These cells are taken up by *T. vaginalis* through phagocytosis and destructed in lysosomes. Eukaryotic lysosomes are acidic organelles that serve for degradation of components deriving from secretory, endocytic, phagocytic, and autophagic pathways. Lysosomes therefor comprise a variety of proteins such as proteases, lipases, and nucleases to fulfill this degradative function.

To investigate *T. vaginalis* lysosomes, we initially tested the localization of several putative lysosomal proteins found in the *T. vaginalis* genome that may serve as suitable lysosomal markers. Genes for Rab7, Atg8, and the beta-amylases BA1-4 have been subcloned to TagVag2 vector enabling the expression of the respective protein with a C-terminal hemagglutinin tag. Immunofluorescence microscopy revealed that Rab7, BA3, and BA4 localized to the lysosomal compartment. Surprisingly, we were not able to observe Atg8 in lysosomes.

Next, *T. vaginalis* lysosomes were isolated with three different approaches. The first approach was based on differential and 45% Percoll gradient centrifugation. To get purified lysosomes, the lysosomal fraction was run on the Percoll gradient twice.
The second approach was based on magnetic Dynabeads coated with FITC-labeled lactoferrin that is known to bind to the trichomonad surface. The cells were incubated with the coated Dynabeads for 60 min at 37°C to allow Dynabead phagocytosis, then the cells were lysed and Dynabeads-containing lysosomes were isolated with a magnet and washed.
The third approach was based on *T. vaginalis* cells expressing a recombinant protein consisting of BioID, a mutant biotin ligase that randomly biotinylates proteins that are in close vicinity, and a lysosomal protein that targets the construct to lysosomes. Therefor the cells were incubated with 1 µl/ml biotin overnight at 37°C. The cells were then lysed. The lysosomal proteins were isolated by streptavidin-covered magnetic beads and a magnet and then washed.
In each approach the isolated proteins were examined by mass spectrometry.
The analyses revealed putative lysosomal proteins such as hexosaminidase, peptidases, nucleases, and phosphatases. Exemplary proteins were chosen for verification of their lysosomal localization with the help of immunofluorescence microscopy.

The knowledge gained from the study is important to uncover pathways for nutrient acquisition and for degradation of host cells and bacteria. The study might reveal attractive targets for the development of new therapies against *T. vaginalis*.

FG4-2

No evidence for Histidine-rich protein 2 deficient P. falciparum in Arsi and East Shewa zone, central Ethiopia

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Introduction:
Rapid diagnostic tests (RDTs) offer great potential to improve the diagnosis of malaria, particularly in remote areas. Most RDTs for *Plasmodium falciparum* infection are based on the detection of *P. falciparum* histidine-rich protein 2 (HRP2) but recently, reports have questioned their sensitivity and reliability. *Plasmodium* species lacking a functional gene coding for HRP2 are increasingly being reported from sub-Saharan Africa, resulting in false-negative results of RDTs. To our knowledge no data on the presence of pfhrp2 gene deficient *P. falciparum* is available from Ethiopia, but from neighboring countries. The aim of this study is to investigate the prevalence of pfhrp2 gene deficient *P. falciparum* from different regions in Ethiopia.
Methods:
In this ongoing study, patients from a health center in East Shewa Zone in Central Ethiopia with microscopy-based diagnosis of *P. falciparum* malaria are included. Rapid diagnostic testing is conducted for each patient using HRP2-based RDT (ACCESS BIO, INC. Ethiopian Branch). In case of negative RDT result, EDTA blood is collected from the patient and transported to HITM for further analysis. Microscopic re-evaluation of blood smears is performed and in case of confirmed microscopic diagnosis, infection is confirmed by PCR amplification of the *P. falciparum* specific gene pf18sRNA, while presence of the pfhrp2 gene is indicated by the successful amplification across exon 1-2 and exon 2 based on known chromosome breaking points for entire and partial gene deletions, adapted from a study of Gamboa et al. 2010. Additionally, stored blood samples from patients presenting to a health center in Arsi Zone, Central Ethiopia with microscopy-positive *P. falciparum* infection were analyzed retrospectively via PCR in the same manner.
Results:
HRP2-based RDT was performed in 99 malaria patients from June to December 2018 in East Shewa Zone. RDT revealed negative results in two patients. Of those, malaria could not be confirmed in one patient and blood sample for confirmatory testing was not available for the other patient. The remaining samples showed positive RDT results and therefore were not further analyzed. In 47 frozen blood samples from *P. falciparum* patients from Arsi Zone, analysis via PCR was performed without prior RDT Testing. *P. falciparum* infection was confirmed in all samples, while no pfhrp2 gene deficiency was detected.
Conclusions:
The preliminary data of this study revealed no evidence for HRP2 deficient *P. falciparum* strains in two malaria-endemic areas in Central Ethiopia. However, only a few blood samples of patients with *P. falciparum* malaria in merely two health centers in two areas of Ethiopia were analyzed. HRP2 deficiency might threaten the malaria management on individual and public health basis, thus continuous surveillance is important.

FG4-3

Bilharziose in der Schwangerschaft

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Bilharziose ist eine weltweit verbreitete Helminthose. Von den weltweit ca. 200 Millionen betroffenen Menschen sind ca. 40 Millionen Frauen im gebärfähigen Alter [1,2]. In einer malawischen Studie wurde bei 60% der Frauen, die Schistosomeneier im Urin ausschieden, auch eine genitale Bilharziose nachgewiesen [3]. Ferner ist die Schistosomiasis des schwangeren Uterus bekannt. Obwohl eine transplazentare Übertragung von Bilharziose bislang nicht beschrieben wurde, steht die plazentare Bilharziose mit Nachweis von Schistosomeneiern in Plazentagewebe [5] in Zusammenhang mit Frühgeburtlichkeit und reduziertem Geburtsgewicht [2, 4]. Eine kürzlich publizierte Studie, mit 1115 im Gabun ausgewerteten Schwangerschaften, konnte zeigen, dass das Geburtsgewicht von Neugeborenen bilharzioseinfizierter Mütter im Vergleich zu denen nicht infizierter Mütter, deutlich niedriger war (2875 vs. 2956g) [6].
Seit 2002 legt die WHO die Verwendung von Praziquantel in der Schwangerschaft nahe, da bereits zu diesem Zeitpunkt kein Hinweis für eine fetale Toxizität bestand [7]. Unter anderem konnte eine in Uganda durchgeführte plazebokontrollierte, randomisierte Studie (n=2507) nach der Gabe von Praziquantel im 2. und 3. Trimester der Schwangerschaft keine Assoziation zwischen dem Medikament und kongenitalen Anomalien feststellen [8]. Vor dem Hintergrund der zur Verfügung stehenden Literatur kann Praziquantel somit nach Abschluss des ersten Trimesters auch in der Schwangerschaft gegeben werden.

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FG4-4

Sandfly dispersal in Central Europe: is temperature really critical?

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Sandflies are inconspicuous, hematophagous insects, inhabiting tropical, subtropical, arid as well as temperate regions worldwide. Of approximately 800 species described, 70 species are of medical relevance, by transmitting protozoan, bacterial or viral pathogens. Within Europe, sandflies were considered to be endemic only to the Mediterranean regions, until the first findings in Germany in 1999 and 2000. Several recent findings of sandfly species in Austria and bordering countries, including Hungary, Slovenia and Slovakia support the assumption, that the sandfly distribution in Central Europe has not been investigated in sufficient detail yet.
The occurrence of sandflies is known to depend on temperature, however the role of other important ecological factors has still not been fully elucidated. The aim of this study was to obtain data on the ecology and seasonality of sandlfy populations in Austria, which is of crucial importance for the evaluation of new trapping sites and modalities. A long-term study was conducted at seven different locations in Lower Austria and Styria. Sandflies were collected from the end of June to the beginning of September, for four consecutive nights a week. Standardized CDC miniature light traps for insect collection were installed at the trapping sites.
Overall, 272 sandflies were caught, of which 214 were female and 58 were male. The number of caught specimens and overall sandfly activity were observed to be different between the trapping sites. Abiotic factors, such as temperature, humidity, precipitation and wind speed were included in the analyses and climatic conditions associated with sandfly activity were assessed. Blood meal host availability and breeding site quality were evaluated and analyzed.
This study provides the first data on sandfly activity and associated factors in a Central European country and further elucidates environmental requirements of sandflies in temperate regions. The results will contribute to detect new sandfly breeding sites and their current distribution and potential expansion.

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FG4-5

Zoonotic pathogens in ticks from migratory birds, Italy

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Migratory birds can act as biological and mechanical carriers of several parasites, allowing them to spread into new areas. This is the case of ticks of the genus Hyalomma spp., which are widely distributed in the Mediterranean and African regions but accidentally found in some Northern European countries as UK [1]. In particular, migratory birds are carriers of immature stages of the ticks which, soon after the blood meal, drop off from the host. In case of suitable weather conditions in the new spot, those ticks are able to moult to the next stage (e.g. adult) to seek for another host. This happened in Northern Austria at the beginning of October 2018, where an adult Hyalomma marginatum was found attached to a horse. At present, limited information are available on the bird species that migrate seasonally from Africa to Europe and on the ticks and tick-borne pathogens that they carry. Therefore, we chose Ponza, an Italian island in the Tyrrhenian sea known to be a resting place for migratory birds along their route, as the site of investigation. Ticks collected from the birds during the standard ringing procedure in spring 2016 and 2017 were firstly identified using the morphological keys and the amplification of the ITS region [2]. Then, they were analysed for the presence of several pathogens like Crimean-Congo Hemorrhagic Fever virus (CCHFv) and Rickettsia spp. using PCR amplification [3]. Totally, 728 birds were captured and 231 ticks were collected, with 104 birds carrying at least one tick. The majority of the ticks belonged to the genus Hyalomma spp. and 20.1% tested positive for Rickettsia spp., while none of the ticks were positive for CCHFv. Sequencing analysis showed the presence of Rickettsia aeschlimannii, Rickettsia africae and Rickettsia raoultii. The tick collected from the Austrian horse was also positive for Rickettsia aeschlimanni. Our results confirm the role of migratory birds as carriers of exotic tick species into new areas, thus leading to the spread of zoonotic pathogens like Rickettsia aeschlimanni into Europe. Even though all the ticks tested negative for CCHFv, the risk of introduction of this virus in Europe is not negligible, and the current climate changes could lead to the establishment of autochthonous population of Hyalomma marginatum ticks, the well-known vector of CCHFv, in this continent.

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FG4-6

Ein Update über einheimische, invasive und neobiotische Stechmücken in Österreich

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Stechmücken sind uns allen als Lästlinge bekannt, aber auch als Überträger diverser Krankheitserreger (z.B. Flaviviren) von Bedeutung. Trotzdem ist das Wissen über die Artzusammensetzung der Stechmückenpopulation, Ökologie und deren Verbreitung lückenhaft. Bis dato sind in Österreich 49 Stechmückenarten bekannt. Die am häufigsten vorkommenden Vertreter sind Hausgelsen (Culex pipiens-Komplex), die zu den einheimischen österreichischen Arten zählen und bekannte Überträger von z.B. dem West Nil Virus sind. Einige neobiotische (gebietsfremde) Arten wurden in den letzten Jahren in Österreich nachgewiesen: die japanische Buschmücke (Ochlerotatus japonicus japonicus) sowie auch Culiseta longiareolata und Anopheles hyrcanus. Die asiatische Tigermücke (Aedes albopictus), ein bedeutender Vektor von Flaviviren wie Chikungunya und Dengue, wurde in Westösterreich entlang von Autobahnen zwar gefunden, eine Etablierung dieser konnte bisher nicht nachgewiesen werden.
Da der Einfluss des Klimawandels nicht vorhergesagt werden kann, ist es um so wichtiger, die gegenwärtige Verbreitung und mögliche zukünftige Ausbreitung invasiver und einheimischer Mücken zu verstehen.

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FG 5: Tropenchirurgie

FG5-1

Burns in low- and middle-income countries – a public health perspective

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Burn injuries in the acute setting require early and highly specialized management, including adequate resuscitation, inhalation injury management, infection control, wound debridement and wound coverage. They are followed by long and extensive rehabilitation phases. Delayed or inappropriate treatment of burn wounds can lead to physical impairment as well as psychological complications.

As burn risk correlates with socioeconomic status, people living in low- and middle-income countries (LMIC) are at higher risk for burns than those living in high-income countries. Burn injuries are amongst the leading causes for lost disability adjusted life years (DALYs). Due to their severe, often long-lasting consequences and the cost intensive, multidisciplinary treatment measures required, burn management in LMICs represents a global public health challenge.

Based on practical medical experiences in the setting of a specialized burns unit in South Africa, ethical dilemmas that arise in areas of burn management with limited resources, such as allocation of resources, social justice and access to care, are presented.

Next, faults in burn management capacity as well as attempts and possibilities of overcoming these, particularly through education and training of local medical care providers, are presented based on examples of a humanitarian aid mission for reconstructive surgery in Bolivia.

By the means of these examples, insights into the epidemiology of burns in LMICs shall be given, the current challenges of burn care in LMICs shall be highlighted and potentials to minimize these health inequities shall be discussed.

FG5-2

Case Presentation: Sigmoid colon carcinoma on the basis of Schistosomiasis in an emigrated nurse

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Clinical case:
A 76 year old female patient presented with a history of bloody stools and abdominal discomfort. After colonoscopy and consecutive resection of the sigmoid colon, histology results showed a highly stenosing adenocarcinoma with a middle grade differentiation (3,5x3cm) pTNM: pT4a, G2, L0, pN0, V0, R0, with the finding of multiple foreign bodies (70x50μm) within and outside the tumor, identified as Schistosoma japonicum eggs.
The patient grew up in Mindanao, Philippines and emigrated to Germany in the 1970s. In her childhood and adolescence, she had frequently been exposed to local fresh water (bathing in lakes, working in rice fields). Neither a diagnostic approach nor an anthelminthic treatment had ever been undertaken. Ever since the emigration the patient lived and worked continually in Germany with short visits to her country of birth. She reported Schistosomiasis with colon and liver cancers in her brothers.

Epidemiological aspects:
Schistosomiasis is one of the world's major helminth infections. More than 800 million people live in endemic areas and over 230 million people are believed to be infected, with more than 20 million people to suffer from severe infection. According to leading textbooks three of the five human pathogenic Schistosomiasis types are endemic in Africa: S. haematobium, S. mansoni, S. intercalatum. Additionally, S. mansoni can be found in South America and the Caribbean. Hotspots of S. mekongi and S. japonicum exist in Asia. S. japonicum is restricted to East Asia, specifically along the Yangtze River, in central Sulawesi and several Philippine islands (1), such as Mindanao (2).
The correlation between S. japonicum and colorectal cancer has long been discussed in scientific literature (3). Data of a matched case-control study showed patients suffering from chronic S. japonica infection to be three times more at risk of developing a colon malignancy than those without (4).

Conclusion:
For a long time, migration associated disease patterns have been discussed. With this case we would like to demonstrate that not only trendy pathologies including psychological disorders occur, but that severe complications of neglected helminth infections also need to be anticipated.

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S14: Global Health 2

S14-1

Global Neurology: The Tsunami of Non-Communicable Diseases

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Rationale: „Brain health is the greatest challenge of societies in the 21st century“ says Dr Elena Becker-Barroso, Editor-in-Chief of The Lancet Neurology. The burden of communicable neurological disorders may have decreased, the burden of non-communicable neurological disorders however has continuously been increasing. In fact, neurological disorders are the leading cause of disability adjusted life years (DALYs) and the second leading cause of mortality globally. It is very common for the burden of neurological diseases to be underestimated, as is the case for example with the calculations carried out by the Institute for Health Metrics and Evaluation (IHME). When revisited, data show the burden of neurological diseases to increase fourfold and when psychiatric disorders are added to the dataset that burden undergoes a fivefold increase.

Methods: The IHME uses a risk-factor based approach for categorization of diseases which causes an underestimation of neurological diseases. We analysed the 2017 Global Burden of Disease estimates by IHME and re-classified the disability-adjusted life years (DALYs) of neurological diseases including those that are not classified as such by IHME. We furthermore compared the burden of neurological diseases with the burden of cardiovascular diseases as number one burden of disease category.

Results: Neurological disorders as defined by IHME accounted for 110 million DALYs. Additional neurological diseases not classified as neurological by IHME, accounted for 234 million DALYs – 102 million DALYs without stroke (Figure 1). Further diseases of which a certain percentage of patients has a neurological involvement, e.g. transport injuries or musculoskeletal diseases, account for an additional 288 million DALYs (20% assumed to have neurological involvement; 66 million DALYs). All of these diseases together account for 410 million DALYs (278 million without stroke) – considerably more than the 366 million DALYs of cardiovascular diseases (234 million without stroke; Figure 2).

Causes	Number of DALYs (both sexes and all ages) in 2017 [thousands]
Neurological disorders not included	**234 000 (102 000 without stroke)**
Meningitis and other infections	
Pneumococcal meningitis	3100 (2600–3600)
H influenzae type B meningitis	5000 (4300–5900)
Meningococcal meningitis	2300 (1900–2700)
Other meningitis	10 000 (8600–12 000)
Encephalitis	5100 (4500–5800)
Tetanus	2500 (1700–3200)
Neglected tropical diseases	
Cysticercosis	1600 (1100–2200)
Rabies	630 (500–840)
Zika virus	2.2 (1.3–4.7)

Causes	Number of DALYs (both sexes and all ages) in 2017 [thousands]
Neonatal disorders	
Neonatal encephalopathy due–birth asphyxia and trauma	57 000 (50 000–63 000)
Neoplasms	
Brain and nervous system cancer	8700 (7700–9600)
Cerebrovascular disease	
Ischemic stroke	55 000 (51 000–59 000)
Intracerebral haemorrhage	65 000 (62 000–67 000)
Subarachnoid haemorrhage	12 000 (12 000–14 000)
Congenital birth defects	
Neural tube defects	6200 (4800–8200)

Figure 1. Additional neurological diseases not classified as “neurological” by IHME

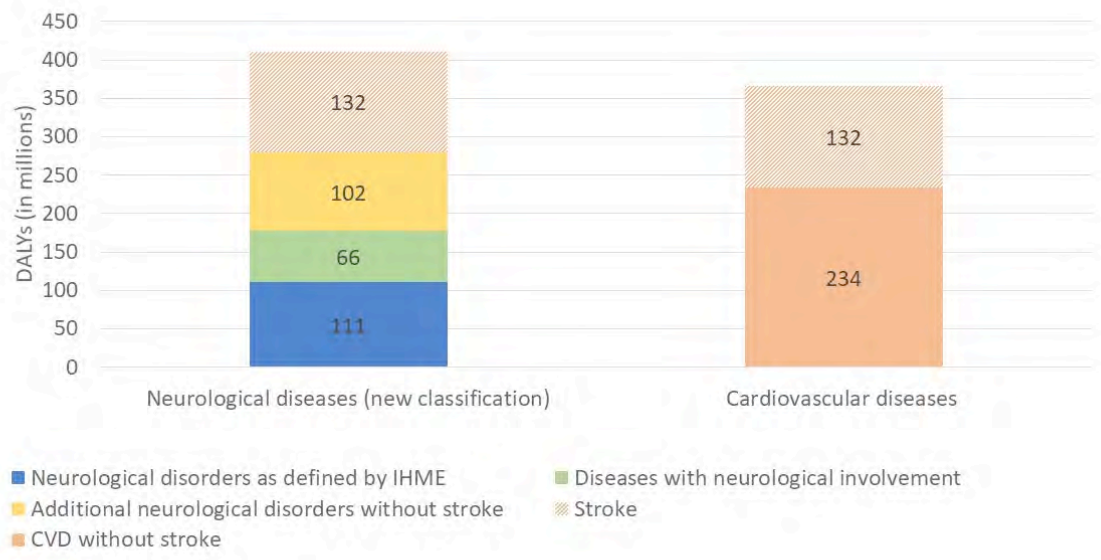

Figure 2. Number of DALYs due to neurological disorders as defined by IHME, and additional neurological disorders, 2017

Discussion: In summary, above data clearly demonstrates the enormous but underestimated global burden of neurological diseases. Considering that life expectancy continues to rise but that the risk for age-related diseases, such as Alzheimer’s disease also increases, we are currently heading towards longer lives with the time lived in poor health also increasing. Considering the above DALY numbers, it becomes clear that more attention from healthcare systems and those responsible as well as from funding agencies is urgently needed in order to address this increasing burden with appropriate resources.

S14-2

Perceived adverse side effects of repeated Praziquantel mass drug administration on Ijinga Island, Lake Victoria, Tanzania

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Background
Mass drug administration (MDA) with Praziquantel (PZQ) is the mainstay of schistosomiasis control in high prevalence areas like the lake region of Tanzania. PZQ is generally considered as well tolerated and therefore suitable for MDA campaigns. Despite this assumption of medical professionals there are contradictory beliefs in the community that can potentially affect the participation in repeated rounds of treatment. We conducted a questionnaire study on the perceived adverse effects after shortly repeated PZQ administration.

Methodology
In early 2017 the community of Ijinga Island, Lake Victoria, Tanzania, received three rounds of PZQ within a schistosomiasis control project (dosage 40mg /kg orally, single dose, directly observed treatment). Prior to the drug administration a meal was provided in an attempt to reduce potential side effects. During the treatment campaign a medical team was available to react on potential adverse events. The interval between each round of treatment was 6 weeks. After each round of treatment, a cross-sectional household survey was carried out using a standardized questionnaire.

Results
328 inhabitants (170 school aged children (SAC), age 7 – 19 and 158 adults, age 20 – 89) participated in the survey.
After the first round of treatment 53% of the participants complained of adverse side effects (60% abdominal pain, 28% vomiting, 22% diarrhoea, 17% dizziness, 10% skin rashes, 1% difficulty in breathing). 8 participants answered that they would refuse to take part again in the next treatment round. After the second round 27% of the participants reported adverse side effects (60% abdominal pain, 26% vomiting, 22% dizziness, 12% diarrhoea, 1% skin rashes, 0% difficulty in breathing). After the third round the rate of reported adverse side effects was 24% (50% abdominal pain, 23% vomiting, 30% dizziness, 13 % headache, 10% diarrhoea, 5% skin rashes, 0 difficulty in breathing).
Compared to the first and second treatment round most of the participants answered that the following treatment round was tolerated a lot better (1st: 76,8%, 2nd: 78,1%) or a bit better (1st 14,8 %, 2nd 16,4%). Despite the reported high rate of perceived side effects, no serious adverse events were seen by the medical team on standby during a 3 hours observation period.

Conclusion
The rate of perceived adverse effects attributed to PZQ was high although no objective serious adverse events were reported by a medical team. There was a substantial decrease in the rate of reported adverse side effects after the 2nd and 3rd MDA round. This indicates that adverse side effects are at least in part caused by the affected parasites rather than by the drug itself. A better understanding of the underlying mechanisms causing adverse side effects by PZQ might be crucial to increase and sustain community participation in MDA campaigns.

S14-3

Kenya´s Health in All Policies strategy: a policy analysis using Kingdon's multiple streams

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Background:
Health in All Policies (HiAP) is an intersectoral approach that facilitates decision making among policy makers to maximize positive health impacts of other public policies. Kenya as a member of the World Health Organization has committed to adopting HiAP, which has been included in the Kenya Health Policy for the period 2014-2030. This study aims to assess the extent to which this commitment is being translated into the process of governmental policy making and supported by international development partners as well as non-state actors.

Methods:
To examine HiAP in Kenya, a qualitative case study was performed, including a review of relevant policy documents. Furthermore, 40 key informants with diverse backgrounds (government, UN agencies, development agencies, civil society) were interviewed. Analysis was carried out using the main dimensions of Kingdon's Multiple Streams Approach (problems, policy, politics).

Results:
Kenya is facing major health challenges that are influenced by various social determinants but intersectoral action focusing on health promotion is still arbitrary. On policy level, little is known about HiAP in other government ministries. Considerable health-related collaborations exist under the concept of intersectoral collaboration, which is prominent in the country's development framework – Vision 2030 with no specific reference to HiAP. Under the political stream, the study highlights that political commitment from the highest office would facilitate mainstreaming the HiAP strategy, e.g. by setting up a department under the President´s Office. The budgeting process and planning for the SDGs were found to be potential windows of opportunity.

Conclusion:
While HiAP is being adopted as policy in Kenya, it is still perceived by many stakeholders as the business of the health sector, rather than a policy for the whole government and beyond. Kenya's Vision 2030 should use HiAP to foster progress in all sectors with health promotion as an explicit goal.

S14-4

Cystic echinococcosis in unaccompanied minor refugees from Afghanistan and the Middle East

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Cystic echinococcosis (CE) is not covered by current refugee screening protocols. After we had detected CE among several refugees attending our clinic from Afghanistan and the Middle East, serological examinations for CE were performed for apparently healthy unaccompanied minor refugees (UMRs) from these regions.
During one year 216 UMR's (136 UMR's from Afghanistan, 41 from Syria, and 39 from Lebanon) were examined serologically with three serologic tests each: an E. granulosus-E. multilocularis-ELISA (Euroimmune, Lübeck, Germany), an in-house-ELISA for E. granulosus, and an indirect hemagglutination test (IHAT) for E. granulosus (Siemens, Marburg, Germany). Among 218 UMRs examined, CE was diagnosed in ten individuals: 7/138 (5.1%) from Afghanistan, 2/41 (4.9%) from Syria, and 1/39 (2.6%) from Lebanon. Eight adolescents had liver cysts, of whom seven had active liver cysts and two had active extrahepatic cysts. 5/10 patients were asymptomatic and were identified by CE serology, only. Another patient had indicative symptoms for CE (urticarial rash after an abdominal trauma), 4/10 had non-specific symptoms.
Compared with another case series, CE was the most frequent and most serious helminthic infection in UMRs from these regions. Furthermore, screening for CE is even more important as half of the UMRs were asymptomatic and only one had indicative symptoms for CE. It is also noteworthy, that only a part of these cases was reported by the central public health board of Germany. This means, that the increase of CE cases would otherwise have passed unnoticed.
Concluding, CE is a serious infection, which refugees from the Middle and Central East should be screened for routinely. Thereby, early diagnosis is achieved which enables timely curative therapy to prevent potentially lethal complications of CE.

Poster

P1

Burden of schistosomiasis in African migrants living in Germany: differential diagnostics and implications for public health

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Background: Schistosomiasis affects more than 250 million people, mainly in sub-Saharan Africa. Morbidity in chronically infected individuals can be subtle, but severe long-term consequences may arise. Imported infections with Schistosoma spp. might increase in Europe due to recent migration from endemic settings in sub-Saharan Africa. Due to the unspecific clinical presentation, a low awareness of schistosomiasis among most clinicians outside endemic areas and the low sensitivity of microscopic diagnostic tools, infections may easily be missed.

Materials/methods: Between April 2017 and July 2018, we collected stool, urine and serum samples from individuals having migrated within the three preceding years from sub-Saharan Africa to the two federal German states of Berlin and Saarland. For detection of schistosomiasis, we employed urine and stool microscopy, serology and a novel point-of-care (POC) rapid diagnostic test that detects a Schistosoma-specific circulating cathodic antigen (CCA) in urine.

Results: 238 individuals were included and most participants were from Eritrea (23.1%), Nigeria (18.1%) and Guinea (15.6%). There were more male than female individuals (80.9% vs. 19.1%) and the mean age was 23 years. The overall prevalence of schistosomiasis found by a combination of all diagnostic tests was 41.2%, with most samples being positive on serology (37.2%). POC-CCA was positive in 13.9%, whereas positive stool or urine microscopy results were rare (4.2%). Only 50% of the POC-CCA positive samples were confirmed by microscopy or serology. Blood eosinophilia was found in 14.7% of all participants and was more frequent in individuals with a positive Schistosoma test result (p=0.02). Other intestinal helminth infections were detected in 7.4% of all participants. Self-reported morbidity indicators such as diarrhoea, haematuria and recent fever were not significantly more common in helminth-infected individuals.

Conclusions: Schistosomiasis is frequent in migrants from sub-Saharan Africa and the true burden of infection is significantly underestimated if only microscopic tests are employed. The POC-CCA test detects additional infections, but further studies are needed to determine its specificity. Our findings call for improved screening strategies to detect and treat chronic parasitic infections in African migrants.

P2

Evaluation of a Strongyloides IgG ELISA with S.papillosus antigen

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Background:
Infections with the nematode Strongyloides stercoralis can either lead to asymptomatic chronic carriage or to life-threatening severe disease. In immunocompromised patients undetected infections can lead to hyperinfection syndrome with frequent fatal outcome. Diagnosis and treatment of strongyloidiasis is therefore crucial for prevention of life-threatening complications. Stool analysis including larval concentration and cultivation on agar exhibits low sensitivity due to the low and infrequent excretion of larvae. Sensitivity of molecular tests also depends on larval shedding. Serological tests are more sensitive and usually are applied in combination with stool analysis. However, available tests using soluble antigens from larvae of S. ratti are prone to cross-reactivity with antibodies to other helminth infections. We have evaluated a new IgG ELISA from Euroimmun AG which uses antigens from S. papillosus larvae and compared the results to our routine ELISA with antigens of S. ratti larvae.

Methods:
The new IgG ELISA was evaluated with a panel of positive sera as well as negative blood donor sera. The S. stercoralis positive sera were selected by means of larval detection and/or sera which were anti-Strongyloides IgG positive in the routine ELISA applying S. ratti antigen. In addition a serum-panel of other helminth infections as well as protozoan infections was tested on both ELISAs for detection of cross-reactivity. Sensitivity and specificity were calculated for both test systems.

Results:
So far 50 strongyloidiasis sera were tested with both ELISAs. The sensitivity of the new IgG ELISA and the S. ratti-ELISA was 84% for both test systems. There was no cross-reactivity with sera of healthy blood donors with both Strongyloides-ELISAs, nor with sera from protozoan infections (E. histolytica, L. donovani, Plasmodium spp. , T. cruzi). Sera from patients with other tissue helminth infections are currently under evaluation.

Conclusion:
Preliminary results indicate that the new IgG ELISA with S. papillosus antigen exhibits comparable sensitivity but increased specificity when compared to the routinely used S. ratti antigen ELISA. Detailed results will be presented.

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P3

Improvements in Patient Safety through online collaboration of a competence network with Liberian district hospitals

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The use of modern information technologies, like e-learning or webinars add more value to traditional, face to face continuous education and collaboration. They have proven their efficiency and sustainability in industrialized countries and continue to become routine procedures in medical practice, especially on hospital level. Taking into account the constantly improving mobile internet connectivity in developing countries, especially Africa, the Academy for Global Health and Development (AGGE) developed a prove of concept approach for district hospitals in Liberia. Pilot partner institutions have been selected and supported in co-operation with the Christian Health Association of Liberia (CHAL).
The project received support by the BMZ sponsored ESTHER academic partnership co-operation, implemented by GIZ. AGGE used a blended learning approach in order to improve specific features of patient safety like infection prevention and control and rational use of antibiotics in order to contribute to the control of antimicrobial resistance.

The initiation and implementation of the project faced challenges on different levels:
• Making continuous and reliable mobile internet connection available in remote district hospital,
• Use and practice of standard IT - devices like smartphones, tablets or laptop with regards to audio and video functions
• Developing familiarity of use of technical devices for written communication or file management
• Change of oral versus reading and writing traditions in continuous medical education linked with self-directed learning discipline

The experience of more than two years of operation of this e-capacity building project proves that:
• Online collaboration can efficiently be implemented even with remote health facilities in Africa,
• The low-threshold approach allowed to establish multidisciplinary teams within hospitals that analyze problems and develop solutions related to patient safety which are informed by international standards and contextualized experiences

More detailed and specific information will be provided during the poster presentation. AGGE concludes besides feasibility of such a project in Africa that the potential of a blended collaboration approach in medical continuous education is that the competence networks continue to collaborate beyond project times. Health professionals acquire experiences to use approved internet resources for international standards and good practices.

P4

Typhoid fever complicated by bowel perforations in children and adults – data and consequences for our main critical care unit in Blantyre (Malawi) from 2006 - 2018.

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Introduction:
Typhoid fever constitutes an important disease in resource poor African countries, partly in epidemic proportions. Perforation is one of the major complications and often needs treatment in critical care. Blantyre provides a mixed tertiary care unit with 4-5 beds (catchment area 3-4 million). We analyse the impact of perforations by typhoid fever on our critical care capacities.
Methods:
We analysed in a clinical audit retrospectively from 2006 to 2014 and prospectively from 2014 to January 2018 all adult and pediatric patients admitted with bowel perforations through typhoid fever.
Results:
Between January 2006 and January 2018 we admitted 57 patients suffering from bowel perforations due to typhoid fever. In 6 patients age, sex or outcome was not longer retrievable. Thirtyeight gentlemen (66.7%) and eighteen ladies (31.6%) were treated. We saw 35 children (61.4%). Seventeen girls (48.6%) and seventeen boys (48.6%) were treated (sex unknown: 4).
During the first 5 years of our study (2006-2011) we only admitted two patients (both children) with such perforations. Eight (3 children/37.5%) from 2011-2013 and then 35 (19 children/54.3%) from 2013-2016. From 2/2016-10/2016 (for 3/16 our ICU files can´t be retrieved) we saw 5 patients (4 children). November 2016 to June 2017 brought 5 patients (4 children/80%) and from July 2017 to January 2018 we saw 2 patients (no child).
The mean age in our audit was 18.2 years with 24.7 years in the male patients and 10.5 years in female patients. All adult women and 16 of 20 male adults were between 18 and 36 years (85%). Children´s mean age was 8.7 years with girls at 8.5 years and boys at 9.1 years. Only 3 children (8.6%) were not between 5 and 13 years of age. No neonates and only 1 baby were seen.
Mortality was high with 29.7% (male: 27.8%, female: 29.4%). Male adult mortality was 46.1% vs. 0% in female adults (only 1). Mortality in children was 20.6%. Mortality for girls was 18.7% and for boys 27.8%. In one girl outcome remained unclear.
Typically several patients suffered from recurrent perforations and posed therefore an additional psychological burden on patients, relatives and staff due to the uncertainty of their surgical prognosis.
Conclusion:
Mortality was high but within our normal range in critical care. Highest risks to develop typhoid fever perforations were in childhood, in the age group of 18-36 and for male adults. Occupying around 2.5% of our beds these patients are not really a challenge for our icu in most years. From 2011-2013, dealing with an epidemic outbreak they represented 7% of our patients and did interfere with our capacities.
Lit.: Pitzer v.E. et al.: Mathematical Modelling to Assess the Drivers of the Recent Emergence of Typhoid Fever in Blantyre, Malawi. Clinical Infectious Diseases, 61 (Suplp.4), S 251-258.

P5

Detection of louse-borne relapsing fever (LBRF) from direct patient blood in migrants – lessons learned from large case series in southern Bavaria

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The human body louse transmits *Borrelia recurrentis*, the causative agent of louse-borne relapsing fever. In the past, large outbreaks have been described claiming millions of lives e.g. during famines and wars. The lethality of untreated disease can easily be above 20% [1]. Although, *B. recurrentis* is susceptible to many antimicrobials, treatment is associated with significant risks, up to 80% of patients develop Jarisch-Herxheimer reactions which require hospitalization and can be fatal [2]. Rapid diagnosis is therefore necessary. Due to very limited numbers of cases in regions with good laboratory infrastructure, little is known about the sensitivity and specificity of current microbiolgical diagnostic procedures for LBRF.

Here, a total of 42 LBRF cases of 2015/16 were investigated [3]. All patients were asylum seekers from east Africa arriving via the Italian route in southern Germany. The main symptoms were fatigue and fever, common symptoms with vast differential diagnoses. Diagnosis is regularly made by microscopy of stained blood films; however this greatly depends on the availability of experienced microscopists to detect also low concentrations of spirochetes in the sample.

Out of all cases ≥80% had positive blood smears in microscopy (Giemsa staining) [34/42] [4], residual cases were negative or unclear [8/42]. However, in blood samples 100% were positiv tested by a modified 16s Borrelia-PCR. As 16s sequences are highly homologous in borrelia, a differentiation was thought to require the sequencing of further genes such as glpQ uvrA and fla. We were able to identify a point mutation in the 16s sequence, which was characteristic in all current and historic isolates and discriminated against the otherwise identical sequences of *B. duttonii*, *B. crocidurae*, *B. miyamotoi* and other borrelia. With quality levels achieved in modern sequencing, this can be used with confidence for identification. Further, we established a simple DAPI based UV-fluorescent microscopy protocol for whole blood smears. Thereby, the diagnosis of *B. recurrentis* is fast and reliable also in otherwise submicroscopic densities due to increased contrast of the bacteria in the sample as well as reduces artefacts. The protocol is also simple and very cost effective without the use of antibodies.

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P6

Erkennung von Erregern globaler Fieber-Erkrankungen - direkt, einfach, schnell, vor Ort

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Akute fieberhafte Erkrankungen können von einer Vielzahl unterschiedlicher Pathogene ausgelöst werden, unter anderem Bakterien, Viren und Parasiten. Derzeit entwickelt BioFire Defense – Partner der deutschen analyticon instruments gmbh –ein Kit (Global Fever – GF) zur Erkennung globaler akuter Fiebererkrankungen (Acute Febrile Illness – AFI). Das Kit läßt sich mit dem semistationären PCR-System Filmarray nutzen. Die Entwicklung erfolgt in Kooperation mit den US-Behörden „Department of Defense“a und „National Institute of Allergy and Infectious Diseases“b. Das FilmArray selbst ist eine in-vitro diagnostische Plattform, die sowohl die Nukleinsäure-Aufreinigung als auch die Multiplex PCR zur gleichzeitigen Identifikation sehr vieler infektiöser Wirkstoffe in weniger als einer Stunde durchführt. Das entsprechende Kit enthält die dafür notwendigen, spezifischen Materialien. Die Kits sind geschlossene Systeme, in denen alle Schritte einer PCR direkt durchgeführt werden. Das GF-Kit detektiert und identifiziert Nukleinsäure des Chikungunya Virus, CCHF Virus, Dengue Virus (Sterotype 1-4), Ebolavirus, Lassa Virus, Marburgvirus, West Nil Virus, Gelbfiebervirus, Zika Virus, Bacillus anthracis, Francisella tularensis, Leptospira spp., Salmonella enterica serovar Typhi und Paratyphi A, Yersinia pestis, Leishmania donovani Komplex und Plasmodium spp. in Proben venösen Bluts von Individuen, die Zeichen und/oder Symptome fieberhafter Erkrankungen haben oder hatten sowie wissentlich oder potentiell in Kontakt mit Krankheitserregern gekommen sind.
Erwartete Studien zu den Bestimmungsgrenzen zeigen klinisch relevante Nachweisgrenzen, zusätzlich zeigen Ausschließlichkeitstests die hohe Spezifität. Bestimmungsgrenzen für die entsprechenden Organismen liegen wie folgend beschrieben bei: Dengue Virus New Guinea C 360 50 Kopien/ml, Marburgvirus Musoke 50 Kopien/ml, Zika Virus 130 Kopien/ml, Leishmania donovani 10 Kopien/ml, Plasmodium 10 Kopien/ml, Bacillus anthracis 64 Kopien/ml, und Yersinia pestis 15 Kopien/ml.c
Vorläufige Off-Panel Ausschließlichkeitsstudien bewerten die Spezifität gegen eng verwandte Organismen oder Organismen, die in ganzem Blut gefunden werden könnten und zeigen keine signifikanten Kreuzreaktionen.
Im Vortrag wird sowohl das semistationäre Filmarray zur schnellen Diagnose von Erkrankungen vorgestellt, als auch die Nachweisgrenzen der einzelnen Erreger sowie weitere Informationen über die Testergebnisse des neuen GF-Kits zur Erkennung globaler Fiebererkrankungen.
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b. NIAID Contract No. HHSN272201600002C, “Advanced Development of Multiplex Diagnostic Platforms for Infectious Diseases (Global Fever Panel)”.
c. Erwartete LoD Grenzen werden aktualisiert, um die neuesten Daten zu zeigen.

P7

Congenital abnormalities associated with ZIKV infection - which co-factors are we looking for?

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Background: Within and beyond Brazil, the variability of the published risk estimates for microcephaly or congenital abnormalities associated with Zika virus (ZIKV) infection during pregnancy is substantial. This highlights a current lack of understanding of co-factors contributing to neurological complications of ZIKV.
Objectives: In this systematic review we assessed the current state of knowledge regarding the variability of the risk of severe abnormalities after maternal ZIKV. We were particularly interested if certain co-factors can potentially explain the variability in the frequency of microcephaly reported. We focused on three different co-factors mentioned in the literature: a) immunological interaction with dengue; b) sexual transmission; c) the toxicological effect of the insecticide Pyriproxyfen.
Methods: We followed the PRISMA guideline. We reviewed PubMed, Cochrane and LILACS online databases from inception to 28 August 2018. The term “zika” and either “microcephaly” or “congenital abnormalities” were combined for the searches in the databases and the different co-factors were added to the search combination.
Results: We identified 328 non-duplicate articles. 66 articles were fully reviewed, of which nine met all criteria for inclusion and exclusion. Six articles highlighted the association between ZIKV and prior dengue virus (DENV) infection, mostly referring to the mechanism of antibody-dependent enhancement. Three analytical studies and three in-vitro studies. Interestingly, the three analytic studies did not postulate a correlation between microcephaly and DENV. Only the in-vitro studies reported enhancement activity between ZIKV and DENV. Three articles discussed the insecticide Pyriproxyfen as potential co-factor. None of these studies described a correlation between the prevalence of microcephaly and Pyriproxyfen. Only one study highlighted sexually transmitted diseases (STDs) in the context of TORCH infections as a co-factor for the variability of microcephaly.
Conclusion: This systematic review concentrated on the three most frequently mentioned co-factors to explain the variability for neurological complications of ZIKV. The reason of the variability, which is well documented in the literature, largely remains inconclusive.
Very few studies addressed the question with a clearly stated methodology. Looking at the existing evidence, immunological interactions with DENV showed some evidence in in-vitro studies.
The insecticide Pyriproxifen is unlikely to be a contributing factor. We did not find any evidence that STDs play a role facilitating sexual transmission of ZIKV. However, many studies suggested that socio-economic status may play a role. The variability of microcephaly and other neurological abnormalities after ZIKV is not well understood and needs to be addressed in future studies. It is of high importance that large ongoing prospective studies include a harmonized assessment of potential co-factors.

P8

Chronology of the discovery of the autochthonous transmission of human schistosomiasis in Corsica

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In actual and retrospective articles on autochthonous schistosomiasis in Corsica the chronology of its discovery is not well reported. Although Napoleon's troups were most likely affected by urinary schistosomiasis after their campaign to Egypt, autochthonous schistosomiasis had never been observed in Corsica until 2014 when a German family assisted the Tropical Medicine Unit of the University in Düsseldorf, Germany on March 2014. The reason of consultation was a hematuria that tone 12-year-old child presented after he had swum in a river in Corsica in August 2013. There, terminal-spined ova were detected in the urine of the boy and of his father, serology was positive in two other siblings. Parasitologists Dr. Moné and Dr. Mouahid from the Laboratory IHPE at the University of Perpignan, France were contacted and urine samples of the family members were analyzed by Dr. Moné and Dr. Mouahid and the hybrid character of the Schistosome species involved was identified (Schistosoma haematobium x Schistosoma bovis).
The cases were notified to the Veille sanitaire, and ECDC and Robert-Koch-Institute were informed on the emergence of autochthonous schistosomiasis in Corsica.
The German (Dr Holtfreter and Dr Richter)-French (Dr Moné and Dr Mouahid) team went to trace the cases to Cavu River together with the family affected in order to investigate the suspected transmission sites in the Cavu River. During the mission, the team unfortunately suffered a serious accident leaving two of the team with severe injuries that required emergency surgical interventions.
The two articles during the time that two team members were inpatients were published in June 2014 (Holtfreter et al., 2014) for the first article regarding the discovery of human schistosomiasis acquired in Corsica by a German family and in July 2015 (Moné et al., 2015) for the first article regarding the hybrid status of the Corsican human schistosome. In September 2014, other cases of human schistosomiasis acquired in Corsica were reported in French families (Berry et al., 2014).

European Centre for Disease Control. Rapid risk assessment: Local transmission of Schistosoma haematobium in Corsica, France – 16 May 2014

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P9

Expect the unexpected A rare cause of hematologic deterioration in a patient from rural Germany

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Background: Hematologic diseases are life-threatening conditions and early diagnosis with consecutive treatment is crucial to prevent serious deterioration. Malignant conditions or a secondary hematologic pathology triggered by infectious diseases (i.e. TTP or AIHA) can share overlapping features and may impede diagnosis. Case: We report a case of a patient who was initially hospitalized with suspicion of hematological malignancy. The 80 year old woman was admitted to our center due to E.coli sepsis. Initial hospital admission was 6 weeks earlier, due to general deterioration, fever and trizytopenia. Weight loss (6 kg) and intermittent fever (40°C) were present for several months. Laboratory findings revealed hemolysis (Hb 8.8 g/dl, LDH 1354 U/l, haptoglobin <0.1 g/l) and thrombocytopenia (6 G/l). CRP, procalcitonin and liver enzymes were increased, coagulation parameters abnormal. Autoimmune parameters were inconclusive. Empirical treatment with piperacillin/tazobactam was initiated and complemented with high dose steroids for hemolysis. While carefully monitoring hemolysis parameters, erythrocytes and thrombocytes were substituted, and fresh frozen plasma was transfused due to impaired coagulation. An ultrasound showed a splenomegaly, while microbiological diagnostics (blood cultures, urine, feces, sputum) remained sterile. A PET-CT scan showed an enhancement of the bone marrow, consistent with a reactive bone marrow morphology but without signs of a malignant disorder or another underlying pathology. While the patient initially reported no trips to a foreign country in recent weeks prior to symptoms, a repeated investigation revealed a stay in Greece several months ago. Consequently, we extended microbiological diagnostics and examined the bone marrow aspirate microscopically for the presence of Leishmania. While microscopy remained negative, PCR confirmed the suspected diagnosis of visceral leishmaniasis. Sequencing of the cytochrome B gene, performed at the Berhard Nocht Institute for Tropical Medicine, showed 99% accordance with L. donovani and L. infantum (members of the L. donovani complex). Liposomal Amphotericin B was applied over 7 days and repeated at day 11 and 18. Both hemogram and coagulation parameters quickly improved after initiating treatment. Conclusions: Despite low incidence of visceral leishmaniasis in Germany, it needs to be considered for patients with unclear hematologic alterations. Incubation time may range from a few weeks to months or even years. It needs to be noted that L. donovani is endemic in Mediterranean countries (including European countries, e.g. Greece, Spain, or Italy). Changes in climate and thus the spread of competent vectors might alter Leishmania epidemiology in addition to the increasing business and touristic mobility. Molecular testing for Leishmania should be performed from qualified clinical samples if clinical and laboratory findings are suggestive, but initial microscopy remains negative.

P10

Diagnosis and outcome of sepsis at a tertiary referral hospital in Central Ethiopia

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Background
Despite recent updates on definition and diagnosis, sepsis remains an underrecognized condition especially in sub-Saharan Africa, where it is associated with high mortality in the context of limited therapeutic options. This study aimed to assess the utility of the SOFA and qSOFA scores for clinical and prognostic purpose at the Asella Teaching and Referral Hospital (ATRH) in Central Ethiopia.

Methods
Patients with a diagnosis of infection admitted to the ATRH were screened for SIRS criteria according to the sepsis 1 definition from 1991. If ≥2 SIRS criteria were present, SOFA and qSOFA scores were assessed and socioeconomic data were recorded. Patients with a SOFA score ≥2 were followed daily until discharge or death. In discharged patients, 28-day mortality was assessed by phone interviews. Data were entered and analyzed by Chi-squared test using IBM SPSS statistics version 24.

Results
From March 2017 until April 2018, 276 patients with SIRS ≥2 were screened for sepsis. Data from 251 patients were available for analysis. Mean age was 33.7 years and 48.6% of study participants were female. Respiratory infections (32.6%) and febrile illness with unknown focus (20.3%) were the most common clinical diagnoses. SOFA score was < 2 in 32.3%, 2 in 25.1%, 3 in 15.5%, 4 in 9.6%, and >4 in 17.5%, respectively. 171 (67.7%) patients with SOFA ≥2 were followed up. Among those, only 12.2% (n=21) were diagnosed with sepsis by the treating physicians and 28-mortality was 28.9% (39/135). In patients with sepsis (SOFA ≥2), mortality was associated with increasing SOFA score (chi-squared test, p<0.001) and qSOFA score (p=0.003) but not with number of positive SIRS criteria (p=0.605). Mortality in patients with SOFA score of 2, 3, 4, ≥4 was 8.5%, 13.8%, 42.1% and 57.5%, respectivelyand mortality of patients with qSOFA score of 0, 1, 2, 3 was 0%, 17.2%, 36.9% and 71.4%, respectively. In comparison with SOFA score as gold standard, sensitivity and specificity of the qSOFA score for the diagnosis of sepsis were 52.4% and 69.1%, respectively.
Age above 65 years was a significant risk factor for mortality (60% vs. 25%, p=0.016). There was a trend towards increased mortality for patients with chronic disease or positive blood cultures. Gender, socioeconomic parameters, HIV status, and clinical diagnosis or recognition of sepsis by the treating physicians were not associated with mortality.

Conclusion
In our setting, sepsis was underrecognized and associated with a high mortality. The easy applicable qSOFA score failed to reliably identify patients with sepsis, but was associated with mortality in this group of patients. The SOFA score was associated with mortality, but its application is impractical in resource-limited settings. New and efficient tools for the early diagnosis of sepsis are needed in resource-limited settings and should be established within clinical studies.

P11

Immunization Coverage among Refugee Children in Berlin

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Background: The Tempelhof refugee camp offers in-camp immunizations. Other camps, like Neukölln, rely on a centralized immunization system. We aimed to determine the impact of conflict on immunization rates of Syrian children and to measure the efficacy of in-camp immunization services.

Methods: Families with children under the age of 5 in Tempelhof and Neukölln camps were surveyed. Surveys included siblings under the age of 18. We organized data into two categories: 1. past immunization history in country of origin, based on parent memory, and 2. existing immunization record provided by host countries and recorded on immunization cards issued by host country. For past immunization history, a child was classified as “fully immunized-memory” or “partially immunized-memory.” For existing immunization record, we reviewed immunization cards issued in the host country and classified children as follows: “no immunizations,” “partially immunized,” “partially immunized but due to return,” and “fully immunized.” Differences among groups were compared using 2 and Fischer’s exact test.

Results: Data on a total of 179 children at Tempelhof and 40 children at Neukölln were collected. At Tempelhof, amongst Syrian children, 28% under the age of 5 were “fully immunized-memory,” in contrast to 74% over the age of 5 ($p=0.005$). This difference in immunization rates by memory between the age groups was not observed in Afghani children ($p=0.34$) or in Iraqi children ($p=0.10$). Furthermore, compared to the 28% of Syrian children, 75% of Afghani children under the age of 5 were “fully immunized-memory” ($p=0.0009$). Compared to Tempelhof, more children at Neukölln were partially immunized (93%) or had no immunizations (5%) ($p<0.001$).

Conclusion: These data suggest that conflict adversely affected immunization rates of Syrian children, and that offering in-camp immunization services may be a solution to increasing immunization rates.

P12

Think globally, but how to act locally? Problems German patients face in getting their medication covered by national health insurances

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A large number of drugs necessary to adequately treat globally widespread neglected parasitic diseases have never been or have ceased to be licensed in Germany. These include intravenous artesunate, intravenous quinine, primaquine, pentavalent antimony, nifurtimox, benznidazole, suramine, melarsoprol, triclabendazole, nitazoxanide as well as all 5-nitroimidazoles besides metronidazole. There are also other drugs that are licensed within Germany but destined for specific therapeutical uses but are not officially licensed for another disease the patient would need them for. This applies e.g. to paromomycine, mebendazole, albendazole and chloroquine which can be used for treating multiresistant giardiasis. In this case these drugs have to be prescribed on an off-label basis. In cases of an acute possibly life-threatening disease such as complicated malaria or acute trypanosomiasis the major threat is the delay until the drug becomes available in the hospital. Although it is mandatory for medical insurances to cover drugs which are not licensed within Germany in the case life-threatening conditions, this does not apply for diseases which are not life-threatening. Examples are drugs for second line treatment of metronidazole-resistant giardiasis or primaquine prevention of malaria relapses which can be handled in outpatient clinics. There is an urgent need to close this gap in German law in order to warrant patients their therapy and meet the ethical criteria which should not only apply globally but also locally in an industrialized country such as Germany.

P13

Open access journals: transparent science or shady business?

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Imagine
Imagine - you are a young European scientist. You submit your excellent article – the reviewers are enthusiastic – but your institution does not have a budget for publishing your article. – you have a family to nourish - well, do you have some 700 to 2.500 USD to pay for publishing your article yourself? The only chance you might have would be to apply to waiving. Maybe you have a friend in the Sudan who will act as first author instead of you in order to get the work published for free because scientists from developing countries have better chances not to be obliged to pay for publication costs.
Imagine - you are a lateral thinker. You are not supported by an academic institution or your head of department or. E.g., Albert Einstein did not receive any funding from his first employer, the Swiss patent office, for publishing his scientific articles. Would he have had the money to publish his pioneering work in an open access (OA) journal?
Imagine – somebody has to pay for the publishing costs. If your institution pays, this means that, eventually, the taxpayer pays the fees.
Imagine - you have to rush towards an airport and you need to take a taxi. After the ride you explain to the taxi driver that he should pay you the fare instead of you paying him, just the condition scientists accept with OA journals now?

Consequences
The more OA journals will predominate, the more science will be biased towards who can afford to publish. Moreover, OA journals are easy to access by everyone. This means that the impact and citation factors will increase more easily as compared with subscription journals.
It is not clear what the money requested by OA journals is destined for. The highly specialized academic reviewers usually are not paid for their work. There are no printing costs. Perhaps this is the reason why OA access journals spring up like mushrooms and inundate email of academics by publication offers?

What can be done?
As a first step, in order to correct the scientific bias caused by this situation, we propose to adjust the impact and citation factors of articles published in OA journals. That could be done be dividing these factors by a defined proportion of the publishing fees and would thereby also contribute to discourage predatory OA journals. Further correcting measures to take must, in our opinion, be urgently addressed and discussed by the scientific community to prevent science from becoming just a business affair.

P14

Predictors and treatment outcomes of Extrapulmonary tuberculosis from an Indian tertiary care hospital

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Background: Studies on extrapulmonary tuberculosis (EPTB) in India is limited. This study was aimed to determine the spectrum of EPTB in the study population and to analyse the risk factors of EPTB in comparison to pulmonary tuberculosis (PTB) and study their treatment outcomes.

Methods: A risk factor analysis was conducted among hospitalised adult TB patients in a tertiary care centre in India from September 2015 to June 2017. Individuals with newly diagnosed EPTB were enrolled as cases, and equal number of newly diagnosed PTB individuals as controls. Cases and controls were defined as per WHO definitions for PTB and EPTB. Chi-square test was used to find association of categorical exposure variable with types of TB. Multivariate logistic regression analysis was done to determine the risk factors of EPTB.

Results: A total of 350 individuals with equal numbers of EPTB and PTB were enrolled. 175 PTB cases were microbiologically confirmed, whereas 62/175 (35.4%) of EPTB cases were microbiologically confirmed. The most common EPTB site among HIV negative patients was pleura and among HIV positive patients it was lymph node. HIV co-infection was found to be associated with EPTB (aOR: 3.12; 95% CI 1.59-6.13), diabetes mellitus (aOR: 0.31; 95%CI 0.17-0.54) and smoking (aOR: 0.32: 95%CI 0.16-0.62) were inversely related. Overall 67.7% opted for non DOTS therapy and 32.3% opted for DOTS (Directly observed treatment, short course). Six (4.3%) of EPTB were cured, 61% completed treatment and 33.3% were lost-to-follow up. Among 96 PTB patients who opted for non DOTS treatment, 15(15.6%) were cured, 39(40.6%) successfully treated and 36(39.5%) were lost to follow up

Conclusions: HIV co-infection was found to be associated with EPTB and diabetes mellitus and smoking were inversely related. High rates of lost-to-follow up calls for urgent measures to improve adherence to treatment and follow up at institutional level and also intervention from the national program once TB is notified.

Keywords: Tuberculosis, extrapulmonary, HIV, DOTS, India, Pulmonary TB

P15

The role of bedaquiline and linezolid in the management of toxicity from rifampicinresistant tuberculosis treatment in Johannesburg, South Africa.

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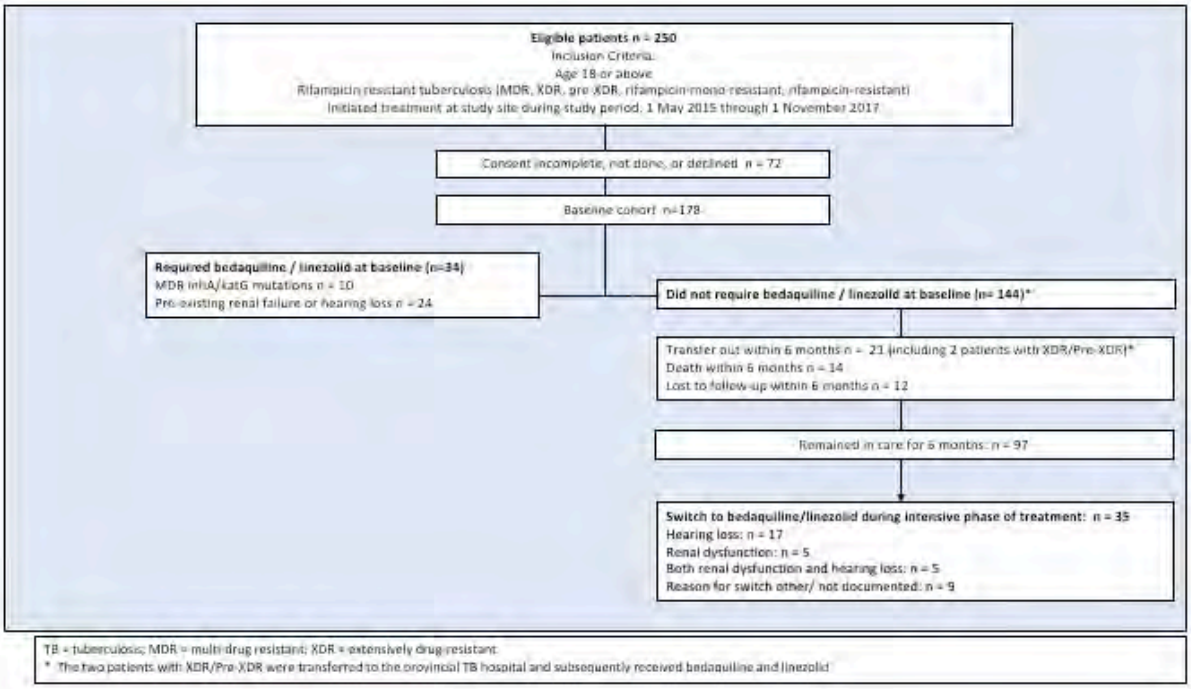
Background:
Bedaquiline and linezolid are substituted for aminoglycosides in the management of rifampicin-resistant tuberculosis (RR-TB) in South Africa in patients with baseline or incident hearing-loss or renal dysfunction or multi-drug-resistant TB (MDR-TB) with inhA and katG mutations. We describe reasons for baseline use of bedaquiline/linezolid and risk factors for switch during the first 6 months (intensive-phase) of therapy.

Methods:
Prospective cohort study at an outpatient RR-TB treatment site in Johannesburg, South Africa. Patients with RR-TB, age>18, who consented to study participation and enrolled between 1/5/2015 and 1/11/2017 were included. A log binomial regression model was applied to determine risk factors for switch to bedaquiline/linezolid during intensive-phase. Patients received monthly monitoring for hearing-loss and renal dysfunction. Bedaquiline/linezolid are co-prescribed for all patients requiring an aminoglycoside-sparing regimen.

Results:
Of 250 eligible patients, 178 consented to enrol in the study. 143/178 (80.3%) were HIV-infected with a median age of 29 (IQR 18 - 36) and median of CD4 54 cells/mm (IQR 19 - 191). Bedaquiline/linezolid were prescribed at treatment start in 34/178 patients: 24 had baseline hearing-loss or renal dysfunction and 10 had MDR-TB with inhA and katG mutations.
Amongst the 97 patients who completed the intensive-phase of treatment an additional 35 switched to bedaquiline/linezolid and discontinued kanamycin (figure): 17/35 developed hearing-loss; 5/35 renal dysfunction; and 5/35 both (reason for switch was not documented in 9/35). The following risk factors for switch to bedaquiline were examined using a log-binomial logistic regression analysis: gender, age, HIV status, CD4, body mass index, baseline anemia.
Only baseline anemia (hemoglobin < 12) was significantly associated with subsequent regimen switch (RR 1.71 95% CI 1.01 - 2.91).

Conclusions:
In an outpatient RR-TB treatment site, close to 40% of patients required a bedaquiline/linezolid based regimen during the intensive-phase of therapy: 19% at baseline and 20% developed aminoglycoside-induced treatment toxicity requiring treatment switch.



Description of Cohort

(This study has been presented at The Union 2018 Conference.)

P16

Socio-demographic Profiling of Tuberculosis Hotspots in Ethiopia: 2014 – 2017

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Poster presentation

Introduction

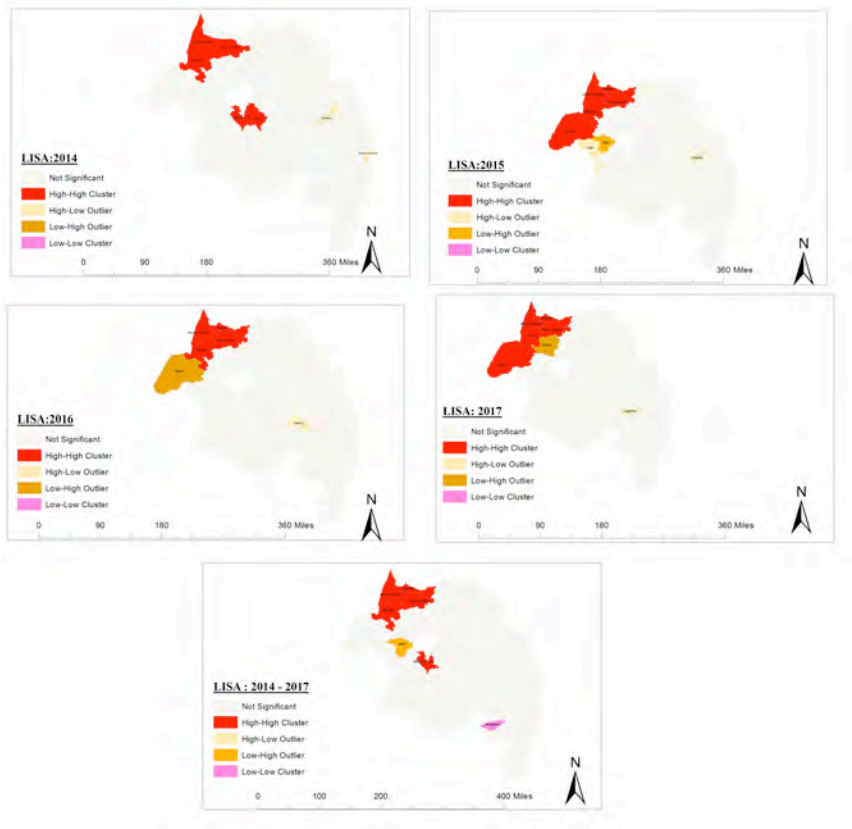
Tuberculosis (TB) notification rates vary across regions in Ethiopia and districts within the Amhara region. The Amhara Region is one of the main TB hotspot regions in the country. In this study, we identified the spatial distribution of TB and characterised the socio-demographic factors of spatial clusters in Amhara region, Ethiopia.

Methods

An ecological spatial analysis of TB notifications from 2014 to 2017 was conducted to quantify the presence and location of spatial clusters of TB notifications at the district level within the Amhara region using global Moran's I statistics and Local Indicators of Spatial Autocorrelation, respectively. Notifications from hotspots and low-risk districts were compared to identify significant socio-demographic difference.

Results

From 2014 to 2017 we estimated an average notification rate of all forms of TB in the Amhara region of 107 per 100,000 population (range 18 to 614/100,000 population). The highest rates in the region were found in the northwest and central regions. District-level TB notification rates were positively spatially auto-correlated, with Moran' I value ranging from 0.207 to 0.276 (p=0.01). Hotspot TB clusters were found in the northwest and central part of the region.



Mean urbanization, proportion of men, household crowding, use of charcoal for cooking, proportion of internal migration for the last 5-years, PLHIV per 1000 population, and health facility coverage were associated with hotspot TB cluster districts.

Variable	F (3,124)	P-value	Cohen's d
Urban residence (%)	7.20	0.001	0.8
Male population (%)	8.47	0.001	0.9
Room crowding (number)	3.63	0.015	0.5
Migration (%)	23.21	0.001	1.4
Use charcoal for cooking (%)	12.40	0.001	1.0
Use dung for cooking (%)	5.76	0.001	0.7
PLHIV per1000 population	5.83	0.001	0.6
Health facility coverage per 100,00 population	3.48	0.018	0.4
Mean elevation	8.46	0.001	0.9

The mean difference and Cohen's d effect size estimates of the social demographic variables of TB notification in Amhara region, Ethiopia, 2014-2015 (n=128)

Notification rates of TB in hotspot, low-low, low-high and not significant TB clusters were 243.6, 43.7, 57.5 and 105 per 100,000 population, respectively. Hotspots accounted for about 244 cases per 100,000 population of notification (57.35%); however, only 0.13% of all TB cases in the population were attributable to the hotspots. Moreover, 9.6% and 6% of TB cases in the under-five and male populations were attributable to the hotspots, respectively.

Conclusion

Our study demonstrated that TB notification rates in the Amhara region of Ethiopia over the past four years were significantly clustered. Distinguishing high-risk areas from low-risk areas and characterizing the social determinants and other risk factors is important for targeted TB prevention and control program.

Keywords: Tuberculosis (TB), hotspots, socio-demographic, Spatial, Amhara, Ethiopia

P17

Using RNA sequencing to describe gene expression signatures for distinct disease states in pulmonary tuberculosis

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Background
Current guidelines recommend treatment for drug susceptible pulmonary tuberculosis (TB) for 6 months, and 9 to 12 months for treatment of extra-pulmonary TB. Our diagnostic tools are unsatisfactory and research is on-going to improve diagnostic capabilities. Several host RNA signatures from whole blood have been described in recent years. All of these were aimed at diagnosing active disease and LTBI in cohorts of adults or paediatric patients or to assess for disease progression. Still, biomarkers to guide treatment and to allow monitoring of treatment response are urgently needed. Hence, we intended to systematically study the impact of host RNA markers on discriminating different “disease states” and early prediction of treatment outcome.

Methods
Whole blood tempus tubes were obtained from the PanACEA MAMS-TB study’s (Boeree et al., 2017) standard treatment arm (HRZE) with additional inclusion criteria for subjects who culture converted within 26 weeks of treatment and number of lung cavities (≤ 1). RNA was extracted for a total of 43 subjects on 4 time-points (baseline, 2, 12 and 26 weeks) followed by RNA quantity and quality checks and library preparation. RNA-sequencing was carried out using Illumina NextSeq500 technology. Data sets were assessed with FASTQC to ensure sufficient quality. Samples were aligned against the Human Reference Genome (Build 38 patch release 12 (GRCh38.p12)) using STAR. Reads mapping to genomic features were counted using FeatureCounts and differential gene expression was computed using DESeq2.

Results
530 genes were found to be significantly differentially expressed (SDE, Adjusted p-value < 0.01 abs (log2 Fold Change >1) between samples taken at week 0 and week 26. Of these 386 genes (72.83%) were up-regulated and 144 (27.17%) were down-regulated at week 0. Key up regulated transcripts included FCGR1A/C, SOCS3, MMP1 and MMP* as well as IL-27. Known diagnostic signatures were successfully evaluated on our data set. Canonical pathways significantly affected by the up-regulation at time of diagnosis encompassed functions such as phagosome formation, inflammasome pathway or interferon signalling. Further analysis towards a transcriptomic signature on treatment response revealed a profound effect 2 weeks into anti-TB treatment.

Discussion
Using the precious biological samples of the PanACEA study, we describe the pattern of differential gene expression between two different “disease states” of TB, the “active TB” and the ‘cured” state, in patients following successful treatment for 6 months with no relapse within a 2 year follow up. We also highlight that a profound effect on the gene expression pattern can be readily detected 2 weeks after treatment initiation. Our results may serve to establish an early gene signature for a favourable treatment outcome, thus enabling a personalized treatment approach.

P18

New techniques to investigate dormant growth states of Mycobacteria on a single cell and ensemble basis for future rapid testing and drug development

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Tuberculosis, caused by *Mycobacterium tuberculosis* is currently the single most deadly infectious disease in the world and a public health priority as defined by WHO [1]. Although the disease is in general curable by antibiotics, treatment success is hampered by the necessity of a long and side effect prone treatment with frequent failures. Low treatment efficiency may be partly due to special growth states mycobacteria enter to survive antibiotics and persist longer within the host. Such growth states have been recently defined as dormant/persistent and are understood now to be of prominent importance as it has been correlated with poor treatment outcome when detected in the sputum of patients under treatment [2, 3]. *In vitro* models could reproduce dormant states and demonstrate less efficient killing of the bacteria by antimycobacterial drugs and slower metabolism than during rapid growth [4]. Understanding dormant growth states and characterizing them *in vitro* is of paramount importance to develop new and more efficient treatments for tuberculosis. Current techniques such as sudan red staining lack precision and are not able to identify growth state without destruction of the organism.
We produced dormant model-organism cultures and characterized those by multilayered approaches using mass spectrometry (MALDI-TOF-MS), microscopy (SEM, Raman), and microbiological techniques (CFU, OD_{600}, ATP) [5]. We developed a fast 96-well-adapted extraction protocol for highly sensitive MALDI-TOF analysis for Mycobacteria and for the first time, could demonstrate growth-state-dependent changes in the mass signatures of the culture, allowing for a reliable differentiation of dormant growth. While MALDI-TOF-MS generates a sum signal of thousands of organisms, Raman spectroscopy is unique due to its high spatial resolution, allowing the analysis of living single cells. Organisms were analyzed individually distinguishing dormant bacteria from their rapidly growing, genetically identical counterparts. This allows for the separation of heterogeneous cultures depending on their growth state using the destruction-free optical Raman microscopy and thus offering the opportunity for future single-cell drug susceptibility testing of dormant bacteria.

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P19

Focused Ultrasound in Pediatric Diagnostic Tuberculosis Work-up: A Case Report from Germany

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Introduction
Establishing a diagnosis of childhood tuberculosis (TB) remains a challenge and microbiological confirmation of TB is achieved only in a minority of children. Focused ultrasound to detect HIV-associated sonographic features of extra-pulmonary TB (EPTB) is established in resource-limited settings with high HIV/tuberculosis prevalence to support the diagnosis of TB where confirmation is restrained by limited diagnostic infrastructure or impeding host conditions such as HIV-infection.
In South Africa focused ultrasound in children with presumptive TB showed that a third of children with pulmonary (PTB) also had ultrasound findings consistent with concurrent EPTB. No studies are available on the use of focused ultrasound for TB in settings with low HIV/TB prevalence where ultrasound is not systematically performed during TB work-up.
Here we report on a pediatric case from Germany where ultrasound was the determining diagnostic factor to establish the diagnosis of active TB.

Case report
A 20-month-old boy was referred to the Department of Pediatrics at RWTH University Clinics Aachen, Germany, to rule out active TB. He was referred because of a tuberculin skin test conversion despite 3 months of TB prophylaxis, which had been administered because the child's mother was diagnosed with PTB.
At presentation TB-related symptoms were absent and clinical examination revealed no pathology. HIV tested negative. Interferon-gamma-release assay was positive. A chest x-ray did not show signs suggestive of TB. Three morning gastric aspirates were negative for acid-fast bacilli on microscopy (Ziehl-Neelsen) but polymerase chain reaction (PCR) was faintly positive, with uncertain significance. After the inconclusive results of routine investigations, a point-of-care ultrasound was performed to search for features of active EPTB and multiple hypoechoic splenic lesions characteristic of TB micro-abscesses were visualized.
Consecutively, the diagnosis of concurrent PTB and EPTB was established and the child was initiated on a 4-drug anti-TB regimen. Liquid culture of gastric aspirates turned positive for non-MDR Mycobacterium tuberculosis after several weeks.
Follow-up ultrasound picked up persisting spleen lesions until 8 months into treatment, anti-TB treatment was extended and splenic lesions had disappeared by 12 months of treatment.

Conclusion
In children first-line TB diagnostic tests may be inconclusive and clinical presentation atypical, as our case portrayed. The additional diagnostic value of focused ultrasound was decisive in establishing TB diagnosis at the time of presentation several weeks before positive culture confirmed the diagnosis. Moreover, focused ultrasound allowed a more accurate delineation of disease extent and was an effective monitoring tool until TB treatment was successfully completed. Focused ultrasound should be studied in settings of low TB incidence and considered as a standard diagnostic tool during pediatric TB work-up.

P20

Interim analysis of the pulmonary tuberculosis sequelae in a multicenter African TB Cohort

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The combined Tuberculosis (TB) related morbidity and mortality remain constantly high in Africa, mainly due to the impact of HIV, sustained poverty and food insecurity and other treatment challenges. National TB programs focus on short-term microbiological cure as opposed to long-term burden of the disease due to sub optimal pulmonary recovery. We aim to have a comprehensive, long-term, TB outcome measure in terms of clinically relevant pulmonary morbidity and disability during and after the course of treatment.
The TB Sequel study (NCT03251196) follows newly diagnosed TB patients in four nations South Africa, Mozambique, Tanzania and the Gambia for two years. They receive anti-TB treatment according to guidelines of the National TB program. We model the joint longitudinal evolution of the lung activity through the correlated outcomes of FVC and FEV1 standardized with respect to the South African healthy volunteer equations. Additionally body weight also evolves positively with time since treatment. These three outcomes constitute an exemplary multivariate composite outcome. We evaluate differences across site and baseline risk factors such as sex, HIV, and age for statistical significance on the composite outcome. In parallel, we model the evolution of pulmonary impairment, including severity grades, and test for the statistical association with the same risk factors as described before, which is the primary objective of the study. We have data from more than 350 participants until now having information on lung function at some specified time point. From the statistical analysis, we obtain a significant positive trend in terms of pulmonary activity and body weight as well as the severity evolution. Age has been a significant risk factor; disease appears to be more severe in younger compared to older subjects. Challenges exist due to non-availability of previous data from healthy participants to standardize pulmonary outcomes in the respective African populations. Additionally age and sex distribution is different across the different sites. This probably affects the classifications of pulmonary severity and partially explains the observed difference across the study sites.

P21

Improving the diagnosis of tuberculosis: Using single-cell transcriptomic profiling of pathogen-specific T cells for the identification of novel biomarkers

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Tuberculosis (TB) caused by *Mycobacterium tuberculosis* (MTB) is one of the leading causes of death worldwide. One of the major obstacles in the fight against TB is the lack of rapid and accurate diagnostic tools for TB detection, especially for a clear differentiation between active and latent disease. The current reference standard relies on the detection of live *Mycobacteria* by culture, a time-consuming process that can only be performed in well-equipped laboratories. Novel non-invasive methods to quickly and accurately diagnose TB are therefore urgently sought.
A novel, flow cytometry based approach assessing T cell activation markers on MTB-specific T cells in peripheral blood has shown great potential in accurately differentiating between the two disease states and provides results within 24 hours. In order to identify additional biomarkers on MTB-specific T cells that differentiate active and latent MTB infection, we applied single-cell transcriptional analysis to MTB-specific T cells from clinically well-characterised patients of the Munich ReFuScreen TB cohort. Live, MTB-specific CD4 memory T cells, producing interferon gamma (IFNg), are sorted after autologous in vitro stimulation, with 1 to 50 sorted cells resulting in sufficient full-length cDNA for transcriptome analyses. Bioinformatic analysis of RNA sequencing data, revealed differential expression in immune regulation pathways, such as antigen processing and presentation.
The biomarkers and pathways differentially expressed in active and latent TB infection, identified and characterized here, will not only contribute to the development of novel TB diagnostic tools, but might also deepen our understanding of the cellular pathways involved in the adaptive CD4 T-cell response against MTB.

P22

Rifampicin dosage and exposure are associated with superior activity in the PanACEA MAMS-TB study

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Background: Higher dosages of rifampicin, at 35mg/kg, were shown to shorten time to negative culture in the MAMS-TB study. We now present pharmacokinetic and dose-response analyses from this trial.
Methods: Adults from Tanzania and South Africa with smear positive pulmonary tuberculosis were randomised to control or one of four experimental arms. One of those arms contained 35 mg/kg rifampicin in weight-banded daily dosages of 1,200 to 2,100 mg; combined with isoniazid, pyrazinamide and ethambutol, for 12 weeks. The primary endpoint was time to stable culture conversion in MGIT. Blood samples for pharmacokinetic evaluation were taken after four weeks of therapy.
Results: Culture conversion occurred much earlier with 2,100 mg RIF (hazard ratio [HR], compared to 450 mg RIF, adjusted for baseline bacterial load and patient gender: 2.76; 95% CI: 1.67 - 4.55;), and it occurred more frequently (91% of 23 patients). With the next lower dosage of 1,500 mg, only 63% of 45 patients achieved conversion (p = 0.015, for difference to 2,100 mg). Intensive pharmacokinetic data was obtained from 97 patients. Rifampicin area under the curve (AUC) was associated with absolute dose and fat free body mass (R2=0.83, p = 0.002 in multivariable regression). Absolute dose explained slightly more variation than dose per body weight. Time to culture conversion was significantly associated with RIF AUC when adjusted for baseline bacterial load and unavailable cultures (HR:1.008 per 1 mg*h/l AUC increase, 95%CI 1.002-1.015, p=0.016).
Hepatotoxic events occurred in 1 (4.3%), 3 (7.3%) and 2 (4.4 %) patients receiving 2,100 mg, 1500mg and 1,200 mg rifampicin, respectively.
Conclusions: A superior rifampicin effect was seen at a 2100 mg dosage, explained by associated higher rifampicin AUC values. Further studies should explore dosage per fat-free mass or individual dosage adjustments based on exposure, to revise the currently used weight banding for rifampicin.

P23

RefuScreen TB: A TB diagnostic study in Munich

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Background: Tuberculosis (TB) remains one of the top 10 causes of deaths worldwide, accounting for 1.3 million deaths annually. One of the populations most at risk for developing active TB are refugees. Current screening and diagnostic algorithms for TB notification among refugees perform sub-optimally, even in settings with satisfactory resources. During the year 2015, when a flow of refugees reached Europe, TB incidence increased by 2/100.000, and efforts have been made to identify more efficient tools for mass-testing and confirmation of disease.

Methods: Since 2017, children and adults were enrolled in the prospective RefuScreen TB study at 4 hospitals in Munich, Germany. Inclusion criteria were suspicion of active TB or recent TB contact history. The screening and diagnostic workup included specimen collection for TB culture and further investigations for active TB as determined by the clinicians. Patients were classified as having confirmed, unconfirmed and unlikely TB based on microbiological, radiological and clinical findings. The new diagnostics have different testing approaches, based on pathogen detection – Xpert MTBRIF Ultra® and a Lipoarabinomannan-assay – and host-based biomarkers, which include a protein signature, RNA transcriptomics and the “T cell activation marker” (TAM TB). Recruitment will continue until April 2019.

Results: So far, 325 patients were recruited; out of those 65% underwent TB testing due to clinical suspicion based on symptoms, while only 14% (n=45) due to an abnormal admission examination (shared shelter). In terms of migration history, 41%, 33%, and 26% were refugees, migrants from safe countries, or German/EU citizens, respectively. Most patients (57%) with non-European background were from countries with a high TB incidence (≥25/100.000). Around 12% of patients reported a history of previous TB treatment, only 4 patients were known HIV+. 155/325 (54%) were diagnosed as having active TB and started on anti-TB treatment. TB was microbiologically confirmed in 106/155 (68%) by PCR and/or culture. The medium duration of residence in non-Germans with active TB was 6 years (n=114), most reported to have lived in Germany for 1-2 years (n=61). The proportion of confirmed TB cases in the subgroup of patients with abnormal admission examination (10/22) was noticeably smaller than when inclusion was based on symptoms (84/109).

Conclusion: RefuScreen TB is a unique study setup, that allows to enrol a significant number of patients for a TB diagnostic study in a well-resourced setting, within short time. We could show that the subgroup with the highest number of active TB cases were immigrants living in Germany for 1-2 years, rather than recent arrivals. Furthermore, the number of Germans/EU-citizens was considerably higher than expected. Analysis is ongoing with further results, including demographics as well as results of new tests and the additional TB work-up, to be presented.

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Tuberculosis and Latent Tuberculosis Infection among Asylum-Seekers in Milan, Italy: Epidemiological Analysis and Evaluation of Interventions

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In low-incidence countries of the European Union tuberculosis (TB) affects mainly marginalized people, including asylum-seekers (AS). Migratory flows from TB high-incidence countries to Italy have increased up to 2017, posing challenges to the national health system in terms of TB and latent TB infection (LTBI) detection and management. This study sought to assess incidence of active TB and prevalence of LTBI among AS in the city of Milan during the biennium 2016-17 and to evaluate interventions in place.
A two-level active surveillance and screening system (Figure 1) was developed to assess AS for both TB and LTBI. AS underwent an initial screening with tuberculin-skin-test (TST) and a questionnaire (QS) at the receiving sites. At the Regional Reference Centre, those with a positive result were subjected to a chest X-ray (CXR). People under 35 years of age with negative CXR underwent further testing by Interferon Gamma Release Assay (IGRA) and were offered LTBI treatment in case of positivity. CXR-positive people were subjected to further microbiological testing to detect TB. Observed TB incidence and LTBI prevalence were compared with official and literature data using incidence rate ratio (IRR) and Chi-square test, respectively. Molecular surveillance was also implemented to evaluate if recent transmission had occurred. The surveillance system was assessed evaluating as indicators: completeness of medical evaluation after a positive screening test, timing of interventions, TB treatment outcomes, and proportion of acceptance and adherence to LTBI preventive therapy.
A total of 5,324 AS, mostly males (89%) from Sub-Saharan African countries (69%), with a median age of 24 years were enrolled in the study.

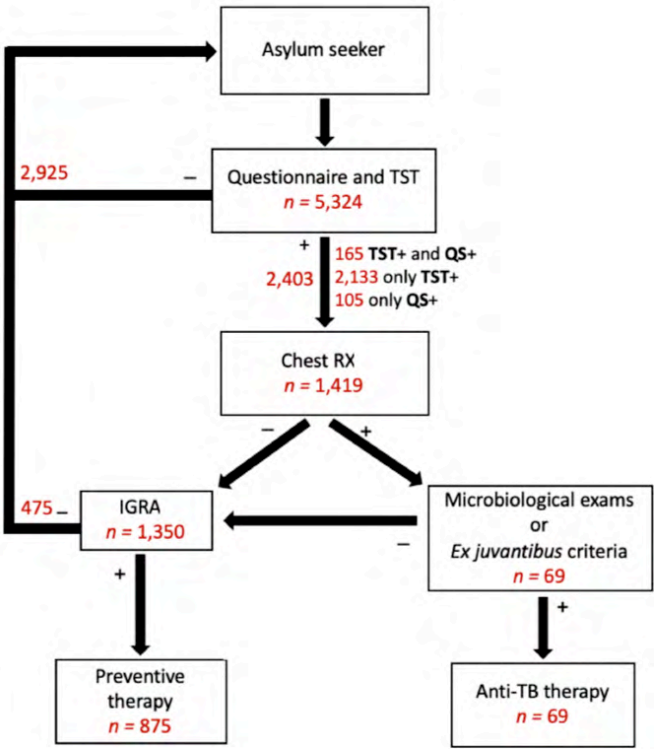

Figure 1 - Sequence of interventions in screening activities for the diagnosis and therapy of TB and LTBI

Sixty-nine active TB cases were diagnosed and 863 LTBI positive individuals were detected. The cumulative TB incidence was high (1,236/100,0000), namely among those coming from World Health Organization (WHO) – East Mediterranean Region (WHO-EMR) (3,043/100,000; IRR = 27; $p<.001$) and WHO – African Region (WHO-AFR) (1,033/100,000; IRR = 4; $p<.001$). LTBI prevalence was 28%, similar to that estimated in WHO-EMR (17%; $p=.545$) and WHO-AFR (32%; $p<.001$). Recent transmission (Figure 2) was observed in only three cases.

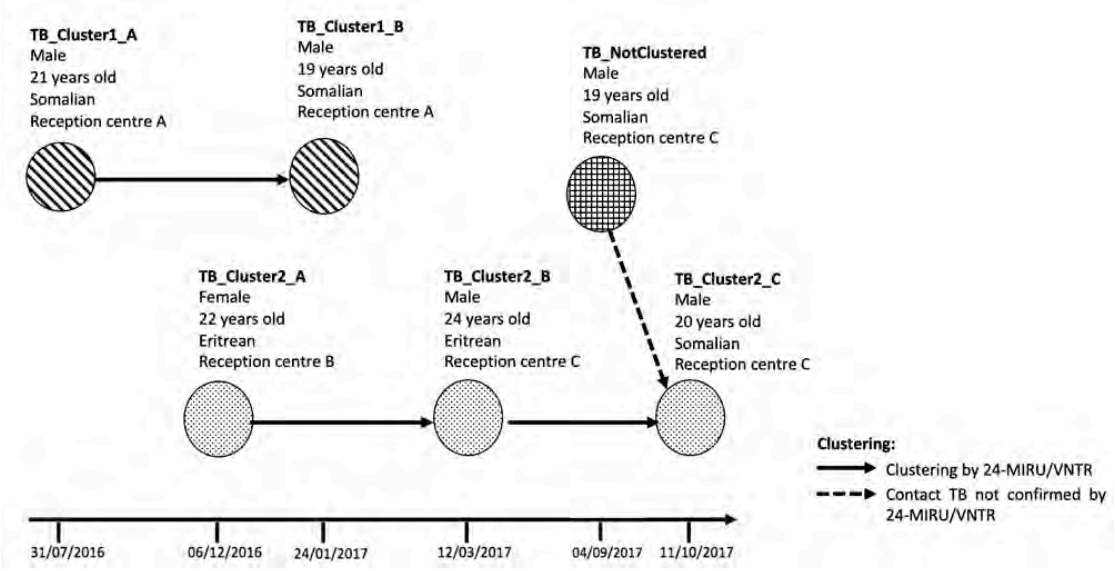

Figure 2 -TB transmission dynamic within Milan reception centres

Despite losses (41%) during the transition from initial screening sites to the diagnostic centre, high TB treatment success rate (85%) and excellent LTBI treatment acceptance (92%) and adherence (94%) were achieved.

Our study shows that TB incidence is high among AS in the Milan area and that well-coordinated screening measures are critical to early diagnosis and treatment. It also proves that rolling out successful at-scale interventions for both preventive therapy and disease management in such hard-to-reach populations is feasible. Maximising effectiveness through digital innovations that allow better inter-connectivity among involved services is a critical innovation to pursue.

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African patient with multi drug resistant, severe pulmonary Mycobacterium avium infection

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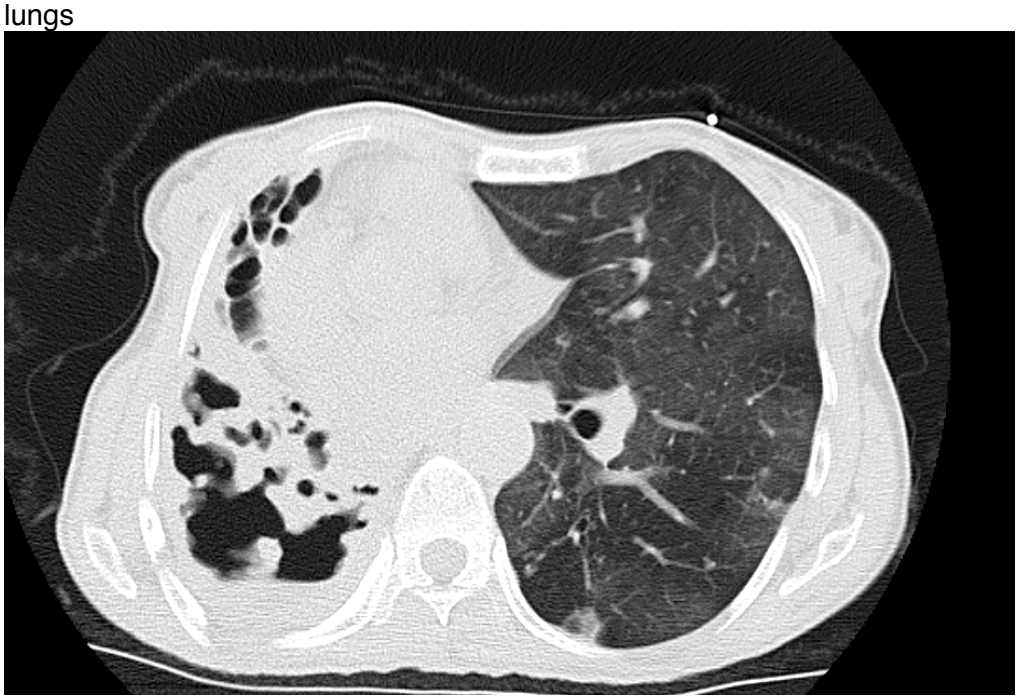
We report a case of a 52 years old HIV-negative female patient from Nigeria who presented with severe pulmonary Mycobacterium avium infection. There was no evidence of disseminated MAI disease . The patient had significant respiratory symptoms due to extensive destruction of both lungs



No image found for uniqueTag: MAI2 with chronic respiratory failure, severe pulmonary hypertension and pulmonary cachexia syndrome. Her past medical history revealed multiple episodes of tuberculosis infections and antimycobacterial treatments since the age of 26. Results of a definite laboratory diagnosis of TB nor susceptibility testing were not available. Opportunistic infections as well as infections due to Salmonella, VZV or fungal disease were denied.
MAC diagnosis was confirmed by acid fast staining, PCR and recurrent isolation of Mycobacterium avium from sputum and bronchial wash. Susceptibility testing confirmed Mycobacterium avium resistance to clarithromycin, moxifloxacin and linezolid but susceptibility to amikacin. Since the severe course of disease was suggestive of an underlying immunodeficiency, an extended immunological workup was performed. The presence of interferon gamma autoantibodies was detected. The patient presented with moderate lymphopenia (CD4 count 350/μl). Other relevant abnormalities in the cellular or humoral (normal or slightly elevated immunoglobulins) immune system were excluded. Repeated HIV screening test was negative.
A course of immunomodulatory therapy with rituximab was initiated in our patient. Our patient did not seem to benefit from this approach.
Our patient received a multidrug regimen consisting of rifampicin, ethambutol, intravenous amikacin and clofazimine. After four months intravenous amikacin administered in our outpatient parenteral antiinfective therapy (OPAT) program intravenous amikacin was switched to aerosolized liposomal amikacin as part of a compassionate use program. Antimycobacterial treatment was well tolerated. There was a partial clinical response with less sputum production. So far, cultures remained positive, but amikacin inhalation salvage therapy improved treatment response and allowed our patient to travel back and forth from Germany visiting friends and family in her home

country in Africa. The inhalative administration of amikacin was well tolerated. A positive effect on health outcome in the long term could be expected by offering the patient the opportunity to travel by avoiding a parenteral administration of amikacin.
This case highlights
a)the need of culture and susceptibility testing to confirm diagnosis and guide antituberculous treatment in case of complicated mycobacterial infections.
b)rare immunodeficiencies may mimic HIV-associated opportunistic infections and have to be taken in consideration in HIV-negative patients from every part of the world.
c)Regarding management of difficult-to-treat nontuberculous mycobacterial lung disease amikacin inhalation therapy could prove to be a valuable new treatment option.

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Increase of nasal colonization with MDR-staphylococci during hospitalization in a tertiary hospital in central Ethiopia

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Background: Staphylococcus species are a common cause of hospital acquired infections (HAI) and are frequently colonizing healthy individuals asymptomatically. They are among the bacteria commonly resistant to antibiotics and constitute a major global concern for patient safety. Nasal carriage of staphylococci, in particular *S. aureus*, is a known risk factor for HAI. Previous studies in Ethiopia showed a high prevalence of nasal colonization with methicillin-resistant organisms. However, the dynamics of colonization during an inpatient stay have not been studied. Since drug resistance can spread between different species of staphylococci, colonization with coagulase-negative staphylococci (CoNS) can serve as a reservoir of resistance genes.

Methods: We conducted a longitudinal observational study in order to determine the prevalence of nasal colonization with multidrug-resistant staphylococci among patients of Asella Teaching and Referral Hospital (ATRH) in Central Ethiopia. Consecutive patients admitted between May and August 2018 were included into the study. Demographic, socioeconomic and clinical data were collected by standardized questionnaires. Nasal swabs were collected upon admission and discharge. Samples were analyzed for methicillin-resistant staphylococci (MRS) at the Hirsch Institute of Tropical Medicine using CHROMagar MRSA. Biochemical testing, identification of colony morphology and gram staining were used for bacterial identification. Collected Data was analyzed with McNemars test and Chi-squared test for proportions and for the trend in proportions using IBM statistics SPSS version 24.

Results: A total of 607 patients was included with a median duration of the hospital stay of 5 days (IQR 3-9 days). Nasal swabs collected upon admission and discharge were available from 381 patients. In total, the rate of nasal colonization with MRS increased significantly from admission to discharge (17.3% vs. 54.2%, $p<0.001$). Upon differentiation, there was a significant increase in the nasal carriage rate of multi-resistant CoNS (MRCoNS) (15.2% vs. 51.6%, $p<0.001$), but not of methicillin-resistant *Staphylococcus aureus* (MRSA) (2.1% vs. 2.9%, $p=0.629$). We found an association (chi-square-test for trends in proportions) between the time spent in hospital and acquisition of a new colonization with methicillin-resistant CoNS ($p=0.008$) but not for MRSA ($p=0.6$). There were no differences in rates of colonization between different departments of the hospital.

Conclusions: We found a significant increase of nasal carriage of MRCoNS during hospitalization. Longer hospital stay was a risk factor for new MRCoNS colonization. There was no evidence for an in-hospital acquisition of MRSA. Nevertheless, strengthening of infection prevention strategies and hospital hygiene are needed to minimize the threat of nosocomial infections and transmission of multi resistant staphylococci within the hospital.

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Extended-spectrum beta-lactamase producing Gram-negative infections and associated mortality in Ethiopia: a systematic review and meta-analysis

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Introduction
Extended-spectrum beta-lactamase (ESBL)-producing Gram-negative bacteria have become a serious threat to global health. The impact is highest in resource-limited settings. The worldwide increase of ESBL-producing bacteria is associated with high mortality. To date, regular surveillance of multidrug resistant pathogens is not established in Ethiopia. For this report, published data regarding ESBL-producing bacteria in different regions of Ethiopia were systematically reviewed. To our knowledge, this is the first systematic review concerning infections and associated mortality caused by ESBL-producing bacteria in Ethiopia.

Methods
A literature search was conducted in PubMed, PubMed Central, Medline, Science Direct, and Google scholar from January 1990 to December 2018 using the following search terms: ESBL producing Enterobacteriaceae, infection, associated mortality, and Ethiopia. Searches were performed irrespective of study types and population by two independent investigators. Potentially relevant original articles were selected by the following inclusion criteria: Gram-negative bacteria pathogenic for humans, human subjects, ESBL producing bacteria defined by double-disk synergy or PCR methods, studies conducted in Ethiopia and published in English. Patient mortality associated with infections by ESBL-producing and or 3rd generation cephalosporins resistant Gram-negative bacteria was recorded.

Results
Twelve publications describing cross-sectional hospital-based studies qualified for review. All reported data on patients attending health care as in- or outpatients. In total, 1129 Gram-negative isolates from 4449 samples were included. The phenotypic pooled prevalence of ESBL among isolated Gram-negative bacteria (n=1079) was 50.3% (n=543). Among different species, ESBL rates were 90.9% (22/24) for Acinetobacter spp.; 75.8% (25/33) for Enterobacter spp., 61.8% (165/267) for Klebsiella spp., 46.2% (240/519) Escherichia coli, 44.6% (83/186) for Salmonella spp., 41.0% (7/17) for Citrobacter spp., 28.6% (14/49) for Proteus spp., and 30.0% (5/17) for others, respectively. The pooled rate of ESBL-producing Gram-negatives was estimated to be 43.7% (95% CI: 40.7%–46.7%). The heterogeneity between the different studies was significant (I^2 92.7 %, $p < 0.0001$). ESBL genes were confirmed in three studies, with blaCTX-M-1 and blaTEM being the predominately detected genes. Associated mortality was only reported in two studies. Here, 86% (12/14) of infected patients died.

Conclusions
In this meta-analysis, the pooled phenotypic prevalence of ESBL-producing Gram-negative pathogens is considerably high. Also, the mortality due to ESBL-producers is high but data is scarce. This highlights the need for establishing and upgrading of clinical microbiology laboratories in the country for routine antibiotic susceptibility testing. The capacity to detect ESBL genes is desirable for continuous surveillance of MDR.

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High rate of Extended-spectrum beta-lactamase producing bacteria among the Gram-negative isolated from patients with febrile illness in the Asella Teaching Hospital, Ethiopia.

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Background: Acute infectious diseases and sepsis are among the leading causes of mortality in Ethiopia. The lack of local data concerning causative pathogens and resistance patterns results in suboptimal empirical treatment and unfavorable clinical outcome. On the long run, an increase in multidrug resistant infections and healthcare service costs are possible consequences. The objective of this study was the characterization of bacterial pathogens in hospitalized patients with febrile infections in Central Ethiopia.
Materials/methods: In total, 684 patients ≥1 year of age with fever admitted to the Asella Teaching and Referral Hospital (ATRH) from April 2016 to June 2018 were included. Blood cultures and cultures from appropriate clinical specimens (e.g. urine, wound swabs) were investigated. Bacterial identification was based on biochemical properties and susceptibility testing was performed using Kirby-Bauer disc diffusion method and VITEK 2. Confirmation of species identification and identification of resistance-genes were conducted using MALDI-ToF and PCR in Germany.
Results: Of 684 study participants, 54% were male and mean age was 26.7 years. Forty-nine blood cultures were positive for bacteria and two grew Candida species. Thus, the overall culture positivity rate was 7.5%. In addition to blood cultures, 19 body fluids, 26 urine samples, 36 swabs of infected skin lesions were cultured with positivity rates of 16%, 27% and 61% respectively. Of 83 cultured organisms, 38 (46%) were Gram-negative, 43 (52%) Gram-positive and 2 (2%) Candida species. Among the 38 Gram-negative isolates, 16 (42%) were E. coli, 15 (39%) Klebsiella pneumoniae and 4 (11%) Pseudomonas aeruginosa. Of 27 Gram-negative available for resistance-gene detection, blaNDM-1 was detected in one K. pneumoniae isolate and blaNDM-1 plus blaOXA-51 in A. baumannii. Eighty-one percent (22/27) of the Gram-negative rods were confirmed to contain ESBL-genes as follows: blaTEM 17(77%), blaCTX-M-1 15(68%), blaSHV 6(27%) and blaCTX-M-9 2(9%). Among ESBL-isolates, 11(50%) contained both blaCTX-M-1 and blaTEM genes.
Conclusions: We found a high prevalence (81%) of ESBL-producing bacteria and 7.4% carbapenem-resistance at the study site. More than half of Gram-negative isolates had two or more mobile resistance genes. These findings warrant the need for local national multi-drug resistant surveillance and revision of local antibiotic treatment protocols. Strengthening of antimicrobial stewardship programs are needed in order to face the threat of multi drug resistant bacteria.
Key words: ESBL, carbapenem resistant, multi-drug resistant, Ethiopia.

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High rate of anal colonization with Extended Spectrum β-Lactamase (ESBL) producing Gram-negative bacteria among hospitalized patients in Central Ethiopia

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Background: A rapidly evolving group of beta-lactamase enzymes commonly produced by Gram-negative bacteria is of great concern for expansion of drug resistance and life threatening infections. Persons regularly presenting to health care institutions are at risk for colonization with such resistant bacteria, but little is known on the acquisition of colonization during an inpatient stay. The objective of this study was to assess the dynamics of colonization rate with ESBL during hospitalization at a tertiary hospital in Central Ethiopia.

Methods: A longitudinal observational study was conducted, including patients admitted to the various wards of the Asella Teaching and Referral Hospital (ATRH) from May to August 2018. Trained nurses took anal swabs immediately after admission and before discharge, using eSwab™ liquid amies preservation medium (COPAN Italia spa, Brescia, Italy). The swabs were examined for Gram-negative bacteria using CHROMagar™ ESBL medium (CHROMagar, Paris, France). Bacterial identification was done based on biochemical properties and agar dilution was used for antibiotic susceptibility testing.

Results: A total of 607 patients were included in the study. 63% of the participants were females. The average hospital stay was 6.8 ± 5.6 days. Anal swabs were available from 91.4% (n=555) patients at admission and from 52.4% (n=318) patients at discharge. Of the 555 swabs cultured on admission on medium for 3rd generation cephalosporin resistant Gram-negative bacteria, 60.5% (n=336) showed single or polymicrobial growth. The total number of identified bacterial species was 401, of which *E. coli* were most common (60.1%, n=241). The other isolated organisms were: *Klebsiella spp.* (19.5%, n=78), *Acinetobacter spp.* (7.7%, n=31), *Citrobacter spp.* (5.5%, n=22), *Enterobacter spp.* (3%, n=12) and *Morganella spp.* (2.2%, n=9). Cultures from the 318 anal swabs collected from patients at discharge showed growth of one or more bacterial species in 84.6% (n=269). Of those, 78.8% (n=212) were identified as *E. coli*, 39.8% (n=107) as *Klebsiella spp.*, 15.6% (n=42) as *Citrobacter spp.*, and 4.8% (n=13) as *Enterobacter spp.* The colonization rate with ESBL producing Enterobacteriaceae significantly increased during the hospital stay (60.5% vs. 84.6%, p<0.001). This increase was also shown for the most commonly isolated organisms, *Escherichia coli* (60.1% to 78.8%, $p < 0.001$) and *Klebsiella spp.* (19.5% to 39.8%, $p < 0.001$).

Conclusion: Colonization rates with ESBL-producing bacteria increased significantly between hospital admission and discharge, with *E. coli* and *Klebsiella spp.* being the most commonly identified bacteria. Extended antimicrobial resistance acquired throughout a hospital stay is potentially leading to hospital-acquired infections associated with clinical complications. Ongoing surveillance, strengthening of infection prevention and hospital hygiene and the introduction of antimicrobial stewardship programs are needed to address this problem.

P30

Prevalence of *H. pylori* infection and efficacy of triple eradication therapy among HIV positive and HIV negative individuals in Central Ethiopia

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Introduction

Gastric *H. pylori* infection and related pathologies are common in Ethiopia and many other regions of sub-Saharan Africa. Besides the known gastrointestinal pathologies, *H. pylori* infection has been associated with iron deficiency anemia and immune modulation.

Objective

To evaluate the prevalence of *H. pylori* infection and the efficacy of the recommended eradication therapy, as well as the effect of *H. pylori* eradication on hemoglobin levels and CD4 cell count among HIV positive and negative patients in the Asella Teaching and Referral Hospital in Central Ethiopia.

Methods

In this interventional prospective study, 306 HIV positive and 201 HIV negative participants were screened for *H. pylori* infection using a stool antigen rapid test kit (GA Generic Assays GmbH, Germany). Results were confirmed using a stool antigen ELISA (Serazym *H. pylori* 2nd Gen. ELISA, VIROTECH Diagnostics GmbH, Germany). 70 *H. pylori* positive participants each from the HIV positive and negative group were randomized to receive *H. pylori* eradication therapy (metronidazole 500 mg bid, clarithromycin 500 mg bid and pantoprazole 40 mg bid for 14 days) or to the control group, not receiving *H. pylori* eradication therapy. Clinical examination, blood count and CD4 cell count were done at baseline and follow-up after three and six months.

Results

The prevalence of *H. pylori* among HIV positive and HIV negative participants was 78.7% and 75.1%, respectively according to the rapid test results (see Table 1). 27 HIV positive and 25 HIV negative participants received *H. pylori* treatment after randomization and were eligible for analysis of follow-up investigations. Of those, eradication was successful in 33.3% (n=9) HIV positive and 68.0% (n=17) HIV-negative participants (p=0.025). In HIV positive patients, there was no significant difference in CD4 cell counts 6 months after eradication (663 ± 331.1 cells/µl vs. 628 ± 274.7 cells/µl, p=0.66), no difference was also observed in the control group of HIV positive participants who did not receive H. pylori eradication therapy. In the group of participants successfully eradicated from *H. pylori* (irrespective of HIV status), there was a significant increase in hemoglobin levels 6 months after eradication (14.4 ± 2.0 g/dl vs. 14.9 ± 1.8 g/dl, p=0.030). No difference was observed in the control group.

Table 1. Prevalence of *H. pylori* among different variables, Asella Teaching Hospital, Ethiopia

Variables		*H. pylori* status		p-value
		positive n (%)	negative n (%)	
Sex				0.657
	Male	140 (78.7)	38 (21.3)	
	Female	252 (76.6)	77 (23.4)	
Age group				**0.043***
	<20	22 (84.6)	4 (15.4)	
	21-30	108 (81.2)	25 (18.8)	
	31-40	134 (70.5)	56 (29.5)	
	>40	128 (81.0)	30 (19.0)	
HIV status				0.386
	HIV positive	241 (78.8)	65 (21.2)	
	HIV negative	151 (75.1)	50 (24.9)	

* Statistically significant

Conclusion

We found a high *H. pylori* prevalence and low efficacy of triple eradication therapy, especially among HIV co-infected patients. Successful eradication of *H. pylori* was associated with a significant increase in hemoglobin level, but not with changes in CD4 cell count. The results have to be interpreted with caution, considering the small number of HIV positive participants which have been successfully eradicated from *H. pylori*.

P31

Getting concrete: What can antibiotic stewardship deliver? A pilot study in sub-Saharan Africa on WHO's Integrated Management of Childhood Illness

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Objective: The aim was to assess if adherence to guidelines on antimicrobial therapy prevents patients from acquiring resistant bacteria in a sub-Saharan African setting. We therefore prospectively analysed the antibiotic prescriptions in accordance with a national guideline and investigated the effects of prescribed antibiotics (AB) on colonisation with antimicrobial resistant bacteria.

Methods: We included children presenting at first-level health care facilities in Lambaréné (Gabon) in a prospective cohort study and analysed if ABs were prescribed according to the national version of WHO's Integrated Management of Childhood Illness (IMCI), which incorporates an antibiotic stewardship.
Rectal swabs taken on the day of medical consultation (baseline), after one and after two weeks were screened for antimicrobial resistant bacteria, in particular extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-E).

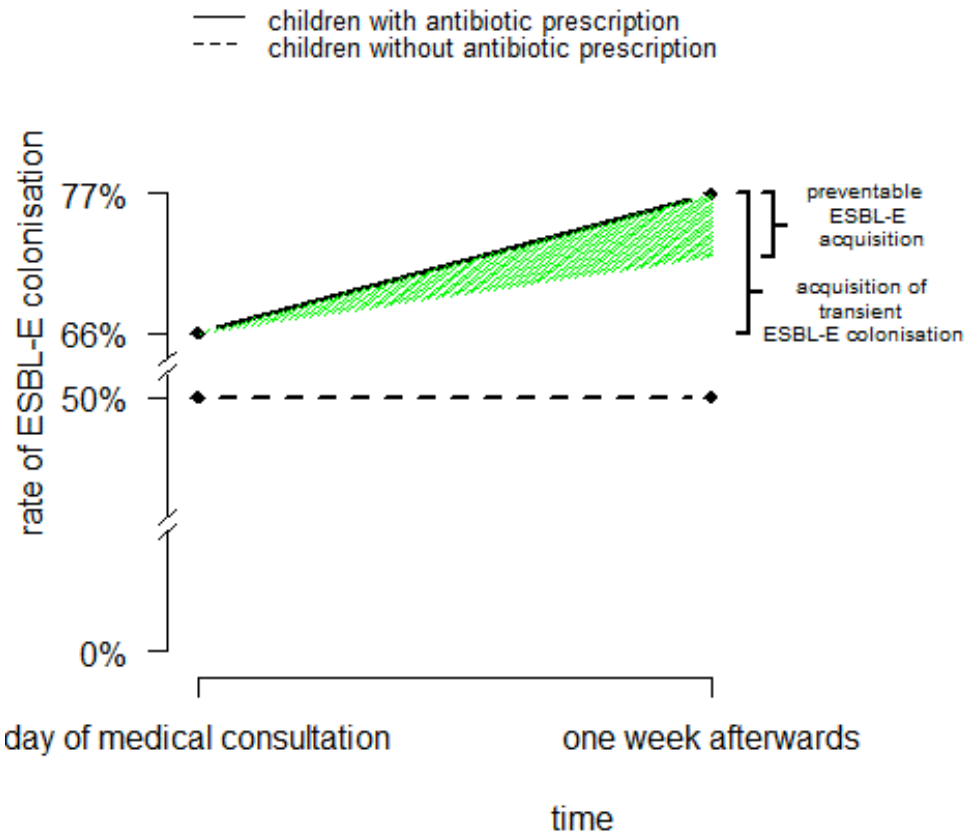
Results: In our study population (n=47), the antibiotic prescription rate was 74% (n=35). According to IMCI, 22 of 35 (63%) antibiotic prescriptions were unnecessary. On the other hand, IMCI had suggested antibiotic therapy in five cases (42%) for the 12 children without antibiotic prescription. Thus -if health professionals adhered to IMCI- the antibiotic prescription rate could be reduced to 38% (18 of 47; confidence interval, 25% - 54%).
In patients without antibiotic prescription, the rate of ESBL-E colonisation did not differ between baseline (6 of 12; 50%) and after one week (6 of 12; 50%). In the group of children with antibiotic prescription the ESBL-E colonisation rate rose from 66% (23 of 35) on the day of inclusion to 77% (27 of 35) after one week. After 2 weeks (n=37), the ESBL-E colonisation rates were similar in both groups (no AB: 8 of 12; 67% vs. AB: 16 of 25; 64%).
We then calculated that if the IMCI guideline had been followed, 2 of 47 children (4%; confidence interval, 1% - 15%) could have been prevented from acquiring ESBL-E colonisation after one week.

Conclusion: Our pilot study suggests that -besides limiting antibiotic prescriptions- antibiotic stewardship might have the potency to reduce colonisation with antimicrobial resistant bacteria. It also highlights the need for regular assessments of the impact of guidelines on relevant outcomes.

	Patients with antibiotic prescription:	**Patients without antibiotic prescription:**	Total:
Patients in need of an antibiotic according to IMCI	13	5	18 (38%)
Patients not in need of an antibiotic according to IMCI	22	7	29 (62%)

Total:	35 (74%)	12 (26%)	47 (100%)

Patients with and without antibiotic prescription: Analysis of accordance with IMCI



Transient acquisition of ESBL-E colonisation in children with and without antibiotic prescription - including an overlay of possible prevention

P32

Comparison effect of Honey bee venom on Pathogen bacteria compared with Common antibiotics

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Statement of the Problem: In recent years, antibiotics resistance has been spreading considerably, so that it is becoming a severe problem in modern medicine. Animal venoms possess antibacterial properties among which honey bee venom shows anticancer, anti-inflammation and antimicrobial properties. The aim of this study in to investigate the effect of unrefined bee venom on some species of pathogen bacteria compare with common antibiotics. Methodology & Theoretical Orientation: Honey bee venom was collected and different concentrations were applied against Staphylococcus aureus, Pseudomonas aeruginosaand Klebsiella pneumonia using disk diffusion method. Then MIC and MBC were calculated compared with 3 common antibiotics. Comparison between concentrations was analyzed in 24, 48 and 72 h. Findings: Results showed that different bee venom concentrations possess inhibitory effect on pathogen species. Among these pathogens, K. pneumonia was the most sensitive against the venom, P.aeruginosa was the most resistant one and the venom had the most effect on S.aureus and K. pneumonia. Comparison between the venom with common antibiotics revealed that the venom possess a low effect while Tetracycline showed a better effect on P.aeruginosa compared with the venom and other antibiotics. Conclusion & Significance: Results showed that honey bee venom has generally antimicrobial properties on pathogens. So more accurate toxicology examinations and derivation its compositions can help us to formulate new natural antibiotics.

P33

12 years of experience in “Barrier Nursing Training” – a review

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At the end of the last century, when smallpox was finally eradicated and infectious diseases faded more and more out of the spotlight, representatives from various institutions in Germany began to wonder again how to deal with the unlikely case of an imported highly contagious disease or with extraordinary epidemic events. In 1998, a working group “Disease Control” was constituted and in 2000, the Act for Prevention and Control of Infectious Diseases in Humans specified that the individual federal states must provide premises for patients with highly infectious, life-threatening illnesses. In addition to the creation of suitable structural conditions and the introduction of protective measures and clothing, the staff had to be trained in a suitable way.
In 2003, the Bundeswehr Medical Service performed the first training in „Barrier Nursing”. The intention was to create awareness for the necessity of preventive measures, although nobody thought, that it would ever be required. Accordingly, the approach was very theoretical. Step by step the focus shifted to the problem of the management within a hospital or health centre. Adapted to all mission areas, plans were created how to handle patients with suspected highly contagious diseases and exercises were performed. But there has never been an actual challenge.
In the Ebola Epidemic in 2014, the Bundeswehr Medical Service became an essential part of the humanitarian aid provided by the German Red Cross and the Bundeswehr in Western Africa (HumHiWa). The challenge was to prepare a lot of people with different knowledge and experience for their task in an Ebola outbreak area as fast as possible. The solution was a modular training that could be arranged according to the needs of each respective group. The experience gained with this form of training was complemented by participation in trainings of WHO, MSF and the Liberian Ministry of Health. More experience with cross-cultural and international training was acquired in work-shops held in Ghana, Tunisia and India on various occasions.
The training for the missions today is kept as simple as possible. The focus is no longer on specific diseases, but on the ways of transmission and the resulting outbreak management. Restriction to basic principles like these enables everybody to be trained and thus “Barrier Nursing” can be implemented in every setting and under all conditions at least temporarily.
Bullet points
• The only salvation is cooperation
• Enlightenment will overcome fear.
• A few experienced persons are sufficient to form a team.
• Drill fights mistakes due to tiredness and habituation.
• The crucial moment is doffing (taking off the PPE).

P34

Yellow Fever Vaccination during methotrexate treatment - a prospective controlled multi-centre study

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Background
The percentage of travelers using immunosuppressive agents is increasing. However, the administration of live vaccines, such as yellow fever vaccination (YFV), to immunodeficient patients bears the risk of replication of the attenuated vaccine microorganism and clinically manifest infection. Therefore, most international guidelines state that YFV is contraindicated in patients on immunosuppression. In Switzerland, new vaccination recommendations were published in 2014. According to these guidelines, YFV may be administered to patients on low dose methotrexate (MTX) therapy (≤20mg/week). The recommendation is based on common practice in several Swiss travel centers, where YFV has been routinely administered to travelers under low-dose MTX without unexpected side effects. However, solid data were missing. In this pilot study, viremia and antibody production after YFV is compared between travelers on low dose MTX therapy and healthy travelers.
Methods
A multi-center controlled observational prospective study was conducted in Switzerland between 2015 and 2017. We enrolled 16 adult patients on low dose MTX therapy who needed a first-time YFV and age-and sex matched healthy controls (HCs).
Safety assessment: On days 3, 7, 10, 14 and 28 vaccination serum samples were collected for viremia measurement. Furthermore, participants were asked to fill in a diary card with regular assessment of local and systemic side effects over the first 10 days after YFV. In addition, side effects were assessed during clinical visits for 4 weeks after vaccination by site staff.
Immunogenicity assessment: Before vaccination and on days 7, 10, 14 and 28 after vaccination serum samples were collected to determine neutralizing antibodies. Laboratory assessment was performed at the Clinical Microbiology Laboratory, Leiden University Medical Center.
Results
Median age in MTX patients and controls was 53 years. In both groups, ten participants were female and six male. Median MTX dosage was 12.5mg with a range of 7.5 to 20mg.
Safety: Solicited local and systemic reactions were comparable between patients and HCs with 38% of controls and 40% of MTX patients experiencing a local reaction (P=0.99), and 69% (HCs) vs. 87% (MTX patients) reporting a systemic reaction (P=0.39). Four MTX patients and eight healthy controls had an unsolicited reaction (adverse event, AE). Two AEs in MTX patients and one AE in a HC were of moderate severity; all others were mild. Two mild adverse events in HCs were possibly associated with YFV (headache, abdominal pain). No serious adverse events occurred. No signs of infection with the vaccine strain occurred.
Laboratory assessments for immunogenicity and safety:
Slightly more subjects on MTX developed viremia after YFV. Viremia occurred between day 3 and 10 post-YFV and was low in both groups.
Neutralizing antibodies developed later in MTX patients. 28 days post-YFV all participants had protective antibody titers.

P35

Envelope-specific epitope recognition patterns of HIV vaccine-induced IgG antibodies are linked to immunogen structure and sequence

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Abstract
Background: A better understanding of the parameters influencing vaccine-induced IgG recognition of individual antigenic regions and their variants within the HIV Envelope protein (Env) can help to improve design of preventive HIV vaccines.

Methods: Env-specific IgG responses were mapped in samples of the UKHVC003 Standard Group (UK003SG, n=11 from UK) and TaMoVac01 (TMV01, n=17 from Tanzania) HIV vaccine trials. Both trials consisted of three immunizations with DNA, followed by two boosts with recombinant Modified Vaccinia Virus Ankara (MVA), either mediating secretion of gp120 (UK003SG) or the presentation of cell membrane bound gp150 envelopes (TMV01) from infected cells, and an additional two boosts with 5μg of CN54gp140 protein adjuvanted with glucopyranosyl lipid adjuvant (GLA). Env immunogen sequences in UK003SG were solely based on the clade C isolate CN54, whereas in TMV01 these were based on clades A, C, B and CRF01AE. The peptide microarray included 8 globally representative Env sequences, CN54gp140 and the MVA-encoded Env immunogens from both trials, as well as additional peptide variants for hot spots of immune recognition.

Results: After the second MVA boost, UK003SG vaccinees almost exclusively targeted linear, none-glycosylated antigenic regions located in the inter-gp120 interphase. In contrast, TMV01 recipients most strongly targeted the V2 region and an immunodominant region in gp41. The V3 region was frequently targeted in both trials, with a higher recognition magnitude for diverse antigenic variants observed in the UK003SG ($p<0.0001$). After boosting with CN54gp140/GLA, the overall response magnitude increased with a more comparable recognition pattern of antigenic regions and variants between the two trials. Recognition of most immunodominant regions within gp120 remained significantly stronger in UK003SG, whereas V2-region recognition was not boosted in either group.

Conclusions: IgG recognition of linear antigenic Env regions differed between the two trials particularly after the 2nd MVA boost. Structural features of the MVA-encoded immunogens, such as secreted, monomeric gp120 versus membrane-anchored, functional gp150, and differences in prime-boost immunogen sequence variability most probably contributed to these differences. Prime-boosting with multivalent Env immunogens during TMV01 did not improve variant cross-recognition of immunodominant peptide variants in the V3 region.

P36

Visualising Virus-T cell Interactions in lymphoid Tissues using combined in situ Hybridisation and fluorescence Immunohistochemistry

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Secondary lymphoid organs play an important role in the pathogenesis of HIV, with the gut-associated lymphoid tissues being a key anatomical site for virus replication. The analysis of cells derived from lymphoid tissues by polychromatic flow cytometry and molecular methods has yielded valuable insight into the cell types involved in the immune response against HIV as well as into the virus preferred target cells. These methods, however, cannot provide information on the spatial localisation of infected cells within tissues or other parameters such as cellular shape, polarisation, and interactions with other cells. In order to determine the localisation and phenotype of productively HIV-infected cells within lymphoid tissues, we set out to establish a dual protocol for the detection of total HIV mRNA by *in situ* Hybridisation (ISH) and cellular markers by fluorescence immunohistochemistry (IHC). To this end, we applied the novel ISH technique RNAscope to formalin-fixed paraffin embedded (FFPE) sections of mesenteric lymph nodes and spleen of HIV-1 infected humanised mice as well as to ileum biopsies of HIV-1 infected patients. Total HIV-1 RNA was detected using a subtype B specific probe and visualised fluorescently. ISH was followed by a standard multiplex fluorescence IHC for cellular lineage markers such as CD3, CD4, and FoxP3, or functional markers such as Granzyme B. This combined method allows us to determine the localisation of HIV-1 infected cells within tissue samples with intact morphology, as well as to study phenotypic characteristics of productively HIV-1 infected cells and their interaction partners.

P37

Effects of *H. pylori* infection on immune activation and regulation of T-lymphocytes

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Introduction
H. pylori is estimated to infect about half of the world's population. Gastrointestinal microbiota has been identified as an important determinant of the immune response, and there is evidence that *H. pylori* infection is associated with systemic immune modulation and progression of HIV-disease. Such a correlation could have major clinical implications, considering the importance of immune activation for a wide spectrum of pathologies.
Objective
To investigate the influence of *H. pylori* infection on markers of immune activation and modulation on T-lymphocytes of HIV-positive and negative individuals
Methods
We report the baseline data of an ongoing prospective study on the effect of *H. pylori* eradication on clinical and immunological parameters in HIV-positive and negative individuals. In randomly selected HIV negative individuals presenting to the voluntary counseling and testing (VCT) unit and HIV positive patients of the antiretroviral therapy (ART) clinic of the Asella Teaching and Referral Hospital in Arsi Zone of Ethiopia, peripheral blood mononuclear cells (PBMCs) were isolated from EDTA blood for the characterization of T lymphocytes. After isolation, PBMCs were stored at -80°C and transported on dry ice to Germany. Using flow cytometry (FACSCanto II flow cytometer, Becton Dickinson, USA), the expression of markers of T cell subpopulations (e.g. regulatory T cells, Treg, and T helper 17 cells, Th17), immune activation (e.g. HLA-DR, CD38) and exhaustion (e.g. PD-1) was assessed (see Table 1). *H. pylori* status of study participants was determined using a stool antigen test (Serazym *H. pylori* 2nd Gen. ELISA, VIROTECH Diagnostics GmbH, Germany) and immune markers were compared according to *H. pylori* status.
Results
Among 63 HIV-positive and 24 HIV-negative individuals, 50% and 81% were *H. pylori* positive, respectively. Mean age was 33.97 + 10.68 and 39.42 + 7.75 years and 50% and 66.6% were female, respectively. All HIV-positive study participants received ART. No HIV-1 viral load measurements were done. We found significantly lower markers of immune activation (HLA-DR+CD38+, 2.73% vs. 7.31 %, p= 0.048) and higher percentage of Treg (CD25+Foxp3+, 7.73 % vs. 2.99 %, P= 0.027) on CD4+ T-lymphocytes of HIV-negative individuals with vs. without *H. pylori* infection (see Table 1). Those differences were not observed in HIV positive individuals.

Table 1. Immunological Parameters According to HIV and *H. pylori* infection Status

Variables	HIV negative			HIV positive		
	H. pylori negative (n=12) Median %(IQR)	*H. pylori* positive (n=51) Median %(IQR)	P-value	*H. pylori* negative (n=11) Median %(IQR)	*H. pylori* positive (n=13) Median %(IQR)	p-value
Ki67+CD4+	37.0 (11.06-84.37)	22.5 (5.31-46.40)	0.128	40.8 (19.8-55.2)	23.7 (15.3-45.9)	0.729
Ki67+CD8+	22.95 (2.16-33.87)	5.06 (2.81-11.1)	0.478	10.2 (4.37-13.8)	6.88 (3.56-11.82)	0.817
HLA-DR+CD38+CD4+	7.31 (2.39-15.52)	2.73 (1.37-6.78)	**0.048***	6.35 (4.78-8.94)	7.63 (4.79-15.2)	0.214
HLA-DR+CD38+CD8+	3.50 (1.53-12.83)	1.97 (1.29-4.41)	0.231	1.27 (1.0-2.63)	2.15 (1.11-2.59)	0.419
CD57+CD4+	5.51 (2.48-13.42)	4.97 (3.12-9.23)	0.958	4.86 (1.3124.3)	3.45 (1.37-6.15)	0.248
CD57+CD8+	41.25 (34.2-60.25)	39.8 (30.5-53.4)	0.739	34.3 (28.9-48.3)	35.6 (20.85-44.5)	0.686
PD1+CD4+	6.55 (4.32-10.33)	6.91 (5.02-10.8)	0.726	11.2 (7.49-20.7)	10.7 (8.1-19.3)	0.817
PD1+CD8+	1.34 (0.5-1.74)	0.79 (0.51-1.5)	0.358	1.63 (1.09-2.79)	2.05 (1.39-3.93	0.094
TIM3+CD4+	1.4 (0.83-3.24)	0.89 (0.42-1.66)	0.07	1.194 (0.78-2.58)	1.67 (1.18-4.54)	0.564
TIM3+CD8+	1.72 (0.97-2.39)	2.01 (0.91-3.21)	0.593	2.6 (2.12-4.72)	3.83 (2.17-7.13)	0.204
CD25+Foxp3+CD4+	2.99 (1.0-4.44)	7.73 (3.53-15.7)	**0.027***	4.39 (2.76-9.45)	6.18 (3.44-10.11)	0.908

* Statistically significant

Conclusion

We found an association of *H. pylori* infection with reduced markers of immune activation on CD4+ T-lymphocytes and increased percentages of regulatory T cells in HIV negative, but not in HIV positive individuals. The results have to be interpreted with caution, considering the low case numbers and the heterogeneity of the HIV positive study population. The immunological implications of H. pylori infection and the effect of *H. pylori* eradication on the immune response will be further investigated within this study.

P38

Mobile instant messaging facilitates clinical consultation and training in HIV care in resource-limited settings

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Background: In resource-limited settings many HIV-infected patients are on antiretroviral therapy (ART) following standardized guidelines. However, some HIV-infected patients, especially those with advanced HIV-related diseases, need specialized individual care that is not represented in guidelines. Training opportunities for health care providers on advanced HIV care are limited. Mobile instant messaging (MIM) offers an easily accessible virtual learning platform free of charge and requiring only a limited bandwidth. MIM has therefore been reported as successful telemedicine and learning tool with special attractiveness for the resource-limited setting.
Objective: To evaluate the educational content and acceptability of MIM as a training and telemedicine tool for HIV care providers in Malawi.
Methods: The project was run at the Lighthouse Clinic treating more than 45,000 HIV patients in Malawi. A MIM messaging group using WhatsApp® was created and moderated by an infectious disease consultant. All clinical officers with access to a smartphone were invited to join the group. The pre-defined MIM group agreement was that questions encountered in the clinics should be shared immediately, that interesting or instructive cases should be shared for educational purposes, and that identifying data is not be posted. Additionally the moderator posted educational cases. MIM conversation was analyzed to describe threads discussed and features of its use. To further understand MIM acceptance and perception by the users in-depth interviews were performed.
Results: The MIM group comprising 21 clinical officers was actively utilized with an average of 2.3 threads/week over the observation period of 15 months. The median number of posts per thread was 10 (min-max 1-52), the median number of active participants per thread was 4 (1-16). Most frequently discussed topics related to tuberculosis (25 threads), adverse drug reaction (22 threads), ART (21 threads), cryptococcal meningitis (12 threads), and drug dosing/logistics. In 20.3% of the threads at least one image file was shared, mainly clinical pictures of skin conditions (10.5%) and chest x-ray images (8.3%). In-depth interviews showed that clinical officers accepted and appreciated MIM group as telemedicine consulting and training tool.
Conclusions: MIM was a successful and well accepted telemedicine tool for support and training of clinical officers providing HIV care in a resource-limit setting. MIM may be integrated in blended training strategies to expand knowledge of HIV care providers.

P39

Systematic HIV care for medical inpatients in a government referral hospital in Malawi: One year results - Inpatient HIV testing and linkage into care

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Background: The HIV prevalence among adults aged 15-64 in Lilongwe district Malawi, is estimated at 11.5%1. Kamuzu Central Hospital (KCH) is a referral hospital in Lilongwe with a catchment population of over 5 million people and is funded through the Ministry of Health (MoH), but resources are often limited. Lighthouse (LH) is a Public Trust for integrated HIV prevention, treatment and care operating on KCH grounds. LH is also funded through MoH but receives significant additional vertical funding from the President's Emergency Plan for AIDS Relief (PEPFAR).

Objective: To implement a system supporting diagnoses and care of inpatients with HIV disease and achieve maximum HIV testing coverage through provider-initiated testing and counseling in medical wards.

Methods: Two HIV-diagnostic assistants (HDA) were full time seconded from LH to the medical wards. Daily, all newly admitted patients identified from ward and admission registers were attempted to be counseled and (re-) tested. Patients already on ART were identified and counseled. If patients were not tested reasons were recorded. The HDA escorted all confirmed HIV positive patients to the HIV care room for enrollment in the national ART program; this was recorded as successful linkage to care. The HDAs used a data sheet to monitor testing coverage, yield and linkage-to-care.

Results: In 2017, 6645 admissions were recorded on the medical wards (Figure 1). 13.2% of the patients died before they were seen by HDAs (e.g. admissions that occurred during weekends). 24.3% were already on ART; the remaining patients were eligible for testing. 3389 (81.6%) patients were tested; reasons for not testing were untraceability (9.4%) or discharge by the time the HDA came to test (8.3%). Only a very small minority of patients (0.7%) declined to be tested. 184 patients tested newly positive (test-yield 5.5%). The number of confirmatory positive tests was higher as some patients had tested previously in other health settings, but had not yet initiated care. Of the 240 patients with a positive confirmatory test, 85.4% were successfully linked to the HIV care.
Of all inpatients with ascertained HIV status, 1854 were HIV positive (including new positives and patients previously on ART) amounting to an inpatient HIV prevalence of 37.0%.

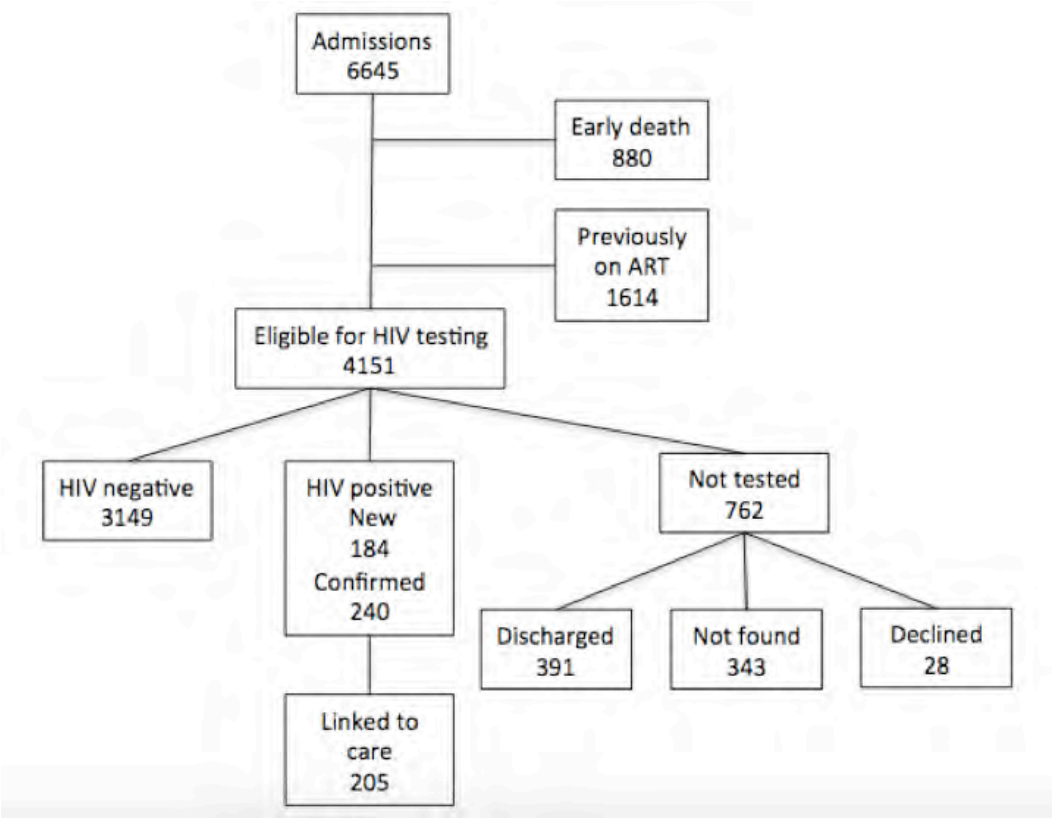

Figure: Medical inpatients HIV testing and linkage-to-care flow

Conclusion: Through this systematic approach the HIV status could be ascertained for a large proportion of inpatients. Nevertheless a significant number of patients were still missed. The yield of newly diagnosed HIV patients was below the estimated regional HIV prevalence. The total HIV prevalence in medical inpatients was more than three times higher than the regional prevalence. Vertically funded HIV programs can successfully support inpatient HIV care.

1Ministry of Health, Malawi. Malawi Population-based HIV Impact Assessment (MPHIA) 2015-16. November 2017

P40

Expansion of HIV Testing in Eswatini: Factors Underpinning Success

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Background
As reported at the 9th International AIDS Conference in July 2017, Eswatini achieved a drop in incidence of 44% between 2011 and 2016 and 85% of people living with HIV know their status. As other countries work to achieve the first 90 target – diagnosing 90% of people with HIV by 2020 – Eswatini's experience and success is highly relevant. This study examines facilitators and barriers to HIV testing services (HTS) uptake over the course of the HIV epidemic.

Methods
This qualitative report draws on (26) semi-structured in-depth interviews with key stakeholders including individuals from the government sector, implementation and donor sectors, local advocacy organizations and academic institutions. Respondents demographics by which results were positioned include time working in the HIV field, experience outside of Eswatini and government versus non-governmental.

Results
In terms of facilitators to improved testing, respondents highlighted the strong political will and governmental commitment to combat the epidemic, task shifting HIV testing to lay counsellors, regionalization of partners who implement health-related programs, and the support and guidance of international policy makers. For HIV testing specifically, a shift to universal testing, the advent of an opt-out policy as well as an incorporation of HIV testing in all entry points to the health system led to increases in terms of testing and mitigated issues of testing stigma. Respondents viewed HIV self-testing and index testing as promising approaches in terms of reaching untested populations.

Stigma was widely regarded as barrier for HIV testing uptake, with a recent shift towards self-stigma. Key populations remain at a heightened risk of acquiring HIV but progress is being made in terms of reaching them. Respondents from the non-governmental sector voiced concerns about future sustainability and funding and also viewed governmental organization as ill-equipped to stem the whole HIV response. Most respondents repeatedly mentioned the need for a transition plan as a high priority. In regard to new testing methods concerns remain over linkage to care and ensuring that individuals who test positive return for treatment. Respondents also described concerns that due to the feminization of the epidemic, clinics and health centers often cater to female patients, but this approach ostracizes men and young adolescents, the groups that are lagging behind most in terms of being tested for HIV.

Conclusions
Stakeholders across the respondent groups were quite homogenous in their views about facilitators and barriers of HIV testing uptake. The recommendations to other countries overlapped a lot with the facilitators named by the respondents. Even though the relatively small size of the country was acknowledged, the factors increasing HTS uptake were seen as replicable in other settings as well.

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Methoden zur Diagnose der Leberfibrose bei chronischer Hepatits C - minimal invasives Verfahren

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Chronische Hepatitis C (CHC) ist eine häufige Erkrankung mit einem hohen Risiko des Übergangs zur Leberzirrhose und zum hepatozellulären Karzinom. Der Hauptfaktor für das Fortschreiten des chronischen Prozesses ist die Fibrose.

Ziel: Untersuchung der Rolle von Serummarkern der Fibrose bei Patienten mit chronischer Hepatitis C als Kriterium für das Fortschreiten der Erkrankung.

Materialien und Methoden. 79 Patienten mit chronischer Hepatitis C wurden beobachtet. Das Stadium der Leberfibrose wurde unter Verwendung des GenoFibroTest-Systems (METAVIR-Skala) bewertet, bei dem vier Leberfibrosestadien isoliert werden: keine Fibrose (F0), Pfortelfibrose ohne Septen oder minimale Fibrose (F1), Pfortelfibrose mit einzelnen Septa oder abgestorbene Fibrose (F2), multiple portocentrale Septen ohne Zirrhose oder ausgeprägte Fibrose (F3), Leberzirrhose (F4). Dazu wurde der Gehalt an alpha2-Makroglobulin, Haptoglobin, Apolipoprotein A1, Gesamtbilirubin sowie die Aktivität von Gamma-Glutamyltranspeptidase (GGT) und Alaninaminotronase (ALAT) im Serum von Patienten mit CHC geschätzt. Die statistische Verarbeitung der erhaltenen Daten erfolgte mit modernen statistischen Methoden: ROC-Analyse (Receiver Operating Characteristic) mit Berechnung des AUC-Koeffizienten (numerischer Indikator Area Under Curve).

Ergebnisse und Diskussion. Das Stadium der Fibrose F0 wurde bei 46,9% der Patienten, F1 - 11,4%, F2 - 16,4%, F3 - 8, 9%, F4 - 16,4% der Patienten diagnostiziert. Bei der Untersuchung der erhaltenen biochemischen Daten haben wir die signifikanteste Beziehung unter Verwendung von Approximationsfunktionen ausgewählt, die auf der Grundlage der Methode der kleinsten Quadrate konstruiert wurden. Es zeigte sich, dass der Wert von alpha2-Makroglobulin, der zum Intervall von 0 bis 3 g / l gehört, F0 - F1 entspricht, von 3 bis 5 g / l F2 - F4 entspricht. Um die Qualität der Studie zu überprüfen, wurde eine ROC-Analyse des verwendeten Werts durchgeführt, die es uns ermöglicht, eine Schätzung der Genauigkeit der vorgeschlagenen Methode zu erhalten - der AUC-Koeffizient unter der Kurve für F und alpha2-Makroglobulin betrug 0,82, was die hohe Qualität der Studie belegt. So zeigt der Gehalt an alpha2-Makroglobulin von 0 bis 3 g / l das Anfangsstadium der Fibrose (F0 - F1) an, von 3 bis 5 g / l eine moderate, schwere oder schwere Fibrose (F2 - F4).

Fazit. Der Gehalt an Serum-alpha2-Makroglobulin kann als vorläufiges diagnostisches Kriterium zur Beurteilung des Stadiums der Leberfibrose bei Patienten mit chronischer Hepatitis C verwendet werden.

P42

Interdisciplinary Management of Alveolar Echinococcosis: Retrospective Analysis of 232 cases from 2011 to 2017

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Background: Alveolar echinococcosis (AE) is caused by the larval stage of Echinococcus multilocularis and affects the liver in the vast majority of cases. It is considered a „malign parasitosis“. Diagnosis and subsequent treatment should follow the recommendations of the WHO Informal Working Group on Echinococcosis (IWGE). Due to the low incidence, controlled clinical studies are hardly feasible. During the years 2011 – 2017, up to 45 newly diagnosed cases per year have been reported to the Robert Koch Institut in Germany, while numbers were lower in the preceding years (2003: 21 reported cases). As a result of rising infestation of fox populations and expansion of endemic areas, an increased incidence of human AE cases has been reported. We delineate the interdisciplinary management of patients with AE with first visit at our center. Methods: This survey includes all patients with AE who were referred to the University Hospital Ulm between 01.01.2011 and 31.12.2017 (n=232). We report demographic data, symptoms with first clinical presentation, therapeutic strategy, follow-up, and outcome. Results: All patients with case classification „confirmed“ (57%, n=130) and „probable (36%, n=82) according to WHO-IWGE received a therapy with benzimidazoles (BMZ). Complete (curative) resection of the parasitical lesion was aspired. For 31% of the patients (n=72), the finding was incidental, 25% (n=59) did not present any specific symptoms. In 13% of the cases (n=31), the disease has been acknowledged as occupational (mostly in farmers). For 98 patients (42%) who underwent operative therapy, resections were recorded as R0 in n=67, R1 in n=12, R2 in n=3, and Rx in n=16 cases. According to the WHO guidelines, we recommended the continued treatment with BMZ following a resection for a minimum of two years. Cases with limited options due to inoperable infestation (50%, n=116) were solely treated with continuous antihelminthic BMZ therapy. Among patients who received BMZ, 15% (n=34) had relevant toxicity. Patients with a „possible“ case classification according to WHO-IWGE (n=18, 7,83%) did not receive therapy, but regular follow-up. We considered 23% (n=53) of the patients cured (no relapse > 2 years after finishing BMZ treatment following the resection), or prospectively cured (follow-up period of less than 2 years after stopping BMZ treatment following the resection). The majority of patients (41%, n=96) has been assessed as chronically stable, only 2% (n=5) had a progress notwithstanding BMZ therapy and 1 patient (0,4%) died due to AE. Conclusions: For a majority of the affected patients, AE remains a chronic disease, which requires a long lasting drug therapy. About 23% of our patients were cured (or prospectively cured) by surgical resection and BMZ therapy. Facing the rising number of cases and overall low number of patients, for whom a curative approach can be provided, improved strategies for prevention and screening are needed.

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Leishmaniases and the Cameroon paradox

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Objectives: Northern Cameroon has been known as an endemic leishmaniasis area as early as 1930, although the sand fly vectors have never been incriminated but were supposedly Phlebotomus duboscqi, like in other sub-Saharan foci. A sound knowledge of the vector-host-parasite transmission dynamics is a prerequisite for adequate control measures of vector-borne diseases. To achieve this and in order to identify the vector(s) of the disease, an entomological investigation was conducted in the cutaneous leishmaniasis (CL) focus of Mokolo District.
Methods: Phlebotomine sand flies were collected in and around Mokolo in a variety of ecotopes using light traps. Individual sand flies were used for morphological species identification, and the remainder of the body for DNA analysis. Sand flies were demonstrated to harbor Leishmania spp. parasites using ITS1 PCR.
Results: This study revealed the presence of Leishmania donovani complex DNA (n=1) in P. duboscqi and of lizard-borne Leishmania tarentolae-like DNA (n=3) in Sergentomyia spp. in 79 sand fly specimens from Mokolo district that were tested. No CL-causing Leishmania major was found. On the other hand, in a pilot survey conducted in September 2012, no Phlebotomus spp. were found. A second series of collections was carried out during 2013 and 14,036 sand flies (6,665 males and 7,371 females) were collected. A total of 5,926 females and 98 males were morphologically identified to species level, representing 19 species of the genera Sergentomyia, Grassomyia and Phlebotomus, with P. duboscqi representing only 0.9% of all females.
Conclusions: The causative agent of CL could not be detected in potential vectors. Instead we found evidence for visceral leishmaniasis (VL) parasites in P. duboscqi as well as enzootic reptile parasites in the Mokolo area. Strangely enough, the suspected vector P. duboscqi was found in extremely low numbers, casting doubts as to whether it could alone be responsible for the local transmission. However, other sand fly species were so far tested negative for human Leishmania parasites.
Recommendation: We recommend an epidemiological survey to be carried out in the area to evaluate the prevalence and eventually to describe the clinical manifestations of VL in the human population. Political instability in neighboring countries and the resulting refugee migration are likely explanations for the emergence of VL in Mokolo. In addition, the transmission dynamics of L. major remains to be investigated and the vector to be incriminated. Sand flies other than Phlebotomus sp. should also be targeted, e.g. Sergentomyia.

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Recurrence behaviour and relapse characteristics of Plasmodium ovale spp. in Gabon

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Plasmodium ovale spp. have long been regarded as relapsing malaria species. In line with Plasmodium vivax, they are thought to form liver dormancies which can induce future recurrence. Yet, other malaria parasites are capable of causing recurrent parasitaemia months to years after the primary malaria episode. Data of incidence patterns and molecular characterisation of reappearing human Plasmodium parasites are scarce. In the last years, doubts about the currently accepted relapse theory of P. ovale spp. have been raised by the scientific community as hypnozoites could so far not be demonstrated in the human host. Also, molecular methods have barely been used to postulate relapses. The aim of this study was to describe P. ovale spp. reappearance and relapse using molecular methods.

This study was conducted at CERMEL, Lambaréné, Gabon. Baseline P. ovale spp. mono or mixed infections were included and treated with artemether-lumefantrine. No primaquine was administered. Participants were followed up biweekly for up to one year. In case of microscopic positivity, blood was drawn for further assessments. Day 7 lumefantrine plasma concentration was measured in plasma samples. Blood samples were analysed by ultra-sensitive Pan-Plasmodium RT-PCR and Plasmodium species-specific nested singleplex quantitative real-time PCR. In case of repetitive occurrence of the same Plasmodium spp. in the same patient, 18S, potra, and porbp2 genes were partially sequenced and isolates were compared. A relapse was postulated in case of documented treatment of the previous corresponding malaria episode, adequate D7 lumefantrine plasma levels, at least one negative PCR result between the two relevant episodes and sameness of isolates in at least two genes.

26 participants were eligible for analyses. The male/female ratio was 1:1, mean age was 8.2 years (range 2-81). At baseline, 17 participants had a real-time qPCR diagnosed P. ovale curtisi (Poc) infection, 13 were positive for P. ovale wallikeri (Pow). 24 reappearances of Poc and 4 reappearances of Pow were found in 12 participants, all before week 32. Partial sequencing of these reappearances combined with the strict pre-defined criteria revealed 10 Poc relapses in 6 subjects. No Pow relapses could be identified.

This is the first prospective analysis postulating P. ovale spp. relapses in a patient cohort using molecular methods. The sequencing results show the reappearance of the same Poc parasites after initial blood stage clearance which is in line with the current relapse theory. These findings are especially relevant for malaria elimination settings as dormancies can lead to sustained malaria transmission and pose a challenge, especially in glucose-6-phosphate deficient communities. Interestingly, there was a higher overall occurrence of Poc as compared to Pow in this Gabonese cohort. The results further show that Poc and Pow occur as sympatric species in Gabon. The absence of Pow relapses remains to be explained.

P45

A common miRNA-146a polymorphism is associated with malaria in pregnancy

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MicroRNAs (miRNAs) are involved in gene regulation, including pathways in immune responses. MiRNA-146a regulates the innate immune response by a negative feedback loop downstream of the TLR machinery. The common miRNA-146a single nucleotide polymorphism (SNP) rs2910164 G>C has been associated with increased risks of several diseases, but no data as to malaria are available. We analysed the association between the miRNA-146a SNP and P. falciparum infection in pregnant women in Ghana. We examined 509 antenatal care (ANC) attendees in 1998 and 296 primiparae in 2000. Infection was assessed by microscopy and PCR and by the detection of leukocyte-associated haemozoin in placental samples of delivering women. Frequencies were compared between the groups by Fisher's exact test and we used logistic regression models to adjust for possible confounders (i.e. season, age and the presence of pyrimethamine in urine or plasma).

In ANC attendees, the SNP distribution was 32.2%, 48.1% and 19.6% for the wild type, heterozygote and homozygote genotype, respectively. In delivering women, these figures were 30.7%, 48.3% and 20.9%. By PCR, P. falciparum infection was present in 63% of ANC attendees and in 67% primiparae. The miRNA-146a rs2910164 G>C SNP was associated with increased odds of P. falciparum infection in both ANC attendees and primiparae. We observed doubled odds of infection among homozygous ANC attendees (adjusted odds ratio (aOR), 2.3; 95% CI, 1.3-4.0, P = 0.005). This effect was particularly strong in primigravidae (aOR, 5.8; 95% CI, 1.6-26, P = 0.01) and only marginal in multigravidae. Similarly, among primiparae, homozygosity was associated with increased odds of PCR detected placental P. falciparum infection (aOR, 5.9; 95% CI, 2.1-18, P = 0.001) and of past or present malaria (aOR, 5.3; 95% CI, 1.9-17, P = 0.002). In terms of the clinical manifestation of infection, the miRNA-146a SNP did not show a significant association with fever, anaemia, low birth weight or preterm delivery.

These findings indicate that miRNA-146a SNP rs2910164 G>C is involved in protective malarial immunity, and likely in the innate immunity component.

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Effect of different albendazole-based treatment regimens on Loa loa microfilaraemia in an endemic region of Gabon: preliminary results of an open-label randomised controlled clinical trial

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Loiasis is a parasitic infection caused by the filarial worm Loa loa. Despite its wide range of clinical symptoms, loiasis is not even considered a neglected tropical disease and its importance was only highlighted when the implementation of mass drug administration programs for lymphatic filariasis and onchocerciasis had to be stopped in Loa Loa co-endemic areas. However, with more than 10 Mio people affected, there is a need for a safe and effective treatment of loiasis. Currently, there is no sufficiently safe treatment option for mass drug administration for the interruption of L. loa transmission available. Potent drugs such as ivermectin or diethylcarbamazine have led to severe post-treatment adverse events in patients with high Loa Loa microfilaremia. While albendazole treatments seem to be safe, it is unclear if this leads to complete suppression of microfilaremia. Here we present an open label clinical trial evaluating different albendazole based regimen alone or in combination with ivermectin for loiasis in Gabon.
Forty-two adults of both sexes with initial filarial count between 7000-50000 were randomized in four arms and followed up to six months. Arm 1 (6 subjects) untreated controls; arm 2 (12 subjects): albendazole 400 mg twice daily for 21 days; arm 3 (12 subjects): albendazole 400 mg twice daily for 21 days followed by additional albendazole 400 mg twice daily for 14 days; arm 4 (12 subjects): albendazole 400 mg twice daily for 21 days followed by a single dose of 150 µg/kg of ivermectin. L. loa microfilaraemia was measured before each treatment and twice weekly for three weeks and then weekly follow-up visits took place from week 4 through week 8; thereafter, twice monthly visits took place until the end of follow-up. Monitoring of adverse events was done through the treatment and re-treatment period.
Post treatment adverse events were similar in the three treatment arms, one adverse event recorded was considered probably treatment related. Microfilarial levels remained stable in the control arm during the follow-up. In all treatment arms, microfilarial levels decreased significantly ($p<0.05$) following the first round of albendazole. More detailed results of the respective treatment arms will be presented at the congress.

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Epidemiologic Features of Imported Malaria in Serbia

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Introduction: After malaria eradication in Serbia 1964, from 1975-1988, 24-57 cases of imported malaria were reported per year. In the nineties, there was a sharp decline, with only three cases in 1993. Since 2000, the incidence rate has been steadily rising. The risk for reintroduction of malaria in Serbia can be increased by a mass influx of migrants from malaria-endemic areas. Most patients with suspected malaria in Serbia are referred to the Clinical Center of Serbia (CCS) in Belgrade for diagnosis and treatment.
Goal: An overview of the epidemiological trend of imported malaria in Serbia.
Method: To determine the epidemiological characteristics of imported malaria in Serbia, we analyzed data of all travelers who examined for malaria at the CCS Parasitological Laboratory (National Reference Laboratory for Tropical Parasitic Diseases) after their return from malaria endemic areas between 2001 and 2018. The study series involved a total of 4365 travelers. Diagnosis of malaria was based on microscopic examinations of Giemsa-stained thick and thin blood smears in combination with rapid diagnostic tests.
Results: In the analyzed period, malaria was diagnosed in 264 cases. Occurring at a rate of 6 (2006) to 39 (2017) cases per year. Plasmodium falciparum was predominated species, with a share of 58%. P. vivax, P. ovale, and P. malariae were each identified in 23%, 8%, and 2% cases, respectively. 4% of infections were mixed, whereas thirteen patients (5%) had submicroscopic malaria. Until 2016, the dominant species was P. falciparum and dominant mode of importing malaria has always been by Serbian workers hired at construction sites in malaria-endemic areas, predominantly from Africa. During 2016 and 2017 P. vivax has taken the primacy over P. falciparum as a consequence of recent migration waves. Since June 2015, 44 P. vivax infections were diagnosed in Afghan and Pakistan's migrants including five relapses occurred due to unavailability of primaquine. Some of them had previous malaria attacks in origin countries and/or during migration route in other countries. All patients were young men with fever. Parasitemia was generally low about 0.2%; maximum 0.9%. In this group the prevalence of gametocyte carriage was 79.5% (35/44), over half during summer. Since 2018, the so-called Balkan Route, used by migrants, has changed and P. falciparum has again taken the primacy over P. vivax.
Conclusion: After years of the dominance of P. falciparum among imported malaria species in Serbia, waves of migrants from P. vivax malaria–endemic countries have increased of imported P. vivax. Curent climatic conditions during summer are conducive to malaria re-transmission in Serbia. In prevention of reintroduction of P. vivax into this area, that containing residual population of former Anopheles vectors, vector control has been increased.

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Further evidence for a gradual dormancy concept in malaria

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Malaria recurrences after an initially successful therapy and malarial fever occurring a long time after infection are well-known problems in malariology. Currently two distinct types of malaria recurrences have been defined: recrudescence and relapse. A recrudescence is thought to originate from circulating asexual Plasmodium blood stages which do not cause symptoms? before a certain level of a microscopically detectable parasitemia is reached (blood-borne recurrence). Contrary, a relapse is thought to originate from quiescent intracellular hepatic parasite stages called hypnozoites (tissue-borne recurrence). Recrudescences would typically occur in Plasmodium (P.) falciparum. P. knowlesi and P. malariae infections, whereas relapses would be caused exclusively by P. vivax and P. ovale. This schematic view is however, insufficiently supported by experimental evidence. For instance, hypnozoites of P. ovale have never been experimentally documented. On the other hand, the non-finding of P. malariae hypnozoites turned into the proof for the non-existence of P. malariae hypnozoites. Clinical relapse-type recurrences have been observed in both P. ovale and P. malariae infections and decade-long incubation times have been also reported in P. falciparum infections. We present two cases of recurrences (P. ovale and P. malariae) and new cases of the actual scientific literature which confirm the gradual hypothesis in accordance with the continuity concept of biological evolution we had proposed for the first time in 2016: both, relapse and recrudescence may be potentially caused by all Plasmodium spp.. We hypothesized that the difference between the various Plasmodium spp. is quantitative rather than qualitative: there are Plasmodium spp. which cause frequently relapses such as P. vivax, species which cause relapses less frequently, such as the P. ovale spp. and sometimes P. malariae, and species which may exceptionally cause relapses such as P. falciparum. All species can cause recrudescences as confirmed by post-transfusion malaria. As clinical consequences we propose that 8-aminquinolines may be considered in a relapse type recrudescence regardless of by which Plasmodium sp. it is caused, whereas routine primaquine relapse prevention might not be always indicated in malaria due to P. ovale.

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Polymorphisms of the Duffy blood group antigens influence malaria in southern India

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Duffy blood group antigens serve as receptors for erythrocyte invasion by Plasmodium vivax, and Duffy blood group negativity confers relative resistance against this parasite. Polymorphisms of the Duffy antigen/chemokine receptor (DARC, also known as Fy glycoprotein (FY)) form the basis the Duffy blood group system. Duffy negativity (Fy (a-, b-)) is rare among non-African populations. Data on DARC polymorphisms and their impact on Plasmodium infections in India are rare.
In a case-control study among 909 malaria patients and 909 community controls in Mangaluru, coastal southern India, we examined associations of the DARC SNPs with the odds of malaria and its manifestation. DARC genotyping by melting curve assays included G125A (rs12075), T-33C (rs2814778), C265T (rs2814778), and G298A (rs13962).
DARC -33C was absent and 265T was non-polymorphic (allele frequency = 0.005). DARC 298 A carriage was associated with increased odds of any Plasmodium infection (aOR, 1.4; 95%CI, 1.1 – 12.0) and of P. vivax infection (aOR, 1.6; 95%CI, 1.1 – 2.2). Vice versa, the genotypes FYA/FYB or FYB/FYB (deduced from the SNP G125A) protected against severe malaria (P = 0.03) and from being hospitalized (P = 0.005).
This report from southern India is the first to show an independent effect of the DARC 298A polymorphism on the risk of Plasmodium infection. Functional studies are required to understand the underlying mechanism. Moreover, FYB carriage appears to protect against severe malaria in southern India.

P50

Molecular markers of antimalarial drug resistance in Mangaluru, southern India

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In most of India, the first-line antimalarials against Plasmodium falciparum and Plasmodium vivax malaria are sulfadoxine-pyrimethamine (SP)-artesunate and chloroquine, respectively. Antimalarial drug resistance in India shows an unequal distribution and in the south of the country, insufficient data is available. By sequencing, we examined molecular markers of drug resistance in 107 P. falciparum and 108 P. vivax isolates obtained from patients attending Wenlock Hospital in Mangaluru, southern India. These markers included P. falciparum dihydrofolate hydrogenase gene (pfdhfr), dihydropteroate synthase gene (pfdhps) multidrug resistance gene pfmdr1, and the Kelch13 propeller domain sequence, as well as the P. vivax multidrug resistance gene pvmdr1.
For pfdhfr, the mutations 59R and 108N co-occurred in 71%, and for pfdhps, the variants 437G and 540E were present in 72% and 24%, respectively. Pfdhfr/pfdhps triple and quadruple mutants were seen in 45% and 25%, respectively. As for pfmdr1, the 86N-184F-1246D haplotype dominated (98%). No Kelch13 variants were observed. Ten pvmdr1 haplotypes were recognized including 958M-976F-1076L (0.9%) but no sextuple or septuple pvmdr1 mutant haplotypes were present.
These data show a substantial degree of P. falciparum SP resistance in the study region but the absence of antifolate super-resistance. No evidence for artemisinin resistance was observed. The dominating pfmdr NFD haplotype suggests that artemether-lumefantrine, introduced in northeastern India because of intense SP resistance, might not be the best alternative option for a potential replacement of SP-artesunate in the study area. On the other hand, by analysis of molecular markers, chloroquine seems to be adequately effective against P. vivax. Monitoring clinical efficacy and drug resistance markers in Mangaluru is warranted to detect a potential intensification of SP resistance and to disentangle the role of pvmdr1 variants in recrudescence and efficacy.

P51

Granzyme B+ CD8+ T cells are associated with complicated malaria

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In Plasmodium falciparum malaria, CD8+ T cells play a double-edge role. Liver-stage specific CD8+ T cells can confer protection, as has been shown in several vaccine studies. Blood-stage specific CD8+ T cells, on the other hand, contribute to the development of cerebral malaria in murine models of malaria. The role of CD8+ T cells in humans during the blood-stage of plasmodium falciparum remains unclear.
As part of a cross-sectional malaria study in Ghana, granzyme B levels and CD8+ T cells phenotypes were compared in the peripheral blood of children with complicated malaria, uncomplicated malaria, afebrile but asymptomatically infected children and non-infected children.
Granzyme B levels in the plasma were significantly higher in children with febrile malaria than in afebrile children. CD8+ T cells were the main cell subsets expressing granzyme B. The proportion of granzyme B+ CD8+ T cells was significantly higher in children with complicated malaria than in uncomplicated malaria, whereas the activation marker CD38 on CD8+ T cells showed similar expression levels. This suggests a pathogenic role of cytotoxic CD8+ T cells in the development of malaria complications in humans.

P52

Non-Burkitt-type malignant tumors of the lower face in southern Malawi

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Introduction:
Many neoplastic conditions affect the oromaxillofacial region and these tumors most commonly affect the lower parts of the face. Histology, location and demography of malignant not Burkitt related tumors of the lower face are not well described for Malawi. To make most use of our limited ressources in anaesthesia in one of the poorest countries in the world we need more information on this type of tumor and on the problems it might present for airway management and equipment.
Objective:
To mine data on the epidemiology of malignant oromaxillofacial tumors and the challenges they impose for anaesthesia providers in a situation where consecutive histopathological results are very difficult to obtain.
Methods:
25 consecutive patients with malignant lower face tumors (excluding Burkitt´s Lymphoma) of the Dentistry Department at Queen Elizabeth Hospital in Blantyre were prospectively evaluated together with the Department of Anaesthesia in a quantitative, longitudinal, monocentric study over almost two years.
Results:
For all 25 consecutive patients (100%) histopathological results could be obtained. 11 patients were male (44%) and 14 (56%) female. Mean age of our patients was 53.8 years, only one patient was a child. Ten female and four male patients were in an age between 50 and 70 years (56%).
Fourteen tumors were classified as Squamous Cell Carcinoma (56%) and three with Kaposi´s sarcoma (12%). Other malignancies were found only once. Either as focal malignancy (adenocarcinoma, adenoidcystic carcinoma, mucoepidermoid carcinoma, basal cell carcinoma, spindel cell malignancy) or as systemic malignancy (non-Hodgkin-lymphoma, plasmocytoma, acute lymphatic leucaemia).
Tumors were predominantly found involving the palate in 8 (32%), the tongue in 5 (20%) and the lips in 3 (12%) patients. Twice (8%) the buccal region, the gingiva and the mandible was affected and once (4%) the maxilla as well as the sublingual and the retromolar region.
All patients (100%) were finally intubated without a bronchoscope or further advanced airway management and all patients could be treated through our experienced „anaesthetic clinical officers“ using different blades, tubes, stylets and bougies.
Results are put into perpective with other sub-Saharan countries and limitations are discussed.
Conclusion:
For the first time we characterized malignant non-Burkitt lower face tumors for southern Malawi. The most common tumor was Squamous Cell Carcinoma, followed by Kaposi´s sarcoma. The prevalence of malignancies for women between 50 and 70 was over-poroportionally high and the palate as main site for the tumors differed from previous findings.
In our study these tumors were not able to impose a significant additional workload on our anaesthetic procedures. Neither through their numbers nor through anaesthetic difficulties they might have had for staff, equipment or drugs.
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P53

Gesundheitliche Hilfe für geflüchtete Frauen und ihre Kinder - Grundlage für eine gelingende Integration. Einrichtung von „Zentralen Frühe Hilfen“

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Bei der Diskussion um Flüchtlinge, ihre Integration und um das Thema „Innere Sicherheit“ wird immer wieder vergessen, dass es tausende geflüchtete Frauen und Kinder gibt.
Was bedeutet es, durch Krieg und Flucht in Lebensgefahr gewesen, heimatlos geworden zu sein?
Wer nimmt sich der geflüchteten Frauen und Kinder an? Wer hat ein offenes Ohr für ihre Sorgen und Nöte – gesundheitlich, emotional und auch im sozialen Bereich. Wie motiviert man diese Frauen aktiv zu werden und ihr Leben auch in die eigenen Hände zu nehmen? Wer informiert Frauen über ihre Rechte in Deutschland?
Gesundheitliche Hilfe ist ein guter Zugang zu allen Frauen und Kindern, auch zu geflüchteten Frauen und Kindern und zu den vielfältigen und meist nicht ausgesprochenen psychosozialen Problemen.
Frauen sind als Mütter weiter vorrangig für die Erziehung ihrer Kinder verantwortlich.
Mütter müssen motiviert werden selbst die neue Sprache sprechen können und ihren Kindern - Jungen wie Mädchen – die gleichberechtigte Stellung und Lebensweise von Mädchen und Frauen in unserer Gesellschaft vermitteln.
Seit dem Jahr 2014 haben wir in niedersächsischen Kommunen fünf „Zentralen Frühe Hilfen“ aufgebaut. Eine Zentrale Frühe Hilfen bedeutet:
• Eine für täglich oder zumindest mehrmals in der Woche besetzte Gesundheits-Sprechstunde als gute Anlaufstelle für gesundheitliche Beratung
• Leitung: Fachkraft Frühe Hilfen (Familienhebamme oder Familien-Kinderkrankenschwester)
• Sowohl eine „Komm-Struktur“ wie auch einer „Geh-Struktur“; d.h. neben einer Sprechstunde wird auch aufsuchend in Familien gearbeitet werden
Aufgaben einer Zentrale Frühe Hilfen sind z.B.:
Ø Beratung für alle gesundheitlichen Probleme von Frauen und Kindern und „Lotsenfunktion“
Ø Aufsuchende Hilfe und Betreuung bei akuten und chronischen Erkrankungen
Ø Gesundheitliche Beratung und Versorgung (u. a. Hygiene, Ernährung, Begleitung zu Ärzten, Empfängnisverhütung
Ø Motivation zum konsequenten Erlernen der deutschen Sprache
Ø Hilfe bei der Lebensgestaltung und zukünftigen Lebensplanung
Die Fachkräfte Frühe Hilfen sind für die geflüchteten Frauen und Kinder:
Ø Lotsinnen für Frauen und ihre Kinder im Wildwasser des Einlebens auf der ungewissen Fahrt in eine völlig neue Kultur und Gesellschaft
Ø Lotsinnen auf dem Weg in eine gelingende Zukunft der geflüchteten Frauen und Kinder, denn diese Lotsinnen können Schutz, Motivation und Perspektive für die Zukunft geben
Ø Helferinnen für Frauen und Kinder gegen physische und psychische Gewalt

Daten aus der laufenden Evaluation werden vorgestellt

P54

Research for the Control of Neglected Tropical Diseases: a Systematic Assessment of the German Commitment

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Background
Neglected tropical diseases (NTDs) are a major cause of poor-health among marginalized populations in low-resource settings. To meet the Sustainable Development Goals health targets by 2030 there is a pressing need to tackle these diseases by intersectoral, interdisciplinary, and international collaborations. The World Health Organization has called on the global health community to capitalize national existing knowledge, experience and political will to priorize implementation of NTDs control and elimination programms. So far no systematic analysis of the german commitment to NTDs exists. The study is the first to systematically investigate the german commitment to neglected tropical diseases research and fomulate a vision for future investments and activities.

Methods
A project team out of 35 experts for specific NTDs from german research institutions and from the german industry was formed of which 1-3 authors worked together to create a condensed expertise on international achievements, setbacks and gaps for research and development of a disease, respectively. The research activities of German institutions were assessed by a systematic methodology following three consecutive steps: 1) a systematic analysis of the literature, 2) a survey of project funding and 3) a data analysis.

Results
The expertise presents key figures on NTD research and development in Germany in a comprehensive and disease-differentiated form. Whilst NTD research of german institutions is often focussing on basic biomedical research, translational research and development is under-represented. This is particular true for the development of drugs, vaccines and diagnostics as well as the investigation of better application of medicines and innovative technologies. The scientific networking and coordination should be further promoted, and integrative and interdisciplinary approaches are needed to develop innovative one-health research approaches.

Conclusion
In terms of efforts to promote Universal Health Coverage (UHC), Germany should increase national commitment to the development of diagnostics and medicines, and should urgently pursue accompanying implementation research. Required scientific structures partly exist already, e.g. the German Center for Infection Research (DZIF) and the Health Networks program in sub-Saharan Africa within the framework of the Africa Strategy of the Federal Ministry of Education and Research (BMBF). In addition, the Public Private Partnership program for new medicines, including German industry colaboration is already involved, should be continued. This is essential to enable excellent preclinical results to be developed.

P55

Transjugular Intrahepatic Portosystemic Shunt (TIPS) for Primary and Secondary Prophylaxis of Variceal Bleeding in Hepatic Schistosomiasis

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Background:
Globally, an estimated 230 million people are affected by Schistosomiasis. In endemic regions hepatic schistosomiasis often is the leading cause for portal hypertension. Due to migration schistosomiasis is also becoming more prevalent in non-endemic countries (e.g Germany, USA). Upper gastrointestinal bleeding secondary to variceal rupture is an important life threatening complication in patients with hepatic schistosomiasis and cause of considerable morbidity and mortality.
Objectives:
The aim of this retrospective case series was to describe and evaluate transjugular intrahepatic portosystemic shunt (TIPS) creation as primary and secondary prophylaxis for upper gastrointestinal bleeding due to portal hypertension related to hepatic schistosomiasis.
Methods:
Case records at the University Medical Center Hamburg-Eppendorf were searched for patients with hepatic schistosomiasis treated with TIPS creation. Outcome parameters of interest were hepatic venous pressure gradient (HPVG), grade of esophageal varices, episodes of upper gastrointestinal bleeding, hepatic encephalopathy, liver function and episodes of hospitalizations post TIPS.
Results: Three patients were treated with TIPS creation for primary prophylaxis (n=2) and secondary prophylaxis (n=1) of variceal bleeding due to portal hypertension caused by hepatic Schistosomiasis. All three patients had oseophageal varices grade III with red spots and hypersplenism but none had ascites on ultrasound. TIPS creation was performed without acute complications and HPVG was successfully reduced in all three patients (24 to 8 mmHg, 23 to 11 mmHg, 21 to 10 mmHg). Two patients showed regression of varices on control endoscopy (one without endoscopic control). During the cumulative 6.5 patient-years of follow-up no episode of variceal bleeding occurred. One patient required hospitalization due to de-novo onset of hepatic encephalopathy grade I. Of note this patient also had hepatitis B co-infection with signs of liver cirrhosis on fibroscan (27.7 kPa).
Conclusion: TIPS placement is a safe and effective intervention to reduce the risk for upper gastrointestinal bleeding in patients with hepatic schistosomiasis. Prospective studies are needed to further evaluate long-term effectiveness and adverse events such as hepatic encephalopathy.

P56

Immune activation in patients with filarial lymphedema before and after treatment with doxycycline

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Background: Lymphatic Filariasis is a mosquito-transmitted helminthic infection caused by Wuchereria bancrofti and Brugia spp., which is characterized by lymphangitis, lymphedema and hydrocele. 68 million people are estimated to be infected worldwide and approximately 30% of the infected individuals suffer from disabling pathology. The treatment (200 µg/kg ivermectin (IVM) and 400 mg albendazole (ALB)) that is currently used mainly acts against microfilariae, the larval stage that is also responsible for transmission, but has limited effect on the adult worm. IVM/ALB reduces the transmission of the parasite, but has to be given repeatedly as the adult worm lives for 10 -15 years in the human body. In addition, no improvement of filarial associated pathology can be demonstrated by IVM/ALB treatment. Doxycycline depletes Wolbachia endosymbionts, which leads to adult worm's sterilization and slow death. Former studies have shown macrofilaricidal activity of 100-200 mg doxycycline given daily for 4-6 weeks. Additionally, Mand et al. could show that Doxycycline 200 mg for 6 weeks leads to a halt of progression or even improvement in the early lymphedema stages independent of active infection.

Methods: Double-blind, randomized, placebo-controlled trials (LEDoxy) are conducted in different countries to confirm the effect of Doxycycline 200 mg and to test the effect of 100 mg per day for six weeks on filarial lymphedema. The LEDoxy studies conducted by the TAKeOFF consortium (Tackling the Obstacles to Fight Filariasis) are carried out in Ghana and Tanzania. In each country it is planned to enroll 420 participants. Patients are characterized at baseline using the lymphedema staging (stage 0-7) according to Dreyer et al., circumference measurements with tape and an infrared scanner (LymphaTech®, Atlanta, Georgia, USA) to measure potential changes in pathology at several time points within 24 months after treatment onset.

Beside the clinical characteristics, immunological aspects of the different treatment groups before and after treatment with doxycycline or placebo will be described. Peripheral blood mononuclear cells of the patients will be characterized for the presence of memory CD4 or CD8 T cells (CD45, CD27), regulatory CD4 T cells (FoxP3, CD25) and immune activation marker (CD38, HLADR).

In Tanzania activities started in July 2018. Data for the first 43 enrolled participants of the Tanzanian cohort, who have measurements at baseline and immediately after 6 weeks of treatment, will be presented in a blinded manner.

Funding: Federal Ministry for Education and Research (BmBF), German Center for Infection Research (DZIF)

P57

Epidemiology and clinical characteristics of (neuro)cysticercosis patients in the EU/EEA: assessment of different data sources from 2000-2016

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Introduction
Human cysticercosis is a neglected disease caused by the zoonotic tapeworm Taenia solium. When the metacestode larval stage of this tapeworm establishes in the central nervous system, it is called neurocysticercosis (NCC). The most common presentation is epilepsy and headache, but patients can also present with other pleomorphic symptoms and signs depending on the localisation and number of cysts amongst others. Reliable data on its prevalence/incidence as well as the clinical presentation of the patients are scarce in the European Union and European Economic Area (EU/EEA).

Methods
The objective of this study, which was embedded in CYSTINET (a European COST Action Network on Taeniosis/Cysticercosis) was to improve knowledge on (neuro)cysticercosis in the EU/EEA (from 2000 to 2016) both regarding epidemiological aspects as well as clinical characteristics of these patients. Therefore, various data sources were taken into account: a) data from relevant national reporting systems on cysticercosis, b) International Classification of Diseases (ICD) coded data, c) a systematic literature search including grey literature, and d) unpublished case reports through contacts with clinicians.

Results
We identified 3763 human cysticercosis cases reported or registered between 2000 and 2016 in the EU/EEA – i.e., 10 cysticercosis cases through mandatory notification, 3489 ICD coded cases (from Italy, Latvia, Portugal, Spain, Sweden), and 264 NCC cases through the systematic literature search and contact with clinicians.
The 264 cases extracted from the literature and the unpublished cases were mostly travel and migration related with almost equal sex distribution (51.9% male, 48.1% female) and a mean age of 36 ± 16 years. The most prominent clinical presentations were epileptic seizures, followed by headache. NCC lesions were mostly seen as viable cysts (89.4%) on neuroimaging. Treatment varied largely with albendazole being mostly used (58.3%).

Discussion
NCC, although classified as a potentially eradicable disease, seems prevalent in the EU/EEA, often related to travel and migration. However, data remain fragmented even though different data

sources were taken into consideration, not allowing reliable prevalence/incidence estimates for human cysticercosis in the EU/EEA. Timely identification of changes in incidence rates for both cysticercosis and *Taenia solium* taeniasis are important for control initiatives, but are challenging with the existing systems. Furthermore, evidence based treatment guidelines as well as training are needed to inform clinicians about best treatment options.

P58

Behavioural and clinical predictors for Loiasis

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Background:
Loiasis is a vector-borne disease in Central and West Africa. While there is still uncertainty to what extent loiasis is responsible for population morbidity, individuals having both loiasis and onchocerciasis have a high risk of fatal encephalopathy when treatment (i.e. ivermectin) for onchocerciasis is given. Therefore, it is current policy that communities of high loiasis-burden are excluded from mass drug administration programmes of ivermectin. To address this treatment gap we present diagnostic scores, based on clinical and behavioural predictors that may help to rapidly identify sub-groups with loiasis within high-burden communities.

Methods:
A cross-sectional survey was performed in the province of la Ngounie, Gabon between December 2015 and February 2016 and 947 participants of all ages were recruited. Clinical parameters and behavioural exposure factors were ascertained by questionnaire-based interviews. Parasitological analysis of blood samples was performed for L. loa detection. Diagnostic scores consisting of clinical and behavioural factors were modelled to predict loiasis in sub-groups residing in endemic regions.

Results:
Increasing sylvan exposure was identified as important risk factor for loiasis with adjusted odds ratios of 5.1 (95% confidence interval CI 2.6-9.9) for occasional forest exposure, 11.1 (95% CI 5.4-22.6) for frequent forest exposure and 25.7 (95% CI 12.5-52.9) for intensive forest exposure. Individuals with loiasis were 7.7 (95% CI 5.4-11.0) times more likely to report recurrent pruritus than those without loiasis. Reporting of regular daily exposure to the deep rain forest and recurrent pruritus was 9-fold (positive likelihood ratio 9.18; 95% CI: 6.39-13.18) more prevalent in individuals with loiasis than in controls. Concordantly, the absence of regular weekly forest exposure was associated with extremely low disease-likelihood (negative likelihood ratio 0.09; 95% CI 0.05-0.16).

Conclusions:
These composite scores may serve as a simple tool to rapidly identify both those most and those least at risk of disease and may simplify loiasis control activities as well as screening procedures for studies on loiasis. Further, they may aid policy-makers to tailor the delivery of ivermectin mass drug administration for onchocerciasis control programmes more effectively and safely in regions of high loiasis-burden.

P59

Diagnosis of Ascaris lumbricoides: comparison of wet mount microscopy, mini-FLOTAC and PCR

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The usual tool for the diagnosis of soil-transmitted helminths in many resource-limited areas is the wet mount microscopy of stool specimens. Other techniques, e.g., Mini-FLOTAC and PCR assays presumably show higher sensitivity. However, it is not well established whether infections additionally detected by the more advanced techniques are clinically relevant. In highland Huye district, southern Rwanda, where Ascaris lumbricoides predominates, 845 schoolchildren were examined for the presence of A. lumbricoides by wet mount microscopy, Mini-FLOTAC, and PCR.
The prevalence of A. lumbricoides infection was 25% by wet mount microscopy, 32% by Mini-FLOTAC and 37% by PCR. Agreement of results was good for Mini-FLOTAC and PCR (Kappa = 0.61) but only moderate for wet mount microscopy and Mini-FLOTAC or PCR. The sensitivity (and 95% CI) in detecting A. lumbricoides (as diagnosed by any of the three methods) was 56.4% (51.3-61.4) for wet mount microscopy, 71.9% (67.1-76.3) for Mini-FLOTAC, and 81.9% (77.6-85.6) for PCR. Clinical manifestation was most strongly associated with A. lumbricoides infections diagnosed by Mini-FLOTAC (e.g. stunting, abdominal pain, weakness). Children with infections detected by PCR exclusively did clinically not differ much from their uninfected peers.
Roughly half of the actually present A. lumbricoides infections were missed by wet mount microscopy. Mini-FLOTAC identified infections undetected by wet mount microscopy and showed the strongest association with clinical manifestation. PCR had the highest sensitivity but also detected clinically silent infections. The use of Mini-FLOTAC in patient management in endemic regions should be encouraged while PCR assays are superior in assessing the actual prevalence of A. lumbricoides in endemic regions.

P60

Helminth infection during pregnancy alters immune responses at the fetomaternal interface

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Background: In recent years it has become clear that the propensity to develop allergies and possibly other autoimmune diseases later in life is already determined by in utero exposure to infections amongst others. We have recently demonstrated that chronic infection with the helminth Schistosoma mansoni during pregnancy suppresses allergic asthma in offspring using an experimental mouse model. The underlying mechanisms of this feto-maternal crosstalk still remain unclear and constitute an intriguing field of research. First steps to unravel the nature of this crosstalk have revealed that inflammatory maternal signals elicited by chronic infection within the placenta imprint a distinct gene expression profile related to the Vitamin-D-receptor (VDR)-inflammation-related axis. Thus, the central hypothesis is that of pro- or anti- inflammatory immune reposnes elicited by maternal infection influence on placental function via regulating the vitamin D metabolism.

Aims and Methods: The main aim of this study is to answer the question whether VDR and vitamin-D-related related gene expression and particularly pro- and anti-inflammatory immune responses within the fetomaternal interface differ (1) between women from helminth-endemic (Germnay) and non-endemic area (Gabun) (2) between Schistosoma haematobium infected and non-infected pregnant women at time point of birth (Gabun).

Results and Conclusion: Preliminary data of 47 German and 54 Gabonese women with a subgroup of 13 Schistosoma haematobium positive women, indicate that Gabonese mothers are at a higher risk for placental inflammation since important anti-inflammatory genes such as IL10 or VDR were less prominently expressed when compared to German placental samples. As a result, the placenta, as an important Vitamin-D production site, might be less prone to react to a rather pro-inflammatory milieu with the production of active vitamin D, known to dampen inflammation. Concerning the immune system of the newborn, we detected IgE in Gabonese cord blood (alongside IgE in the maternal blood), which was not found in any German cord blood sample. Moreover, living in an helminth endemic area in general leads to a possibly partial protection against helminth re-infection. In this context we found a significantly higher IgE/IgG4 ratio in the Gabonese cohort. We are currently investigating the cellular composition and functional cytokine responses of maternal PBMC and offspring CBMCs to relate these to environmental (geographical) as well as infection-driven (helminth) factors as well as the above mentioned parameters within the vitamin D metabolism.

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Modulation of innate and adaptive immune responses by parasitic secretions of *Taenia solium* cysticerci

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INTRODUCTION: Neurocysticercosis, the larval stage of the pork tapeworm *Taenia solium* in the human central nervous system, is a neglected tropical disease with significant neurological morbidity and an increasing concern for non-endemic European countries. In endemic regions, the immune response in affected individuals is very diverse involving a complex Th1/Th2 immune response. However, little is known about how the parasite modulates immunity to escape potential harmful immune responses in the brain.

OBJECTIVE: The present work aimed to investigate the effect of *Taenia solium* larval cyst and related products on innate and adaptive immune responses in non-endemic individuals.

MATERIALS AND METHODS: *Taenia solium* cyst antigen lysate (CLys), membrane/scolex lysate (CMS), cyst vesicular fluid (CVF) and culture supernatant (CSN) were prepared from cysts collected from an infected pig and cultured with peripheral blood mononuclear cells (PBMC) from healthy German volunteers and murine bone-marrow derived dendritic cells (BMDDC). The effect of the lysates was investigated by flow cytometric analysis of Th subsets (Th1/Th2/Th17/Treg) and TNFα, IL-6 and IL-10 cytokines secretion. Underlying mechanistic aspects were explored using TLR and TGF-ßR neutralizing antibodies.

RESULTS: In contrast to CVF, which induced significant levels of TNFα and IL-6, CLys induced IL-10 production in BMDDC. In periphery, significant induction of peripheral Tregs ($CD4^{+}CD25^{high}FoxP3^{+}IL\text{-}10^{+}$) was observed in presence of CLys. Unexpectedly, both CVF and CLys were not prominent Th2 inducers as revealed by decreased expression of IL-5 and GATA-3.

CONCLUSION: Our findings suggest that in non-endemic individuals, lysate antigen from cysticerci may modulate peripheral immune responses by inducing Tregs and anti-inflammatory cytokines to favor a suppressive environment and parasite establishment. Current work focuses on identification of the underlying cellular pathways as well as of the nature of the immunomodulatory parasitic molecules acting on immune cells in the brain.

P62

Development of molecular diagnostic method for soil-transmitted helminthiases: Epidemiological implications for disease control

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Soil-transmitted helminthiases (STH) affect more than 2 billion people worldwide with the highest prevalence in Asia and Africa. Belonging to neglected tropical diseases with preventive chemotherapy, WHO has set their elimination as public health problem by 2020. As the prevalence drops and their elimination approach, it is becoming important to develop sensitive tools to have the real epidemiological situation of the disease, to validate the elimination and to monitor the post-elimination period. It is in this context that we have undertaken to search for supports and conditions to store stools under the field conditions in order to develop an easy to perform molecular diagnosis methods for epidemiological surveillance of STHs.
Stool samples were collected from inhabitants of Menoua villages in the western region Cameroon. STHs infections were identified in stools with Kato–Katz and flotation techniques. Different supports (filter paper) were tested to find those appropriate for long time storage of stool samples. Commercial kit, Chelex 100, Boiling-freezing and Cethyl Trimethyl Ammonium Bromide (CTAB) were tested to extract DNA from stored and fresh stools. Published molecular markers for STHs' detection were selected and used for identification.
A total of 1040 samples were collected and analyzed. The Kato-Kazt and flotation techniques identified 136 (13.08%) samples with soil transmitted helminthes including 11.83% of Ascaris lumbricoides, 2.02% of Trichuris trichiura and 0.96% of Necator americanus. Molecular identification of DNA from fresh stool obtained by different extraction methods revealed no amplification with Chelex and Boiling-freezing. Amplification rates of 60% and 80% were obtained for CTAB and Kit respectively. Stools preserved for one and two weeks on filter paper 1 to 6 (Whatman) revealed papers 1, 2 and 4 as appropriate support to keep stool samples at room temperature. Amplification rates varied according to the stool weight. The higher amplification rates were observed with 10 mg and 20 mg stools.
Results of this study show that the preservation of 10 and 20 mg of stool on Whatman papers 1, 2 or 4 provided optimal conditions to store stools for molecular diagnosis of STH. CTAB extraction method appeared as the appropriate method for DNA extraction from fresh and preserved stools. Whatman papers and CTAB could be used during post-elimination monitoring of STHs.

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Cystic echinococcosis: degeneration of protoscolices under subsequently combined albendazole-praziquantel therapy in vivo

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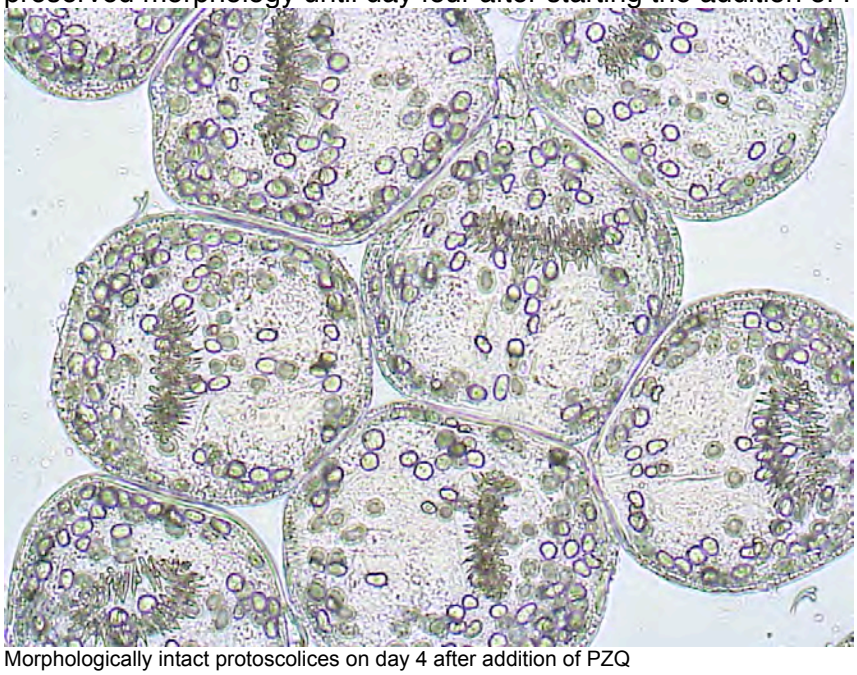
Antihelminthic drugs are used as conservative therapy or for covering invasive therapy of cystic echinococcosis (CE). Benzimidazoles, particularly albendazole (ALB) are effective against the larval metacestode stage affecting ungulates as well as humans whereas adult worms harboured by dogs are susceptible to praziquantel (PZQ). The effect of PZQ on protoscolices has been shown in vitro and studies have shown a faster treatment response in patients treated with the combination of ALB+ PZQ as compared to ALB alone. This has been also attributed to the observation that PZQ increases serum concentration of ALB sulfoxide.
We present a case of a female 30-year-old Kurdish patient from Syria who had undergone cholecystectomy due to a gallbladder hydrops caused by a large liver cyst compressing the cystic duct. The patient presented a typical unilocular anechoic liver cyst measuring 15.5 x 8.1 x 9.2 cm constituting a CE1 cyst according the classification of a WHO expert group. The suspicion of CE was confirmed by positive specific antibody test results. A catheter was placed inside the liver cyst by interventional radiology under coverage with ALB initiated 21 days earlier. Instillation of a scolicide was not performed due to the large volume of the cyst and possibly eroded bile ducts. Instead, the intra-hepatic catheter was fixed in situ with a suture thread and PZQ was added to ABZ at a daily dosage of 50mg/kg per os. Allergic events were not observed during and after the intervention. During the following days more than 1.5 litres of fluid spontaneously drained out of the cyst. The microfiltrated cyst fluid still contained viable protoscolices as supported by their preserved morphology until day four after starting the addition of PZQ.



Morphologically intact protoscolices on day 4 after addition of PZQ

Microscopy of cyst fluid revealed the degeneration of protoscolices eight days after PZQ co-administration was begun.

Degenerated protoscolices on day 8 after addition of PZQ

This finding persisted during further follow-up examinations.
It is still a matter of debate which is the best therapy for large CE 1 cysts, although the WHO has recommended a minimally invasive interventional therapy as early as in 2000. The same applies to the medical coverage with antihelminthic drugs prior, during and after the intervention. ALB is considered the drug of choice to cover invasive interventions for treating CE. There is evidence that the addition of PZQ increases the efficacy of therapy by a direct protoscolicidal effect and possibly also by increasing the intracystic and seric concentration of ALB sulfoxide.
In the present case, the persisting intrahepatic catheter permitted treatment monitoring by repeated microscopic examinations of the cystic fluid. Thereby, the degeneration of protoscolices under antihelminthic therapy could be visualized in vivo.

P64

Pre-clinical development of Corallopyronin A, an antibiotic with activity against filarial nematodes, STIs and Staphylococci

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The natural compound Corallopyronin A (CorA) inhibits the bacterial DNA-dependent RNA polymerase by binding to the switch region rather than the active site, making this antibiotic active against rifampicin-resistant Staphylococcus aureus. We demonstrated efficacy of CorA towards Wolbachia, endobacteria of filarial nematodes. The depletion of these endosymbionts blocks embryogenesis and development of the worms, and slowly kills the nematodes. Accordingly, CorA is a promising antibiotic for the treatment of human filarial infections onchocerciasis and lymphatic filariasis. Within DZIF we also showed activity against Rickettsia and Orientia spp., Chlamydia trachomatis, Neisseria gonorrhoeae and multi-resistant S. aureus. Thus, we are developing CorA for the primary indication of treating human filarial diseases and the secondary indications sexual transmitted infections (STIs) and antimicrobial resistant infections, including MRSA.
Using high-quality research grade material (HQ-RGM) we performed several non-GLP ADME pre-clinical studies that demonstrated that CorA has protein binding equivalent to ibuprofen, is stable in plasma >240 min, and is also stable in fed state intestinal stimulated fluid. Compared to rifampicin the induction by CorA of CYP3A4 via PXR is eight-fold lower and the expression of CYP450s is not modified, suggesting drug-drug interactions that would alter dosing of other chemotherapeutics are not expected. CorA oral and intraperitoneal bioavailability is equivalent and its metabolism in human and dog microsomes is slow: t1/2 >45 min, resulting in oxidation metabolites.
Within DZIF we achieved heterologous expression of CorA in Myxococcus xanthus, allowing for a more simplified fermentation process to achieve a cost-effective, high purity production at industrial-scale. Moreover, the downstream process was optimized including only one RP-chromatography consistently yielding CorA at >90% purity, confirmed by HPLC and NMR. During our first scientific advice at the German Federal Institute for Drugs and Medical Devices (BfArM), this purity was accepted as sufficient for the non-GLP toxicity and safety pharmacology studies. Using this HQ-RGM CorA we will finalize the non-GLP preclinical studies, including hERG and micronucleus in vitro toxicity, and also start the first non-GLP in vivo toxicity tests in 2019. In parallel, we will prepare the transfer of the production protocol to a GMP-certified CMO that will produce GMP-conform CorA for the GLP studies.

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"Test and Treat" with Doxycycline or Ivermectin plus Diethylcarbamazine plus Albendazole as tools for the elimination of lymphatic filariasis

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Background: Lymphatic filariasis (LF), one of the 20 neglected tropical diseases (NTDs) listed by the WHO, is caused by the filarial worms *Wuchereria bancrofti* and *Brugia species*. Since the start of the Global Programme to Eliminate LF (GPELF) in 2000 the worldwide number of people requiring mass drug administration (MDA) was reduced by 554 million (38% reduction from 2000 to 2017). Despite this remarkable progress it is a great challenge to eliminate the remaining LF cases in hot spot areas that went unnoticed during the surveys and could reintroduce LF in adjoining areas. "Test and Treat" strategies could be a valuable tool to find and treat the (remaining) positive cases in these areas.
The TAKeOFF consortium is a collaboration of German and African partners to "tackle the obstacles to fight filariasis" which is funded by the German Federal Ministry for Education and Research (BMBF). The overall goal of this consortium is to establish a multinational clinical trial platform to harmonize and improve clinical trials investigating LF. As one out of nine work packages a community based trial was designed to evaluate possible "Test and Treat" strategies in comparison to the standard MDA with Ivermectin (IVM) plus Albendazole (ALB). As the drugs used for MDA are mainly microfilaricidal, drugs that target the adult worms and therefore the reservoir of the microfilariae (Mf) are needed. Since the "Test and Treat" strategies are based on individual drug administration the use of drugs that are not feasible for large scale treatment is possible in this setting.
Methods: Two "Test and Treat" approaches, carried out in two communities in Ghana, will be compared to a third community where only the standard MDA will be administered.
The first approach is the treatment with doxycycline (DOX), an antibiotic targeting the endosymbiotic bacteria *Wolbachia* in the filarial worms and thereby exerting a long-term sterilizing or even macrofilaricidal effect. The efficacy of 100mg DOX for 4-5 weeks against *W. bancrofti* has been proven and shown to be safe in several clinical trials.
The second approach will adapt the triple drug therapy for LF (IVM plus diethylcarbamazine (DEC) plus ALB, IDA) which is recommended by the WHO in areas which are not co-endemic for *Onchocerca volvulus* or *Loa loa*. One course of this combination cleared Mf from the blood of LF infected patients for at least three years in two clinical trials and proved to be superior to two-drug-regimens. Since onchocerciasis and LF are co-endemic in Ghana, IDA will only be given to patients not infected with *O. volvulus* (OV16 negative) to avoid possible severe adverse reactions from DEC. As an additional safety measure, all patients for IDA will receive IVM alone 4 weeks before the triple combination to clear all *O. volvulus* Mf in possibly false OV16-negatives.
All patients from the third community and patients that are not eligible for DOX or IDA will receive IVM plus ALB in the scope of the standard MDA.

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Modulation of allergy and vaccine responses through maternal *S. mansoni* infection

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Chronic infection with the parasitic helminth Schistosoma mansoni is characterized by a modified Th2 response coupled to immunosuppression. This protects the host against overwhelming inflammatory responses against the parasite, but has spillover effects to bystander antigens, such as allergens. There is recent evidence that schistosomiasis during pregnancy similarly influences offspring allergic responses, as well as to vaccines. We have shown that allergic airway inflammation (AAI) in adult murine offspring from schistosome-infected mothers is strongly modified by the phase of maternal infection, and suppressed when pregnancy was initiated during late chronic stages. Further, this was associated with changes at the fetomaternal interface, specifically in terms of an infection-phase-specific shifts in placental transcriptional profile as well altered cytokine production to schistosome antigens. We have since further investigated the potential effect of this maternal infection within the immune cell compartments of these offspring, and in our in vivo model begun exploring the early sensitization stages of allergic response in these offspring, as well as other vaccination models. In line with epidemiological trends, we have found differential T and B cell responses to vaccination of offspring exposed to transmaternal schistosomiasis, with these changes relying heavily on vaccine vector and the mode of antigen delivery. Through altered vaccine strategies, we have been able to further modify these antigen-specific responses, and our continued work investigates the mechanisms underlying this. Our studies will help to understand the effects of the maternal immune status during pregnancy on immune predisposition in later life, and mechanisms for fine tuning immune responses.

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The TAKeOFF ("Tackling the Obstacles to Fight Filariasis and Podoconiosis") consortium

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In the course of the Research Networks for Health Innovations in Sub-Saharan Africa initiative, the TAKeOFF consortium is one of five consortia that are funded by the German Federal Ministry for Education and Research with the overall goal to improve health research capacities and strengthening local health systems in African countries. Five partners from Africa and Germany with high expertise in the research fields of lymphatic filariasis (LF) and podoconiosis (Podo) have joined forces to tackle the obstacles to fight LF and Podo together:
1) Kumasi Centre for Collaborative Research in Tropical Medicine (KCCR, Ghana),
2) National Institute for Medical Research (NIMR, Tanzania),
3) University of Buea (Cameroon),
4) University Hospital of Bonn (UKB, Germany),
5) University of Munich (LMU, Germany)
TAKeOFF receives funding for a five year period to work on nine interconnected work packages (WPs) which address several aspects on the way to an integrated disease management for LF and Podo. Even though LF (infection with filarial worms) and Podo (prolonged contact with red clay soils of volcanic origins) have different causes, they share the development of lymphedema of the leg as a disease symptom that can account for severe disabilities.
Investigated tasks in the course of TAKeOFF include i) possibilities to reach the affected population, ii) to evaluate the geographical distribution, iii) to develop new, preferably non-invasive diagnostic markers and iv) to reduce the burden of the diseases by improving morbidity management. A multinational Filarial Clinical Trial & Research Platform (F-CuRE) with the overall goal to improve research in LF and Podo will be developed to combine the different tasks. F-CuRE includes ICH-GCP training for trial staff as well as harmonisation of standard operating procedures, monitoring strategies, pharmacovigilance processes and electronic data capture systems. All trials will acquire samples to establish biobanks in the African and German partner institutions providing a basis for the search of biomarkers in blood,urine and saliva.
To achieve sustainable effects, TAKeOFF does not only stimulate intensive exchange about ideas, challenges and their solutions between the partners but is also well-connected to other health institutions. Close collaborations with competent authorities,like the national FDAs and local ethics committees, have helped both sides to improve the processes. By engaging the Ministries of Health in the respective African countries and the WHO as well as experts from other institutions working on LF or Podo, we hope to achieve long-term progress even beyond the funding period.
Currently TAKeOFF focuses on the clinical trials for LF and Podo morbidity management (WP4, WP5). Recruitment and treatment are already finalized in Ghana and are ongoing in Tanzania and Cameroon. If these trials prove the impact of doxycycline on morbidity management, the treatment strategies will be adopted by the WHO.

P68

Detection of Histoplasma DNA from pathology blocks by specific and broadrange qPCR

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Histoplasmosis is a fungal infection by the obligate fungal pathogen Histoplasma. The burden of histoplasmosis is difficult to assess due to the unspecific clinical presentation and a lack of sensitive diagnostic tests. Tissue biopsies are frequently needed to establish the diagnosis, but cultures may remain negative and histopathology may not differentiate histoplasmosis from other invasive fungal infections.
We evaluated a specific qPCR assay targeting the ITS-1 region of Histoplasma on Formalin-fixed, Paraffin-embedded (FFPE) tissue specimens in order to improve specificity and to provide insights into the epidemiology of histoplasmosis. To gain further insights into the optimal molecular strategy to identify fungal DNA a broadrange fungal PCR assay targeting the 28s gene was also applied. Diagnostic accuracy was evaluated using 67 FFPE samples from patients with proven invasive fungal infection, including 36 samples from patients with suspected histoplasmosis and 31 samples with other fungal infections as assessed by histopathology.
The clinical sensitivity of the specific and broadrange qPCR for histoplasmosis could be determined at 94% and at 48,5%. All samples from other fungal infections were negative with the specific qPCR demonstrating 100% clinical specificity. However, the broadrange assay amplified DNA from Emergomyces (n=1) and Paracoccidioides (n=2) in samples suggestive for histoplasmosis by histopathology.
In conclusion, amplification of Histoplasma DNA from FFPE samples by a specific qPCR is more sensitive than with a broadrange qPCR. However, identification of other fungal pathogens from suspected histoplasmosis suggests that a combination of both assays improves the diagnoatic accuracy and allows a better insight in the epidemiology of endemic mycosis.

P69

The addition of albendazole to ivermectin does not reduce female worm fertility in onchocerciasis

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Background: The question whether ivermectin (IVM) combined with albendazole (ALB) at higher doses and given twice per year might generate sustained reduction in microfilariae (Mf) by reducing female fertility or by killing adult worms in onchocerciasis led to the implementation of a randomised open-label clinical trial in an endemic area in Central Ghana.
Methods: The trial was carried out for a total duration of 36 months. Treatment was administered annually at 0, 12 and 24 months or semiannually at 0, 6, 12, 18 and 24 months. Skin snips to assess the Mf-load were taken at 0, 6, 18 and 36 months. The trial ended at 36 months with the surgically removal of the onchocercomata (nodulectomy) to histologically determine the drug effects on the adult worms. In total 272 Mf-positive participants, with at least one palpable onchocercoma were treated with either 1) IVM 200µg/kg annual (N = 68), 2) IVM 200µg/kg semiannual (N = 68), 3) IVM 200µg/kg plus ALB 800mg annual (N = 70) or 4) IVM 200µg/kg plus ALB 800mg semiannual (N = 66). 80% of the treated patients (N = 218) took part in the nodulectomies.
Results: The histological analysis showed normal embryogenesis in 11 – 23% of the adult female worms with no significant difference comparing the four treatment groups (p = 0.1229). With a range of 55 - 59% the proportion of dead worms did also not differ between the 4 groups (p = 0.9198). The proportion of individuals that completely cleared Mf at 36 months (after 3 annual/5 semiannual rounds of treatment) was 35/56 (63%, 95% CI [49-74]) in the IVM annual, 42/59 (71% [59-81]) in the IVM semiannual, 39/64 (61% [49-72]) in the ALB+IVM annual and 43/53 (81% [69-89]) in the ALB+IVM semiannual group. The addition of ALB did not improve the efficacy, however, the increase from annual to semiannual drug administration resulted in a sustained decrease of Mf-positive individuals (annual: 46/120, 62% [53-70]; semiannual: 27/112, 76% [67-83], p = 0.024).
Conclusion: The results confirm that semiannual administration of IVM leads to significantly lower MF-positive rates after one year without drug(s). However, addition of ALB did not have a significant impact neither on microfiladermia nor worm fertility so that it may be omitted in areas that are not co-endemic for LF. Alternative treatment strategies for the treatment of onchocerciasis are still needed and clinical trials with newly developed drugs, re-purposed drugs or new drug combinations are planned or already ongoing to reduce female worm fertility and will be discussed in the presentation.

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Seroprevalence and Risk Factors of Human Cysticercosis in Mocuba District, Central Mozambique: A pilot study

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INTRODUCTION
Taenia solium cysticercosis constitutes a serious but under-recognised public health problem, particularly, in developing countries. Neurocysticercosis, the larval stage of Taenia solium in the central nervous system, is a leading cause of epilepsy in endemic areas. This study was conducted to generate baseline information regarding the seroprevalence and risk factors of human cysticercosis, and the association with epilepsy in Mocuba district, located in Zambezia province, Central Mozambique.

METHODS
A total of 1087 persons were investigated in a cross-sectional study carried out in 8 selected villages in the study district using Western Blot IgG kits from LDBIO Diagnostics (www.ldbiodiagnostics.com) and HP10 Ag-ELISA assay (http://www.apdiagroup.com) after informed consenting was given by the participants. Socio demographic and clinical data including gender, age, education, sewage disposal, religion, history of epilepsy and pork consumption were taken.
A 5 ml sample of venous blood was taken by venepuncture and blood serum was removed, put into 3 aliquots and frozen at -20 ºC until transported to the Parasitology Laboratory at Faculty of Medicine, Eduardo Mondlane University in Maputo. Here serological testing was carried out to determine the presence of antigens and antibodies against Taenia solium larva.

RESULTS AND DISCUSSION
The study revealed that 54 (4.97%) persons had T. solium circulating antigens as detected by Ag-Elisa test, while immunoblot test on the same sample found 19 (1.6%) persons seropositive. Among 111(10%) reportedly persons with epilepsy, 3 (2.7%) and 2 (1.8%) were found positive by Ag-Elisa and immunoblot test, respectively, and did not differ significantly ($p > 0.05$) with that of non-epileptic persons (51/975, 5.2% and 17/975, 1.7%, by Ag-Elisa and Immunoblot, respectively). Older age (OR = 4.46; 95% CI = 1.37 - 14.54) was significantly associated with seropositivity to T. solium cysticercosis by Ag-Elisa, but not by Immunoblot (OR = 4.31; 95% CI = 0.57 - 32.85). Other risk factors such as gender, education, sewage disposal, religion, epilepsy and pork consumption were not statistically different between those with epilepsy and without epilepsy.
In our study, we found more patients Ag ELISA positive than western blot positive. This could be in part due to the fact that the HP10 Ag-ELISA detects both T. solium and T. saginata antigens, while the western blot assay detects only T. solium larva antibodies. In addition the sensitivity of the

western blot assay is influenced by the number of cysts in the brain and can vary from 65% to 97%.

CONCLUSION

Our findings confirm that human T. solium cysticercosis is present in the area and plays an important role as aetiological cause of epilepsy though it might not be the unique cause of epilepsy in the area. Further epidemiological, clinical and imaging studies are needed to generate more baseline information regarding the burden of disease and its clinical features.

P71

The German-African Projects MAP2CO/MAP-TB and TAKeOFF – Avenue to target the sustainable developmental goals (SGDs) raised by the WHO

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The long lasting working relationship between IMMIP in Bonn (Germany) and the Department of Microbiology and Parasitology in Buea (Cameroon) enables numerous possibilities to target the challenges of the SGDs raised by the WHO. Indeed, during a German Research Foundation (DFG)-funded project (MAP2CO) which focused on the filarial nematode *Mansonella perstans*, we were able to characterize ecological zones prerequisite for *M. perstans* infection and identified the so far unknown vector for transmission in the South-West region of Cameroon. Whereas mass drug administration with ivermectin had limited efficacy on *M. perstans* prevalence in areas with optimal vector habitat, we could show that doxycycline treatment effectively reduced *M. perstans* microfilarial burden. Moreover, we established an in vitro culture system for long-term maintenance of *M. perstans* and thus, for the first time, used a *M. perstans*-specific worm antigen extract from the cultured parasites to decipher the specific T-cell responses in *M. perstans*-infected individuals. We also revealed that *M. perstans*-microfilaremic individuals have a distinct immune profile, which is characterized by increased Th2 and regulatory cell populations concomitant with reduced systemic cytokine/chemokine and increased filarial-specific IgG4 levels. In conclusion, the *M. perstans*-specific down-regulation of immune responses might be an explanation for the increased susceptibility and worsened disease course of tuberculosis (TB) in *M. perstans* endemic regions. Therefore, within the next 3 years, we will perform a follow up project in Cameroon (MAP-TB) including two observational studies that aim to determine the influence of *M. perstans* infection on i) TB disease manifestation and on time the recovery under treatment and ii) on Bacillus Calmette-Guérin vaccination which is applied to protect children against TB disease progression. Besides the research about the filarial nematode M. perstans, the Bonn-Buea collaboration is part of the TAKeOFF consortium which is funded by the German Federal Ministry of Education and Research and aim to tackle the obstacles to fight filariasis and podoconiasis to make Africa and the world free of both of these diseases. In Cameroon, we will focus on the non-filarial lymphedema and aim to establish podoconiasis treatment centers in which afflicted individuals will be educated about the disease by trained health personal. Moreover, we will perform a randomized placebo controlled pilot trial to decipher if doxycycline can lead to an improvement or halt of the disease progression and reduces the frequency of attacks.
In summary, these projects are excellent examples how German-African collaboration provide a platform to tackle the SDGs, especially goal 1 “Quality and Education” that aim to create sustainable development and thus improve quality of life and goal 3 “Good Health and Well-Being” that aim to eliminate tuberculosis and neglecting tropical diseases.

P72

Barriers to facility-based delivery in post-Ebola Sierra Leone

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Background: Sierra Leone has one of the highest maternal mortality rates in the world. Encouraging the use of skilled birth attendance in health facilities is an important step in the endeavor to increase the number of safe deliveries. However, public trust in health facilities has greatly been damaged during the Ebola epidemic outbreak in Sierra Leone in 2014/2015, and little is known about external and intrinsic barriers to facility-based delivery (FBD) in the country after recovering from Ebola.
Methods: We conducted a qualitative study on FBD in Princess Christian Maternity Hospital, Freetown, which is the national referral maternity hospital in Sierra Leone. We performed six focus group discussions with a total of 35 participants including providers, pregnant women and recent mothers. The discussed topics included personal experiences, attitudes and behaviors regarding FBD and potential barriers. Discussions were tape recorded, transcribed and evaluated through content analysis.
Results: The women in our study were overall technically aware of the higher safety linked with FBD, in particular regarding emergency care in case of obstetric complications. However, this awareness often diverged from women´s individual desire to deliver in a supportive and trusted social and traditional environment, offering not only medical care but also emotional support. Close relatives and community members seemed to be highly influential regarding birth practices. Many women associated FBD with negative staff attitudes which they had experienced, and feared being left alone or not being treated well in hospital. Logistic issues regarding transportation problems or late referral from smaller health centers were also identified as frequent barriers to FBD.
Conclusions: Accommodating delivering women´s emotional state of insecurity and fear by more supportive staff attitudes and by acceptance of an accompanying familiar person throughout the delivery procedure could be promising approaches to increase confidence in health institutions and FBD. However, these approaches also imply revising health systems structures, like working conditions of overloaded hospital staff that are conducive for a friendly atmosphere, sufficient space in delivery wards allowing the women to bring a birth companionship, or like the establishment of a reliable peripheral ambulance system to ensure transportation and fast referral.

P73

Prospective case-control study in African children: Is the number of stool pathogens associated with acute diarrhea?

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Background: Diarrhoea represents the second leading cause of mortality in children aged <5 years. In low-income countries, many children suffer from multiple diarrhoea episodes per year with the highest incidence in the age group ≤12 months. However, data on the prevalence of enteric pathogens in African infants are scarce. This prospective case-control study aims to assess the causes of acute diarrhoea in Ghanaian children aged ≤12 months.
Methods: Ghanaian children aged 0-12 months who visited the outpatient department (OPD) of a rural Ghanaian hospital in 2014-2015 were assigned to case or control group depending on existence of acute diarrhoea (cases) or other conditions (controls). In addition to demographic and clinical data, stool samples were collected and analysed for 18 potential pathogens using multiplex polymerase chain reaction (PCR) at the University Medical Center Hamburg-Eppendorf. To assess the association of diarrhoea with different variables such as positive PCR and the cycle threshold (Ct) value, univariate and multivariate analyses were performed to identify risk factors for diarrhoea.
Results: A total of 204 infants at a median age of 7 months (range, 0.5-12 months) were included in the study. While 107 patients (52%) suffered from acute diarrhoea, 97 were recruited as controls (48%). In univariate analyses, diarrhoea was significantly associated with female sex (p=0.048), a higher number of detected pathogens (median 3 versus 2, p=0.001) and a positive PCR result for Rotavirus (RV; p=0.011), Enterotoxigenic Escherichia coli (p=0.005), Giardia lamblia (p=0.036) and Cryptosporidium (CS; p=0.044). A significant association between a lower Ct value and presence of acute diarrhoea was observed for CS (p=0.015). After adjusting for gender and the number of pathogens, RV was the only pathogen associated with the presence of diarrhoea (p=0.034).
Conclusions: Enteric pathogens were highly prevalent in Ghanaian children aged 0-12 months visiting the OPD, with a higher average number in children with diarrhoea compared to the control group. Acquisition of enteric pathogens occurs very early in life. The presence of only four pathogens could be attributed to the occurrence of acute diarrhoea in univariate analysis, while RV seems to be the most important pathogen.

P74

Interjections of pain: are they biological pre-linguistic or cultural?

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The way speech evolved in human beings is yet to be elucidated. Pain interjections (PIs), i.e. spontaneous vocalization in response to an acute painful stimulus, e.g. in English ouch [[ɑwʧ], are elementary utterances which typically lack integration into the respective grammatical systems and might reflect early language development.stages.
In order to investigate cross-linguistic phonetic variations in PIs. native speakers of different languages from 148 countries were interviewed for the most common pain interjection used in their language.
PIs in 120 languages (Ls) belonging to 17 diverse language families (LF) and 1 language isolate were recorded. In all languages PIs start with a vowel. PIs are prototypically monosyllabic with a lengthened open, non-fronted initial vowel nucleus in almost all Ls and LFs examined (in the IPA range from [ɑː] to [ɔː]). PIs in most Ls and LFs start with [ɑ-] (93 Ls of 14 LFs, 1 isolate), followed by [u-] (16 Ls / 3 LFs), [ɔ-] (7 Ls / 5 LFs), [i-] (3 Ls / 3 LFs), and [e-](1 L / 1 LF). Expressive lengthening of the nucleus may lead to instability of the vowel which produces velar or palatal closing of the syllable coda: [ɑː] > [ɑw] > [ɑwʧ].
PIs have both, universal and culturally differing characteristics. In all Ls observed PIs start with a vowel, indicating a universal aspect of PIs, so far not covered in any list of human universals. Our main assumption is that open, non-fronted vowels are preferred in pain articulations because they can be rapidly articulated with least effort and with minimal conscious input. This assumption is supported by a distribution of prototype variants in 15/17 different language families. This observation may be related to the inconscious contraction of facial musculature in response to pain as also observed in non-human primates. The subsequent sounds of PIs vary in relation to different Ls and/or geographical areas suggesting a cultural coding. This may occur when the child needs to communicate to the caretaker that it suffers pain. Interestingly, the distribution of different PIs was only partly congruent with the distribution of LFs and/or subfamilies.
On one hand there is evidence pointing at a universal pre-linguistic starting point of PIs. On the other hand the only partial congruence of different PIs with various LFs either point at cross-lingual transmission or a convergent cultural evolution of PIs. Possibly, all three phenomena still take place. Studies in infants and toddlers are required in order to study the development from a universal cry pattern to a PI characteristic for a specific language. The timing of its emergence might be used as an indicator of physiological child development.

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Intravenous Artesunate for Imported Severe Malaria in Children treated in Four Tertiary Care Centers in Germany: a retrospective study

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Background
Intravenous artesunate (ivA) is the standard treatment for severe malaria. Data systematically evaluating the use of ivA in paediatric patients outside malaria endemic regions are limited. The aim of this case series was to summarize efficacy and safety of ivA for imported severe malaria in children in Germany.
Methods
Our retrospective case series included pediatric patients with imported severe malaria treated with at least one dose of ivA (Artesun®, Guilin Pharmaceutical; Shanghai, China) at four German tertiary care centers. Severe malaria was defined according to WHO criteria.
Results
Between 2010 and 2018, 14 children with a median (IQR) age of six (1;9.5) years were included. All children were of African descent. All but two patients had P. falciparum malaria; one child had P. vivax malaria and one child had P. falciparum and P. vivax co-infection. Median (IQR) parasitaemia at admission in patients with P. falciparum was 9.5% (3;16.5). Patients were treated with 1 to 10 (median (IQR) 3 (3;4)) doses ivA. All but one patient consecutively received a full course of oral antimalarial treatment. Parasite clearance was achieved within 2-4 days, with the exception of one patient with prolonged clearance of peripheral parasitaemia. Three patients experienced post-treatment hemolysis but none needed blood transfusion. Otherwise ivA was safe and well tolerated.
Conclusion
Intravenous artesunate was highly efficacious and safe in this pediatric cohort. We observed episodes of mild to moderate post-treatment hemolysis in approximately a quarter of patients. The legal status and usage of potentially lifesaving ivA should be revalued in Europe.

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Spektrum Der Gesundheitsprobleme Minderjähriger Flüchtlinge Und Asylbewerber Im Raum München

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Hintergrund: In den Jahren 2015 und 2016 kamen aufgrund andauernder, gewaltsamer Auseinandersetzungen in Nordafrika und dem Nahen Osten über eine Million Flüchtlinge in die Bundesrepublik Deutschland. Besonders unbegleitete wie auch begleitete minderjährige Flüchtlinge gehören zu einer überdurchschnittlich gefährdeten Gruppe, da sie in besonderem Maße den körperlichen und seelischen Belastungen der Flucht ausgesetzt sein könnten. Zur Erkrankungslast und den Erkrankungsarten der in Deutschland untergebrachten minderjährigen Flüchtlinge gibt es bislang kaum verfügbare Daten. Selbstverständlich treten auch bei Migranten unter 18 Jahren Erkrankungen auf, die dem bekannten pädiatrischen Spektrum entsprechen. Allerdings müssen auch spezielle Infektionserkrankungen wie z.B. Masern, Tuberkulose, Hepatitis B, Malaria, HIV oder selten auch Läuserückfallfieber bedacht werden.

Methoden: Im Rahmen einer deskriptiven retrospektiven Querschnittsstudie wurden bisher knapp 1900 vorwiegend ambulante aber auch stationäre, irreversibel anonymisierte Patientenkontakte in zwei Einrichtungen im Raum München (REFUDOCS e.V. Bayernkaserne und Dr. von Haunersches Kinderspital) aus den Jahren 2015 und 2016 retrolektiv statistisch ausgewertet. Ein weiterer Datensatz mit knapp 7000 ambulanten Patientenkontakten befindet sich derzeit noch in der Auswertung. Die Datenanalyse erfolgt mit Microsoft Excel und STATA®.

Ergebnisse: Die Analyse der ersten Daten lässt bereits erkennen, dass sich das Spektrum der Gesundheitsprobleme minderjähriger Flüchtlinge und Migranten nicht wesentlich vom Spektrum der in Deutschland lebenden minderjährigen Durchschnittsbevölkerung unterscheidet. Auch bei minderjährigen Asylbewerbern machen Hauptdiagnosen wie grippale Infekte, Atemwegsinfektionen oder Gastroenteritiden den mit Abstand größten Anteil der Erkrankungen aus. Auffällig ist jedoch das gehäufte Auftreten von parasitären Erkrankungen wie Skabies (40 Fälle bei 856 Patientenvorstellungen, Prävalenz in Europa: 0,5-2 pro 1.000 Einwohner). Zudem wurden Diagnosen wie Tuberkulose (13 Fälle bei 856 Patientenvorstellungen, Inzidenz 2010 in Deutschland: 5,3 pro 100.000 Einwohner) oder posttraumatische Belastungsstörungen (12 Fälle bei 856 Patientenvorstellungen) häufig gestellt.

Diskussion: Die Studienergebnisse zeigen deutliche Parallelen zu bisher bei erwachsenen Asylbewerbern erhobenen Daten. Einflussfaktoren wie Herkunftsland und Art der Unterbringung scheinen dabei das Auftreten bestimmter Erkrankungen, wie beispielsweise Tuberkulose oder Skabies, zu begünstigen.
Nach Abschluss kann die Gesamtanalyse dieses umfangreichen Datenkollektivs sicher dazu beitragen, eine bessere Planung und Umsetzung der Versorgung von minderjährigen unbegleiteten und begleiteten Flüchtlingen in der Zukunft zu ermöglichen.

P77

Liposomal amphotericin B for the treatment of old world CUTANEOUS LEISHMANIASIS in children. A case series.

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Introduction: Cutaneous leishmaniasis (CL) of the old world is caused by the protozoa *L. major* and *L. tropica* and is transmitted by sandflies. It usually presents as papules, nodules, and ulcers at the site of the bites, which heal over time with scarring and sometimes cosmetic disfigurement. *L. tropica* can also cause disseminated lesions and relapsing disease. With the migration of refugees from the middle east and central Asia into Austria we were seeing an increasing number of children suffering from cutaneous leishmaniasis. There are several treatment options, but the optimal management for pediatric L.tropica infections has not been defined. We present a case series of five children treated successfully with liposomal amphotericin B (L-AmB) in our hospital.
The characteristics of the five cases are shown in the table.

Case	Age/sex	Origin	Number lesions	Site of lesions	Species	Treatment before L-AmB	L-AmB	Outcome
1	10a/m	Afghanistan	3	face, arm	*L.tropica*	Cryotherapy Fluconazole p.o. 6 weeks	3mg/kg 6 days	healed
2	9a/m	Afghanistan	1	retroauricular	n.a. (*L.tropica* in sibling)	none	3mg/kg 6 days	healed
3	6a/f	Afghanistan	4	face, arm, foot	*L.tropica*	none	3mg/kg 6 days	healed
4	13a/m	Pakistan	7	face, wrists, arm	*L.tropica*	Fluconazole p.o. 6 weeks	3mg/kg 6 days	healed
5	4a/m	Syria	1	shin	*L.tropica*	none	3mg/kg 6 days	healed

Discussion: Leishmaniasis due to *L.tropica* is more resistant to treatment compared to lesions caused by *L. major*. All the children recently seen in our centre had infections with *L.tropica*. Topical treatment is either not very effective (paromomycin ointment) or too painful to be administered to small children without sedation (cryotherapy, phototherapy, intralesional sodium stibogluconate). Only one of our children had been treated with cryotherapy before referral to our centre. Systemic treatment was indicated in 2 children due to number or location of lesions, and it had been started with fluconazole as the leishmania species was not yet known at treatment initiation. Fluconazole has to be given for 6 weeks, raising concerns with compliance. Furthermore, *L.tropica* can be intrinsically resistant to fluconazole. We finally used intravenous liposomal amphotericin B in all 5 cases, giving 3mg/kg for five consecutive days and a sixth dose on day 10. It was very well tolerated and effective in all children. With the predominance of *L.tropica* as causative species in leishmaniasis patients currently presenting to our centre, we are now using liposomal amphotericin B as the preferred first line treatment in all children with this disease.

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Transjugular Intrahepatic Portosystemic Shunt (TIPS) for Hepatic Schistosomiasis

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Background: Globally, an estimated 230 million people are affected by schistosomiasis. Upper gastrointestinal bleeding secondary to variceal rupture is an important life-threatening complication in patients with hepatic schistosomiasis. The aim of this retrospective case series was to describe and evaluate transjugular intrahepatic porto-systemic shunt (TIPS) creation as prophylaxis for gastrointestinal bleeding related to hepatic schistosomiasis.

Methods: Case records at the University Medical Center Hamburg-Eppendorf were searched for patients with hepatic schistosomiasis treated with TIPS creation. Results: Three patients received TIPS creation for primary prophylaxis (n=1) and secondary prophylaxis (n=2) of variceal bleeding. All patients had esophageal varices (III°) with red spots and hypersplenism without ascites. TIPS creation was performed without acute complications and HPVG was significantly reduced in all patients (24 to 8 mmHg, 23 to 11 mmHg, 21 to 10 mmHg). Two patients showed Regression of varices on control endoscopy (one without endoscopic control. During the cumulative 6.75 patient-years of follow-up no episode of variceal bleeding occurred. Conclusion: TIPS placement can be a safe and effective intervention to prevent upper gastrointestinal bleeding in patients with hepatic schistosomiasis. Prospective studies are needed to further evaluate long-term effectiveness and adverse events such as hepatic encephalopathy.

P79

Tropenmediziner in der Bundeswehr – Zwischen Einsatzrealität und Präventivmedizin

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In den vergangenen Jahren hat sich das Einsatzspektrum der Bundeswehr deutlich verändert. Aufgaben der Bündnisverteidigung mit vielfältigem internationalem Engagement kamen zur nationalen Verteidigung hinzu. Die Konsequenz sind Einsätze auch in subtropischen und tropischen Regionen, die in besonderer Weise Anforderungen an die medizinische Betreuung der entsandten Soldaten stellen.

Der Sanitätsdienst der Bundeswehr reagiert auf diese Herausforderung mit der Bereitstellung von Fachärzten mit der Zusatzbezeichnung Tropenmedizin, die – zusätzlich zu ihrer jeweiligen Spezialisierung – über breite infektionsmedizinische Kenntnisse mit tropenspezifischem bzw. tropentypischem Fokus verfügen. Gewünscht ist ein klinisch versierter Generalist, der in der Lage ist, trotz limitierter Ressourcen und unter sehr unterschiedlichen Rahmenbedingungen, die die tropische Umgebung und der jeweilige Einsatz bedingen, kompetent und entscheidungssicher zu agieren.

Auch jenseits der Einsatzverpflichtungen haben Tropenmediziner der Bundeswehr im militärischen System vielfältige Verwendungen. Im klinischen Bereich arbeiten sie als Ansprechpartner für infektionsmedizinische Fragestellungen in ambulanten Sanitäts-Versorgungszentren (SanVersZ) oder an einem der fünf Bundeswehrkrankenhäuser in Deutschland, wo sie stationäre Patienten mitversorgen. Ein weiterer Schwerpunkt kann auf der präventivmedizinischen, gutachterlichen Tätigkeit und Beraterfunktion, z. B. im Kommando Sanitätsdienst der Bundeswehr oder anderer Behörden, liegen, wo verbindliche präventivmedizinische Empfehlungen anhand von fundierten epidemiologischen Risikoevaluationen erarbeitet werden.

Für den Erwerb der Zusatzbezeichnung „Tropenmedizin“ ist eine anspruchsvolle, bislang fast dreijährige Weiterbildung notwendig, wovon ein Jahr obligat im tropischen Ausland absolviert werden muss. Ziel dabei ist nicht nur der Erwerb fachlicher Expertise und Handlungssicherheit, sondern auch die Auseinandersetzung mit unterschiedlichen Gesundheitssystemen und sozioökonomischen Gegebenheiten in den Ländern des Südens, deren Kenntnis insbesondere für etwaige Verwendungen in beratender Tätigkeit notwendig ist.

Um den Bedarf an Tropenmedizinern für die eigene Verwendung zu decken, ermutigt und fördert der Sanitätsdienst der Bundeswehr deren Ausbildung. Diese ist in curricularer Form organisiert und beinhaltet bislang eine 12monatige Ausbildung im Inland am Fachbereich Tropenmedizin zusammen mit den Kooperationspartnern Bernhard-Nocht-Institut und Universitätsklinikum Hamburg-Eppendorf, einen 3monatigen Diplom-Tropenkurs sowie die 12monatige klinische Ausbildung im tropischen Ausland (Standorte Moshi/Tanzania und Dakar/Senegal). Dieser Karriereweg steht auch zivilen Seiteneinsteigern offen, die sich ohne oder nur mit teilweise abgeschlossener tropenmedizinischer Weiterbildung als Zeitsoldat für mehrere Jahre verpflichten.

P80

When Rare Meets Seldom - Unusual Complication in the Therapy of an Uncommon Disease

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Case presentation: A 60-year-old female patient of Turkish origin was admitted for fatigue, loss of appetite, intermittent vomiting and night sweats. The symptoms had started 8 months ago and the patient had lost 12 kg of weight during this period. Endoscopy of the upper and lower gastrointestinal tract had been normal. A few days prior she had returned from a stay in Turkey where she had received electrolyte infusions in a hospital for weakness and dehydration. Her medication included Opipramol for depression.
On presentation the patient appeared weak, emaciated and febrile (39.2 °C). Laboratory abnormalities included sodium of 126 mmol/L, C-reactive protein of 42 mg/L and venous plasma glucose of 58 mg/dL. Potassium and creatinine were normal as well as serum cortisol (82 µg/L).
Blood cultures grew Brucella melitensis and therapy with Doxycycline and Gentamicin was started. Computed tomography showed abdominal lymphadenopathy and splenomegaly, with no signs of spondylitis. Transesophageal echocardiography was normal. Opipramol was switched to Mirtazapine for suspected drug-induced syndrome of inappropriate antidiuretic hormone secretion. Fever subsided and C-reactive protein declined. After one week the antimicrobial therapy was changed to Doxycycline and Rifampicin and the patient was discharged.
Four days later she was readmitted with prostration, persistent vomiting and inability to eat or drink. Laboratory showed acute renal failure, hypoglycemia of 38 mg/dL and sodium of 128 mmol/L. The patient was started on intravenous fluids and parenteral nutrition. Central nervous system involvement of brucellosis was ruled out with cranial magnet resonance imaging and spinal tap.
At this point the whole clinical course was reconsidered. It was conspicuous that shortly after discharge the clinical state of the patient was worse than ever before. Evaluation of the pituitary adrenal axis was repeated and now showed a marked elevation of adrenocorticotropic hormone (1280 ng/L) with a low serum cortisol (58 µg/L). A diagnosis of Rifampicin-exacerbated primary adrenal insufficiency was made. Supplementation therapy with hydrocortisone and discontinuation of Rifampicin led to marked clinical improvement.
Discussion: Brucellosis is a rare condition in Germany with less than 50 notified cases annually. Addison's disease (primary adrenal insufficiency) has an incidence of roughly 5 cases per million persons per year (400 new cases per year) in Germany. The combination of two unrelated rare diseases with systemic symptoms is challenging for the clinician. Even recognizing the second disease – in apparent contradiction of Ockham's razor – is not easy and requires vigilance and readiness to question the working hypothesis. Exacerbation of Addison's disease during treatment with Rifampicin is well documented in several case reports.

P81

Strongyloides stercoralis Hyperinfection Syndrome Presenting as „Mechanical“ Ileus After a Short Course of Oral Steroids for Chronic Obstructive Lung Disease (COPD) Exacerbation

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We report a case of a fatal Strongyloides stercoralis hyperinfection syndrome (SHS) in a migrant from Kenia, who had been living in Germany for three decades. A short course of steroid treatment (5 days oral 40 mg Prednisolone) for COPD exacerbation had been administered 4 weeks prior to the presentation.
A 56-year-old female patient presented with a 7-day history of obstipation, malaise, and dyspnea at rest. A computed tomography (CT) scan of the abdomen and pelvis showed a thickening of the bowel wall (Figure 1A). Signs of proximal mechanical small bowel ileus were noted (Figure 1B). The patient underwent an urgent diagnostic laparatomy with retrograde bowel decompression. No mechanical obstruction was detected. The patient was discharged from the surgical department but was re-admitted to the emergency department 5 weeks later with constipation, abdominal discomfort, fatigue, weight loss and malaise. The esophagogastroduodenoscopy revealed an edematous duodenal mucosa with diffuse erythema, the colonoscopy showed diffuse mucosal erythema with shallow fibrin-covered ulcers of approx. 6 cm size in diameter in cecum, patchy erythema with small aphtoid ulcers in colon as well as diffuse erythema with ulcers in rectum. Histopathological examination of biopsy revealed diffuse erosive proctocolitis with xanthomatous and granulomatous inflammation and slightly increased infiltration of eosinophil granulocytes. Moreover worm-like elements were detected in some crypts as well as in deeper parts of the mucosa and submucosa as tissue infiltrating larves. (Figure 1C). The helminth was identified morphologically (Figure 1D) as Strongyloides stercoralis, confirmed by a S. stercoralis-specific 18S rRNA-gene -qPCR (CT 28,6). S. stercoralis DNA was also detected in the bronchoalveolar lavage. Treatment with oral Ivermectin (200 µg/kg) and Albendazole 400 mg BID was initiated urgently. The patient developed a septic shock with E. coli bacteremia and died despite intensive care treatment.
Our case highlights the importance of maintaining a high index of suspicion for strongyloidiasis in patients from endemic areas even years after they left the country of origin. It demonstrates that even a 5-day course of prednisolone is able to trigger SHS in patients with underlying strongyloidiasis. History of frequent administration of oral Prednisolone for COPD exacerbations in the past raises the question why and how the last steroid regimen provoked SHS. SHS can present with plethora of gastrointestinal symptoms including ileus, and the absence of eosinophilia during the whole course of the disease should not lower the level of suspicion in the appropriate clinical setting.

P82

The impact of traditional herbal medicine on the prevalence of bacterial and fungal pathogens in chronic wound infections in rural Ghana

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Background
Chronic wound infections (CWI) are health complications with high socioeconomic impact but are frequently neglected in sub-Saharan Africa. Studies on wound infections in this setting are rare, because the polymicrobial bacterial infection of most wounds makes microbiological analysis demanding. Herbal medicine is frequently used as first-line treatment in most African countries and we hypothesized that pathogen distribution in wounds depends on the kind of treatment.
Patients and methods
Wound swabs of 302 patients coming in 2017/2018 for treatment to the St. Martin de Porres Hospital in Eikwe WR, Ghana were analyzed by standard microbiology cultivation techniques. Species of pathogens were identified by MALDI-TOF MS and antimicrobial susceptibilities by VITEK. Obtained data were compared with data collected in 2014 from the same region.
Results
Of 302 analyzed wound swabs, 68 (23%) where obtained from patients with CWI.
32/68 (47%) of the respective patients had previously been treated with herbal medicine, and 31/68 (46%) did not receive any herbal medicine, respectively. However, partly patients in both groups also received antibiotics. No precise information on treatment with herbal medicine was available for 5 (7%) of 68 patients.
Wound origins were unknown in 33 of 68 (49%) cases and average duration of the wound was 27.5 months (range 3-240 months). 58 of 68 (85%) CWI were located at the lower extremity. 66 of 68 (97%) CWI were polymicrobial. A total of 281 different pathogens were isolated consisting of 71 different bacterial and 5 different fungal species. On average 4.1 (range 0-12) species per wound were identified. Gram-negative pathogens, n=178 (63%), were predominant followed by gram-positive bacteria, n=97 (35%) and fungal pathogens, n=6 (2%). The most frequently detected bacterial species was *Proteus mirabilis*. Wounds treated with traditional medicine showed a broader bacterial spectrum (56 vs 44 different species), especially with more different gram-positive bacteria.
Compared to our previous study in 2014 with no MRSA found, this time half of the 18 *Staphylococcus aureus*-isolates were MRSA. Detected antimicrobial resistances of gram-negatives were in the range of our previous study. However, three non-fermenting gram-negative bacterial isolates were resistant to carbapenemes.
Conclusion
Herbal medicine is frequently used in the Western Region of Ghana to treat wound infections. Herbal treatment does not seem to influence the composition of bacterial key pathogens and their antimicrobial resistance. The emergence of multi-resistant bacteria pose a dangerous threat for patients. Meanwhile, there is a high percentage of resistant gram-positive and gram-negative bacteria with limited or even no antimicrobial treatment option. Cultural microbiology should be an essential part of offered laboratory investigations to limit inappropriate use of antimicrobials.

P83

A Live Worm Emerging from the Eyelid

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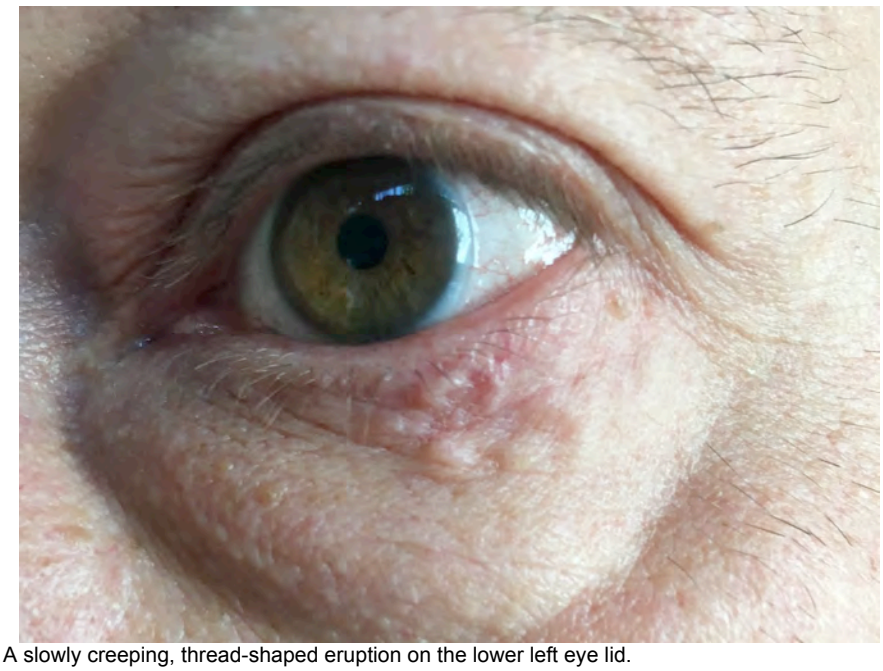
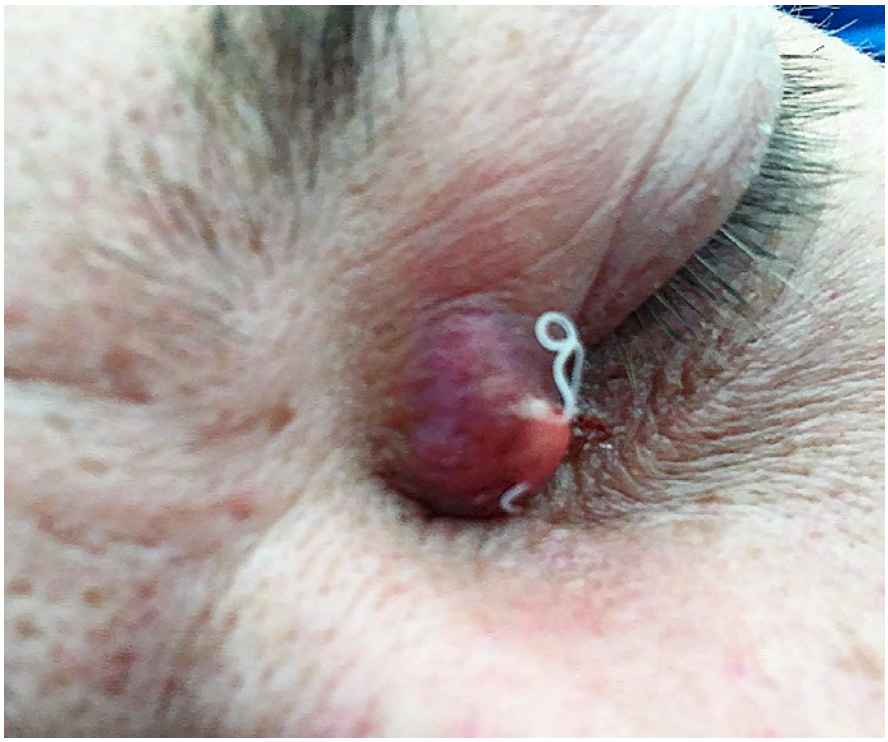
A 42-year-old German traveller presented with a 2-day history of a transient creeping eruption on the left palpebral region, occurring several times a day for a few minutes. Six months previously, he had travelled to Sri Lanka.
During consultation, a slowly creeping, thread-shaped subcutaneous eruption was observed on the left lower eyelid (Figure 1) for duration of approximately two minutes.
A blood eosinophil count and serology testing for filariae and Strongyloides stercoralis were unremarkable. Microscopy of microfiltrated blood also after diethylcarbamazine (DEC) provocation did not reveal any microfilariae.
Probatory antihelminthic treatment with ivermectin for 2 days was started. Ten days later, inflammation of the complete upper eyelid started developing into a nodule. A live thread-like, 12 cm long nematode spontaneously emerged from the upper eyelid (Figure 2). The patient extracted the worm himself without seeking medical care and documented the actively moving worm in a video.

Differential diagnosis was based on the periocular localization and included dirofilariasis or an Onchocerca lupi infection. A Loa loa infection could be ruled out as the patient had never travelled to sub-Saharan Africa.
A nematode-specific 12S rRNA gene polymerase chain reaction (PCR) from a sample of the worm was positive. Sequence analysis of the 510 bp amplicon using BLAST (www.blast.ncbi.nlm.nih.gov) revealed 99% sequence similarity with Dirofilaria (D.) repens sequences deposited in GenBank. An ELISA using a crude D. immitis antigen extract was negative.
Dirofilaria spp. are nematode parasites of dogs and other carnivores, transmitted by various mosquito species, with humans as accidental hosts. Human subcutaneous/ocular dirofilariasis is commonly caused by D. repens. In humans, the parasite development is impaired and microfilariae are usually not produced. An increasing number of reported human cases suggest that it is an emerging, albeit rare, infection. Cases are reported worldwide, especially from the Ukraine, Russia, Italy, and Sri Lanka, where our patient most likely acquired the infection.
D. repens infection most frequently presents as a single subcutaneous nodule, growing over weeks and months. Local swelling with changing localization occurs when the worm migrates. Approximately one third of cases reported occurred in the ocular region. The spontaneous emergence of a filaria from the eyelid has been observed only exceptionally.



A slowly creeping, thread-shaped eruption on the lower left eye lid.



A live worm spontaneously emerging from the upper left eye lid.

Literature:
Lindner AK, Tappe D, Gertler M, Equihua Martinez G, Richter J. A live worm emerging from the eyelid. Journal of Travel Medicine, September 2018. https://doi.org/10.1093/jtm/tay066

P84

Successful use of Quinacrine in five patients with treatment-refractory Giardiasis, Berlin 2017/18

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Nitroimidazole-refractory infections with Giardia intestinalis have been reported frequently in several countries including Germany, where only metronidazole is licensed for the treatment of giardiasis. Non-responders may be treated with other drugs or combinations of drugs which are licensed for other uses but not for giardiasis (off-label use) including paromomycine, mebendazole, albendazole and chloroquine. Other possible medications are not or no longer licensed in Germany including tinidazole, ornidazole, secnidazole, nitazoxanide and furazolidone.
Quinacrine (QC) – also not licensed in Germany – has been reported recently as an alternative drug for multi-resistant giardiasis. Developed in Germany in 1932, QC was extensively used for treatment and prophylaxis of malaria until the 1950s when it was superseded by chloroquine. Since the 1940s, QC was already the drug of choice for treatment of giardiasis until the better tolerated 5-nitroimidazoles were introduced in the 1970s.

Five cases of giardiasis with multiple treatment failure who attended our clinic were treated with QC. All cases (4 male, 1 female; ages 27 to 67 years) aquired the infection in the Indian subcontinent and denied other preexisting pathologies. Prior to QC treatment, patients had undergone several therapy attempts consisting of one to three drugs each. Patients had taken from three to eight different drugs without clearance from Giardia before attempting QC (table1).

Patient	Regime 1	Regime 2	Regime 3	Regime 4	Regime 5	Regime 6	Treatment regimes	Number of Substances used	Duration of Illness (months)
1	TNZ 1day	TNZ, 3days	MTZ + PMC	QC			4	4	5
2	MTZ	TNZ + PMC	ODZ+MBL+CHL	QC			4	7	6
3	MTZ + PMC	TNZ+MBL+CHL	QC				3	6	3
4	MTZ	TNZ	PMC	ODZ+PMC+MBL	SDZ+MBL+CHL	QC	6	8	7
5	MTZ	TNZ	PMC	ODZ + PMC	QC		5	5	9
							Median	**6**	**6**

legend:

Metronidazole MTZ; Secnidazole SDZ; Paromomycine PMC; Chloroquine CHL
Tinidazole TNZ; Ornidazole ODZ; Mebendazole MBL; Quinacrine QC

All Treatment Regimes used in five Patients with Quinacrine Treatment

All five persons treated with QC had negative results in repeated post-treatment microscopy and reported clinical improvement. None of the five patients reported significant adverse drug events during or after QC treatment. The duration of illness from diagnosis until cure ranged from 3 to 9 months (median 6 months).
QC appears to be an efficient therapy alternative for multi-resistant giardiasis. Logistic difficulties, restricted availability and high cost of QC in Europe as well as in-availability of drug resistance testing contributed to an unnecessarily prolonged disease duration and high consumption of antimicrobials.

P85

Proposed improvements of the WHO ultrasound protocol to assess schistosomiasis associated morbidity

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The WHO has published standardized ultrasound protocols for the assessment of schistosomaisis in 1993, and 2000 (1,2). To improve the WHO ultrasound protocols for schistosomiasis all relevant publications had been reviewed (3,4) and analyzed for their practicabilty and reliability. The following improvements are proposed:
Schistosoma (S.) haematobium:
1. to provide height adjusted minimal urinary bladder fillings. 2. to state whether or not the bladder contains blood clots, sediment, sludge or calculi. 3. to simplify and improve the urinary bladder findings scoring. 4. to provide a more fine-grained urinary tract obstruction (UTO) scoring. Optional investigations: “fibrosis of the renal pelvis” should be omitted. Presence of ureteric lesions, of calcifications, of prostatic echogenic lesions, of hydrocele or any other possible sign of genital involvement should be added. In pregnant women fetal growth parameters should be specifically compared with gestation time and placenta should be scanned
Portal hepatic and gallbladder fibrosis due to S. mansoni:
1. to omit all measurements except for the portal stem.
2. to obtain a more fine-grained grading also covering “in-between”-findings and to reduce intra- and inter-observer variance the ultrasonographist should have a second image pattern (IP) choice and a gradual grading scale. 3. risk scoring for gastrointestinal bleeding should be simplified. 4. gallbladder changes including external echogenic wall protuberances, sludge, calculi as well as the result of a ultrasonographic Murphy manoevre should be part of the standard protocol.
Interseptal and portal fibrosis due to S. japonicum or S. mekongi:
1. ultrasound pictures should be compared to standard image patterns (IP) covering both, interseptal fibrosis (“network patterns”) and portal fibrosis. 2. combined network- and portal fibrosis patterns are proposed. 3. network patterns should be sub-devided into two classes with predominant mesh size < 2.5 and >2,5 cm.
All reports on hepatic abnormalities must state how many patients have been screened for HBV, HCV, HDV and in Asia for concomitant liver fluke co-infections. If available, platelet count should also be taken into account.in the assessment of gastrointestinal bleeding risk.

References:
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2. Niamey Working Group, J. Richter et al. eds. WHO 2000; World Health Organization / TDR / STR/ SCH / WHO-Dokument: 1-51. www.who.int/tdr/publications/publications/ultrasound.htm; last accessed Oct 03,2012
3. El-Scheich, et al. Parasitol Res. 2014 113(11):3915-25; Erratum corrige: Parasitol Res. 2015 Jan;114(1):347.
4. Akpata et al. Parasitol Res 2015; 114:1279-1289

P86

Chronic oral ulceration and lip swelling after a long term stay in Guatemala: A diagnostic challenge

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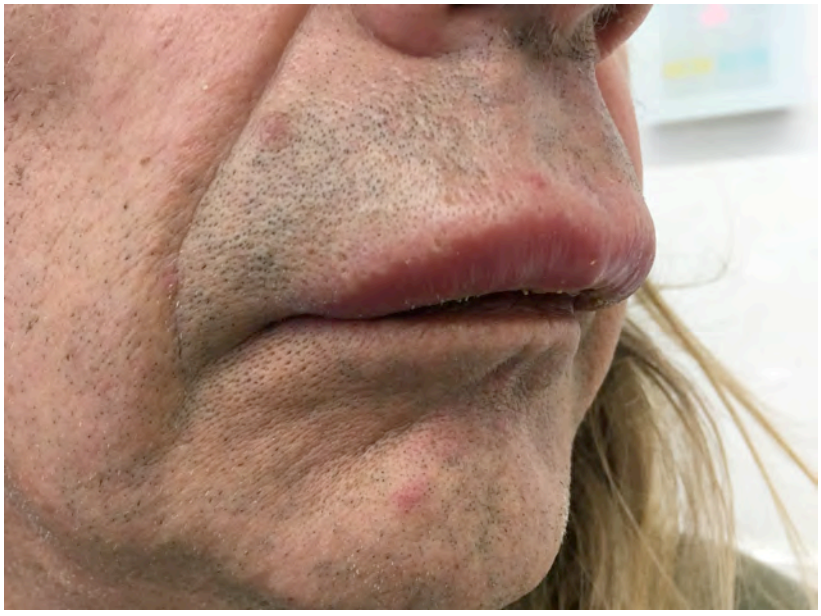
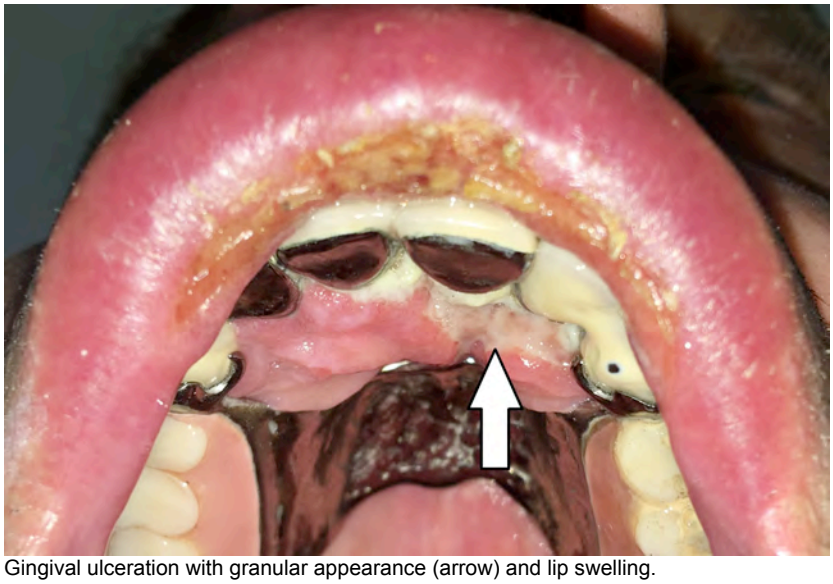
A 55-year-old German traveler presented to our clinic with an oral ulceration and swelling of the upper lip. The patient described gradual onset of a gingival swelling, slowly progressing into a painful ulceration and swelling of the lip over a period of 4 months (Fig. 1 and 2). He had no further complaints. He returned to Germany recently after a 3-year stay in Guatemala. The patient had a previous medical history of severe peripheral artery occlusive disease, cerebral stroke and tobacco abuse (30 pack-years).
Repeated empirical antibiotic treatments provided no relief. Previously, a bacterial culture and testing for sexually transmitted infections (HIV-, herpes-, chlamydial-infection, gonorrhoea, syphilis, chancroid, donovanosis) were negative. The initial histopathological examination of a lesional biopsy revealed a severe chronic, partly granulomatous gingivitis, without identification of pathogens in the Ziehl-Neelsen and periodic acid-Schiff (PAS) stains. Computed tomography revealed five peripheral pulmonary nodules<6 mm in diameter.
We considered the differential diagnosis of mucocutaneous leishmaniasis, atypical mycobacteriosis and systemic mycosis. The mucosal biopsies were further analyzed. Polymerase chain reaction (PCR) for Leishmania DNA was negative. A broadrange fungal-specific 28S ribosomal DNA qPCR and a Histoplasma specific ITS 1 ribosomal DNA qPCR were both positive for Histoplasma capsulatum. Antibodies against Histoplasma yeast cell antigen were detected using a western blot and a complement fixation test (Titer 1:8).
Antifungal therapy with oral itraconazole at a dose of 200–400 mg daily was initiated. The patient did not fully adhere to the recommended treatment. He took itraconazole 100 mg daily no longer than 6 weeks and stopped after having achieved complete clinical remission. A follow-up of the small peripheral pulmonary nodules was recommended, because disseminated histoplasmosis was suspected.
Chronic progressive histoplasmosis can be a diagnostic challenge presenting with an oral ulcer in an apparently immunocompetent patient.



Upper lip swelling slowly progressing over a period of 4 months.



Gingival ulceration with granular appearance (arrow) and lip swelling.

Literature:

Lindner AK, Rickerts V, Kurth F, Wilmes D, Richter J. Chronic oral ulceration and lip swelling after a long term stay in Guatemala: A diagnostic challenge. Travel Med Infect Dis. 2018 May - Jun;23:103-104. doi: 10.1016/j.tmaid.2018.

P87

The use of medical Point of Care Ultrasound (POCUS) in inpatients in Queen Elizabeth Central Hospital, Blantyre, Malawi.

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Background:
Ultrasonography has been categorised as “essential” to improving patient care in low resource health systems. Point of care ultrasound (POCUS) is ultrasound delivered at the bedside by a clinician, is relatively low cost, easily taught and can impact management in up to 70% of cases when used in low resource settings. In 2018 a POCUS training program was initiated in the Department of Medicine at the College of Medicine in Blantyre. The aim of this study is to analyse the distribution of the scans performed in the radiology department versus POCUS and describe common pathologies.

Methods:
Adult inpatient records were screened for eligibility. Data was collected from consenting inpatients over the age of 16, receiving an ultrasound scan for medical indications as part of routine care within the period of the study.

Results:
Up to 10.01.2019, data from a total of 163 patients was collected. Median age was 38 (range 16 to 82) and 51% were female and 82 (50%) were HIV positive. 171 ultrasound examinations were performed of which 87 (51%) were POCUS (defined as a scan delivered by a clinician at the bedside). Most common examinations were abdominal scans (n=61), echocardiograms (n=37) and focused assessment with sonography in HIV for TB (FASH) scans (n=37). While the proportion of POCUS among FASH-scans was high (88%), the attending clinician performed only 36% of abdominal scans and 33% of echocardiograms. Overall, pathology was reported in 38% of FASH-scans, 67% of abdominal ultrasound and 81% of echocardiograms. The median time from requesting to performing the ultrasound was 2 days (IQR 1-4) for formal ultrasound examinations and 0 days (IQR 0-2) for POCUS (p=0,002). A high proportion of scans had an impact on the management of the patient (123 of 171 examinations, 72%).

Discussion:
In a resource limited setting there is a high burden of pathology on ultrasound examination. Six months after introduction of POCUS-Training in Queen Elizabeth Central Hospital, over half of all medical sonography is performed as POCUS, shortening the time to diagnosis and changing the clinical management of patients.

P88

Training in Point of Care Ultrasound at Queen Elizabeth Central Hospital in Blantyre, Malawi – an ESTHER-Project

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Background:
One of the biggest challenges for helath systems in resource poor settings is the lack of qualified personnell, especially in the field of diagnostic imaging. This is true for both diagnostic imaging and imaging for guiding procedures. At Queen Elizabeth Central Hospital in Blantyre (QECH) most procedures are performed without imaging and waiting time for diagnostic ultrasound can be up to ten days, directly impacting patients safety and timely diagnosis.

Methods:
To improve this situation at QECH, a training program for Point of Care Ultrasound (POCUS) was initiated in the frame of the ESTHER cooperation between the University Medical Centre Hamburg-Eppendorf (UKE) and the College of Medicine in Blantyre (COM). Through a combination of short-courses, continuous evaluation and mentoring and external supervision the programme aimed to make POCUS available and routinely used for all patients admitted to the medical department.

Results:
This abstract reports the initial steps of the cooperation, the training methods, the current situation and the measures to increase the chance for sustainability. First, clinical questions that were accessible to POCUS examinations in the Malawian setting were identified. Main fields were the guidance of interventions, focused assessment with sonography for HIV-associated tuberculosis (FASH), identification of kidney pathologies, lung pathologies, deep vein thrombosis and basic echocardiography. To date total of 25 doctors and clinical officers have been trained in the use of POCUS, including 5 doctors who have acted as trainers in courses at COM and have been invited as trainers to external courses. POCUS is now routinely used and available for 80-90% of the patients on admission.

Discussion:
Systematic training in POCUS is feasible in the Malawian setting, adoption in to routine use can be achieved and sustainability is likely. Future training will extend to other departments and include income-generating courses for external staff to increase the chance for sustainability.

P89

Increased liver enzymes after Ayurvedic therapy

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In July 2018 a 70 year old female patient of South-Indian origin went back to her home in Kerala. She was taking a non-specified ayurvedic medicine during and after her trip to Kerala. She attended our clinic because she felt generally unwell and suffered from headache since her return. As part of her medical history had been operated for cataracts on both eyes and was suffering from moderate hypercholesterolemia. Her previous history was otherwise unremarkable. She was taking glucosamine 300mg/d due to chronic joint pain and phosetamine and methylsulfonylmethane p.o as nutritional supplements. Previous intake of Dehydroepiandrosterone acetate (DHEA) had been stopped.
Her liver enzymes were slightly increased (ALAT 49 and ASAT 47 U/l) before her first consultation in August 2018. The day she attended our clinic ALAT was found increased to 312 U/l. During the following three days ALAT further increased to 535 U/L and ASAT to 321 U/l, gamma GT to 47 U/l. Alkaline phosphatase remained normal as well as the white and red blood count, differential blood count and creatinine. Other results showed a past HAV-infection but no indication of a previous or active HBV, HCV, HEV or Dengue virus infection. Antibodies against Fasciola hepatica and Strongyloides stercoralis were not found. Malaria testing was negative. Three parasitological stool examinations after pre-patency period had elapsed were also negative. Markers of autoimmune hepatitis or primary biliary cirrhosis were all negative. Abdominal ultrasonography showed slightly irregular liver parenchyma without splenomegaly. Fibroscan elastography showed increased liver stiffness to 14.6 KPa (normal < 7.2 kPa).
During the following months, liver enzymes gradually decreased to ALAT 73 and ASAT 45 U/l. Considering an infectious etiology of the liver damage was ruled out, toxicology examinations were performed in the beginning of October. Increased mercury (1.6 microg/l, normal<1.0) and arsenic (1.6 microg/l; normal < 1.2) concentrations were found in blood and are likely to be a result of the chronic intake of Ayurvedic medication. Other hepatotoxic substances including heavy metals were not found. Within a month mercury and arsenic levels normalized completely. Ayurvedic medications should be taken into account in the differential diagnosis of liver injury.

Reference

Philips et al Clinical outcomes, histopathological patterns, and chemical analysis of Ayurveda and herbal medicine associated with severe liver injury-A single-center experience from southern India. Indian J Gastroenterol. 2018 Jan;37(1):9-17. doi: 10.1007/s12664-017-0815-8. Epub 2018 Feb 24.

P90

Returning Travelers in an interdisciplinary Emergency Department of a Tertial Referral Center (University Hospital Bonn): Experiences with Manchester Triage System and correlation with recent reports on emerging infections and outbreaks

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Aim: International travel activities are increasing. A significant proportion of travelers experience medical problems (travel accidents, infections) during or after the travel. Most infections are cosmopolitan diseases such as upper respiratory infections, flu-like-illness or traveler's diarrhea/gastroenteritis. Identifying patients with potential life threatening infectious diseases is challenging. Here we evaluate the Manchester Triage System (MTS) used in the Emergency Department and the value of reports on recent outbreaks and local epidemiology.

Methods: We performed a retrospective survey between 2012 and 2018 in the interdisciplinary Emergency Department of the University Hospital of Bonn using the hospital electronic database. Including criterion was presenting/referral with a recent history of international travel and suspected travel-associated infection. Manchester Triage System (3rd revised version) had been applied on all patients on presentation in the emergency department. Triage class and vital signs were analyzed on significant differences between patients with tropical infectious diseases and those with suspected cosmopolitan infections. Epidemiological Information were assessed from National surveillance systems and other information systems (e.g. CRM, Promed mail)

Results: We included 891 patients (47% female/53% male, average age 36.7 years) with a recent travel history presenting with fever and gastrointestinal complaints. 75% were self-presenters, 75% returned from a tropical destination. The spectrum of diseases included flu-like-illness/respiratory infection (30%), gastroenteritis/traveler's diarrhea (24%), malaria (9%), urinary tract infection (4%), dengue fever (3%), Rabies-prophylaxis after animal bite (1%), typhoid fever (7 cases), Hepatitis A (7 cases), Rickettsiosis (5 cases), chikungunya (3 cases) and amebic liver abscess (3 cases). Patients with potential life-threatening infections and suspected cosmopolitan diseases showed no significant differences in Triage class and clinical/vital signs. Triage-cassifier "Report on recent international travel“ was an important operator for identifying patients with need for further evaluation as only a minority of patients were assessed with pathological vital signs. Correlation of proven infections in our cohort with local epidemiology in the travel destination and recent outbreaks showed coincidence with emerging infections (dengue, chikunguya) while endemic infections (Malaria (except for P. vivax), Leptospirosis, Rickettsia, Hepatitis A, Typhoid fever) showed no noticeable correlation with local epidemiology.

Conclusion: Manchester Triage system is a reliable measure for identifying patients at risk in our cohort of returning travelers, especially when travel history was systematically included. Reports on recent outbreaks provide relevant information for diagnosing patients with emerging infections in our cohort even in a non-specialized general emergency department.

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Autochthonous human brucellosis in non-endemic Germany: Are travel and migration the only drivers?

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Background and objectives: In Germany, brucellosis evolved from an endemic occupational disease in the 1960s to a travel-associated foodborne zoonosis. The infection is mainly transmitted through the consumption of raw milk and unpasteurized dairy products in endemic regions surrounding the Mediterranean Sea. Although Germany is officially free from ovine/caprine and bovine brucellosis autochthonous human cases without any travel history are still reported. The actual source of these domestic human brucellosis cases remains to be elucidated.

Materials and methods: We therefore investigated 200 raw milk cheese samples imported from endemic regions and sold by retailers in Berlin (Germany) as well as online. Loose, non-labelled as well as pre-packed, labelled cheeses of five types (brine, cream, soft, semi-hard and hard cheese), made from bovine, ovine and caprine milk were included in our study. The presence of *Brucella* spp. was evaluated using both molecular assays and Farrell's selective culture medium. Two genus-specific qPCRs targeting IS711 and *bcsp31* were applied for screening and confirmation, respectively.

Results: *Brucella* DNA was found in 20.5% (n=41) of the investigated cheese samples. However, using classical culture methods viable brucellae could not be isolated from the samples tested positive by PCR. In contrast to the vendor information, essentially only three positive cheese samples were made from raw milk. Logistic regression indicated that *Brucella* was significantly more often detected in cheese from Bulgaria, France, Greece and Turkey (p=0.017) and in late summer purchases (p=0.036). Positive samples clustered at certain vendors indicating large-scale illegal imports.

Conclusions: Uncontrolled import of dairy products from endemic regions might explain human *Brucella* infections acquired in non-endemic EU countries. Hence, even in non-endemic countries consumers should be educated about potential health risks related to the consumption of raw animal products imported from endemic regions. However, consumers cannot easily identify hazardous dairy products if cheeses are sold with fraudulent intent and misleading information is provided. *Brucella* in raw milk cheese from endemic regions seems to be an ongoing challenge for food safety standards in the European Union which is why official sanitary control measures have to focus on pathogen detection and product quality in all segments of the food market.

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Verfügbarkeit der Impfungen gegen Influenza und Tollwut für die Reisemedizin: Tübinger Erfahrungen 2017

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Die über 7500 Immunisierungen des ITM im Jahr 2017 wurden mit Fokus auf Tollwut- (als schwer erhältlicher Impfstoff) und Influenza-Vakzine (als nur saisonal verfügbarer Impfstoff) retrospektiv evaluiert einschließlich anamnestischer und epidemiologischer Parameter sowie der jeweiligen Indikationen.
Influenza: Die Immunisierungen gegen Influenza begannen Ende des 3./Anfang des 4. Quartals und endeten Ende des 1./Anfang des 2. Quartals; ca. 5 Monate lang konnten wegen fehlender Verfügbarkeit des Impfstoffs keine Impfungen durchgeführt werden. Chargen mancher Hersteller wurden mit Ablaufdatum 31.03.2018 auf den Markt gebracht. Während sich das Auftreten der Influenza in Ländern gemäßigten Klimas hauptsächlich auf die Wintermonate beschränkt, kommen Grippefälle in den Tropen ganzjährig vor, in Ländern mit gemäßigtem Klima auf der Südhalbkugel entsprechend in unserem Sommer (1). Gemäß Dokumentationsauswertung ist davon auszugehen, dass im Einzugsgebiet des ITM in Tübingen im Jahr 2017 über 2000 Impfwillige mit Indikation für eine Influenza-Immunisierung wegen jahreszeitlicher Nichtverfügbarkeit nicht immunisiert werden konnten. Jährlich wären somit bei sehr vorsichtiger Hochrechnung bundesweit – basierend auf 17 reisemedizinischen Ambulanzen auf der Homepage der DTG (Stand: Januar 2019) – viele zehntausende Impfwillige mit Indikation nicht immunisiert worden. Um den Schutz der Reisenden und deren Mitmenschen gegen Influenza zukünftig zu gewährleisten, wäre geboten, den Impfstoff ganzjährig verfügbar zu haben.
Tollwut: 2017 wurden am ITM knapp 3000 Immunisierungen gegen Tollwut durchgeführt, gemäß Herstellerangaben sowie STIKO bei präexpositioneller Grundimmunisierung mit drei konsekutiven Gaben. Laut Empfehlung der WHO sollen nun jedoch zwei Impfungen für suffizienten Schutz ausreichen, Auffrischungen seien nicht zwingend (2). Hierdurch ergäbe sich eine wesentliche Kosten- und Zeitersparnis. Zudem stehen dadurch der Allgemeinbevölkerung insgesamt mehr Impfstoffe zur Verfügung, die den Engpässen entgegenwirken könnten, ggf. wäre ein off-label-use zu erwägen (2). Die Studie zu diesem reduzierten Impfschema basiert auf einer Altersgruppe <50 Jahre und auf nicht-standardisierten Testzeitpunkten bzgl. AK-Titer. Eine Langzeitstudie hierzu fehlt. Um einen einheitlichen Standard zu garantieren, sind Ergebnisse von Langzeitstudien abzuwarten sowie eine Einigung bezüglich der Impfrichtlinien wünschenswert.

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Incidence of MRSA among travelers (MRE-Trav)

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Methicillin-resistant Staphylococcus aureus (MRSA) is one of the most relevant multidrug resistant bacteria. In this study we prospectively determine the incidence of MRSA in nasal swabs among German travelers in the travel medicine outpatient clinic of the University Medical Center Hamburg-Eppendorf (UKE) at the Bernhard-Nocht-Institute for tropical medicine (BNITM). Between June 2018 and January 2019, we recruited 358 participants of whom 163 have returned specimens after travel so far. Nasal swabs were obtained from the participants before and after the journey and cultured on MRSA-selective media. After biochemical confirmation, the specimens positive for MRSA were tested for antimicrobial susceptibility. So far, we only detected one case of MRSA after travel in the screened population, indicating that there is no increase of MRSA colonization in travelers. We report from this currently ongoing study.

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Making the case for tinidazole as first-line treatment in giardiasis - experiences from a small Tropical Medicine Department in Germany

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In Germany there are no current guidelines for the treatment of the intestinal parasite *Giardia lamblia*, which is a common parasite in returning travellers from tropical countries as they are usually aquired by fecal-oral transmission in low-hygiene environments.

Traditonally, nitroimidazole drugs are used as first-line therapy, most commonly metronidazole 250-500 mg tid for 7 days. Efficacy with one course is reported as a range of 60 - 100%. Second-line courses are increasingly used, due to the emerging of resistances, but also due to difficulties adhering to a full therapy course.

Tinidazole is not available in Germany and must be imported by an international pharmacy. It is usually administered as a single dose of 2g (4 tablets of 500 mg) and efficacy is reported as ranging between 85 - 100%. Attack mechanism to the parasite is essentially the same, but in vitro slight advantageous differences like a higher amount of toxic radicals are reported. Side effects and adverse events are not substantial and similar or less common than in metronidazole.
The obvious advantage of tinidazole over metronidazole is clearly overcoming the compliance problem - even direct observed therapy is possible - and by that successfully administering an effective dose at once.

We present our experience with treating *Giardia lamblia* with tinidazole in our small Tropical Medicine Department since 2016. Medical, diagnostic, logistic, legal, financial aspects as well as the follow-ups are addressed. So far, we had no treatment failure documented and intend to continue to use tinidazole over metronidazole.

At the poster presentation we would like to invite poster exhibition visitors to participate in a small questionnaire about their preferences in first-line and second-line treatment of Giardia lamblia.

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