ABSTRACT-BOOK

O01

Rapid ResaImipenem/Acinetobacter NP test for rapid detection of carbapenem susceptibility/resistance in Acinetobacter baumannii.

P Nordmann[1]; M Sadek[2]; L Poirel[1]
[1] National Reference Center for Emerging Antibiotic Resistance (NARA) and Molecular and Medical Microbiology, University Fribourg; [2] University of Fribourg, Fribourg, Switzerland

Background
Acinetobacter baumannii is a significant nosocomial pathogen, especially as a cause of pneumonia intensive care units, and is associated with a prolonged hospitalization and increased mortality rates . Carbapenems are often considered to be drugs of choice for treating Acinetobacter spp. associated nosocomial infections . However, during the last few years, the increasing reports and outbreaks due to carbapenem-resistant Acinetobacter spp. represents a worldwide challenge. Consequently there is a need for rapid diagnostic testing of carbapenem susceptibility for that species.

Methods
The principle of the test is based on the reduction of resazurin (a viability colorant) by metabolically active bacterial cells, hence detecting bacterial growth, in the presence of a defined concentration of imipenem chosen to be slightly above that defining imipenem resistance (6 µg/ml). The bacterial growth is visually detected by a color change from blue (resazurin) to purple or pink (resorufin product). A total of 110 A. baumannii isolates, among which 61 were imipenem-resistant, were used to evaluate the test performance

Results
The sensitivity and specificity of the test were found to be 100%, by comparison with broth microdilution taken as the reference standard method. The Rapid ResaImipenem/ Acinetobacter NP test is highly specific and sensitive, and easy to implement in any routine microbiology laboratory and results are obtained within 2 h 30

Conclusion
Taking into account the common cross resistance between imipenem and meropenem in A. baumannii, use of the Rapid ResaImipenem/Acinetobacter NP test may contribute to optimize the antibiotic stewardship in infections due to A. baumannii that are increasingly multidrug resistant, even in Switzerland. Once culture is obtained, the gain of time by using the result of this test would be 18 h (in clinical practice one day) for implementing or not a carbapenem-containing strategy for treating A. baumannii infections.

O02
Implementation of simulation training in nursing homes during CoVID-19 pandemics

L Qalla-Widmer; C Petignat; D Héquet
Unité cantonale HPCI Vaud

From March 2020, the nursing homes (NH) staff has been on the front line of the battlefield linked to the CoVID-19 pandemics. The healthcare workers (HCW) are at the heart of the institutional system as they provide care for residents and fight to prevent the spread of the virus within the institution. CoVID-19 highlighted the lack of knowledge regarding infection control measures in NH. In this context, the Cantonal Unit for Infection Control and Prevention developed a simulation-training program to remain these gaps urgently.

Aim
The goal was to strengthen the capacity of NH staff to provide safe and effective care, while protecting the residents and themselves from the spread of infection.

Methods
The infection control nurses defined learning objectives, identified the infection control academic content, developed a teaching strategy fitted to any learning styles and selected interactive teaching resources. After drafting scenarios of simples and complex care situations of targeting learning objectives, they defined the ideal environment and the equipment. Finally, a training was organized and simulations scenarios were recorded on video.

Results
Each session consisted of a simulation conducted by an infection control nurse with a selected scenario. A session averaged 12 participants including nurse, assistant nurse and medico-technical staff.
Participants were placed in work situations through role-playing. Before each simulation session, participants were reminded of the mode of transmission of microorganisms, standard precautions and additional precautions. Debriefing was conducted after each session.
Pertinent identified issues included the misuse of disposable gown, (droplet precautions), the failure to comply with the standards of hand hygiene and gloves wearing. The lessons learnt from each session were quickly disseminated to other NH staff.
From June 2020 to March 2021, 67/160 (42%) NH participated in this simulation-training program. 109 sessions of simulation were conducted over 10 months. Over 1,800 HCW were trained (Fig.1).

Conclusion
Through simulation scenarios, essential elements of infection control can be emphasized. NH staff can be exposed to critical care scenarios and have the opportunity to respond without fear or risk for the resident.

O03

Epidémiologie locale de la pandémie de CoVID-19 dans les établissements médico-sociaux: Expérience Vaudoise.

C Riccio[1]; C Petignat[2]; L Qalla Widmer[2]; M Nahimana-Tessemo[2]
[1] Unité cantonale HPCI Vaud ; [2] Unité cantonale HPCI Vaud

L'épidémie de Sars-Cov 2 a touché beaucoup d'établissements médico-sociaux (EMS). Les résidents sont des personnes à risques de complications de par leur âge, leurs comorbidités et parfois leurs pathologies psychiatriques. L'identification et la prise en charge précoce des résidents positifs à la Covid-19 permet de limiter la propagation virale dans les EMS.

Objectifs
L'objectif est de récolter des données disponibles afin de comprendre le mode propagation du SARS-CoV 2 et de freiner la transmission du virus en EMS. Le but étant d'améliorer les pratiques de contrôle de l'infection et d'adapter les stratégies préventives.

Méthode
Récolte des données via l'Office du Médecin Cantonal, les EMS ou la plateforme de déclaration centralisée. Chaque alerte est traitée par un infirmier en prévention et contrôle des infections (PCI) qui contacte l'EMS ou se déplace si besoin pour définir ensemble d'une stratégie. L'infirmier rédige une consultation qui reprend les recommandations de prise en charge et de dépistages afin d'éviter une flambée de cas. Un suivi quotidien ou pluri-hebdomadaire est assuré jusqu'à résolution de l'épidémie. Lorsque l'EMS ne compte plus de résident CoVID-19 positif, un rapport final est rédigé pour clôturer l'épidémie.

Résultats
La première vague a durée du 9 mars 2020 au 23 juin 2020. 62 EMS/163 ont été touchés soit 38% des EMS vaudois et certains EMS ont eu deux épisodes. Le taux d'attaque moyen est de 16% (1-62%). Environ 700 résidents/5178 (14%) ont été affectés par l'épidémie. 400 résidents ont eu une infection documentée et 300 résidents ont présenté une clinique compatible avec la CoVID-19 mais sans résultat microbiologique ; avec 5% des décès (255/5178)
Lors de la deuxième vague allant du 10 Aout 2020 au le 31 décembre 2020, 104 EMS/163 (64%) ont été touchés. Le taux d'attaque moyen est de 38% (6-91%). 1914/5178 (37%) résidents affectés par l'épidémie, soit deux fois plus que lors de la première vague avec un taux de décès de 8% (426/5178). La durée moyenne des flambées de cas était de 5 semaines (2 -10 semaines).

Conclusion
Les EMS ont été fortement impactés par la deuxième vague plus longue et plus forte. Le dépistage systématique a conduit à une détection précoce des résidents asymptomatiques. Le renforcement des mesures de prévention, la collaboration avec les EMS et les multiples interventions des infirmiers en PCI ont permis de détecter et de combler certaines lacunes en PCI et de maitriser des nombreuses flambées.

O04
Introduction of a peer review system in infection control for acute care hospitals

J Notter[1]; L Clack[2]; M Rossi[3]; W Zingg[4]; M Schlegel[1]
[1] Kantonsspital St. Gallen; [2] Institut für Implementation Science in Health Care; [3] Luzerner Kantonsspital (LUKS); [4] Universitätsspital Zürich

Aim
At most Swiss hospitals, there is currently no external quality control performed in infection prevention and control (IPC). Some hospitals participate in Sanacert®, which among other standards, reviews the hospital hygiene standard based on methodological quality measures. The main problem is the lack of technical expertise specific to IPC and thus insufficient inputs for improvement. Interprofessional peer reviews are increasingly important in the context of continuous quality assurance in healthcare and are a proven procedure for improving quality with the involvement of external specialists.
To continuously assess and ensure the quality of IPC programs while offering a practical tool for improvement, we aim to develop and introduce a peer review system for the external examination and quality control of IPC programs.

Methods
The peer review system includes 3 phases:
Pre-visitation phase: Prior to the peer review visit, the IPC service will complete a structured questionnaire including detailed information on IPC service and structure including general information on the hospital/IPC service, existing guidelines, surveillance, intervention projects and educational activities. Additionally, general hospital staff will be asked to complete an online survey to reflect frontline perceptions of IPC.
Visitation: Peer reviewers will conduct semi-structured interviews with selected staff members (e.g. head of the IPC service, IPC staff, medical director, head of nursing) to further explore issues identified from the questionnaire and deepen the understanding of possible areas of concern. On-site hospital visits will be conducted with observations in selected areas if deemed necessary.
Feedback: After the peer review visit, a structured final report will be generated by the peers including identified strengths and weaknesses of the IPC program as well as suggestions for improvement.

Implementation
The peer review system will be piloted at the cantonal hospital of St. Gallen. After the pilot, the peer review process will be evaluated and adaptations will be undertaken if necessary. If successful, the availability of the peer system will be extended to other Swiss hospitals.

Conclusion
In summary, a peer review system for the external examination and quality control of IPC programs at Swiss hospitals will not only provide a possibility to ensure quality but also for the programs to receive meaningful input for improvement from peer experts in this field.

O05

Alerte Infection, a tool for an innovative public management of health care professionals to prevent epidemics in the Vaud canton

M Ku Moroni
HPCi Vaud

Aims

The objective of this public management is to control epidemics by reducing the communication time with the health care professionals, main actors on the field. The goal of this Public Health administration is to protect patients in acute care and nursing home residents from infections and communicable diseases in the Vaud canton.

Methods

With a first observation of information problem in epidemic cases, it was noted that health care professionals don't have time to get informed by themselves about hygiene hospital news or protocols last updates. The cantonal unit of Hygiene Prevention and Control of Infection in Vaud (HPCi Vaud) in charge of epidemics monitoring in health facilities, worked on a strategy to push in the fastest possible way important information to the health care professionals to prevent diseases' spread as soon as a situation has been detected. This solution has been managed according to communications methods and strategies.

Results

A free mobile application has been created in 2019 and released on mobile app stores.
It applies to care workers in Vaud health facilities: hospitals, clinics, CTR (Center for readaptation), EMS (nursing homes). This app sends PCI alerts classified by category that users can enable/disable according to their needs:

- Epidemics: outbreaks and cantonal guidelines (eg. epidemic notifications for gastroenteritis clusters, or wearing of mask regulation activation, or CoVID-19 updates for professionals)
- Prevention: awareness info, campaign and focus attention (eg. contaminated industrial materiel recall)
- HPCI courses and events in hospital hygiene
- HPCI documentation and recommendations updates
- School eviction HPCI updates

Conclusion

The priority of Alerte Infection is to reduce the communication time between the public administration and the care workers for major information to prevent and control epidemics. In the current context of the CoVID-19 pandemic, this tool has been very useful to communicate as fast as possible with the health care professionals about the details of the patient care and the multiple updates of pandemic recommendations. After 9 000 installations, the evolution of use shows that it has not been yet adopted by all the care workers in the Vaud canton. This implicates launching complementary communications and thinking about new improvements.

O06

Covid_kidz – an internet based information platform on Covid-19 testing targeting (pre-)school children

F Barbey; D Suter; P Haberstich; M Oberle; C Fux; S Haubitz
Kantonsspital Aarau

Aims
While the wild type Covid-19 pandemic in its first and second wave in Switzerland was merely driven by young adults the shift to variant of concern B.1.1.7 shows increased susceptibility not only in adults but also in younger children (Volz E, medRxiv 2021). Still there is an unresolved debate about the role of younger school children in population-wide transmissions, as outbreaks in schools seem to be very limited so far. A large body of evidence shows that children rarely suffer from severe disease (e.g. less general and respiratory symptoms (Bi. Lancet Infect Dis 2020; 20: 911–19), and rare MIS-C, (Multisystem Inflammatory Syndrome). Rigorous outbreak investigations of contact tracing authorities in school and even preschool children cause collateral damage: Nasopharyngeal swab testing in children may be associated with significant anxiety and discomfort while lacking impact on these children's health. Adapted sampling strategies using saliva instead of nasopharyngeal swabs are more children-friendly, but limited by significantly prolonged collection times and limited sensitivity due to low mucosal viral load, particularlyin children under 12 years of age (Euser S, medRxiv 2021). This is particularly true in an asymptomatic setting. Our project aims to overcome these fears by providing an age-appropriate information on Covid-19 testing for young school (and even preschool) children.

Methods
We build a webpage for children in preschool and primary school age with custom-made videos, pictures and text providing information on Covid-19 infection, its prevention and the different test modalities, all presented in an age-appropriate manner. The webdesign is optimized for mobile devices (i.e. smartphones).

Results
The webpage will be presented as ksa.ch/covid_kidz soon.

Conclusion
Age-appropriate information is key to prevent anxiety and refusal in younger children facing Covid-19 testing by the authorities. An interdisciplinary approach including hospital clowns and involving children themselves are helpful.

O07 - Keynote Lecture
Caught in the cat: RNA-Seq of Toxoplasma gondii cat intestinal stages reveal essential genes for transmission

C Ramakrishnan[1]; S Maier[1]; B Nugraha[1]; L Raupach[1]; A Hehl[1]; P Deplazes[1]; N Smith[2]
[1] University of Zurich; [2] University of Technology Sydney

The only definitive hosts of the zoonotic and globally prevalent apicomplexan parasite Toxoplasma gondii are felids. Until recently, these stages could only be obtained by experimental cat infections and studies of these stages were limited to microscopy. However, understanding the mechanisms of parasite development in cats is key for novel intervention strategies as oocysts produced in the small intestine of felids are directly or indirectly responsible for all the infections of intermediate hosts including humans.

In the small intestine of cats, T. gondii undergoes several rounds of asexual replication (merogony) before sexual differentiation (gamogony) takes place which results in oocysts that become infectious by sporulation and persist in the environment. As a first step to understand the biology of the cat stages, we aimed to study the gene expression of T. gondii in the cat intestine at different stages of development using deep Next Generation Sequencing. Experimental infections of cats with T. gondii bradyzoites were performed and parasites harvested at distinct time points. To obtain high quality data, isolation and enrichment of parasites from intestinal tissue was optimized. RNA-Seq and subsequent differential expression analyses of cat intestinal stages compared to tachyzoites, which mediate acute infection, or to bradyzoites, which mediate chronic infection and initiate merogony, revealed genes specific to asexual cat stages (merozoites) and sexual stages. One of these gene is the male gamete-specific gene hap2 that has been shown to be essential to membrane fusion. Targeted deletion of hap2 resulted in oocysts that were morphologically aberrant and sporulation-incompetent, but still conferred protective immunity making it a novel live vaccine strain (1).

To perform high through-put intervention studies or molecular analyses of the cat stages, in vitro platforms are essential. We have recently established various cat enteroid-based culturing systems that are stable and reproducible as well as achieved optimization of long-term in vitro cultures of T. gondii bradyzoites that are necessary to initiate merogony.

Taken together, RNA-Seq has enabled us to describe the cat stage transcriptome, identify protentially essential genes and generate a live attenuated vaccine. The data will also be crucial for further molecular and cellular studies in in vitro systems and thus open the door for novel intervention strategies.

O08

Activity and mechanism of action of mefloquine derivatives against Echinococcus multilocularis

R Memedovski[1]; R Rufener[1]; R Zurbriggen[1]; S Braga[2]; M Heller[2]; J Müller[1]; M Vinícius Nora de Souza[3]; B Lundström-Stadelmann[1]
[1] Institute of Parasitology, Vetsuisse Faculty, University of Bern, Switzerland;
[2] Inselspital, Bern University Hospital, Bern, Switzerland; [3] Fundação Oswaldo Cruz, Instituto de Tecnologia em Fármacos-Far Manguinhos

Alveolar echinococcosis (AE) is a zoonosis caused by the fox tapeworm E. multilocularis. The disease is caused by the metacestode (secondary larval stage), exhibiting silent invasive growth primarily in the liver and metastatic potential. The current chemotherapeutic treatment is based on benzimidazoles, which have only limited curative capabilities and can cause severe side effects in some cases. Therefore, novel and markedly improved treatment options for AE are needed.
Mefloquine, an antimalarial agent, had previously been shown to be active against various helminth species, and also showed activity against E. multilocularis metacestodes in vitro and in experimentally infected mice.(1) Mefloquine was shown to bind to E. multilocularis ferritin, an iron-storage protein, which sequesters ferrous iron.(2) However, whether this interaction is relevant for the mechanism of action of mefloquine is not known.
We here present a structure-activity relationship (SAR) study of mefloquine derivatives and their physical interaction with E. multilocularis proteins. Three different assays were employed, namely i.) the phosphoglucose isomerase assay (integrity of metacestodes) with 24 compounds, ii.) the Alamar blue assay (metabolic activity of metacestodes) with 17 compounds, and iii.) the motility-based activity assessment of protoscoleces with 15 compounds. None of the derivatives showed higher activity compared to mefloquine. However, nine compounds caused limited physical damage in metacestodes and four of them impaired the movement of protoscoleces at a low level. Comparative affinity chromatography of mefloquine, one active and two non-active mefloquine derivatives was performed, and bound Echinococcus metacestode proteins were analysed by LC-MS/MS. Final data analysis is ongoing and will be presented at the conference. The comparison of derivatives of mefloquine will help in understanding its mode of action in the fight against AE.

O09

Antibodies against hidden glyco-antigens from the liver fluke Fasciola hepatica targeting potential vaccine candidates

RM Eichenberger
Univeristät Zürich

Sonja G. Rechsteiner, Sina Hasler, Ramon M. Eichenberger
Institute of Parasitology, Vetsuisse Faculty, University of Zurich, Winterthurerstrasse 266a, CH-8057 Zurich, Switzerland

The zoonotic liver fluke Fasciola hepatica is responsible for major economic losses to the agriculture industry worldwide. Triclabendazole (TCBZ) has been the drug of choice. However, resistance to TCBZ is becoming prevalent with cases of resistance detected globally. This emphasizes the urgent need for alternative control methods. Vaccines as an economically viable strategy has been discussed, especially with regards to the subclinical appearance and high prevalence of F. hepatica. A significant focus is on the development of protein vaccines. In this process however, glycoproteins (GPs) have been mostly ignored. GPs are present throughout the organ systems of F. hepatica and such GPs could serve as ‘hidden’ antigens. Hidden antigens are not exposed to the host’s immune-system during the course of natural infections, but have proven to be effective vaccine candidates, notably for antigens that are expressed in the intestine of blood-feeding parasites. Here, we purified GPs from flukes by different lectins with known unspecific binding to the parasite gut and produced monoclonal antibodies against these fractions for specific antigen purification. We identified various antibodies by immunohistochemistry binding specifically to the gut of F. hepatica. We evaluated the in vitro protective capacity of these antibodies against parasites. Further, we started to profile their proteomic identity by pull-down approaches. Overall, these sweet proteins offer promising candidates for anthelmintic vaccine design.

O10

Schistosomiasis and fascioliasis: Making the case for a one health approach to trematode control in Côte d'Ivoire

J Giovanoli Evack[1]; JN Kouadio[2]; LY Achi[3]; B Bonfoh[4]; EK N'Goran[5]; O Balmer[1]; J Utzinger[1]; J Zinsstag[1]
[1] Swiss Tropical and Public Health Institute / University of Basel; [2] Swiss Tropical and Public Health Institute / University of Basel / Centre Suisse de Recherches Scientifiques en Côte d'Ivoire / Unité de Formation et de Recherche Biosciences, Université Félix Houphouët-Boigny; [3] Centre Suisse de Recherches Scientifiques en Côte d'Ivoire / Ecole d'élevage et des métiers de la viande de Bingerville; [4] Centre Suisse de Recherches Scientifiques en Côte d'Ivoire; [5] Unité de Formation et de Recherche Biosciences, Université Félix Houphouët-Boigny / Centre Suisse de Recherches Scientifiques en Côte d'Ivoire

Schistosoma spp. and Fasciola spp. are zoonotic trematodes that infect humans and animals and are associated with human morbidity and decreased livestock production. Both infections have been identified as neglected tropical diseases (NTD) by WHO and are targeted for control in the 2021-2030 NTD Roadmap.
Since 2010 significant resources have been devoted to the prevention and control of human schistosomiasis in Côte d'Ivoire, resulting in decreasing prevalences, but elimination still remains elusive. Conversely, fascioliasis receives little attention, despite high prevalences in livestock and rising human prevalences globally. Despite the call from WHO for an integrated One Health approach to control and eliminate NTDs, neither infection is monitored in animals and no prevention or control programme exists.
Over the last four years we conducted numerous investigations using a One Health approach to examine Schistosoma spp. and Fasciola spp. prevalences and transmission dynamics in humans, livestock and snails in villages, farms and abattoirs in Côte d'Ivoire. Samples of urine and feces were collected from humans and livestock and the livers and small intestines of slaughtered livestock were inspected. Polymerase chain reaction of microsatellites, ITS1/2 and cox1 loci were performed on DNA from flukes and miracidia in order to identify species and perform population genetic analyses.
Schistosoma spp. prevalences in slaughtered cattle, sheep and goats were higher than expected at 24.6% (95% CI: 14.1-37.8%), 7.1% (0.2-33.9) and 6.9% (0.8-22.8), respectively. Humans were infected with hybrids of livestock and human schistosomes. In slaughtered livestock, Fasciola spp. were found only in cattle (10.5%, 95% CI: 4.0-21.5), but during a triclabendazole clinical trial, the overall prevalence in farm cattle was 79.1%. High prevalences of these infections in livestock pose a risk for human health and cause farmers significant economic losses. The added value of a One Health approach in our research is the detection of hybrid schistosomes and their variable representation in cattle and humans. To ensure the gains made are not lost, and to further improve the health and well-being of farming communities, surveillance and control of these parasitic infections in animals is necessary. A One Health observatory, would be ideal for establishing an understanding of schistosomiasis and fascioliasis in humans and animals and their health implications.

O11

Safety evaluation and efficacy assessment of a Listeria monocytogenes-based vaccine against abortion and vertical transmission of Neospora caninum.

D Imhof[1]; W Pownall[2]; A Oevermann[3]; A Hemphill[4]
[1] Institute of Parasitology, Vetsuisse Faculty, University of Bern, Switzerland; [2] Small Animal Clinic, Vetsuisse Faculty, University of Bern; [3] Vetsuisse Faculty, University of Bern; [4] Institue of Parasitology

The apicomplexan parasite N. caninum is the worldwide leading cause of abortion and stillbirth in cattle due to vertical transmission of the parasite. There is currently no vaccine against neosporosis on the market. In this study, the gram-positive, facultative intracellular bacterium Listeria monocytogenes was used as a vaccine vector, because it induces potent innate and adaptive immune responses. L. monocytogenes expresses several important virulence genes such as InlA and InlB, which are surface proteins essential for invasion of most cells, and ActA, an actin-assembly inducing protein important for cell-to-cell spread. An attenuated mutant L. monocytogenes strain (Lm3Dx) was engineered deleting actA, inlA, and inlB virulence genes in order to avoid sytemic infection and target the vector to antigen presenting cells (APCs), because phagocytosis of L. monocytogenes by APCs is independent of InlA and InlB. Bacteria are either processed by the phagolysosome and antigens presented via MHC class II to CD4+ T-cells, or escape the phagosome, reach the cytoplasm, proteolytically degraded in the proteasomes, and peptides are presented via MHC class I for CD8+ T-cell presentation. Insertion of sag1, coding for the major surface protein NcSAG1 of N. caninum tachyzoites yielded the vaccine strain Lm3Dx_NcSAG1. The safety and efficacy of this vaccine strain was evaluated in non-pregnant and pregnant mouse models. Female BALB/c mice inoculated intramuscularly with 1x106, 5x106, and 1x107 CFU of Lm3Dx_NcSAG1 three times at two week intervals showed no clinical signs, and no Listeria could be detected in any organ two weeks after the 3rd immunization. In contrary, mice inoculated with the WT strain were euthanized after 36 h due to clinical signs (lethargy, hunched back and ruffled fur). Immunization of pregnant mice did not have a negative influence on fertility or number of viable pups. To evaluate vaccine efficacy, mice were vaccinated as described, and challenged by subcutaneous inoculation of 1x105 N. caninum NcSp7 tachyzoites 7 days post-mating. Follow-up studies after birth showed that vaccination with 107 CFU of Lm3Dx_NcSAG1 resulted in a postnatal offspring survival rate of 67%, while upon vaccination with 1x105 CFU only 31% postnatal survival was achieved. Results on vertical transmission, and cerebral parasite load in dams and pups are in progress and will be presented at the meeting.

O12

Bloodstream infections in allogeneic Hematopoetic Stem Cell Recipients from the Swiss Transplant Cohort Study

M Sava[1]; V Baettig[1]; S Gerull[1]; JR Passweg[1]; N Khanna[1]; C Garzoni[2]; N Mueller[3]; U Schanz[3]; C Berger[4]; Y Chalandon[5]; C van Delden[5]; F Franzeck[1]; M Weisser[1]
[1] University Hospital Basel; [2] Clinica Luganese Moncucco, Lugano; [3] University Hospital Zurich; [4] University Children's Hospital Zurich; [5] Geneva University Hospitals

Background
Bloodstream infection (BSI) is the most common infectious complication during aplasia after hematopoietic stem cell transplantation (HSCT) ranging from 28 to 56%. In this study we aimed to assess the evolution of BSI incidence and the frequency of resistant bacteria causing BSI in HSCT recipients included in the Swiss Transplant Cohort Study (STCS).

Methods
This is an observational multi-centre cohort study from prospectively enrolled patients receiving allogeneic HSCT included in both the STCS and the European Group for Bone Marrow Transplantation (EBMT) between 10/2009 and 10/2018.

Results
Out of 1688 HSCT performed at three transplantation centres in Switzerland, 1432 transplantations in 1364 patients were included. Patients were mostly male (834, 61.1%); median age at the first transplantation was 53 years (IQR 42-61). In 725 (53.2%) patients the underlying hematologic condition was acute leukemia. In 64 (4.7%) patients more than one HSCT was performed. Among 451 (33%) patients 676 BSI episodes were registered during a median follow-up time of 1.88 patient-years (0.75-4.03). Patients with BSIs had more frequently > 1 HSCT (10.4% vs 2.1%; $p < 0.001$), received more often a full-intensity myeloablative conditioning (57.2% vs 49.7%; $p = 0.010$), had a longer median time to engraftment (16 vs 15 days; $p < 0.001$), a higher incidence of grade III/IV GVHD (18.2% vs 8.0%; $p < 0.001$ and a shorter follow-up time (1.4 vs 2.03 years $p > 0.001$). The BSI incidence was 7.3/100 vs. 14/100 person-months in the first 3 months after the first and second transplantation, respectively. Of 781 pathogens causing BSI, 322 (41.2%) were isolated in the pre-engraftment phase, 67 (8.6%) day 30 - 100 and 392 (50.2%) > day 100 post-transplant. Gram-positive isolates contributed to 454 (58.1%) BSIs, gram-negatives to 270 (34.6%) and 28 (3.6%) were of fungal origin. No increase in resistant pathogens was noted (21% ESBL-production in enterobacterales, 22% resistance to quinolones and 20% resistance to carbapenems in P. aeruginosa).
The mortality rate was 58.3% in patients with BSI vs. 32.6% in those without ($p < 0.001$), most deaths occurred within one year post-HSCT.

Conclusions
One third of all HSCT recipients and more than half of patients undergoing a second HSCT had at least one BSI episode. Most BSIs occurred in the pre-engraftment phase leading to increased mortality. We did not observe an increase in antibiotic resistance of BSI-causing pathogens over the years.

O13

Incidence, causative pathogens and risk factors for surgical site infections in thoracic-organ transplant recipients registered in the Swiss Transplant Cohort Study

PW Schreiber[1]; BM Lang[2]; K Boggian[3]; D Neofytos[4]; C van Delden[4]; A Egli[5]; M Dickenmann[2]; S Hillinger[6]; C Hirzel[7]; O Manuel[8]; F Desgranges[8]; M Koller[2]; S Rossi[2]; S Stampf[2]; M Wilhelm[6]; SP Kuster[1]; N Müller[1]; _ and the Swiss Transplant Cohort Study[2]
[1] University Hospital Zurich and University of Zurich; [2] Basel University Hospital; [3] Cantonal Hospital St.Gallen; [4] University Hospitals Geneva and University of Geneva; [5] University Hospital Basel; [6] University Hospital Zurich; [7] University Hospital Bern; [8] University Hospital (CHUV) and University of Lausanne

Background
Surgical site infections (SSI) represent one of the most common hospital-acquired infections (HAI). The occurrence of SSIs in the early post-transplant course poses a relevant threat for heart (HTR) and lung transplant recipients (LTR). Considering the paucity of data on this important HAI, we analyzed HTR and LTR registered within the Swiss Transplant Cohort Study (STCS).

Methods
The STCS dataset was used to identify adult HTR and LTR with a potential follow up of at least 90 days post-transplant between 2008 and 2020. Diagnosis and categorization of SSIs was based on adapted Centers for Disease Control and Prevention (CDC) criteria (extension of the time period for a transplant-related SSI to 90 days post-transplant). Except the categorization of SSIs, all other data were prospectively collected. Risk factors for SSIs were investigated with logistic regression.

Results
Of 356 HTR, 31 (8.7%) individuals with totally 32 transplant-related SSIs were identified: 5 (15.6%) superficial incisional, 17 (53.1%) deep incisional and 10 (31.2%) organ/space SSIs. Among 450 LTR, 23 SSIs occurring in 21 (4.7%) individuals were reported: 3 (13%) superficial incisional, 11 (47.8%) deep incisional SSIs and 7 (30.4%) organ/space SSIs. The majority of SSIs were caused by bacteria, most frequently by coagulase-negative staphylococci (HTR 36.4%, LTR 18.5%) and enterococci (HTR 18.2%, LTR 22.2%). Fungal SSIs were rare, with 1 (3.1%) fungal SSI after HTR and 3 (13.0%) fungal SSIs after LTR. All fungal SSIs were caused by Candida spp.. Nine (28.1%) SSIs after HTR and 7 (30.1%) SSIs after LTR were diagnosed on clinical findings. Among HTR, preexisting diabetes mellitus tended to a higher risk for SSI (odds ratio (OR) 2.1, 95% confidence interval (95%CI) 0.923-4.81; P=0.075), whereas male sex was a risk factor for LTR (OR 3.28, 95%CI 1.18, 9.06; P=0.02).

Conclusions
After both, HTR and LTR, SSIs were observed at a low frequency. The majority of SSIs were classified as deep incisional SSIs. Most SSIs were caused by bacteria with a predominance of gram-positive pathogens, all fungal SSIs were caused by Candida spp..

O14

Real-life food-safety behaviour and Epidemiology and Outcomes of Bacterial Foodborne Infections in Solid Organ Transplant Recipients

L van den Bogaart[1]; M Lindup[1]; BM Lang[2]; D Golshayan[1]; J Aubert[1]; J Vionnet[1]; J Regamery[1]; M Pascual[1]; D Neofytos[3]; A Egli[2]; LN Walti[4]; K Boggian[5]; C Garzoni[6]; C Berger[7]; C van Delden[3]; NJ Mueller[8]; O Manuel[1]; M Mombelli[1]
[1] Lausanne University Hospital (CHUV); [2] Basel University Hospital; [3] Geneva University Hospital; [4] Inselspital, Bern University Hospital; [5] Cantonal Hospital St. Gallen; [6] Clinica Luganese Moncucco; [7] University Children's Hospital of Zurich; [8] University Hospital and University of Zurich

Aims: Food-safety measures are generally recommended in solid organ transplant (SOT) recipients. However, adherence of patients in a real-life setting after transplantation and the burden of bacterial foodborne infection in SOT recipients remain largely unexplored. We performed a survey in order to describe the observance of food-safety recommendations and we assessed the epidemiology and outcomes of bacterial foodborne infections in a nationwide cohort of SOT recipients.

Methods: In the first study a single-center survey concerning food safety behavior among SOT recipients followed in Lausanne University Hospital between 2012 and 2017 was conducted. In the second study we identified episodes of microbiologically-confirmed bacterial foodborne infections among patient transplanted between 2008 and 2018 and enrolled in the Swiss Transplant Cohort Study. The incidence rate of bacterial foodborne infections and patient and graft survival at 30 days after the infection were analyzed.

Results: In the first study 197 SOT recipients participated in the survey. Overall, 17.7% of the participants observed all food-safety recommendations (22.0% avoided food at risk of contamination while 67.9% applied hygiene recommendations). Patients within the first year after transplantation (OR 5.42; p = 0.001) and females (OR 4.67; p = 0.001) followed food-safety recommendations more closely.
In the second study, among 4405 SOT recipients prospectively followed for a median of 4.2 years, we identified 151 episodes of bacterial foodborne infections (131 [88%] Campylobacter spp. and 15 [10%] non-typhoidal Salmonella) with an overall cumulative incidence of 4% (95% CI 3.4-4.8). Standardized incidence rates of Campylobacter and Salmonella infections were 7.4 (95% CI 6.2-8.7) and 4.6 (95% CI 2.6-7.5), respectively. Median time from transplantation to infection was 1.57 years (IQR 0.58-3.40). Invasive infection occurred in 7.6% (11/145) of the episodes and was more common with Salmonella (33.3% [5/15]) compared to Campylobacter (3.2% [4/125]; p = 0.001). A composite endpoint of acute rejection, graft loss, or death occurred within 30 days in 3.3% (5/151) of cases.

Conclusion: Our findings highlight that the majority of SOT recipients do not systematically follow food-safety recommendations. Moreover, bacterial foodborne infections in SOT recipients were common and were associated with significant morbidity, supporting the need for implementation of food-safety recommendations.

O15
Predictive factors for HIV-1 CSF escape in neurocognitive impairment

P Filippidis[1]; J Damas[1]; B Viala[2]; F Assal[3]; A Calmy[3]; P Tarr[4]; T Derfuss[5]; M Oberholzer[6]; I Jelcic[7]; T Hundsberger[8]; L Sacco[9]; M Cavassini[1]; R Du Pasquier[1]; KE Darling[1]
[1] CHUV Centre Hospitalier Universitaire Vaudois (CHUV); [2] Centre Hospitalier Alpes Léman; [3] HUG Hôpitaux Universitaires Genève; [4] Kantonsspital Baselland, University of Basel, Bruderholz; [5] Basel University Hospital; [6] Bern University Hospital; [7] University Hospital of Zurich; [8] Kantonsspital St Gallen; [9] Ospedale regionale di Lugano

Aims
Among people with HIV (PWH) enrolled in the Neurocognitive Assessment in the Metabolic and Aging Cohort (NAMACO) study, we have observed a neurocognitive impairment (NCI) prevalence of 40 %. In the current study, we examined the characteristics of patients with HIV viral escape in the cerebrospinal fluid (CSF).

Methods
We pooled data from NAMACO study participants and from patients attending a neuro-HIV platform in Switzerland. The NAMACO study is an ongoing, prospective, longitudinal, multicentre study of aging (≥ 45 years old) PWH enrolled in the Swiss HIV Cohort Study (SHCS). NAMACO participants in whom HIV-related NCI is diagnosed are invited to pursue investigations with a neurological examination, brain MRI and CSF analysis. The neuro-HIV platform is a multi-disciplinary full outpatient assessment at Lausanne University Hospital for PWH of any age, enrolled in the SHCS or not, in whom NCI is suspected. We analysed the demographic, clinical, immunological, neurocognitive and radiological characteristics of PWH who underwent lumbar puncture (LP) as part of the NAMACO study or the neuro-HIV platform between 1 March 2011 and 30 April 2019. CSF viral escape was defined as 1) the presence of quantifiable HIV RNA in the CSF at any level when plasma HIV RNA was suppressed or 2) CSF HIV RNA greater than plasma HIV RNA when the latter was detectable.

Results
Of 1166 PWH assessed, 287 underwent LP. The majority had suppressed plasma HIV RNA. CSF viral escape was observed in 29 patients (10.1 %) of whom 18 (62.1 %) had supressed plasma HIV RNA and 11 (37.9 %) had detectable plasma HIV RNA. Characteristics of patients were comparable whether they had CSF viral escape or not, including demographic profile, cardiovascular and metabolic comorbidities, time since HIV diagnosis (12 vs 16 years, p = 0.4), median current CD4 count (558/mm3 vs 611/mm3, p = 0.1) and median CD4 nadir (170/mm3 vs 171/mm3, p = 0.7), antiretroviral CSF Penetration-Effectiveness score (7 vs 8 points, p = 0.2), neurocognitive diagnosis based on Frascati criteria and presence of MRI abnormalities.

Conclusions
In this large pooled sample of PWH assessed for NCI, CSF viral escape occurred in 10.1 % of patients. Patients with CSF viral escape presented no significant demographic, clinical, immunological, neurocognitive or radiological differences compared to patients without CSF escape. We conclude that LP remains the only reliable means of diagnosing HIV-1 escape in the CSF.

O16

Prevalence of HIV-related stigma among participants of the Swiss HIV Cohort Study: a pilot study

E Kampouri[1]; J Damas[2]; D Jackson-Perry[2]; I Cobos Manuel[2]; A Scherrer[3]; M Cavassini[1]; K Darling[1]
[1] Lausanne University Hospital (CHUV) and University of Lausanne (UNIL); [2] Lausanne University Hospital (CHUV); [3] University Hospital Zurich, University of Zurich

Background
HIV-related stigma presents a challenge to the health and well-being of people with HIV (PWH). As a first step to address such stigma, we aimed to quantify its prevalence in Switzerland.

Methods
We conducted a pilot study at Lausanne University Hospital, Switzerland, between March and June 2020 using a validated 12-item HIV Stigma Scale [1]. This questionnaire examined personalized stigma, disclosure concerns, beliefs regarding public attitudes and negative self-image. Two questions were added regarding healthcare-related stigma. The Stigma Scale was translated and backtranslated
from English into French, German and Italian and completed electronically by the treating physician during a standard follow-up visit. Inability to speak one of the four available languages was the only exclusion criterion. Responses were graded using a 4-point Likert-type scale (strongly disagree, disagree, agree, and strongly agree) to give a score of 1-4 for each item (higher scores indicating higher stigma).

Results
351 participants were included: 118 (34%) were women, median age was 51 years (IQR:42;59); 227 (65%) patients were from Europe; 93 (26%) from Africa. HIV acquisition mode was men having sex with men in 126 participants (36%), heterosexual in 177 (50%), other in 48 (14%). Median duration of HIV infection was 15.2 years (IQR:8;25). Disclosure concerns represented the highest stigma burden across all demographic subgroups (age, sex, origin, mode of HIV acquisition). The item, ‘I am very careful who I tell that I have HIV' had a positive answer (agree or strongly agree) in 89% of participants and the highest score (median 4; IQR:3;4). Personalized stigma was significantly higher in African patients ($P < 0.001$), as was health-care associated stigma ($P = 0.02$).

Conclusions
Stigma is prevalent in our study population across all demographic groups while stigma subtypes vary. This pilot study has been expanded into an ongoing multicentre cross-sectional study across Switzerland. Quantifying stigma and stigma subtypes is key in designing interventions and improving care for PWH.

O17

A trial platform to assess approved SARS-CoV-2 vaccines in immunocompromised patients: A pilot trial comparing the mRNA vaccines Comirnaty® and Covid-19 mRNA Vaccine Moderna®

B Speich[1]; F Chammartin[1]; D Smith[2]; MP Stoeckle[3]; P Amico[4]; AL Eichenberger[5]; B Hasse[6]; MM Schuurmans[6]; T Müller[6]; M Tamm[3]; M Dickenmann[5]; IA Abela[2]; A Trkola[2]; HH Hirsch[3]; O Manuel[7]; M Cavassini[7]; LG Hemkens[1]; M Briel[1]; NJ Mueller[6]; A Rauch[5]; HF Günthard[2]; MT Koller[3]; K Kusejko[2]; HC Bucher[1]
[1] Basel Institute for Clinical Epidemiology and Biostatistics, University Hospital Basel; [2] University of Zurich; [3] University Hospital Basel / University of Basel; [4] University of Basel / University Hospital Basel; [5] Inselspital - Universitätsspital Bern; [6] University Hospital Zurich; [7] Lausanne University Hospital and University of Lausanne

Background
Well conducted randomised controlled trials (RCTs) provide the best evidence when assessing the efficacy and safety of a medical intervention. However, RCTs usually require large resources and are time intensive to set-up and perform. The current SARS-CoV-2 pandemic has highlighted that new and more flexible clinical trial approaches, such as trial platforms are needed to assess the efficacy and safety of interventions in a timely manner. The Swiss HIV Cohort Study (SHCS) and the Swiss Transplant Cohort Study (STCS) are an ideal foundation for a trial platform leveraging routinely collected data. In the recently established trial platform we assessed the efficacy of the two in Switzerland available SARS-CoV-2 vaccines in immunocompromised patients in the frame of a pilot study while at the same time assessing the functionality of the trial platform.

Methods
We conducted a multicentre, open-label, 2-arm RCT pilot study nested into two cohorts. We randomised patients from the STCS and the SHCS to receive either the mRNA vaccine Comirnaty® (Pfizer / BioNTech) or the Covid-19 mRNA Vaccine Moderna®. The primary clinical outcome is the change in pan-Ig antibody response (pan-Ig anti-S1-RBD; baseline vs. 12 weeks after first vaccination). The pilot study also allows us to collect endpoints related to trial conduct feasibility (i.e. duration of RCT set-up; time of patient recruitment; patient consent rate; proportion of missing data). Assuming vaccine reactivity of 90% in both vaccine groups we powered our trial, using a non-inferiority margin such that a 95% two-sided confidence interval excludes a difference in favour of the reference group of more than 10%. A sample size of 380 (190 in each treatment arm) was required for a statistical power of 90% and a type I error of 0.025.

Results
The study received final approval from the ethical committee on the 19 April 2021. The first patient was randomised on the 19. April 2021 and by the 30. May 2021 400 patients have received their first SARS-Cov-2 vaccine. The follow-up is currently ongoing until the middle of August 2021 and we expect to present first primary results on the Joint Annual Meeting 2021.

Conclusion
We set an example how existing cohort structures can be used to set-up trial platforms that facilitate the conduct of efficient RCTs.

O18

The Achilles' heel of the fox tapeworm? - Investigation of the threonine metabolism of Echinococcus multilocularis

M Kaethner[1]; P Grossenbacher[2]; M Lochner[2]; S Schürch[3]; C Regnault[4]; D Villalobos Ramírez[5]; B Lundström-Stadelmann[1]
[1] Institute of Parasitology, Vetsuisse Faculty, University of Bern, Switzerland; [2] Institute of Biochemistry and Molecular Medicine, University of Bern, Switzerland; [3] Department of Chemistry and Biochemistry, University of Bern, Switzerland; [4] Glasgow Polyomics, College of Medical, Veterinary and Life Sciences, University of Glasgow, UK; [5] Department of Bioinformatics, University of Würzburg, Germany

Alveolar echinococcosis (AE) is a severe zoonotic disease caused by the metacestode larvae of the fox tapeworm Echinococcus multilocularis. Treatment options are the surgical removal of all parasitic tissue, or lifelong treatment with benzimidazoles, since these drugs fail to kill the stem cells of the parasite. New drugs are urgently needed as treatment might fail and adverse side effects of benzimidazoles can lead to treatment discontinuation.

Like other parasites, E. multilocularis highly depends on nutrients from its host. Recent in vitro experiments elucidated that besides glucose, E. multilocularis metacestodes scavenge high amounts of the amino acid threonine from the culture medium (Ritler et al., 2019). Therefore, we currently trace 13C4 L-threonine and its metabolites in in vitro cultured metacestodes to give new insights into how threonine is metabolized in E. multilocularis and the data will presented at the conference. Additionally, we investigate a potential effect of L-threonine on the growth rate of in vitro cultured E. multilocularis metacestodes. The results are currently obtained via a newly established metacestode growth assay that allows the assessment of growth of individual metacestodes using a macro in ImageJ.

Threonine dehydrogenase (TDH) is known to metabolize threonine in other organisms, and the enzyme is actively expressed also in E. multilocularis metacestodes. EmTDH is potentially an interesting future drug target against AE, as human TDH is expressed as a non-functional pseudogene. Our current studies focus on EmTDH, which is recombinantly expressed, and its activity is measured by NAD+ reduction at 340 nm. In a next step, we will treat EmTDH with quinazoline carboxamide inhibitors in a target-based approach (Alexander et al., 2011) and also against E. multilocularis by various established in vitro tests in a whole-organism based approach (Lundström-Stadelmann et al., 2019). These tests will show whether EmTDH can be specifically targeted by inhibitors, and if they affect the parasite. With these approaches we aim at understanding and targeting the threonine metabolism of E. multilocularis.

O19
Dual inhibition of the Echinococcus multilocularis energy metabolism

S Chaudhry[1]; R Zurbriggen[1]; JS Doggett[2]; B Lundström-Stadelmann[1]
[1] Vetsuisse Faculty, University of Bern; [2] Oregon Health and Science University

Alveolar echinococcosis (AE) is caused by the metacestode stage of the zoonotic parasite Echinococcus multilocularis. Current chemotherapeutic treatment options rely on benzimidazoles, which have limited curative capabilities and occasionally cause severe side effects. Therefore, alternative treatment options are urgently needed.
We have previously shown that the parasite relies on energy generation by two mitochondrial pathways functioning in parallel: The classical oxidative phosphorylation including the electron transfer chain (ETC) and the malate dismutation (MD) (Ritler et al. 2019). We have further investigated the energy metabolism of E. multilocularis as a potential target.
We repurposed endochin-like quinolones (ELQs) for inhibition of the ETC: 15 ELQs were screened in vitro against two isolates of E. multilocularis metacestodes and isolated germinal layer cells by the phosphoglucose isomerase (PGI) assay and the CellTiter Glo assay, respectively. For the most active ELQs, EC50 values against metacestodes were assessed by PGI assay, and IC50 values against germinal layer and mammalian cells were assessed by CellTiter Glo and Alamar Blue assay. Further focus was laid on ELQ-400, and it was shown with the Seahorse XFp Analyzer that cytochrome bc1 complex is a direct target of ELQ-400 in E. multilocularis. When tested under microaerobic conditions, ELQ-400 was not active against metacestodes. Under ELQ-400 treatment, increased succinate levels compared to control-treated parasites suggested for a block of the ETC and respective switch to MD for energy generation. Thus, the parasite applied an alternative way for energy generation.
Therefore, MD was also inhibited by the previously described experimental compound quinazoline (Matsumoto et al. 2008), and effects on metacestodes were assessed by PGI assay and succinate measurements. Whereas quinazoline alone did not induce any damage to the metacestodes under microaerobic conditions either, it reduced the production of succinate compared to control-treated parasites (i.e. inhibited the MD), and it strongly improved the activity of the bc1 inhibitor ELQ-400 when applied in combination.
We conclude that targeting the energy metabolism of E. multilocularis as a possible novel treatment approach can only be successful if both pathways are blocked simultaneously.

O20
Neuropeptidergic systems in the different life stages of a model cestode

M Preza[1]; S Van Bael[2]; L Temmerman[2]; E Castillo[3]; U Koziol[3]
[1] Facultad de Ciencias de Montevideo, UdelaR, Uruguay & Institute of Parasitology, Vetsuisse Faculty, University of Bern, Switzerland.; [2] Department of Biology, KU Leuven, Belgium.; 3 Facultad de Ciencias de Montevideo, UdelaR, Uruguay.

Neuropeptides are small peptides produced by nerve cells, which are derived from longer precursors by proteolytic cleavage and can have different functions. In this work, we studied the neuropeptidergic systems of the model cestode H. microstoma, which allows easy access to all of the stages of its life cycle: oncosphere (first larval stage), cysticercoid (second larval stage) and adult. Previously, we developed a bioinformatic method for the detection of neuropeptide genes in the genomes of different flatworms, identifying 39 genes in H. microstoma [1]. In this work we experimentally confirmed 21 of these genes through peptidomics, many of which are specific to parasitic flatworms. RNAseq and RT-PCR were used to analyze the expression of neuropeptide genes in the life stages of H. microstoma, finding several genes with differential expression or stage-specific [2]. The adult stage expressed the highest number of neuropeptide genes, but surprisingly a large number of neuropeptide genes were also expressed in the oncospheres. Subsequently, we performed fluorescent in situ hybridization for selected neuropeptides in adults and oncospheres. In adults we detected complex and distinct expression patterns of the different neuropeptides in the nervous system as well as in individual cells in the neck region. In oncospheres, we detected the expression of one cestode specific neuropeptide in two putative nerve cells, out of a total of three nerve cells found in this larva as determined with different molecular markers. At this moment we are carrying out functional studies for these neuropeptides in the different life stages of H. microstoma, based on their effects on motility, cell proliferation and development. This work is a contribution to the understanding of peptidergic systems in the life cycle of cestodes using a powerful model, which is of importance as these systems have been described as candidates for the generation of new anthelmintics.

O21
How to steal nucleotide and energy from your host cell: a Microsporidia perspective

R Hirt
Newcastle University

Plasma membrane-located transport proteins are considered key adaptations for obligate intracellular Microsporidia parasites, because they can use these to steal host metabolites needed by the parasite to grow and replicate. However, despite their importance, the functions and substrate specificities of most Microsporidia transporters are unknown. Here, we provide functional and cellular data for two families of transporters encoded in all microsporidian genomes and also in the genomes of some related endoparasites. The universal retention of the two families of transporters among otherwise highly reduced Microsporidia genomes indicates an important role for these transporters for these strict intracellular parasites. Our work identifies different routes for the acquisition of essential energy and nucleotides for a major group of intracellular parasites that infect most animal species including humans.

O22
Identifying the essentialome of Theileria-infected leukocytes

M Maurizio[1]; K Woods[1]; J Doench[2]; M Masid[3]; V Hatzimanikatis[3]; S Rottenberg[1]; P Olias[1]
[1] University of Bern; [2] Broad Institute of MIT and Harvard; [3] École Polytechnique Fédérale de Lausanne (EPFL)

Theileria are tick-transmitted apicomplexan parasites that cause East Coast Fever and Tropical Theileriosis, severe leukoproliferative disorders of cattle with a substantial economic impact in developing countries. Theileria is unique in biology as it is the only eukaryotic organism known to transform its eukaryotic host cell, inducing continual proliferation of the infected bovine leukocyte. Despite advances in identifying signalling pathways that the parasite hijacks to transform its host, we only have limited knowledge about the essential host factors that Theileria parasites need to thrive. We hypothesized that there are host cell factors required for Theileria-transformed leukocytes, but dispensable for uninfected host cells. In this project we leveraged recent advances in genome-wide CRISPR/Cas9-based forward genetic screening technology to identify the essentialome of Theileria-induced transformation. We have generated a bovine genome-wide CRISPR/Cas9 library, allowing us to perform drop out screens in Theileria-infected and non-infected bovine cell lines. Initial genome-wide screens identified 1561 genes whose depletion lead to reduced cell fitness. These preliminary hits were stringently validated using a targeted sgRNA library consisting of 10 guides per gene. After filtering out genes that were also essential in the non-infected bovine cells, a set of 111 genes that are exclusively essential for Theileria-infected cells was obtained. Further validation and characterization of selected hits is currently ongoing.
Since intracellular apicomplexan parasites are highly dependent on the metabolism of the host cell, we performed gene knock-out simulations in a human hepatocyte-Plasmodium falciparum metabolic model. 41 genes in the Theileria essentialome are related to metabolism and, within this group, 6 genes were predicted to be dispensable for human hepatocytes but essential for Plasmodium falciparum-infected hepatocytes. In order to test whether bovine genes that are essential for the survival of Theileria schizonts are also required for related apicomplexan parasites, we are generating CRISPR/Cas9-based individual knockouts in the human haploid cell line HAP1 to allow for subsequent infection with Toxoplasma and Plasmodium. We hope that the identification of host factors required for Apicomplexan parasites will open up new therapeutic opportunities to combat these important human and veterinary pathogens.

O23

Exploiting parasitic auxotrophies: In vitro activities of 9-(2-Hydroxyethyl)adenine-tagged trithiolato-bridged arene ruthenium complexes and proteomic analysis in Toxoplasma gondii and Trypanosoma brucei

N Anghel[1]; J Müller[1]; J Jelk[2]; G Boubaker[1]; D Imhof[1]; J Ramseier[1]; Y Amdouni[1]; O Desiatkina[3]; E Păunescu[3]; S Braga[4]; J Furrer[3]; P Bütikofer[2]; M Heller[4]; A Hemphill[1]
[1] Institute of Parasitology, Vetsuisse Faculty, University of Bern, Switzerland; [2] Institute of Biochemistry and Molecular Medicine, University of Bern, Switzerland; [3] Department of Chemistry and Biochemistry, University of Bern, Switzerland; [4] Proteomics and Mass Spectrometry Core Facility, Department for Biomedical Research, Faculty of Medicine, University of Bern, Switzerland

Toxoplasma gondii is an apicomplexan intracellular parasite, causing infections in virtually all warm-blooded animals, including humans and livestock. Important outcomes of the infections are abortions, stillbirths, and serious impairments in immunocompromised patients. Trypanosoma brucei is an extracellular kinetoplastid that causes human African trypanosomiasis and Nagana disease in cattle, with important medical and veterinary importance primarily in rural sub-Saharan Africa. Current treatments against both parasitic infections have limitations including drug resistance and serious side effects. Purine salvage represents an essential function in all parasitic protozoa, and exploiting these auxotrophies could be an asset from a therapeutic point of view. Ruthenium complexes have been shown previously to be active in vitro against T. gondii and T. brucei, showing structural alterations in both parasites.
We report on the activities of 9-(2-Hydroxyethyl)adenine and two trithiolato-bridged arene ruthenium complexes bearing 2-thioxanthine (1) and 9-(2-Hydroxyethyl)adenine (2) respectively, against T. gondii and T. brucei in vitro. 9-(2-Hydroxyethyl)adenine alone did not inhibit parasite growth in vitro, and complex 1 was not active in T. gondii, but in T. brucei (IC50: >600nM). Complex 2 was the most active compound in both parasites, with IC50s of 60 nM for T. gondii and 29 nM for T. brucei. Transmission electron microscopy (TEM) revealed ultrastructural modifications in both protozoan in a comparative treatment of the three compounds, most notably induced by complex 2 within the parasite mitochondrion in both species, but not by the other two compounds.
Differential affinity chromatography using 9-(2-Hydroxyethyl)adenine, compounds 1 and 2 followed by mass spectrometry analysis revealed 128 proteins in T. gondii and 46 proteins in T. brucei, which specifically bound to compound 2. Both datasets contained many proteins involved in key steps of metabolism, such as ATPases. Moreover, metabolic pathway analyses revealed that in both parasites, homologous acyltransferases (two in T. gondii, one in T. brucei) are proteins binding to compound 2. Such transferases are involved in many essential metabolic processes.

O24

Prospective multicenter surveillance study of azole resistance among clinical Aspergillus spp. isolates in Switzerland

S Ragozzino[1]; D Goldenberger[1]; PR Wright[1]; S Zimmerli[2]; K Mühlethaler[2]; D Neofytos[3]; A Riat[4]; K Boggian[5]; O Nolte[6]; A Conen[7]; H Fankhauser[7]; PW Schreiber[8]; R Zbinden[9]; F Lamoth[10]; N Khanna[1]
[1] University and University Hospital of Basel; [2] University Hospital of Berne; [3] University Hospital of Geneva; [4] University Hospitals and University, Geneva; [5] Cantonal Hospital St. Gallen; [6] St. Gallen; [7] Cantonal Hospital Aarau; [8] University and University Hospital of Zurich; [9] University Hospital of Zurich; [10] Lausanne University Hospital

Aims
To describe the clinical characteristics of patients with Aspergillus spp. in respiratory samples in Switzerland and to provide an update of azole resistance prevalence with molecular characterization of the resistant strains.

Methods
Prospective study conducted at 7 hospitals participating in the Fungal Infection Network of Switzerland (FUNGINOS). All patients with detection of Aspergillus spp. in respiratory samples were included (2018-19). Clinical and microbiological data were collected. Antifungal susceptibility testing was performed by Sensititre YeastOne panel at reference laboratories. Non wild-type Aspergillus isolates, i.e. minimum inhibitory concentration (MIC) above the epidemiological cut-off value for any triazole, were submitted for sequencing of cyp51A gene and promoter region. The groups were compared using Fisher's exact test for categorical and Wilcoxon rank sum test for continuous variables. $P < 0.05$ were considered significant.

Results
Overall, 400 Aspergillus spp. from 365 patients were included. They were mainly obtained from sputum (n=237/400; 59%), tracheobronchial aspirate (94/400; 24%), and bronchoalveolar lavage (38/400; 10%). The most frequent species were A. fumigatus (355/400; 89%), A. niger (20/400; 5%), A. flavus (12/400; 3%). Clinical information was available for 94% (342/365) of the patients. The most prevalent underlying diseases were chronic lung diseases (170/342; 50%), cystic fibrosis (97/342; 28%), solid or hematological malignancies (50/342; 15%). Forty patients (40/342, 12%) were classified as invasive pulmonary aspergillosis (IPA). Patients with IPA more often received prior azole therapy, had an underlying hematologic malignancy or were transplant recipients, required hospital admission and intensive care and had a significantly higher mortality. Non-fumigatus Aspergillus spp. were significantly more prevalent among solid organ transplant recipients and patients previously treated with azoles. Nine of 400 (2%) strains (1 A. calidoustus and 8 A. fumigatus) showed higher MIC to azoles. Among A. fumigatus isolates, 3 showed the environmental TR34/L98H and 1 the M220K mutation.

Conclusions
A. fumigatus is the most frequently identified Aspergillus spp. in respiratory samples with a low prevalence of azole resistance in Switzerland. The detection of the environmental mutation TR34/L98H in 3 clinical samples highlights the importance of systematic surveillance studies.

P01

Control of Nosocomial Transmission of SARS-CoV-2 in the Service of Internal Medicine in Lausanne University Hospital

E Kampouri[1]; E Glampedakis[2]; E Moulin[2]; G Chaillou[3]; I Federli3; M Gouffon[2]; J Vaucher[2]; C Sartori[2]; P Vollenweider[2]; B Grandbastien[2]; L Senn[2]
[1] CHUV Lausanne; [2] Lausanne University Hospital (CHUV) and University of Lausanne (UNIL); [3] Lausanne University Hospital (CHUV)

Aims
Transmission of SARS-CoV-2 inside the hospital has significant implications for patients and healthcare workers. In February-March 2021, Lausanne University Hospital experienced a surge in nosocomial SARS-CoV-2 infections leading to a strengthening of infection prevention and control (IPC) measures. Here we describe this nosocomial outbreak, the implemented IPC measures and their impact on the control of SARS-CoV-2 transmissions in non-COVID units of the Service of Internal Medicine.

Methods
We report all consecutive nosocomial cases in a 206-bed service from February 8 until April 8, 2021 (weeks 6-14). Nosocomial COVID-19 cases were defined as microbiologically documented cases (PCR performed on nasopharyngeal swab, saliva or other respiratory specimen), diagnosed ≥ 5 days after admission. A nosocomial cluster was defined based on the detection of ≥ 2 healthcare-associated COVID-19 cases within a given period (< 72 hours between each infection) or geographically linked. IPC measures implemented on week 10 to control SARS-CoV-2 transmissions in all non COVID units were: 1) systematic screening at day 3 after admission; 2) weekly screening of all patients by PCR on saliva; and 3) decreasing the occupancy of all patient rooms with 5 patients (n=8) to 3 patients.

Results
A total of 69 cases were identified, with 57 attributed to 21 separate clusters and 12 cases considered isolated. Median age was 74 years (IQR 65, 80) and 40.6% were female. Median time from admission to positive test was 12 days (IQR 8, 17). All cases had a previous negative test and median time from previous negative test to diagnosis was 6 days (IQR 4, 8). 45.1% of nosocomial cases were completely asymptomatic. 60.9 % of patients stayed in rooms with 5-patients. Death occurred in 23.2% of cases. The incidence of nosocomial cases was the highest between weeks 8 and 10 with 18 and 17 new cases per week, respectively. After the introduction of IPC measures on week 10, there was a rapid decrease in the number of cases until complete absence of new cases on week 14.

Conclusion
Nosocomial infections were frequently asymptomatic, potentially hampering fast diagnosis which is crucial for control of nosocomial transmission, and were often associated with high mortality rate. The implementation of additional IPC measures led to a gradual decrease in nosocomial transmissions and allowed controlling the outbreak.

P02

Double Dose Cefuroxime Surgical Antimicrobial Prophylaxis and the Risk of Surgical Site Infection in Patients above Eighty Kilogram

R Sommerstein; A Atkinson[1]; SP Kuster[2]; D Vuichard[3]; S Harbarth[4]; N Troillet[5]; A Widmer[5]
[1] Inselspital - Universitätsspital Bern; [2] Privat; [3] Spital Thurgau AG; [4] Uni Genf; [5] Swissnoso

Objectives
Many guidelines recommend a weight adopted dose increase of cefuroxime for surgical antimicrobial prophylaxis (SAP). However, the evidence of this approach for lowering surgical site infection (SSI) rates is limited.

Methods
Swiss nationwide cohort study from 142 hospitals after the introduction of optional guideline recommendations to increase SAP dose for patients ≥80kg in 2015. We assessed the relationship between the cefuroxime SAP dose (1.5 vs 3gr) and the likelihood of an SSI among patients ≥80 kg in the Swissnoso SSI surveillance system between 2015 and 2019 in the nine most common surgical procedures. We used mixed-effects logistic regression model adjusted for institutional, epidemiological and perioperative variables. Results were stratified by weight categories, as well as by wound contamination class.

Results
Among 37,640 patients with complete follow-up, 1,203 developed an SSI (3.2%). Double dose cefuroxime SAP was administered in 13,246/37,640 patients (35%) and did not significantly reduce the rate of SSI rate (aOR 0.94 [95% CI 0.82-1.07], p=0.355). We identified significant interaction with weight categories and wound contamination class: SSI rates were significantly lower with the double dose in patients ≥80-90 kg (aOR 0.79; 95% CI 0.63-0.99, p=0.040), but not in the other weight categories (≥90-100kg: aOR 1.19, CI 0.92-1,55, p=0.185; ≥100-120kg: aOR 1.06, CI 0.82-1,38, p=0.643; ≥120kg: aOR 0.76; CI 0.50-1.16, p=0.200). SSI were lower in patients with contaminated wounds (aOR 0.51, CI 0.31-0.85, p=0.010), but not with clean (aOR 1.00; 95% CI 0.82-1.22, p=0.984), nor

Conclusion
Double-dose of cefuroxime SAP for patients ≥80 kg failed to demonstrate a significant overall effect on the SSI rate. The lower SSI rate within the weight category of 80-90kg and for contaminated wounds merits further investigation.

P03

Secondary attack rate following isolation of patients with suspected SARS-CoV-2 infection in multiple-bed rooms

S Ragozzino; R Kühl; L Maurer Pekerman; M Wicki; A Durovic; S Zingg; M von Rotz; M Battegay; A Widmer; S Bassetti; S Tschudin Sutter
University Hospital Basel

Aims
The implementation of isolation precautions for patients with suspected SARS-CoV-2 infection may be challenged by the limited availability of single-bed rooms in many healthcare settings. Due to such limitations, we isolated patients with suspected Coronavirus Disease 2019 (COVID-19) together with patients without suspected COVID-19 in multiple-bed rooms until PCR-test results were available. We here report the secondary attack rate among patients sharing multiple-bed rooms with a patient initially suspected and later confirmed with SARS-CoV-2 infection.

Methods
Observational study performed at the University Hospital Basel, Switzerland from 01/20-11/20. Patients admitted due to suspected COVID-19 were placed under combined droplet and contact isolation precautions while PCR-test results for detection of SARS-CoV-2 were pending. Isolation precautions comprised wearing surgical masks, gloves and gowns for all direct contacts with the patient or his/her immediate surroundings. The patients' compliance with surgical mask wearing was prerequisite for isolation in multiple-bed rooms. The patient area was delineated by room dividers or floor markings and dedicated toilets were assigned. After confirmation of SARS-CoV-2-infection, patients were reallocated to single-bed rooms. To calculate secondary attack rates, the medical records of all patients sharing the same multiple-bed room while microbiological confirmation was pending, were screened for subsequent diagnosis of SARS-CoV-2-infection.

Results
Among 1218 patients admitted with suspected COVID-19 during the study period, 67 (5.5%) were tested positive for SARS-CoV-2. Of these, 20 (30%) were initially isolated in multiple-bed rooms potentially exposing 26 patients sharing the same room. Median contact time was 11.5 hours (IQR 6.5-18 hours). Subsequent SARS-CoV-2 infection was identified in one out of 26 exposed patients. However, this patient also had a four-day exposure to another patient with initially not detected COVID-19. Therefore, our calculated secondary attack rate from isolation in multiple-bed rooms lies at 0-3.8%.

Conclusions
Isolation of suspected COVID-19-patients in multiple-bed rooms avoided single room occupation and subsequent in-hospital relocation for a large number of patients without confirmation of SARS-CoV-2-infection. Our estimate of the resulting secondary attack rate allows for assessment of the risk/benefit ratio given the limitation of a small sample size.

P04

Low secondary attack rate after prolonged exposure to sputum smear positive miliary tuberculosis in a neonatal unit

R Pop[1]; MB Kälin[1]; SP Kuster[1]; H Sax[1]; SK Rampini[2]; R Zbinden[3]; C Relly[4]; B Zacek[5]; D Bassler[2]; J Fontijn[2]; C Berger[2]
[1] University Hospital Zurich and University of Zurich, Switzerland; [2] University Hospital Zurich; [3] University of Zurich; [4] University Children's Hospital Zurich; [5] Lung Association of Canton Zurich (Verein Lunge Zürich)

Aims
Several neonatal intensive care units (NICU) have reported exposure to sputum smear positive tuberculosis (TB). NICE Guidelines give support regarding the investigation and treatment intervention, but not for close contact definitions. Additionally, data regarding the reliability of interferon gamma release assay (IGRA) in infants as a screening test for TB infection is scarce. We report an investigation and management strategy and evaluated the viability of IGRA in infants and its concordance to TST.

Methods
We performed an outbreak investigation of incident TB infection in a NICU after prolonged exposure to sputum smear positive miliary TB of an infant's mother. Our team of experts defined individual contact definitions and interventions. In addition, we evaluated the concordance of IGRA and TST at baseline investigation and its technical viability in infants.

Results
71 of 90 (78.9%) exposed infants were investigated at baseline, in 51 (56.7%) of the 54 (60%) infants, follow-up TST at the age of 6 months was performed. No infant in our cohort showed a positive TST or IGRA. At baseline investigation all infants showed a negative TST and a concordant negative IGRA. All infants responded to Mitogen, which was used as a positive control of the IGRA, demonstrating that cells are viable and react upon stimulation by mitogen.
149 of 160 (93.1%) exposed health care works (HCW) were investigated. 1 HCW was tested positive, having no other reason than this exposure for latent TB infection. 5 of 92 (5.5%) exposed primary contacts were tested positive, all coming from countries with high TB burden.
In total, 1 of 342 exposed contacts was newly diagnosed with latent TB infection. The secondary attack rate in this study including pediatric and adult contacts was 0.29%-0.32%.

Conclusion
This investigation highlights the low transmission rate of sputum smear positive miliary TB in a such highly susceptible population as infants. Our expert definitions and interventions proved to be useful in terms of feasibility of a thorough outbreak investigation. Furthermore, we demonstrated concordance of IGRA and TST. All infants responded to Mitogen, indicating IGRA as a well-functioning test in infants. Based on our findings, we assume that IGRA could be considered as a reliable investigation tool to rule out TB infection in infants.

P05

Wie oft stimmt die angegebene Indikation für liegende Dauerkatheter?

P Martic; D Saleschus; W Zingg; PW Schreiber
Universitäts Spital Zürich

Hintergrund
Eine der wichtigsten Massnahmen zur Vermeidung von Blasenkatheter-assoziierten Harnwegsinfektionen (CAUTI) ist die Reduktion der Anzahl Kathetertage. Dies bedeutet, dass Blasenkatheter nur eingesetzt werden, wenn deren Gebrauch indiziert ist.

Methoden
Mit dem Projekt «Überprüfung der Indikation von Blasenkathetern und tägliche Evaluation-repetitive Prävalenzstudien», wird punktuell gemessen, welcher Anteil aller an einem Tag kontrollierten Katheter wirklich notwendig ist. In 2017 wurde eine tägliche Dokumentation der Katheterindikation durch das betreuende Behandlungsteam eingeführt, i.e. «angegebene» Indikation. Für die zehn Medizinbereiche, die die höchste Dichte an Blasenkatheter aufweisen, erfolgte für eine Stichprobe von zehn Patienten eine Überprüfung der Katheterindikation durch eine Fachexpertin Infektionsprävention, i.e. «effektive» Indikation. Wir prüften die Übereinstimmung zwischen «angegebener» und «effektiver» Indikation bei durchgeführten Erhebungen in zwei Messperioden (2. Halbjahr 2019 und 1. Halbjahr 2021) und verglichen Veränderungen mit Fisher's Exact Test.

Resultate
In den Messperioden 1 und 2 wurde bei jeweils 120 bzw. 118 Patienten die «effektive» Indikation für einen Dauerkatheter evaluiert und mit der «angegebenen» Indikation verglichen (siehe Abbildung 1). Die am häufigsten «angegebenen» Indikationen waren Urinmonitoring/Bilanzierung (51,5% in Messperiode 1, 47,5% in Messperiode 2, gefolgt von Operation (25,4% in Messperiode 1, 22,9% in Messperiode 2). Bei diesen beiden Indikationen zeigte sich die höchste Diskrepanz zwischen «angegebener» und «effektiver» Indikation. Im Vergleich der Messperioden fand sich eine bessere Übereinstimmung in Messperiode 2 (P=0.008).

Schlussfolgerung
Eine kritische Überprüfung der Dauerkatheter-Indikation zeigte in Messperiode 1 in 37.2% keine Übereinstimmung mit der «effektiven» Indikation. In Messperiode 2 sank dieser Wert erfreulicherweise auf 16,5%, was einer signifikanten Verbesserung entspricht.

P06

It never rains but it pours: outbreak of carbapenem-resistant Acinetobacter baumannii during the COVID-19 pandemic

R Thoma[1]; M Schlegel[1]; D Flury[1]; K Boggian[1]; J Männer[1]; M Filipovic[1]; G Kleger[1]; O Nolte[2]; SN Seiffert[2]; P Kohler[1]
[1] Kantonsspital St. Gallen; [2] Center for Laboratory Medicine

Background
The COVID-19 pandemic might facilitate the spread of multidrug-resistant organisms (MDRO) due to high patient turnover, overuse of broad-spectrum antibiotics, altered handling of personal protective equipment (PPE) and shortage of staff. We investigated the outbreak of a carbapenem-resistant Acinetobacter baumannii (CRAB) in two intensive care units (ICU) of a tertiary care centre.

Methods
In September 2020, a COVID-19 patient was diagnosed with CRAB bacteremia 11 days after transfer from South-eastern Europe (admission screening for MDRO negative). After detection of a second case, an outbreak investigation was started including description of patient histories, isolation of colonized or infected patients, contact screening, weekly cross-sectional and routine screenings after discharge from the ICU, and environmental sampling. Environmental cleaning was intensified, observations and training regarding correct use of PPE and hand hygiene were held, and carbapenem use was restricted on the medical ICU. All screening- and environmental samples were analysed using routine diagnostic procedures. Whole genome sequencing (WGS) and analysis by SeqSphere allowed in-depth phylogenetic differentiation.

Results
From September 30th to December 28th 2020, 10 CRAB positive patients were identified, all of which were treated in the medical- or surgical ICU. Five had clinically relevant CRAB infection, whereof four were treated with cefiderocol. Fatality rate was 6/10, whereof at least 2/6 were attributable to CRAB infection. WGS data revealed ST2 (MLST Pasteur) with an OXA-23 carbapenemase in all isolates. Single nucleotide polymorphism analysis differentiated a medical- and a surgical ICU cluster with 8 and 2 cases, respectively. Environmental sampling (n = 15) remained negative, on-site observations revealed inadequate handling of PPE, particularly of non-sterile gloves. On the medical ICU, carbapenem use decreased from 340 defined daily doses (DDD) in October to 30 DDD in December. After December 28th, no further cases were detected.

Discussion
Our observations suggest inadequate PPE-handling and frequent carbapenem use as driving factors for the spread of CRAB among these mostly COVID-19 patients. Of note, both presumable index patients were transferred from South-eastern Europe underlining the importance of repetitive MDRO admission screenings of transfers from high-risk countries. Although not always related to CRAB, case fatality was considerable.

P07

Nosocomial transmission of SARS-CoV-2: Experience from the contact tracing activity of the Infection Control Unit for the University Hospital of Lausanne.

E Glampedakis; E Kampouri; E Moulin; F Boiron; P Bressin; G Chaillou; I Federli Hanachi; D Gustin; M Gyger Wanzenried; L Kalbermatter; I Koenig; A Lacot; M Limet-Dutoit; H Salehi-Gysel; M Thevenin; E Viaccoz; A Vital-Heilbronn; B Grandbastien; L Senn
CHUV Centre hospitalier universitaire vaudois

Aims
The high transmissibility of SARS-CoV-2 is of particular concern for hospitals given that hospitalized patients often have comorbidities putting them at risk of severe COVID-19- and related death. Here we describe the contact tracing activity related to nosocomial SARS-CoV-2 cases conducted in the University Hospital of Lausanne.

Methods
Physicians and nurses of the Infection Control Unit received automatic alerts for positive SARS-CoV-2 PCR results performed by the Microbiology laboratory in hospitalized patients. Hospital-acquired SARS-CoV-2 infections, defined as those occurring after at least 5 days of hospitalization, were further investigated. Contact tracing was performed via an institutional software allowing tracing index patients' movements and their roommates. Patients were considered as "contacts" at risk and were placed in quarantine if they shared the same room with the index-case up to 72 hours before index's first positive PCR or first symptoms, whichever came first. Additionally, contacts systematically had nasopharyngeal SARS-CoV-2 PCR testing at days 0 , 10 counting from last contact with the index or at symptom onset.

Results
Between November 1st 2020 until March 31st 2021, 322 nosocomial SARS-CoV-2 cases were identified, of whom 195 (61%) had previously been in contact with a known nosocomial case while for 127 (39%) source of infection was unknown. Median time from admission to positive PCR was 13 days (IQR 8 – 25). COVID-19 associated symptoms where present in 67% of cases with a median time of onset of 12 days (IQR 6 - 22). Median age was 76 years (IQR 64 – 84). Of all episodes, 75% were diagnosed in medical units (including 50 cases, 16% in geriatric sections),24% in surgical sectors and 1% in the ICU. Contact tracing activity identified 605 contacts with a median of 2 contacts per index case (IQR 0-2, range 0-19). Of these, 195 (32%) had a positive PCR result during follow-up.

Conclusion
Our experience shows that a thorough contact tracing with systematic PCR screening of contacts is necessary after detection of a nosocomial SARS-CoV-2 case as transmissibility is high and more than 1/3 of cases are asymptomatic. The non-identification of a source for more than a third of nosocomial cases raises concerns of potential implication of healthcare workers in transmission and their inclusion in screening is to consider if cases without evident source are found in a unit.

P08

Whole genome sequencing sustains cross-transmission of Pseudomonas aeruginosa in a neonatal intensive care unit during an outbreak

D Blanc; L Senn; I Federli; E Giannoni; F Legault; M Roth-Kleiner; B Grandbastien
Centre Hospitalier Universitaire Vaudois

Introduction
Pseudomonas aeruginosa is a rare pathogen in neonatal intensive care unit (NICU). Following P. aeruginosa infections in three NICU patients in June 2020, we performed an epidemiological investigation to find possible sources of infection and routes of transmission.

Methods
Retrospective analysis of P. aeruginosa isolates from patients hospitalized in NICU was performed and we initiated a prospective weekly screening of all patients for P. aeruginosa (which included naso-pharyngeal and rectal swabs). Based on previous investigation, environmental samples targeting sink traps were performed to identify P. aeruginosa. Isolates were first typed by double locus sequence typing (www.dlst.org/Paeruginosa) and all isolates identical to the outbreak isolates, were further analysed by whole genome Multi Locus Sequence Typing (wgMLST, BioNumerics v.7.6.3).

Results
The three patients harboured isolates from the same DLST62-56 genotype. Retrospective analysis of isolates from patients hospitalized in the NICU revealed five other patients with this genotype from April to July 2020. Weekly screening implemented in August revealed eight new patients with P. aeruginosa, of whom only three with the epidemic genotype. No isolate from the environment belonged to this genotype. Whole genome sequencing revealed that all DLST62-56 isolates belonged to the MLST ST667. wgMLST of NICU isolates from this genotype revealed they clustered all in the same group with 0 to 6 loci differences between isolates.

Conclusions
The absence of the epidemic DLST in the environment favoured the hypothesis of cross-transmission. This was corroborated by the fact that the outbreak stopped when weekly screenings were implemented and additional contact measures were taken with positive patients. Molecular typing with DLST in the first approach allowed a rapid identification of a putative problem and selecting isolates for finer typing with whole genome sequencing. wgMLST confirmed the close genetic relatedness between these isolates, sustaining the patient-to-patient chain of transmission.

P09
COVID-19: rôle et implication d'une équipe de prévention et contrôle de l'infection

I Koenig; L Senn; G Chaillou
Centre Hospitalier Vaudois

Introduction
L'augmentation rapide du nombre de patients hospitalisés pour une infection à SARS-CoV-2 a nécessité plusieurs réorganisations des services de soins pour les accueillir aux urgences, en unités et aux soins intensifs. Notre objectif est de décrire le rôle joué par l'équipe de prévention et contrôle de l'infection (PCI) dans la prévention de la diffusion du virus pour un centre hospitalier universitaire.

Méthode
L'équipe PCI a suivi une approche multimodale d'information, de sensibilisation et d'évaluation des pratiques en collaboration interprofessionnelle avec les équipes médico-soignantes des secteurs cliniques concernés et les services de support (communication, logistique, infrastructures).

Résultats
L'évolution des recommandations a nécessité une mise à jour régulière des procédures internes. Pour accompagner leur mise en application, l'équipe PCI a assuré l'information en continu et le coaching des équipes sur le terrain. Elle a également participé aux cellules de gestion de crise des différents secteurs cliniques, aux points d'informations quotidiens des secteurs impliqués dans la prise en charge des patients COVID, afin de répondre aux questions et appréhensions des équipes. En étroite collaboration avec le service de communication, elle a élaboré des affiches, réalisé des vidéos expliquant l'utilisation des équipements de protection individuelle lors de la prise en charge des patients et des mesures de prévention à appliquer en tout temps. Le cours PCI dispensé chaque mois pendant la semaine d'intégration du nouveau personnel soignant a été repensé en incluant une sensibilisation à la situation COVID et aux mesures de protection.

Conclusion
L'équipe PCI a gagné en visibilité et ses compétences spécifiques ont été régulièrement sollicitées, contribuant ainsi à la protection des patients, des collaborateurs et des visiteurs. Cette présence accrue sur le terrain a permis à de consolider des partenariats multidisciplinaires, qui se sont avérés bénéfiques pour la prise en charge du patient. La participation à la création de vidéos et l'élargissement des formations à d'autres corps de métiers (logistique, protection civile, armée) nous a conduit à élargir nos champs d'activité et à faire preuve de créativité et d'adaptabilité. Aujourd'hui encore, l'équipe PCI reste engagée auprès des diverses structures de gestion de crise, provisoires ou pérennes pour une prise en charge optimale des patients.

P10

Expertise en Prévention et Contrôle de l'infection dans un service de Médecine intensive adulte au cours de la pandémie Covid

M Thevenin
CHUV - Hôpital universitaire

Introduction
Le 4 mars 2020, un 1er patient Covid 19 était admis en Médecine intensive. La progression de la pandémie et l'afflux d'admissions a conduit l'établissement, notamment les soins intensifs (SI) à se restructurer.
Cette gestion de crise a impliqué une coordination entre de multiples partenaires impliquant largement l'équipe PCI, experte en gestion du risque infectieux.
Les objectifs de ce retour d'expérience sont 1) de décrire la mise en place de stratégies exceptionnelles aux SI et 2) d'évaluer l'impact de ces changements sur les indicateurs ciblés PCI.

Méthodes
L'équipe médico-soignante des SI a dû réorganiser complètement ses activités : locaux, matériel et personnel. L'évolution temporelle de l'épidémie, des connaissances scientifiques et des recommandations ont guidé ces remaniements.
Parallèlement, la surveillance en routine des indicateurs PCI a été poursuivie.

Résultats
Cinq unités de SI supplémentaires ont été créées (passage de 36 à 85 lits). Selon la géographie (open space, types de box) et la modularité des régimes de pression, les mesures de PCI ont été adaptées : choix de la protection respiratoire, signalétique à chaque lit, circulations sécurisées, identification de zones de stockage.
Les difficultés d'approvisionnement ont conduit à devoir évaluer de nombreuses références d'équipements de protection individuelle (masques : n=16).
Les équipes médicales et soignantes ont été renforcées par 600 collaborateurs issus de 17 secteurs ; tous ont bénéficié d'un encadrement et de formations spécifiques, dont 80 sessions assurées par l'équipe PCI.
Les collaborateurs PCI ont apporté leur soutien aux équipes médico-soignantes des SI : actualisation constante des recommandations (17 versions successives), présence accrue sur le terrain, rencontres médico-soignantes tri-hebdomadaires pour le suivi PCI des patients.
Les indicateurs d'impact, comparés à 2019 étaient l'observance de l'hygiène des mains (86% vs 81%), l'incidence des bactériémies (10,2/1000 patient-jours (pj) vs 7,3), de MRSA (0,4/1000 pj vs 0,6) non statistiquement différents ou encore les cas Covid nosocomiaux (aucun).

Discussion/Conclusion
La collaboration entre les équipes médico-soignantes PCI et SI a permis d'adapter les recommandations et de maîtriser le risque infectieux Covid ou non. Ce défi a montré les élans de solidarité, la complémentarité avec la PCI, la réactivité de ces 2 équipes et l'importance de communiquer avec cohérence dans un contexte médiatique parfois

P11

Interactive Access to Current Hospital-specific Antimicrobial Consumption Data: the ANRESIS Dashboard

L Renggli; M Gasser; O Friedli; C Plüss-Suard; A Kronenberg
Universität Bern

Background and aims
Surveillance of antibiotic consumption is a crucial element in "antibiotic stewardship", and it has been shown, that optimizing use of antibiotics may prevent spread of resistant bacteria1,2,3,4.
The Swiss Centre for Antibiotic Resistance (ANRESIS) collects aggregated antibiotic consumption data from 70 hospitals distributed all over Switzerland since 2006. Data analyses from ANRESIS are transmitted as feedback and benchmark reports to individual hospitals to support them in defining aims for antibiotic stewardship programs.
The main aim of this project was to develop an interactive dashboard in order to supplement the printed reports with customised visualisations according to the hospital-specific needs.

Methods
Data source for the ANRESIS dashboard is antibiotic consumption data, which was provided by the hospitals, that are part of the ANRESIS surveillance system. The dashboard was programmed by the R software environment (Version 4.0.4, R core team, Vienna, Austria), using packages such as Shiny and Plotly.

Results
The ANRESIS dashboard is a web application with hospital-specific login providing free access to interactive graphics and interactive tables to hospitals which are part of the ANRESIS surveillance system (https://www.anresis.ch/shinyapps/Website_personalised/Example/). The current beta version contains data of 64 Swiss hospitals (including 17 hospital groups) and will be updated yearly. The temporal course of the user's hospital antimicrobial consumption is depicted graphically. Data can be filtered by users according to antibiotics or antimycotics, antimicrobial categories and substances, departments, consumption units (DDDs/100 bed-days vs. DDDs/1000 admissions) and additional parameters. A benchmark boxplot enables the user to compare the consumption of his hospital with other hospitals of the same size or the same linguistic region.

Conclusion
The ANRESIS dashboard conveys antimicrobial consumption data in an interactive form to hospitals and provides state-of-the-art information technology to antibiotic stewardship programs. Due to its flexible design, the ANRESIS dashboard may be adjusted to the users' needs and extended with further panels.

P12

Influence du port du masque en période de pandémie CoVID-19 sur le taux de vaccination contre la grippe saisonnière chez le personnel soignant des EMS du canton de Vaud - saison 2020/2021

B van der Kaa[1]; C Petignat[2]; M Attinger[1]; I Nahimana - Tessemo[1]; D Hequet[1]
[1] Unité cantonale HPCI Vaud ; [2] Direction générale de la santé

La vaccination contre la grippe du personnel soignant permet de diminuer la morbidité et la mortalité chez les personnes vulnérables dont font partie les résidents des établissements médico-sociaux (EMS). Le personnel soignant des EMS est donc incité à se faire vacciner contre la grippe chaque année. Dans le canton de Vaud (Suisse), le vaccin est offert par la Santé Publique au personnel soignant des EMS qui pourra se faire vacciner gratuitement sur son lieu de travail.
Suite à une diminution de la couverture vaccinale chez le personnel soignant sur plusieurs années, le port du masque est devenu obligatoire en 2015/16 pour le personnel soignant non-vacciné contre la grippe, dès le franchissement du seuil épidémique et durant toute la période épidémique.

But
Nous souhaitons estimer l'impact de l'obligation du port de masque dès 2015/16 pour les non-vaccinés ainsi que l'impact de la pandémie de CoVID-19 avec le port du masque pour tous les professionnels sur le taux de vaccination contre la grippe dans les EMS du canton de Vaud.

Méthode
Sur mandat de la Santé Publique, l'Unité Cantonale Hygiène, Prévention et Contrôle de l'Infection (UHPCi) récolte annuellement les taux de vaccination du personnel soignant des EMS du canton de Vaud. Elle les reporte ensuite dans un rapport qui est adressé aux EMS. Nous analysons ces taux pour les saisons 2008/09 à 2020/21.

Résultats
Le taux de vaccination contre la grippe du personnel soignant des EMS vaudois était de 42% en début de surveillance (2008/10) et a ensuite diminué à 35%. Suite à la directive imposant le port du masque pour le personnel non vacciné, ce taux a augmenté progressivement pour atteindre 47% en 2019/20. Avec la mise en place de l'obligation du port du masque pour tout le personnel durant la saison 2020/21 ce taux a chuté à 37%.

Conclusion
L'obligation du port du masque pour les non-vaccinés dès 2015 a permis d'augmenter le taux de couverture vaccinale contre la grippe des professionnels travaillant en EMS. Le port du masque obligatoire pour tous en 2020/21 en raison de la pandémie de CoVID-19 a eu un impact direct sur les taux de vaccination contre la grippe du personnel soignant avec une chute de 10%. Le taux de vaccination contre la grippe saisonnière est directement lié aux mesures de protection imposées au personnel et donc au port du masque. Il conviendra de revoir la prévention primaire dans la lutte contre la grippe saisonnière avec le personnel des EMS, car le gold standard reste la vaccination.

P13

Evaluation of “ward-level" risk factors for nosocomial COVID-19 outbreaks: a matched case-control study

R Thoma; D Flury; S Haller; J Männer; P Kohler; M Schlegel
Kantonsspital St. Gallen

Introduction and Aims
The prevention of nosocomial SARS-CoV-2 infection and outbreaks is a major challenge during the COVID-19 pandemic. During the second wave of the pandemic, we observed several wards with outbreaks whereas others were spared. We aimed to investigate risk factors for nosocomial COVID-19 outbreaks on a ward level.

Methods
We conducted a matched case-control study by retrospectively defining outbreak- (≥ 2 noso-comial patients infected within a 14-day time period) and control wards. Matching was done 1:1 for approximate number of beds (+/- 5) and the period in which data on ward-level risk factors was collected (3 months preceding the start of the outbreak on the case ward). The beginning of the outbreak was defined as the day of diagnosis of the first nosocomial COVID-19 case on the ward. Nosocomial COVID-19 cases were defined as patients with diagnosis of the disease 5 or more days after hospital admission. Intensive Care Units and designated COVID-19 wards were excluded. We used a paired Wilcoxon signed-rank test to compare variables between outbreak- and control wards.

Results
From July to December 2020, we observed 9 outbreak- (total of 40 patients and 26 HCW infected) and 9 control wards (total of 2 patients and 8 HCW infected). The only factor significantly associated with outbreak wards was the percentage of HCW tested positive within a period of 14 days prior- until 2 days after the start of the outbreak (mean 9.7% of HCW vs 2.7%, p = 0.04). Further, outbreak wards trended towards a higher mean number of beds per room (2.22 vs 1.97, p = 0.09) and younger mean HCW age (33.3 vs 36.2 years, p = 0.17) compared to control wards. No clear association was found for factors reflecting workload (mean subjective LEP (Leistungserfassung in der Pflege) -score 4.8 vs 4.3, p = 0.23), for the number of admissions per bed, or for the mean years on duty of HCW.

Conclusion
Our study reveals increased numbers of infected HCW shortly before the outbreak to be a risk factor for SARS-CoV-2 ward outbreaks. This supports the notion that infected HCWs are an important source of nosocomial COVID-19 outbreaks and underscores the importance of compliance with infection control- and prevention measures - especially between HCW and patients and among HCW.

P14

Use of respirator vs. medical masks in Swiss healthcare personnel and its impact on SARS-CoV-2 acquisition – a prospective cohort

S Haller[1]; S Güsewell[1]; T Egger[1]; OB Leal Neto[2]; G Scanferla[1]; R Thoma[1]; D Flury[1]; A Brucher[3]; E Lemmenmeier[4]; JC Möller[5]; P Rieder[6]; M Ruetti[7]; R Stocker[6]; D Vuichard-Gysin[8]; B Wiggli[9]; U Besold[10]; S Kuster[11]; A McGeer[12]; L Risch[13]; A Friedl[9]; P Vernazza[1]; M Schlegel[1]; CR Kahlert[14]; P Kohler[1]
[1] Cantonal Hospital St. Gallen; [2] University of Zurich; [3] Psychiatry Services of the Canton of St. Gallen (South); [4] Clienia Littenheid AG; [5] Center for Neurological Rehabilitation Zihlschlacht; [6] Hirslanden Clinic Zurich; [7] Hospital Region Fürstenland Toggenburg; [8] Thurgau Hospital Group; [9] Cantonal Hospital Baden; [10] Geriatric Clinic St. Gallen; [11] Federal Office of Public Health; [12] Sinai Health System; [13] Labormedizinisches Zentrum Dr Risch Ostschweiz AG; [14] Children's Hospital of Eastern Switzerland

Aims: To date there is insufficient evidence to determine if respirators offer an advantage over medical masks for the prevention of SARS-CoV-2 infection. We analysed the impact of filtering face piece class 2 (FFP-2) respirators vs. medical masks on the risk of SARS-CoV-2 acquisition among healthcare workers (HCW).

Methods: Our prospective multicentre study enrolled Swiss HCW between June 22nd and August 15th 2020. Participants answered a baseline questionnaire followed by weekly surveys capturing the type of mask participants preferentially used while caring for COVID-19 patients outside of aerosol generating procedures (AGP). For those performing AGPs, we also asked whether they preferentially used FFP-2 masks during AGPs for patients without COVID-19 suspicion (i.e universal use). We performed Cox regression analysis to assess the impact of mask type on the hazard of COVID-19, as evaluated by self-reported SARS-CoV-2 positive swab results in weekly follow-ups, accounting for time-independent (e.g. age, sex, profession, use of personal protective equipment) and time-dependent (e.g. household or patient/co-worker exposure) co-variables. Subgroup analyses for those with infrequent (having cared for ≤10 patients during follow-up) and frequent exposure (>10) were performed.

Results: We followed 3’137 participants from 9 healthcare networks in 4 cantons over a median period of 27 weeks; 694 (22%) reported mostly wearing FFP-2 masks while caring for COVID-19 patients. SARS-CoV-2 tests were positive in 77/694 (11%) of FFP-2 compared to 330/2443 (14%) of medical mask users (OR 0.80; 95% CI 0.61 - 1.04; P = 0.096). In multivariable analysis, FFP-2 use was associated with a decreased risk of acquiring SARS-CoV-2 (HR 0.75, 95% CI 0.61 - 0.93, P = 0.008). A positive SARS-CoV-2 test was most strongly associated with exposure to a positive household (HR 8.6, 95% CI 6.4 - 11.4, P < 0.001). In subgroup analyses, the protective effect of FFP-2 use was not significant for those with infrequent (n=1740, HR 0.78, P = 0.38), but for those with frequent exposure (n=1397, HR 0.68, P > 0.001). Universal FFP-2 use during AGPs showed no effect compared to medical masks (HR 1.09, 95% CI 0.73 - 1.63, P = 0.68).

Conclusion: Our findings show a lower SARS-CoV-2 infection risk for HCW using FFP-2 masks for those with frequent exposure to COVID-19 patients. However, household exposure remains the strongest risk factor. Universal use of FFP-2 during AGPs offers no additional benefit.

P15

Hospital-acquired respiratory viral infections while applying droplet precautions on-site (DroPS) - prospective observational study during the 2019/20 influenza season, Bern, Switzerland

M Birrer[1]; K Draps[1]; F Hobi[1]; M Laguardia[1]; E Hofmann[1]; A Atkinson[1]; M Blatter[2]; M Perrig[1]; M Luginbühl[2]; D Aujesky[1]; J Marschall[1]; R Sommerstein[1]
[1] Inselspital, Bern University Hospital, University of Bern, Switzerland; [2] Tiefenauspital, Bern, Switzerland

Background
The guideline-driven and widely implemented single room isolation strategy for respiratory viral infections (RVI) such as influenza or respiratory syncytial virus (RSV) can lead to a shortage of hospital beds. Alternative strategies to prevent hospital-acquired respiratory viral infections (HARVI) are needed. Based on promising results of a pilot study using droplet precautions on-site (DroPS) during the influenza season 2018/19, this strategy was implemented in multiple hospital wards. We assessed the “real-life” safety of DroPS by measuring the rate of HARVI after its implementation.

Methods
Prospective observational study during the influenza season 2019/20 at a tertiary and secondary referral hospital. The study was prematurely stopped at the beginning of the COVID-19 pandemic (17th March 2020). DroPS was used for patients hospitalised with suspected or proven RVI. Hospitalised patients with no respiratory isolation in the two days following admission were considered “at risk” for the acquisition of HARVI. They were screened daily for the onset of new respiratory symptoms. Once an “at risk” patient developed symptoms, an influenza/RSV molecular rapid test was performed. The two main outcomes were the rate of clinical and laboratory-confirmed HARVI (influenza or RSV).

Results
We included 1’996 hospitalisations with a total of 8’955 “at risk” hospital days for HARVI. Median age was 71 years [IQR 56 – 81]. HARVI was clinically diagnosed in 11/1’996 (0.6%) hospitalisations. All patients with clinical diagnosis were microbiologically screened and three confirmed (0.15%; 2x RSV, 1x influenza B).

Conclusion
Droplet precautions on site (DroPS) appear to represent a safe, simple and resource-saving alternative to the traditional pathogen-based single room strategy for RVI in non-pandemic circumstances.

P16
Enhancing Infection Prevention and Control in Mozambique

G Diakité[1]; A Charrier[2]; S Makohliso[2]; M Hobbins[1]; A Jores[1]
[1] SolidarMed; [2] Ecole Polytechnique Fédérale de Lausanne (EPFL), EssentialTech C E N T R E

Aim
Infection prevention and control (IPC) is an essential part of health care at all levels in preparing for and preventing outbreaks. It prevents patients and health staff of being harmed by Healthcare Associated Infections (HAI) or as the result of antimicrobial resistance (AMR). The current study was designed in order to gain in-depth understanding and gap analysis of the IPC system in a rural area in Northern Mozambique to inform future project development.

Methods
We performed an in-depth assessment at 5 health facilities in the province of Cabo Delgado to understand IPC at various levels. On-site visits were organised with semi-structured assessments of equipment, processes, SOPs. We also performed interviews with the IPC managers, health facility hygienists, health staff to assess the successes and challenges of IPC management in the facilities.

Results
The in-depth study showed:
- None of the health centre had a hygiene committee to facilitate coordination, development of IPC intervention strategies and supervision. Insufficient training in IPC management resulted in SOPs not being reinforced, poor personal and environmental hygiene and non-adequate sterilisation of medical equipment.
- Health care waste management: biological infectious waste was properly disposed, but improper management of remaining infectious waste resulted in cross contamination of non-infectious waste. No recycling or composting of waste was in place.
- Only one health facility had a functioning incinerator; the other HFs used open pits to burn waste. Burning HC waste can lead to the release of hazardous chemicals (i.e. dioxins, furans) and infectious micro-organisms. This represents a serious threat of contamination of the environment and population.
- Monitoring of IPC indicators and HAI, evaluation of IPC quality was not implemented properly.

Conclusions
The assessment led to the development of a project to reduce the spread of HAI and AMR through a comprehensive approach to IPC in 3 key health facilities of Cabo Delgado Province, Northern Mozambique. It will ensure personnel is trained and SOPs are in place, while testing innovative combined approaches to incineration, energy use, composting and recycling in close collaboration with the EPFL in Lausanne, Switzerland

P17

Covid-19 immunity through vaccination or past infection in health care workers (HCWs) of a tertiary care hospital in Switzerland as of March 2021

B Jakopp; S Koch; C Schmutz; K Müller; A Gross; S Haubitz; CA Fux
Kantonsspital Aarau

Aims
The Covid-19 pandemic has confronted HCWs with both severe patient morbidity and a high burden of occupational infections. The availability of highly potent mRNA vaccines promises excellent protection. At the Kantonsspital Aarau, vaccination of HCWs caring for Covid-19 patients on ICUs and dedicated wards started on January 7th 2021. Preparing for a third wave caused by the more virulent B.1.1.7, the Canton Aargau allowed vaccination of all HCWs with direct patient contact mid February 2021. With an information campaign including biweekly online conferences, a chat platform and an easily accessible booking tool we tried to reach vaccination rates approaching herd immunity as of March 2021

Methods
Profession and workplace of every HCW receiving a first Covid-19 vaccine were collected prospectively. The comparison of these anonymized data with the head counts of every department and ward provided the vaccine coverage by profession (physicians; nurses; diagnostic and therapeutic services; others) and by workplace. Vaccine data were complemented by data on occupational Covid-19 infections (again provided by profession and workplace) to describe the proportion of HCWs immune to Covid-19 infection.

Results
Among 4706 employees of our hospital, 3599 (76 %) are HCW with direct patient contact, including 26 % physicians and 55 % nurses. By the end of March 2021, 382 (11 %) HCWs had suffered from Covid-19 and were thus considered immune (52 physicians, 261 nurses, 69 others). The immunity against Covid-19 by vaccination or past infection was 53 % / 10 % overall, 65 % / 5 % for physicians, 48 % / 13 % for nurses and 42 % / 11 % for the remainder. Paediatricians showed the highest vaccination rate with 93 %, followed by intensivists and anaesthesiologists with 78 % and 70 %, respectively. ICU nurses were immune in 60 % / 13%. On Covid wards, more nurses were immune due to past infection (38 %) than vaccination (32 %) for 70% immunity overall. Vaccination rates between wards differed between 13 % and 71 %. Physiotherapists were vaccinated in 34%, cleaning services in 6 % only.

Conclusion
Despite extensive information and low-threshold registration options, HCWs in our hospital did not reach the goal of 70 % immunity suggested to define herd immunity within the first 6 weeks of vaccine availability. Employees with restricted access to online information, language as well as cultural barriers need special attention.

P18

Evaluation von Prüfindikatoren zur Qualitätssicherung der Reinigungsleistung von RDG-E

Y Fietze; T Thalmann; W Steiger; J Marschall
Inselgruppe AG, Inselspital Bern

HINTERGRUND: Reinigungs- und Desinfektionsgeräte zur maschinellen Aufbereitung von flexiblen Endoskopen (RDG- E) müssen eine gleichbleibende Reinigungsleistung über die jährliche Validierung hinaus garantieren (DIN SN EN 15883-4). Die Reinigungsleistung ist 4x jährlich anhand von Reinigungsindikatoren (Prüfindikatoren) nachzuweisen (Swissmedic 2018).
ZIEL: Zur Etablierung eines standardisierten Prozesses (SOP) zur Qualitätssicherung der Reinigungsleistung der RDG-E wurden in unserer Spitalgruppe Prüfindikatoren verschiedener Hersteller getestet mit dem Ziel, einen für alle RDG-E geeigneten, praktikablen und möglichst kostengünstigen Prüfindikator einzusetzen.
METHODE: Es wurden 3 Prüfindikatoren verschiedener Hersteller ausgewählt.
Mit jedem Prüfindikator wurde eine Testserie auf 6 unterschiedlichen RDG-E- Typen gefahren. Nach dem Testdurchlauf wurden die Ergebnisse der Reinigungsleistung und weiterer Parameter in eine Tabelle eingetragen und miteinander verglichen.
RESULTATE: 17 RDG-E der Firmen BHT (2), Mositech (2) und Olympus (13) wurden in die Evaluation einbezogen. In 10 RDG-E wird für den Desinfektionsprozess Peressigsäure verwendet, in 3 RDG-E Glutaraldehyd.
Die Resultate der Testserien mit 3 verschiedenen Prüfindikatoren wurden in einer Tabelle zusammengefasst (Tabelle 1).
DISKUSSION: Der standardisierte Einsatz von Prüfindikatoren kann helfen, Funktionsstörungen der Reinigungsleistung eines RDG-E frühzeitig zu erkennen.
Herausfordernd bei der Einrichtung der Testreihe war die technische Adaptation der Prüfindikator- Vorrichtung an die verschiedenen RDG-E Typen. Die Kosten für die Anschaffung passender Adapter sowie der Personalaufwand für die Durchführung der Tests sind nicht zu unterschätzen.
Einfluss auf das Reinigungsergebnis hatte die angewendete Chemie bzw. die Druckleistung einiger RDG-E Typen.
Für unsere Einrichtung entschieden wir uns in Rücksprache mit den Herstellern der RDG-E für das Produkt 3.
Eine Limitation ergibt sich aus der kleinen Auswahl an Prüfindikatoren, welche zur Testung herangezogen wurden.
Die Einführung von Prüfindikatoren in unserer Einrichtung hatte bereits Konsequenzen: Nach einer ersten Prüfserie wurde ein RDG-E aufgrund des schlechten Resultates ausser Betrieb genommen.

Literatur

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P19

Transcriptomic signature differences between SARS-CoV-2 and Influenza virus infected patients

S BIBERT[1]; N Guex[2]; J Lourenco[3]; T Brahier[1]; M Papadimitriou-Olivgeris[1]; L Damonti[1]; O Manuel[1]; R Liechti[4]; L Götz[4]; J Tschopp[1]; M Quinodoz[5]; P Vollenweider[1]; J Pagani[1]; M Oddo[1]; O Hügli[1]; F Lamoth[1]; M Delorenzi[4]; V Erard[6]; C Voide[7]; N Rufer[8]; F Candotti[1]; C Rivolta[5]; N Boillat-Blanco[1]; P Bochud[1]
[1] University Hospital and University of Lausanne; [2] University of Lausanne; [3] Swiss Institute of Bioinformatics and University of Lausanne; [4] University of Lausanne and SIB Swiss Institute of Bioinformatics ; [5] Institute of Molecular and Clinical Ophthalmology Basel (IOB)/Department of Ophthalmology, University Hospital Basel; [6] HFR-Fribourg; [7] Central Institute, Valais Hospital; [8] University Hospital and University of Lausanne

Background & Aims: Worrying features of the outbreaks of coronavirus disease 2019 (COVID-19), caused by infection with SARS-CoV-2, included the difficulty to control transmission, the increasing number of patients requiring mechanical ventilation and the absence of specific treatment. Indeed, patients severely infected with SARS-CoV-2 are likely to present dysfunctional and/or dysregulated immune responses involving the up-regulation of inflammatory genes. Identifying mechanisms making individuals susceptible to severe COVID-19 may shape prevention strategies to the most-at-risk ones, and/or identify novel management strategies.

Methods: Here, we established transcriptomic profiles in 103 patients infected with SARS-CoV-2 that we have compared to that of 27 healthy individuals and 22 influenza-infected patients. SARS-CoV-2 infected patients were stratified according to the level of respiratory failure; 23 did not even require oxygen support, 40 received oxygen but no mechanical ventilation and 40 required mechanical ventilation. Differential gene expression analyses, and KEGG pathway enrichment were performed. To assess whether differentially expressed genes were associated with biological process, gene set enrichment analyses based on functional annotation were conducted.

Results: The transcriptome data from patients infected with SARS-CoV-2 compared to those infected with Influenza revealed that unfavorable outcomes in COVID-19 may result from delayed or impaired interferon responses leading to a compromised virus control and prolonged activation of inflammatory cytokines. In addition, immune features of COVID-19 also included a reduced maturation and toxicity in NK cells, which may not be able to migrate towards infected tissues, an increased degranulation of neutrophils and a dysregulation of T cells activity. Finally, data suggested an important activation of B cells with a high increased immunoglobulin production, as well as an important over-expression of genes involved in metabolism and cell cycle.

Conclusion: Altogether, our results suggest that severe COVID-19 presentation may results from a defect in or escape from innate immunity associated with an unbalanced adaptive immune response. Collectively, this study improves our understanding of COVID-19 pathogenesis and may guide to characterize the severity level of COVID-19.

P20

High rates of asymptomatic Mycoplasma genitalium infections with high proportion of genotypic resistance to first-line treatment azithromycin among men who have sex with men initially presenting with a primary HIV-infection

A Ring[1]; S Balakrishna[1]; F Imkamp[2]; S Burkhard[1]; F Triet[1]; F Brunschweiler[1]; C Grube[1]; R Kouyos[1]; R Bodmer[2]; H Günthard[1]; DL Braun[1]
[1] University Hospital Zurich, University of Zurich; [2] University of Zurich

Background. Mycoplasma genitalium (Mg) is an emerging sexually transmitted disease (STI) and can lead to serious sequela in men who have sex with men (MSM). Resistance to recommended antimicrobial agents (macrolides and quinolones) are rapidly increasing. To date, guidelines recommend treatment only in symptomatic individuals.

Aims
To investigate the prevalence and incidence of Mg infections in HIV-1 positive individuals who were initially diagnosed during primary HIV (PHI) infection and now on suppressive antiretroviral therapy and to determine the proportion of Mg strains with resistance to antibiotic treatment options.

Methods
Participants of the Zurich Primary Human Immunodeficiency-Virus Infection Study (ZPHI) (NCT 00537966) were systematically offered a STI screening between April 2019 and September 2020. We established a 6-pathogen STI-screening PCR including genotypic resistance testing of Mg strains to macrolides and quinolones.

Results
We included 147/265 (55.4 %) participants from the ZPHI with overall 410 follow-up visits. The majority (90.5%) were MSM. There were 29 participants (19.7 %) with at least one Mg infection, reflecting a period prevalence of 21%. The overall incidence rate was 39 Mg infections per 100 person-years (95% CI [27.54, 55.07]). The distribution of infection sites was: 6 urethral, 4 rectal and the remaining were pooled. Seven out of the 29 participants (24 %) were symptomatic. Eighteen participants (62.1 %) showed resistance to macrolides and 5 (17.2 %) to both macrolide and quinolones respectively. Treatment guided by genotypic resistance test was initiated in 4 (6.9 %) participants: lead in with tetracyclines 2x100 mg for 7 days followed by i) azithromycin 1g on day 1, 500mg day 2-4 (n=1); ii) moxifloxacin 400mg for 10-14 days (n=2) or iii) pristinamycin 4x1g for 10 days (n=1). The remaining 3 symptomatic patients were treated for co-occurring STI's. All treated individuals were tested negative for Mg at the subsequent visit.

Conclusion
In our systematic STI screen of MSM who initially presented with a primary HIV-1 infection, we found a high prevalence of mostly asymptomatic Mg infections. The very high proportion of macrolide-resistant strains suggests that the genotypic determination of resistance to macrolides and quinolones should be standard of care in clinical routine and moxifloxacin should be the preferred treatment option for symptomatic Mg infections if genotypic resistance testing is unavailable.

P21

Trained immunity increases lung antimicrobial activity of PMNs and protects from pneumococcal pneumonia

C Théroude[1]; R Porte[2]; B Bottazzi[2]; I Schrijver[1]; E Ciarlo[1]; D Leroy[1]; M Reverté Royo[1]; T Calandra[1]; C Garlanda[2]; T Roger[1]
[1] Lausanne University Hospital and University of Lausanne, Switzerland; [2] Humanitas Clinical and Research Center IRCCS

Background
Trained immunity characterizes innate immune memory in mammals. We reported that trained immunity confers broad-spectrum protection against bacterial infections (Ciarlo JID 2020). Yet, whether it protects from pneumococcal pneumoniae remains largely unknown.

Aim
To test whether, and if so how trained immunity protects from lethal pneumococcal pneumonia.

Methods
Control mice and mice trained with b-glucan were challenged i.n. with S. pneumoniae. Blood, lungs, spleen and bone-marrow were collected to quantify bacteria, hematopoietic stems cells, leukocytes, cytokines and lung injury, and to isolate PMNs used to measure metabolic activity, phagocytosis, and NETosis.

Results
The induction of trained immunity increased 2-4-fold PMNs and inflammatory monocytes in lungs, did not affect macrophages and innate lymphoid cells (ILCs), but increased the proportion of inflammatory ILC1. Trained mice survived pneumococcal infection and had reduced bacterial burden, lung injury and blood cytokines ($P < 10e-3$-$10e-4$). The numbers of PMNs, monocytes, macrophages and ILCs remained stable in lungs of trained mice, while PMNs increased parallel to bacterial burden in lungs of control mice. Lung ILC2/ILC1 (i.e. tissue repair/inflammatory ILCs) ratio increased in trained mice but decreased in control mice. In response to S. pneumoniae, PMNs from trained mice showed increased metabolic activity, phagocytosis and NETosis.

Conclusions
The accumulation of PMNs with enhanced antimicrobial activity, and the shift of ILCs toward ILC2 in the lungs suggest that the establishment of trained immunity promotes early antimicrobial defense mechanisms and later resolution/repair mechanisms associated with bacterial pneumonia.

P22

Co-infection with rhinovirus and influenza determines replicative capacity of SARS-CoV-2 in the upper respiratory tract

M Essaidi-Laziosi[1]; C Alvarez[1]; P Sattonnet-Roche[2]; G Torriani[1]; L Kaiser[3]; I Eckerle[1]
[1] Faculty of Medicine, University of Geneva; [2] Geneva University Hospitals, Geneva; [3] Geneva University Hospitals

Although frequently reported since the beginning of the pandemic, questions remain regarding the impact of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) interaction with circulating respiratory viruses in coinfected patients. We here investigated co-infections of SARS-CoV-2 with the most prevalent respiratory viruses, namely rhinovirus (RV) and Influenza A and B viruses (IAV and IBV), in reconstituted respiratory airway epithelial cells cultured at air-liquid interface.
We found that SARS-CoV-2 replication was impaired in tissues pre-infected, but not post-infected, with RV, IAV or IBV. In contrast, SARS-CoV-2 had no effect on the replication of these three respiratory viruses. Inhibition of SARS-CoV-2 correlated better with immune response triggered by RV, IAV and IBV than the virus entry. Using neutralizing antibody against type I and III interferons, SARS-CoV-2 blockade in dual infections could be partly prevented.
Altogether, these data suggested the involvement of innate immunity in SARS-CoV-2 interaction with other respiratory viruses. This study extended our understanding of viral co-infection that might be more frequently observed after the pandemic and would play a key role in SARS-CoV-2 epidemiology.

P23

Pharmacological target achievement with cefazolin standard bolus administration of cefazolin in complicated Staphylococcus aureus infections: a prospective single-centre cohort study

P Charitos Fragkakis; S Rehm; S Moser; V Hinic; S Dräger; R Kühl; KM Rentsch; P Sendi; M Osthoff
University Hospital Basel

Background
Complicated methicillin-susceptible Staphylococcus aureus infections (MSSA-CSAI) are an important cause of mortality. Contemporary data regarding the pharmacology of cefazolin (CFZ), a highly protein bound cephalosporin, are scarce. The primary purpose of this study is to determine the achievement of pharmacological targets and its association with clinical outcome and toxicity with standard intermittent bolus administration of CFZ in patients with MSSA-CSAI.

Methods
30 patients with MSSA-CSAI were prospectively enrolled in a Swiss tertiary care center. Total and unbound plasma CFZ concentrations were measured by high performance liquid chromatography-mass spectrometry at five time points during the first week of treatment and minimal inhibitory concentration (MIC) for all MSSA strains were determined by CFZ MIC test strips (Liofilchen). Target attainment (%fT > MIC) and associated factors were analyzed.

Results
Patients were predominately male (83%) with a median age of 76 years [interquartile range (IQR) 56-81]. Bloodstream infection was present in 83% of patients and the most frequent sources were catheter-associated and musculoskeletal infection (both 25%). Intensive care unit admission was required in 50% of patients. The median MIC was 1 mg/L (IQR 0.75-1.5). The median mid-dose concentration of unbound CFZ was 14 (IQR 6-31) and 19 (IQR 4-31) mg/L on day 1 and 3, respectively, and the median trough concentration was 5 (IQR 2-17), 7 (2-16) and 4 (2-15) mg/L on day 1, 3 and 7, respectively. Optimal (100% fT > MIC) target attainment was achieved by 83% patients throughout the study period. At least one trough concentration above 10x the ECOFF MIC (20mg/L) was encountered in 27% of patients.
The unbound fraction correlated positively with the SOFA score and negatively with renal function and albumin ($p < 0.01$). Optimal target achievement was significantly associated with higher age, comorbidities, renal impairment and hypoalbuminemia.

Conclusions
In contrast to healthy individuals, the unbound plasma fraction of CFZ is substantially higher in MSSA-CSAI patients with impaired renal function, hypoalbuminemia, and severe disease. Unbound concentrations below but also above the desired therapeutic range (1-10x MIC) were observed in approximately 20% of patients. Therefore, therapeutic drug monitoring of unbound CFZ concentrations in MSSA-CSAI is desirable.

P24

Novel Echinacea formulations for the treatment of acute upper respiratory tract infections in adults – a randomized controlled trial

J Sumer[1]; K Keckeis[1]; G Scanferla[1]; M Frischknecht[1]; J Notter[1]; A Steffen[1]; P Kohler[1]; P Schmid[1]; B Roth[2]; K Wissel[3]; P Klein[4]; R Schoop[5]; P Vernazza[1]; W Albrich[1]
[1] Kantonsspital St. Gallen; [2] Kantonsspital Luzern; [3] Checkpoint Zürich; [4] statistical services GmbH; [5] A. Vogel

Aims
Echinacea purpurea has clinical and antiviral activity against respiratory viruses. This randomized, double-blind, controlled trial compared higher doses of new Echinacea formula-tions with conventional formulations for therapy of upper respiratory tract infections (URTIs) in adults.

Methods
Healthy adults (n = 409) were randomized to one of four Echinacea purpurea formula-tions, which were taken in case of a URTI for up to 10 days (“d”). New formulations A (lozenges: 5 x 1 on d 1 - 3, 1 x 1 on d 4 - 10) and B (spray: 7 x 2 puffs on d 1 - 3, 2 - 3 x 1 puffs on d 4 - 10) delivered an increased dose of 16’800 mg / d Echinaforce® extract during days 1 - 3 and 3’360 mg / d afterwards; conventional formulations C (tablets: 6 x 1 on d 1 - 10) and D (drops: 6 x 10 on d 1 - 10) constantly 2’400mg. Primary endpoint was time to clinical remission of first URTI episodes based on inves-tigator-confirmed patient-reported diaries for up to 10 days. Novel and conventional formulations were compared using Kaplan-Meier analysis. In a sensitivity analysis, mean time to remission beyond day 10 was calculated extrapolating treatment effects observed on days 7 to 10.

Results
246 participants (mean age 36.2 years, 78% female) treated at least one URTI. Recov-ery by day 10 was achieved in 56% and 44% of patients with the new and conventional formula-tions, showing median time to recovery of 10 and 11 days, respectively ($p = 0.10$ in intention-to-treat analysis, $p = 0.07$ in per-protocol analysis). In the extrapolated sensitivity analysis, new for-mulations resulted in significantly shorter mean time to remission (9.6 vs. 11.0 days, $p < 0.001$). (Very-) good efficacy ratings were given by participants more commonly for new formulations (63% vs. 48%, $p = 0.02$). Among those with an identified respiratory virus, clearance until day 10 based on real-time PCR from nasopharyngeal swabs was more frequent with new formulations (70% vs. 53%, $p = 0.046$). Tolerability and safety (adverse events: 12% vs. 6%, $p = 0.19$) were good and similar between formulations with only one severe adverse event with a potential hy-persensitivity reaction to the novel spray.

Conclusions
In healthy adults with acute URTI, new Echinacea purpurea formulations with high-er doses resulted in faster viral clearance than conventional formulations and a trend for faster clinical recovery with significant differences in sensitivity analyses with good safety.

P25

Upper respiratory tract infection in outpatients before and during the SARS-CoV-2 pandemic

A Frey[1]; V Kufer[2]; S Schmutz[2]; M Zaheri[2]; S Burkhard[1]; A Plate[1]; A Trkola[2]; M Huber[2]; N Mueller[3]
[1] University Hospital Zurich; [2] University of Zurich; [3] UniversitätsSpital Zürich

Background
Acute upper respiratory tract infections (URTIs) are among the most common reasons for consultations in primary care and frequently result in unnecessary antibiotic treatment. In order to improve the clinical decision making, the distinction between viral and bacterial infections is crucial. Here, we investigated the utility of viral metagenomic next generation sequencing (mNGS) in an outpatient setting. By providing a comprehensive viral detection, mNGS may allow for an adjustment of the clinical diagnosis, less antibiotic use and thus impacting antibiotic resistance development.

Methods
Viral mNGS was applied in a prospective cross-sectional study aimed at investigating the potential of mNGS in immunocompetent patients suffering from an acute URTI. Pharyngeal swabs were collected by GPs and analyzed using viral mNGS. Demographic and medical data were obtained by questionnaire. The detected pathogen(s) were subsequently communicated to both the GPs and the patients. EC approval was obtained (2019-01120).

Results
A total of 281 patients (mean age 42.5 years, 58% female) were recruited by 21 GPs between 10/2019 and 12/2020. In 209 patients, mNGS identified one or more viral species. In 91% of patients a viral etiology was suspected by the GP. Only 23 patients received antibiotic treatment, of which in four cases mNGS revealed a possible viral cause. Rhinoviruses were the most frequently detected respiratory viral species (20% of all patients). The study showed the seasonal occurrence of influenza viruses in early 2020 and the arrival of the SARS-CoV-2 pandemic in Switzerland in March 2020. During the lockdown, with hygienic measures in place, respiratory viruses other than SARS-CoV-2 continued to be recorded.

Conclusions
In the case of URTI, viral mNGS analysis enables the re-evaluation of the GPs presumed diagnosis. In certain cases, this may reduce inappropriate antibiotic use. Given future reduction in turnaround time, this method could prospectively influence URTI treatment. On an epidemiological level, mNGS allows to anticipate circulating viruses in a population, guiding informed choices on prevention. Retrospectively, such data could provide essential information on implemented hygiene measures, particularly during a pandemic.

P26

High rates of advanced liver fibrosis and cirrhosis in patients with chronic hepatitis B in Macenta, Republic of Guinea | interim analysis.

D Leuenberger[1]; J Hébélamou[2]; C Henzen[3]; Y Guilavogui[2]; S Onivogui[2]; CA Fux[1]; M Seydi[4]; C Ottiger[1]; A Rauch[5]; C Staehelin[3]
[1] Kantonsspital Aarau, Aarau, Switzerland; [2] Centre Hospitalier Régional Spécialisé; [3] Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland; [4] Fann University Hospital; [5] Inselspital, Bern University Hospital, Bern, Switzerland

Aims
In patients with chronic hepatitis B, we aimed to assess the prevalence of advanced liver fibrosis and cirrhosis and the proportion of patients qualifying for treatment with a nucleos(t)ide analogue (NA) at the Centre Hospitalier Régional Spécialisé (CHRS) in Macenta, Forest Region, Guinea. The final aim is to provide data on the burden of advanced chronic hepatitis B infection in the region to the Ministry of Health to lobby for a separate hepatitis B treatment programme.

Methods
Interim analysis covering the period between 01.11.2018 and 07.04.2021 of a study running over 3 years. Patients with active hepatitis B (at least one positive hepatitis B antigen (HBsAg)) were assessed with non-invasive methods – the aspartate-to-platelet ratio index (APRI score), ultrasound and/or transient elastography (TE) using the FibroScan®. Severe fibrosis was defined as TE of ≥ 9.0 kPa (corresponding to metavir stage ≥ F3). Cirrhosis was defined as APRI score > 2 or consistent ultrasound imaging or TE of ≥ 12.0 kPa. Patients were considered to qualify for treatment with tenofovir according to WHO guidelines 2015* (any of: HIV-coinfection; APRI score > 2; clinical or ultrasound diagnosis of cirrhosis; age > 30 years with persistent ALT elevation and HBV viral load > 20000 IU/mL) or if TE was ≥ 9.0 kPa.

Results
A total of 390 patients, or 68% of those who ever had at least one positive HBsAg in the above period, were included in the hepatitis B cohort; their median age was 35 years (interquartile range 27-45), 38% were women. Among these patients, 88%, 8% and 0% had ever been tested for antibodies against HIV, hepatitis C or hepatitis D virus respectively, and 11% had ever received a viral load measurement. This resulted in 341 (87%) patients with hepatitis B mono-infection (HBV-mono), 49 (13%) with HIV/HBV and 0% with HBV/HCV dual infection. In the entire active HIV cohort (n= 2424), 31% had ever been tested for HBsAg (26% of whom were positive). Among HBV-mono patients, 22% (36 of 163 available measurements) had an APRI score > 2, 33% (48 of 144) had values on TE ≥ 9.0 kPa, and 29% (77 of 266) had either one of these criteria, thus qualifying for treatment with a NA.

Conclusion
Nearly one in three hepatitis B mono-infected patients show signs of advanced fibrosis or cirrhosis and are therefore in need for hepatitis B treatment.

P27

SARS-CoV-2 Seroprevalence in Health Care Workers after the First and the Second Wave of COVID-19 in the Canton of Grisons in Switzerland

K Szajek[1]; S Hutter[1]; S Robitt[1]; M Risch[1]; T Bechmann[1]; S Güsewell[2]; A Cusini[1]
[1] Cantonal Hospital Graubuenden, Chur, Switzerland; [2] Cantonal Hospital St. Gallen

Background
Health care workers (HCW) are exposed to SARS-CoV-2 through contact with COVID-19 patients. We aimed to assess the seroprevalence for SARS-CoV-2 among HCW in the canton Grisons, to analyze risk factors associated with seropositivity and report COVID-19 specific symptoms in HCW.

Methods
HCW from 13 health care institutions were included. Sera for SARS-CoV-2 antibodies were measured using an electro-chemiluminescence immunoassay (ECLIA, Roche Diagnostics) in mid-2020 (suvey I) and early 2021 (survey II). Participants reported risk factors and symptoms in an online questionnaire. Odds ratios (OR) and 95% confidence intervals (95% CI) for the association of seropositivity with each risk factor were determined by logistic regression.

Results
Positive SARS-CoV2 serology was present in 99 of 2794 (3.5%) participants in survey I and in 376 of 2315 (13.5%) participants in survey II. By suvey II, 86 of 99 (86.9%) initially seropositive participants remained positive whereas two (2%) reverted to negative. Seropositivity was associated with patient contact: seroprevalance in study participants with and without patient contact was 4.2% versus 2.1% in suvey I, [OR 1.99, (95% CI: 1.22−3.44) p-value: 0.009] and 13% versus 18% in survey II [OR: 1.47, (95% CI: 1.14−1.9) p-value: 0.003]. The association was even stronger among participants with contact to patients with COVID-19 [OR in survey II: 1.78 (95% CI: 1.37-2.32 p-value: < 0.001)]. Further risk factors for seropositivity included: working as a nurse [OR: 1.86, (95% CI: 1.36−2.58) p-value: < 0.001], working in COVID-19 specific wards [OR: 1.98, (95% CI: 1.47−2.66) p-value: < 0.001], contact with SARS-CoV-2 positive coworkers [OR: 1.57, (95% CI: 1.21−2.02) p-value: 0.001], private contact with a SARS-CoV-2 positive person [OR: 2.82, (95% CI: 2.08−3.79) p-value: 0.001] and most significantly contact with a positive household member [OR: 6.27, (95% CI: 4.55−8.65 p-value: 0.001]. COVID-19 specific symptoms were more frequently reported by seropositive participants, especially taste or olfactory disorders, followed by fever and limb pain. 15% of seropositive participants were asymptomatic.

Conclusion
Seroprevalence for SARS-CoV2 among HCW increased in the second wave of COVID-19. Contact with COVID-19 patients was an important risk factor for seroconversion, though nonprofessional contacts were equally important. These findings highlight the need to optimize preventive measures against SARS-CoV2 among HCW.

P28

Safety evaluation of a medical congress held during the COVID-19 pandemic – a prospective cohort

J Sumer[1]; D Flury[1]; W Albrich[1]; C Kahlert[1]; N Müller[2]; L Risch[3]; S Nigg[1]; M Seneghini[1]; P Vernazza[1]; M Schlegel[1]; P Kohler[1]
[1] Kantonsspital St. Gallen; [2] UniversitätsSpital Zürich (USZ); [3] Labormedizinisches Zentrum Dr Risch Ostschweiz AG

Aims
Worldwide, scientific congresses are cancelled because of the COVID-19 pandemic. Yet, scien-tific exchange is more important than ever, especially for infectious diseases and infection pre-vention specialists. Within a prospective cohort of congress attendees, we evaluated the safety concept of the 2020 congress of the Swiss Societies of Infectious Diseases and Hospital Hy-giene.

Methods
The congress was held between September 2nd and 4th 2020 in Geneva (Switzerland), where COVID-19 incidence in the week during the congress was 65 cases /100 000 population within 7 days. A rigorous safety concept was implemented including universal face masking, physical distancing during sessions, and maximal reduction of social events. We invited congress at-tendees to participate in this prospective cohort and used an anonymized online questionnaire to assess risk perception, risk exposures, symptoms and diagnosis of SARS-CoV-2 of attendees before, during and after the congress. Dried blood spots were taken from attendees on-site and four weeks later to detect specific antibodies against SARS-CoV-2 and to document seroconver-sions.

Results
A total of 365 people attended the congress, thereof 271 healthcare professionals. Of these, 196 (54%) either answered the questionnaire (N=150) or provided baseline and follow-up blood sam-ples (N=168). None of the study participants reported a positive PCR result in the 2 weeks after the congress. Five of 168 (3%) participants were seropositive at follow-up, all of which had al-ready been positive at baseline. The safety concept was deemed appropriate by 92% of the study participants and hygiene measures were performed correctly by the vast majority.

Conclusion
In this prospective cohort of congress attendees, no PCR positive cases or seroconversions could be documented after attending an on-site medical congress. These findings indicate that congresses with a rigorous safety concept may take place, even in areas with moderately-high COVID-19 activity.

P29

Comorbidities in children with severe malaria admitted to hospitals in the Democratic Republic of the Congo and Uganda

G Delvento[1]; N Brunner[1]; T Lee[1]; P Awor[2]; P Athieno[2]; G Tumukunde[2]; J Kimera[2]; A Tshefu[3]; J Okitawutshu[3]; M Lambiris[1]; M Hetzel[1]; C Lengeler[1]; C Burri[1]; A Signorell[1]
[1] Swiss Tropical and Public Health Institute / University of Basel; [2] Makerere University School of Public Health; [3] Kinshasa School of Public Health

Background and aims
Malaria remains one of the main causes of child mortality in Sub-Saharan Africa, yet, some of these deaths may not be attributed exclusively to malaria. Comorbidities are common in malaria-endemic settings and they may complicate the diagnosis and treatment of severe malaria.(2) It is therefore critical to properly diagnose severely ill children to ensure adequate case management. In the frame of a multi-country observational study on the use of pre-referral rectal artesunate (CARAMAL Project), we assessed the frequency of comorbities in patients presenting with severe malaria at local referral health facilities in the Democratic Rrepublic of the Congo and Uganda.

Methods
We investigated predictors and health outcomes for severe malaria cases associated with comorbidities. The sample included children aged 6 months to 5 years admitted at hospitals/tertiary health facilities with severe malaria between September 2019 and August 2020.

Results
In DRC, 72% of 1744 children had at least one comorbidity reported. The main comorbidities were anaemia (55%) and unspecified helminthiasis (24%). Measles, meningitis, typhoid fever, and respiratory tract infections together accounted for an additional 8% of the comorbidites. Comorbidities were more common in younger children (51% in age groups 0-1 years , 37% in age 2-3 and 12% in 4-5 years;chi-square test, p =0.02). In Uganda 29% of 1410 children presented with a comorbidity, most frequently with aneamia (16%), pneumonia (7%), or respiratory tract infections (5%). Younger children were more likely to be diagnosed with a comorbidity (55% in age group 0-1 years, 33% in age 2-3 and 12% in 4-5 years chi-square test, p = 0.02).There was no statistically significant difference in the frequency of reported comorbidities between male and female children. Within one month of initial treatment seeking, 15 (1%) of the children with severe malaria died in Uganda and 70 (4%) died in DRC. We found no statistically significant association of the deaths with reported comorbidity (Fisher's test, Uganda p = 0.16, DRC p = 0.41).

Conclusion
Comorbidities in severe malaria were common, particularly in children less than 1 year old, but they did not appear to influence case fatality. Further investigations into the quality of diagnosis and treatment of severe malaria and comorbidities may help to improve overall case management.

P30
Verification and characterization of SAG1 knockouts in Toxoplasma gondii

K Hänggeli[1]; G Boubaker[1]; B Schimanski[2]; A Hemphill[1]
[1] Institut für Parasitologie der Universität Bern; [2] Department of Chemistry and Biochemistry, University of Bern, Switzerland

In humans and animals, toxoplasmosis is caused by the apicomplexan parasite Toxoplasma gondii. It represents a major health problem with considerable economic losses. The major surface protein in T. gondii tachyzoites is named SAG1 and it is estimated that the amount of SAG1 in the whole tachyzoite proteins ranges between 3 to 5%. Despite the extensive research on transcriptome and proteome, the exact role of SAG1 in the biology of Toxoplasma especially, its function in the tachyzoites stages and its involvement in the lytic cycle remains largely non-elucidated.
This work aimed to study the function of SAG1 by generating and characterizing knockout parasites. Thus, we created T. gondii mutants lacking SAG1 by CRISPR-Cas9 using a drug-selectable marker. Mutants were first selected for their acquired resistance to pyrimethamine. Then, through a highly elaborated verification process, mutants were checked for sag1 interruption and expression by PCR sequencing, immunofluorescence assay, and Western Blot Furthermore, we have addressed the critical issue related to the off-target effects of CRISPR/Cas9, thus mutants were also examined for single insertion of the selection cassette within sag1 by southern blot using two restriction patterns.
As a more accurate alternative to the southern blot, we developed a single- and multiplex real-time qPCR for quantifying the copy number of the selection cassette within the genome of the mutants.
To the end of this, three mutants were validated for single insertion and taken for in vitro phenotypic characterization using quantitative assays addressing various steps of the lytic cycle. Differences were observed between the mutants and the parental strain on the one hand, and on the other hand among the three mutants. Two clones showed similar results but were different from the third one, despite a common genetic background.
Further work is planned for (i) deeper in vitro and in vivo characterization of the mutants, (ii) validation of T. gondii RH ∆sag1 phenotypes by genetic complementation, and (iii) comparative proteomic analysis which may reveal subsequent changes in protein expression pattern.
In conclusion, this work highlights the importance of the verification of the correctness of generated knockout mutants − such a fundamental step requires more than one technique.

P31

Swiss Interprofessional Guidance Of Good Practice Of Acute and Complicated Diabetic Foot Infections and Syndromes – A National Project

I Uçkay[1]; A Czock[2]; B Peter-Rüesch[3]
[1] Balgrist University Hospital; [2] QualiCCare; [3] Diabetology

Aim
Diabetic foot infections (DFI) and syndromes (DFS) have multiple negative outcomes in a patient population marked with co-morbidities and frailty. Their management requires a quality of care consisting of evidence-based, practical guidance tools for primary care providers together with the implementation of an interprofessional care system including nationally standardized diagnose-relevant best practice recommendations.

Objective
We implement a national best practice guidance for timely and qualitative care of patients with DFI and DFS.

Methods
Under the umbrella of the national non-profit association QualiCCare, an interprofessional and comprehensive Swiss practical guidance for the timely and standardized quality of care management of acute DFI, DFS and diabetic foot ulcers (DFU) was elaborated in a multi-stakeholder approach including all relevant professions. Before the nation-wide implementation of the primary care triage and treatment guidance and indication-specific recommendations for interprofessional networks and footcare centers, three Swiss regions will pilot the implementation in different possible primary care settings in collaboration with the respective interprofessional footcare centers.

Results
Twenty experienced stakeholders from twelve different professions issued four protocols for various aspects of DFS between March 2018 and January 2020 and defined criteria for the triage and treatment in primary care as well as the timely referral of patients with DFS and DFU to multidisciplinary footcare centers. All invited professional societies agreed to work together and have a representative in the working group. The resulting guidance were endorsed by all national professional societies.
We propose a framework for specialized footcare networks as well as multidisciplinary footcare centers. The piloting of the proposed concepts is under way. Website www.qualiccare.ch

Conclusions
We provide evidence-based tools for Swiss primary care providers and specialists while increasing the accessibility for patients to specialized care of DFS, DFU and DFI.

P32

Pseudomonas diabetic foot infections: Is a combined antibiotic therapy better than monotherapy?

I Uçkay[1]; K Gariani[2]
[1] Balgrist University Hospital; [2] Geneva University Hospitals (HUG)

Aim
The consequence of infection with Pseudomonas aeruginosa, on the outcome of diabetic foot infections (DFI), remain unknown. Many Infectious Diseases physicians treat P. aeruginosa infection in combination therapy, at last initially; not because of synergy but to avoid a possible development of resistance in monotherapy. P. aeruginosa in DFI is very common, especially in (sub)tropical climates.

Objective
We evaluate this attitude in a single-center cohort of DFI in Switzerland, a Pseudomonas-poor country in terms of DFIs.

Methods
We analyzed data from DFI patients, comparing those with and without infection with Pseudomonas spp, employing multivariate Cox regressions to adjust for the large case-mix.

Results
We assessed 1018 DFI cases - 392 with osteomyelitis, 626 with soft tissue infections. The prevalence of P. aeruginosa on wound culture was 10% (104/1018), of which 82 were polymicrobial, and 46 had osteomyelitis. Overall, patients were treated with a median of 1 surgical debridement and 20 total days of antibiotic therapy. The proportion of clinical failures was significantly higher in those infected with Pseudomonas than with other pathogens (36/104 [35%] versus 218/914 [24%], p=0.02). By multivariate analysis, DFI caused by Pseudomonas DFIs did not recur more often than non-Pseudomonas DFIs (hazard ratio 1.0, 95% CI 0.6-1.7). Among the fifteen Pseudomonas microbiological recurrences, two cases (13%) developed resistance to an antibiotic agent of the index episode.

Conclusions
For DFI caused by P. aeruginosa, other than choosing an antibiotic agent active against the organism, it does not appear necessary to treat with a different therapeutic regimen than for non-pseudomonal DFIs. There was no difference in our tertiary center in Switzerland.

P33

Does the amputation level influence the infectious outcome in diabetic toe osteitis? Comparing the transarticular (cartilage level) versus the transosseous amputation levels (bone level)

I Uçkay; F Waibel; M Schöni; M Berli
Balgrist University Hospital

Aim
In diabetic toe osteomyelitis (DTO), revisions due to new or recurrent infection episodes are common. It is unknow if the level of amputation is associated with a particular outcome.

Objective
We assessed the long-term effect of amputations at the trans-articular (articular exarticulation; “Joint”) compared to the transosseous level (“Bone”) in diabetic patients with chronic DTO on the incidences of clinical and microbiological failure.

Methods
We investigated all episodes of DTO amputations. We assessed the outcome “surgical revision” using comparative statistics, log-rank-survival analyses, Kaplan-Meier curves and multivariate Cox regressions.

Results
We actively followed 543 minor toe amputations (203 Joint-Amp, 340 Bone-Amp) in 284 adult diabetic patients during a mean of 4.2 years. Overall, in 122 of the amputations (22.5%) there was clinical failure that lead to a surgical revision. There was no significant difference in the risk of clinical failure in the Joint group compared to the Bone group (n= 44, 21.7%, versus n=78, 22.9%, respectively; p=0.73). Similarly, there was no significant difference in microbiological failure (32 episodes, 5.9% overall) between the Joint and Bone groups (11, 5.4% (n=11) and 21, 6.1%, respectively; p=0.72). The average time between the index surgery and clinical failure was 2.2 months for Joint; and 3.2 months for Bone (Mann-Whitney-U-Test; p=0.39). Equally, the survival analyses showed similar evolutions for each of the amputation levels (log-rank-test; p=0.85). In the multivariate Cox regression analysis, the type of amputation did not significantly influence clinical or microbiological failures.

P34

Point of care lung ultrasonography for early identification of mild COVID-19: a prospective cohort of outpatients in a Swiss screening center

S Schaad[1]; T Brahier[1]; M Hartley[2]; J Cordonnier[3]; L Bosso[1]; T Espejo[1]; O Pantet[1]; O Hugli[1]; P Carron[1]; J Meuwly[1]; N Boillat-Blanco[1]
[1] Lausanne University Hospital; [2] Ecole Polytechnique Fédérale de Lausanne (EPFL)/Lausanne University Hospital; [3] EPFL

Background
Early identification of SARS-CoV-2 infection is important to guide quarantine and reduce transmission. Current diagnostic tests take time or rely on consumables, which are susceptible of shortage during transmission peaks. This study evaluates the diagnostic performance of lung ultrasound (LUS)—an affordable, consumable-free point-of-care tool—for COVID-19 screening.

Methods
This prospective observational cohort included adults presenting with cough and/or dyspnea at a SARS-CoV-2 screening center of Lausanne University Hospital between March 31st and May 8th, 2020, and a group of sex- and age-matched healthy controls. Investigators recorded standardized LUS images and videos in 10 lung zones per subject. Two blinded independent experts reviewed LUS recording and classified abnormal findings according to prespecified criteria to investigate their predictive value to diagnose SARS-CoV-2 infection according to PCR on nasopharyngeal swabs (COVIDpos vs COVIDneg). We finally combined LUS and clinical findings to derive a multivariate logistic regression diagnostic score.

Results
Of 134 included patients, 23% (n = 30/134) were COVIDpos and 77% (n = 103/134) were COVIDneg; 85%, (n = 114/134) cases were previously healthy healthcare workers presenting within 2 to 5 days of symptom onset (IQR). Abnormal LUS findings were significantly more frequent in COVIDpos compared to COVIDneg (45% versus 26%, p = 0.045) and mostly consisted of focal pathologic B-lines. Combined LUS findings in a multivariate logistic regression score had an area under the receiver-operating curve of 63.9%to detect COVID-19 but improved to 84.5% with the addition of clinical features.

Conclusion
COVIDpos patients are significantly more likely to have lung pathology by LUS. Our findings have potential diagnostic value for COVID-19 at the point of care. Combination of clinical and LUS features showed promising results, which need confirmation in a larger study population.

P35

Decreased incidence of carbapenemase-producing Enterobacterales in Switzerland in 2020

M Gasser[1]; P Nordmann[2]; J Kessler[2]; A Kronenberg[1]
[1] Swiss Centre for Antibiotic Resistance (ANRESIS), Institute for Infectious Diseases, University of Bern; [2] National Reference Center for Emerging Antibiotic Resistance (NARA) and Molecular and Medical Microbiology, University Fribourg

Background
Carbapenemase-producing Enterobacterales (CPE) represent a great concern since they are frequently associated to resistance to multiple antibiotics thus reducing therapeutic options. Increasing CPE rates have been observed in Europe and all over the world. Gasser and Ramette et al. [1] reported an aggravation of the situation in Switzerland over the last years with an increase from 66 yearly isolates in 2013 to 189 in 2018. In this current study it is examined if this increasing trend continues on national and regional levels and how species and genotypes are distributed within Switzerland.

Methods
Since 2019 all suspected human CPE isolates from primary laboratories are sent to the national reference laboratory (NARA) which performs the genotyping. Data from NARA were analysed and interactive graphics were built by the Swiss Centre for Antibiotic Resistance (ANRESIS) using R 4.0.4.

Results
After a further increase from 189 isolates in 2018 to 286 in 2019 (+51%*) a decrease to 238 isolates was observed in 2020 (-17%). Klebsiella pneumoniae (93 isolates, 39%) and Escherichia coli (89, 37%) were found to be the most abundant species in 2020, OXA-48 (72, 30%), NDM (68, 29%), KPC (37, 16%), OXA-181 (28, 12%) and OXA-244 (20, 8%) were the most abundant genotypes. OXA-48 was the predominant genotype observed in western parts (e.g. Geneva 49%) whereas NDM was the most frequently detected genotype in northern and eastern parts (e.g. North-East 38%). Total numbers of CPE decreased or remained stable in all regions in 2020 except of the Centre-West where a doubling of OXA-48 isolates (from 13 in 2019 to 26 in 2020) lead to an overall increase of 33% from 40 to 53 isolates. These trends and further analyses of CPE data can be accessed via https://www.anresis.ch/antibiotic-resistance/resistance-data-human-medicine/#CPE, an interactive platform, which was recently developed to visualize the latest resistance data from Switzerland.

Conclusion
Our analyses of CPE data in Switzerland show a decrease in total numbers from 2019 to 2020. This finding is in contrast to the long-term increase observed from 2013 to 2018 [1] and may be explained by a reduced population mobility and virtually sharp decrease of worldwide travel during the global COVID-19 pandemic. Actually, this decrease is very likely related to decreased patient transfers from foreign to Swiss hospitals.

References: 1. Gasser and Ramette et al. Eurosurveillance, manuscript accepted.

P36

Antibiotic treatment durations for community-acquired pneumonia, cholangitis and cellulitis in Switzerland – real-life vs. guidelines

C Schaub[1]; S Barnsteiner[2]; L Schönenberg[1]; A Conen[3]; W Albrich[2]; M Osthoff[1]
[1] Universitätsspital Basel; [2] Kantonsspital St. Gallen; [3] Kantonsspital Aarau

Aims
Shortening the length of antibiotic therapy (LOT) for common infectious diseases is one of the most effective strategies to tackle antimicrobial resistance. Shorter treatments have been proven safe and effective for community-acquired pneumonia (CAP), cellulitis and cholangitis. We retrospectively assessed the appropriateness of LOT for these three indications in Switzerland.

Methods
Medical records of patients hospitalized with CAP, cellulitis and cholangitis in 2017 and 2018 were randomly selected (at least 40 records per disease, year and hospital) at three tertiary-care hospitals in Switzerland. Appropriateness of LOT was assessed according to international and local guidelines.

Results
Records of 271, 260 and 239 patients with CAP, cellulitis and cholangitis were assessed, respectively (median age 71, 62 and 72 years, respectively). Infectious diseases physicians were involved in the minority of patients (10-30%). For CAP, median time to clinical stability was 2 days (IQR 1-3), intravenous antibiotics were ceased after only 4 days (IQR 2-5) and LOT was 7 days (IQR 6-9). Serial measurement of procalcitonin, which was performed in only one hospital, did not reduce LOT. Overall, LOT for CAP was longer than recommended by local and international guidelines in 87 (32%) and 100 (37%) patients. For cellulitis, median LOT was 10 days (IQR 8-13), and oral antibiotics were administered after a median of 4 days. Interestingly, the proportion of excessive LOT was 23% vs. 73% according to local vs. international guidelines, respectively. Antibiotics were continued for a median of 5 days after discharge in patients with cellulitis. In patients with cholangitis, intravenous LOT was the longest (median 5 days (IQR 3.5-7)), and median LOT was 9 days (IQR 6-13). LOT was longer than recommended by local and international guidelines in 33% and 37% of patients, respectively. There were no inter-hospital differences in LOT except for a shorter LOT for cholangitis in one hospital (8 vs. 10 days).

Conclusions
LOT exceeded local and international recommendation in a significant proportion of patients with community-acquired infections. This was particularly evident for cellulitis, where local and international guidelines differed considerably. These observations suggest substantial opportunities to improve antibiotic prescribing in Swiss hospitals.

P37
Post-COVID-19 syndrome in outpatients: a cohort study

F Desgranges[1]; E Tadini[1]; A Munting[1]; J Regina[1]; P Filippidis[1]; E Karachalias[2]; B Viala[1]; V Suttels[1]; D Haefliger[1]; E Kampouri[1]; M Van Singer[1]; J Tschopp[1]; L Rochat Stettler[1]; S Schaad[1]; T Brahier[1]; O Hugli[1]; Y Mueller Chabloz[3]; A Gouveia[3]; O Opota[1]; P Carron[1]; B Guery[1]; M Papadimitriou-Olivgeris[1]; N Boillat-Blanco[1]
[1] Centre Hospitalier Universitaire Vaudois (CHUV); [2] Data Scientist; [3] Centre universitaire de médecine générale et santé publique - Unisanté

Background
Some patients experience long-term symptoms after COVID-19. We aimed to describe persisting symptoms more than 12 weeks after diagnosis of COVID-19 in outpatients in comparison with a control group. We also aimed to identify predictors of persisting symptoms.

Methods
This prospective cohort study was conducted in outpatient clinics of Lausanne University Hospital, Switzerland, between February and April 2020. Symptomatic outpatients with PCR-confirmed COVID-19 (COVID-positive) during their initial visit were included. We also included a control group of outpatients who presented with similar symptoms but had a negative SARS-CoV-2 PCR (COVID-negative). We performed a phone interview 12 to 41 weeks after diagnosis to assess 14 persisting symptoms and outcomes. Associations between long-term symptoms and PCR test result, as well as patients' characteristics in COVID-positive, were evaluated by multivariate analysis.

Results
We included 465 COVID-positive with a median age of 42 (interquartile range: 35–55) years, 61.9% women and 63.7% health-care workers; 34.0% had a comorbidity, mainly overweight/obesity; 10.1% required a secondary hospitalization within 30 days of diagnosis. We included 89 COVID-negative with similar demographics and initial symptoms. Long-term symptoms were reported by 256 (55%) COVID-positive and 33 (37%) COVID-negative (p 0.002). Overall, 23% COVID-positive and 15% COVID-negative (p 0.07) consulted a doctor for these symptoms. Four surveyed symptoms were independently associated with COVID-19: fatigue (33% in COVID-positive vs 17% in COVID-negative, p 0.003), smell/taste disorder (22% vs 1%, p < 0.001), dyspnea (18% vs 8%, p 0.015), and memory impairment (13% vs 3%, p 0.006). Frequencies of long-term symptoms in COVID-positive were similar between three time-periods of phone survey. Among COVID-positive, overweight/obesity, hospital admission, female gender and smoking were associated with persisting symptoms.

Conclusion
More than half COVID-positive reported persisting symptoms 12 to 41 weeks after COVID-19 diagnosis, which led to a medical consultation in a quarter of them. Also, proportions of long-term symptom stayed stable during the study period. It is of prime importance to better understand the natural evolution of COVID-19 and determine groups with higher risk of long-term symptoms in order to plan a dedicated follow-up of those with disabling symptoms.

P38

COVID-19 in outpatients: can we predict secondary Hospital ADmission? – The CHAD study

F Desgranges[1]; P Filippidis[1]; J Regina[1]; A Munting[1]; E Tadini[1]; E Karachalias[2]; B Viala[1]; V Suttels[1]; D Haefliger[1]; E Kampouri[1]; M Van Singer[1]; J Tschopp[1]; L Rochat Stettler[1]; O Hugli[1]; Y Mueller Chabloz[3]; A Gouveia[3]; O Opota[1]; P Carron[1]; B Guery[1]; M Papadimitriou-Olivgeris[1]; N Boillat-Blanco[1]
[1] Centre Hospitalier Universitaire Vaudois (CHUV); [2] Data Scientist; [3] Centre universitaire de médecine générale et santé publique - Unisanté

Background
Among outpatients who initially consult with a mild Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) infection, some will develop a more severe disease and require hospital admission on a subsequent medical visit. The aim of the present study was to define predictors of secondary hospitalization in outpatients.

Methods
This prospective study was conducted at the Lausanne University Hospital from February to April, 2020. Adult patients that consulted the emergency department or outpatient clinics for PCR-confirmed SARS-CoV-2 infection and discharged after the initial visit were included. We performed a prospective phone interview to assess for secondary hospitalization within 30 days from the initial visit.

Results
A total of 721 outpatients with SARS-CoV-2 infection were included, of which 63 (8.7%) were hospitalized within 30 days from the initial visit. Patients that were eventually hospitalized were older (57 vs 44 years old; $p < 0.001$), had higher Charlson Comorbidity Index (2 vs 0; $p < 0.001$), had higher rates of overweight/obesity (63.9% vs 31.8%; $p < 0.001$), reported more often fever (72.1% vs 39.8%; $p < 0.001$), dyspnea (34.4% vs 17.0%; p 0.001) and thoracic pain (13.1% vs 4.4%; p 0.009) and had higher temperature in their initial visit (38.0°C vs 37.1°C; $p < 0.001$) than outpatients. Multivariate analysis revealed that overweight/obesity (p 0.009; OR 2.3, CI 1.2-4.2), dyspnea (p 0.040; OR 2.1, CI 1.0-4.1), thoracic pain (p 0.019; OR 3.1, CI 1.2-8.2), and high temperature at initial visit (p 0.002; OR 2.0, CI 1.3-3.1) were independently associated with secondary hospitalization.

Conclusion
Secondary hospitalization is uncommon (< 10%) among outpatients with SARS-CoV-2 infection. Overweight or obesity can predict a secondary hospitalization, as well as, the presence of dyspnea and thoracic pain at the initial visit. Young patients with normal BMI have an extremely low risk of secondary hospitalization.

P39

Functional activity of the complement system in hospitalized COVID-19 patients with a focus on the lectin pathway

P Charitos Fragkakis; I AFM Heijnen; S Bassetti; M Trendelenburg; M Osthoff
University Hospital Basel

Aims
Although the exact factors promoting disease progression in COVID-19 are not fully elucidated, unregulated activation of the complement system (CS) seems to play a crucial role in the pathogenesis of acute lung injury (ALI) induced by SARS-CoV-2. In particular, the lectin pathway (LP) has been implicated in previous autopsy studies. The primary purpose of our study is to investigate the role of the CS in hospitalized COVID-19 patients with varying degrees of disease severity.

Methods
In a single-center prospective observational study, 154 hospitalized patients with confirmed SARS-CoV-2 infection were included. Serum samples on admission to the COVID-19 ward were collected for analysis of CS pathway activities and concentrations of LP proteins (mannose-binding lectin (MBL) and ficolin-3) and C1 esterase inhibitor (C1IHN). Associations with clinical outcomes were analyzed.

Results
The patients were predominately male (61%) with a median age of 62 years (interquartile range (IQR) 49-73). ICU admission was required in 16% of the patients and death (3%) or invasive ventilation (WHO ordinal scale score 6-8) occurred in 23 patients (15%).

There was no significant difference in LP activity and serum concentrations of MBL and ficolin-3 according to different peak disease severities. Classical pathway (CP) activity was slightly lower in patients with more severe disease (median 101% for WHO score 6-8 vs 109% for WHO score 3-5, $p = 0.014$). C1INH concentration – the most important inhibitor of the LP & CP – correlated positively with length of stay, inflammatory markers and disease severity on admission but not during follow-up.

The median alternative pathway (AP) activity was significantly lower (64%, IQR 47-92) in patients with WHO score 6-8 compared to patients with WHO score 3-5 (86 % (65-100), $p < 0.05$). An optimal cut-off of < 65.5% for the AP activity was derived from a ROC curve analysis (AUC 0.65, $p=0.026$) resulting in increased odds for death or invasive ventilation (OR 3.67; 1.47-9.16, $p < 0.005$), even after adjustment for other confounding factors.

Conclusion
Our results point to an overactivated AP in critically ill COVID-19 patients in vivo leading to complement consumption and consequently to a significantly reduced AP activity in vitro. In contrast to the AP, the LP does not seem to play a role in the progression to severe COVID-19. Apart from its acute phase reaction the significance of C1INH in COVID-19 requires further studies.

P40

Fast and sensitive multiplex PCR to detect Cutibacterium periprosthetic joint infections

J Prinz[1]; B Schmid[1]; R Zbinden[2]; P Bosshard[1]; Y Achermann[1]
[1] University Hospital Zurich and University of Zurich, Switzerland; [2] Institute of Medical Microbiology, University of Zurich

Background
Diagnosis of Cutibacterium periprosthetic joint infections (PJI) is challenging due to long cultivation time of up to 14 days. We developed and evaluated a PCR for Cutibacterium species (formerly Propionibacterium spp.) that allows accurate and fast PJI diagnosis.

Methods
We designed specific primers and probes for Cutibacterium acnes, Cutibacterium avidum and Cutibacterium granulosum based on the 16S ribosomal RNA gene and tested them in a multiplex PCR format. Quantification cycle cutoff values were determined based on 20 culture-negative cerebrospinal fluid samples. The multiplex PCR was evaluated in 57 inguinal skin swabs with high colonization rate of Cutibacterium and 41 sonication fluid samples from removed implants from PJI patients infected with different pathogens.

Results
Both in skin swabs and sonication fluid samples, we found a high concordance between culture and multiplex PCR for C. acnes (70%, 100%), C. avidum (95%, 95%), and for C. granulosum (97%, 100%). In the PJI cohort, all five Cutibacterium culture-positive sonication samples were detected by PCR and C. avidum was additionally detected in two samples with staphylococcal growth.

Conclusion
The new Cutibacterium multiplex PCR provides faster diagnosis in PJI that allows an early and accurate antibiotic treatment. A prospective diagnostic trial in orthopedic infections is needed for further evaluation.

P41

Risk factors and predictors of mortality of candidaemia among patients hospitalized in a Swiss University Hospital

M Papadimitriou-Olivgeris; F Lamoth; L Senn
CHUV Centre hospitalier universitaire vaudois

Aims
Candidaemia is associated with high morbidity and mortality. The aim of the present study was to identify predictors of mortality among patients with candidaemia hospitalized in a university hospital.

Methods
This retrospective study was conducted at the University Hospital of Lausanne, Switzerland. All adult patients with positive blood culture for Candida spp. from 2014 to 2019 were included. Susceptibility of antifungals was assessed by Sensititre YeastOne and was interpreted according CLSI.

Results
During the study period, 155 candidaemias (from 158 patients) were included. C. albicans predominated (74; 47.7%), followed by C. glabrata (48; 31.0%), C. tropicalis (11; 7.1%) and C. parapsilosis (10; 6.5%). Fifty-seven cases (36.7%) were attributed to primary candidaemia, 46 (29.7%) were catheter-related and 38 (24.5%) were secondary to abdominal infection. Forty-five patients (29.0%) developed septic shock. Thirty-day mortality was 27.7% (43 patients). Survivors were more likely to have benefited within 72h from infection onset from i) infectious diseases consultation (89.3% vs 67.4%, P 0.003) and ii) appropriate empiric antifungal administration (75.0% vs 48.8%, P 0.004). A source control (catheter removal for catheter-related or primary candideamia; operation or imaging-guided drainage of infected collections) was warranted in 142 patients; 89 patients (62.7%) benefited from a source control within 72h from infection onset. Multivariate analysis found that septic shock (P 0.009; OR 3.4, CI 1.4-8.5) was independently associated with mortality, while infectious diseases consultation within 72h from infection onset (P 0.044; OR 0.30, CI 0.09-0.97) and source control within 72h from infection onset (P < 0.001; OR 0.09, CI 0.04-0.22) were associated with better survival.

Conclusion
Most candidaemias were primary or catheter-related, with C. albicans being the predominant species. The development of septic shock was related with mortality, while source control within 72h from infection onset was associated with better survival.

P42

Role of throacoabdominal or cerebral imaging studies in patients with suspected infective endocarditis

M Papadimitriou-Olivgeris; P Monney; G Tzimas; M Kirsch; B Guery
CHUV Centre hospitalier universitaire vaudois

Aims
Presence of embolic phenomena impacts diagnosis and treatment of patients with suspected infective endocarditis (IE). The aim of the present study was to describe the effect on diagnosis and treatment of thoracoabdominal (TAIS) or cerebral imaging studies (CeIS).

Methods
This prospective observational study included all patients with suspected IE hospitalized at Lausanne University Hospital, Switzerland during a two year period (2018-19). IE was defined according to modified criteria of 2015 European Society of Cardiology Guidelines. Patients with clinical manifestations (neurologic deficit, confusion, pain, dyspnea, etc) that led to imaging studies were considered as symptomatic.

Results
Among 517 patients with suspected IE, 90 (17.4%) patients had definite endocarditis, 35 (6.8%) possible. A total of 312 (60.3%) patients had a TAIS of which 113 (36.2%) patients were symptomatic. TAIS revealed at least one embolic lesion at 55 (17.6%) patients (29 symptomatic and 26 asymptomatic lesions). Of the 312 patients, 27 had lung, 16 splenic, nine liver and nine kidney lesions. A total of 156 (30.2%) patients had a CeIS of which 87 (55.8%) patients were symptomatic. CeIS found at least one lesion at 74 (47.4%) patients (50 symptomatic and 24 asymptomatic lesions). Of the 157 patients, 67 (42.7%) had ischemic stroke, 11 hemorrhagic stroke, eight mycotic aneurysm and two cerebral abscesses. Without imaging studies, the vascular criterion was present in 33 patients (6.4%); imaging studies in symptomatic patients added the vascular criterion in 63 patients (96 in total; 18.6%) and in asymptomatic patients in another 26 patients (122 in total; 23.6%). Despite that, imaging studies upgraded the diagnosis classification from possible to definite endocarditis in only two patients (0.4%). Of the 62 patients having benefited from cardiac surgical procedure, 36 patients had embolic lesions found by either thoracoabdominal or cerebral imaging. For 11 of them (17.7%; four were asymptomatic), the indication for surgery was given by the results of either TAIS and/or CeIS.

Conclusion
Imaging studies didn’t affect diagnosis but they triggered the indication for cardiac surgery in 18% of the operated patients.

P43

Utility of polymerase chain reaction in nasopharyngeal swabs for identifying respiratory bacteria causing community-acquired lower respiratory tract infections (sUsPENSE)

Y Demars; T Brahier; O Opota; K Jaton; D Rotzinger; N Boillat-Blanco
CHUV Centre Hospitalier Universitaire Vaudois (CHUV)

Background
Timely identification of a pathogen in patients with lower respiratory tract infections (LRTI) is essential to limit inappropriate antibiotics use. We aimed to assess the performance of multiplex polymerase chain reaction (PCR) in nasopharyngeal (NP) swab for detection of Streptococcus pneumoniae (SP), Haemophilus influenzae (HI) and Moraxella catarrhalis (MC).

Methods
We retrospectively included all adults who attended the emergency department of Lausanne University Hospital between February 2019 and August 2020 for a community-acquired LRTI and with both a NP swab and a high quality (≥ 25 neutrophils and < 10 epithelial cells per low-power field) LRT sample available. All respiratory samples were tested with the BioFire FilmArray Pneumonia plus panel (PP ; positive cut-off at 10^4 copy/ml). Sensitivity and specificity of FilmArray PP in NP swab were calculated, using (1) PCR in LRT sample and (2) standard microbiological tests as gold standard. To assess if a lower detection cut-off in NP swabs could increase the performance, samples were also tested with an in-house PCR for SP and HI. Correlation between patients' constellation (clinical, biological and radiological) and molecular diagnosis on NP swab was evaluated by Kruskal-Wallis and chi-squared test.

Results
118 patients were included. FilmArray PP in LRT sample and standard microbiology detected SP in 19/118 and 12/118, HI in 44/118 and 19/118 and MC in 14/118 and 0/118 respectively. Using LRT FilmArray PP as gold standard, PCR on NP had a sensitivity and specificity of 58% and 100% for SP, 61% and 100% for HI, 57% and 99% for MC. Using standard diagnostic tests as gold standard, sensitivity and specificity were 58% and 96% for SP, 74% and 87% for HI, indefinite and 92% for MC. Using a lower detection cut-off (≥ 102) on NP with in-house PCR, the sensitivity was 68% for SP and 77% for HI. The only significant correlation between patients' constellation and positive NP PCR for SP, HI or MC was a higher median C-Reactive Protein (114 mg/l in the positive group versus 65 mg/l in the negative group, p = 0,02).

Conclusions
Our data showed that FilmArray PP results in NP swabs for identifying the most common etiologies of community-acquired LRTI has a limited sensitivity, preventing its use for withholding antibiotics, but an excellent specificity, suggesting its use for targeting antibiotics in case of positive result. The low sensitivity is not explained by the PCR detection cut-off

P44

Switching to DTG/3TC fixed-dose combination is non-inferior to a TAF-based regimen (TBR) for 96 weeks: TANGO subgroup analyses

P Benson[1]; C Kinder[2]; MJ Pérez Elías[3]; DE Smith[4]; S Scholten[5]; M Ait-Khaled[6]; KA Pappa[6]; R Wang[6]; J Wright[7]; B Wynne[6]; M Aboud[6]; J van Wyk[6]; S Buergi[6]; KY Smith[6]
[1] Be Well Medical Center; [2] AIDS Healthcare Foundation; [3] Hospital Universitario Ramón y Cajal; [4] Albion Centre; [5] Praxis Hohenstaufenring; [6] ViiV Healthcare; [7] GlaxoSmithKline

Aims
The 2-drug regimen (2DR) of DTG/3TC reduces the number of antiretroviral agents taken by individuals treated for HIV-1 infection, when compared to traditional 3DRs. DTG/3TC is non-inferior to DTG + TDF/FTC in HIV-1 infected ART-naive adults (GEMINI) through Week 144 and in ART-experienced, virologically suppressed participants switching from a TAF-based 3/4DR (TANGO) through Week 96. Here we present a key Week 96 secondary endpoint from the TANGO study: Snapshot virologic success by baseline regimen third agent class, disease and demographic characteristics.

Methods
TANGO is a randomized, open-label, multicenter, non-inferiority phase III study evaluating the efficacy and safety of switching to DTG/3TC once daily versus remaining on a current TAF-based regimen. HIV-1 infected adults, with HIV-1 RNA < 50 c/mL for > 6 months, on a TAF-based regimen for at least 3 months and without prior virologic failure or historical NRTI or INSTI major resistance mutations, were eligible to participate. Randomization was stratified by baseline third agent class: PI, NNRTI, INSTI. The primary endpoint was the proportion of participants with plasma HIV-1 RNA ≥ 50 c/mL at Week 48 (FDA Snapshot algorithm, intention-to-treat–exposed [ITT-E] population) with secondary analyses at Week 96.

Results
741 randomized/exposed participants (DTG/3TC: 369; TBR: 372) were included. Snapshot success rates across subgroups were generally consistent with the overall TANGO Week 96 study results and were similar between arms, including subgroups by age (< 35, 35-50, ≥ 50), sex (male, female), race (White, African heritage, Asian, other), baseline third agent class (PI, NNRTI, INSTI) and baseline CD4+ cell count (< 350 or ≥ 350 cells/mm3). Zero participants on DTG/3TC and 3 participants (< 1%) on TBR met confirmed virologic withdrawal criteria with no resistance mutations observed at failure.

Conclusion
Switching to DTG/3TC FDC was non-inferior to continuing a TAF-based 3/4DR in maintaining virologic suppression in HIV-1 infected ART-experienced adults through Week 96. Efficacy by subgroups was consistent with overall Week 96 study results, demonstrating that switching from TAF-based regimens to DTG/3TC is effective at maintaining virologic suppression regardless of baseline regimen, patient or disease characteristics.

P45
Mycoplasma pneumoniae genotypes and clinical outcome

PM Meyer Sauteur[1]; E Pánisová[1]; M Seiler[1]; M Theiler[1]; C Berger[1]; R Dumke[2]
[1] University Children's Hospital Zurich; [2] RKI German Reference Laboratory for Mycoplasma, Institute of Medical Microbiology and Hygiene Dresden

Aims
Mycoplasma pneumoniae (Mp) is a common cause of community-acquired pneumonia (CAP) in children. Apart from the respiratory tract, Mp can cause a wide range of extrapulmonary manifestations. We recently described the occurrence of Mp-induced mucocutaneous disease among CAP patients, which was associated with increased systemic inflammation, morbidity, and a higher risk of long-term sequelae. In contrast, Mp can be carried in the upper respiratory tract (URT) without causing any symptoms in up to 56% of healthy children. However, factors leading to the wide range of clinical outcomes are unclear. We investigated whether Mp genotypes are associated with specific clinical outcomes.

Methods
We compared Mp loads and genotypes of children with mucocutaneous disease to those with CAP, family members with URT infection (URTI), and carriers from a prospective cohort study (n = 47; 2016 – 2017), and to other children with mucocutaneous disease from a case series (n = 7; 2017 – 2020). Genotyping was performed using macrolide resistance determination, P1 subtyping, multilocus variable-number tandem-repeat analysis (MLVA), and multilocus sequence typing (MLST). Comparisons were performed with pairwise Wilcoxon rank sum test and Fisher exact test with corrections for multiple testing, as appropriate.

Results
Mp loads did not statistically differ between patients with mucocutaneous disease and CAP or carriers. Macrolide resistance was detected in 1 (1.9%) patient with mucocutaneous disease. MLVA types from 2016 – 2017 included 3–5–6–2 (n = 21, 46.7%), 3–6–6–2 (n = 2, 4.4%), 4–5–7–2 (n = 14, 31.1%), and 4–5–7–3 (n = 8, 17.8%), and they correlated with P1 subtypes and MLST types. MLVA types were not associated with specific outcomes such as mucocutaneous disease, CAP, URTI, or carriage. They were almost identical within families, but varied over geographic location. MLVA types in patients with mucocutaneous disease differed between 2016–2017 (3–5–6–2, n = 5, 62.5%) and 2017–2020 (4–5–7–2, n = 5, 71.4%) (P = 0.02).

Conclusion
Our results suggest that Mp genotypes vary over time and geographic location, but may not determine specific clinical outcomes. It is hypothesized that host factors determine which children exposed to Mp are more likely to develop pneumonia, extrapulmonary manifestations, or carriage.

P46

Durable efficacy of DTG + 3TC in GEMINI-1 and -2: Year 3 subgroup analyses

C Orkin[1]; N Porteiro[2]; M Berhe[3]; R Dretler[4]; F Pulido[5]; S Cheng[6]; C Oprea[7]; M Johnson[8]; S Kizhlo[9]; J Sievers[10]; C Man[10]; R Urbaityte[11]; M Underwood[10]; B Wynne[10]; M Mika[10]; J van Wyk[10]
[1] Queen Mary University; [2] Fundacion IDEAA; [3] Texas Infectious Diseases Consultants; [4] Infectious Disease Specialists of Atlanta; [5] Hospital Universitario 12 de Octubre; [6] Taipei Medical University; [7] Dr. Victor Babes Clinical Hospital for Infectious and Tropical Diseases; [8] Royal Free Hospital; [9] Centre for Prevention and Control of AIDS and Infectious Diseases; [10] ViiV Healthcare; [11] GlaxoSmithKline

Aims: In GEMINI-1 and GEMINI-2 (ClinicalTrials.gov: NCT02831673, NCT02831764), dolutegravir + lamivudine (DTG + 3TC) was non-inferior to the 3-drug regimen DTG + tenofovir/emtricitabine (TDF/FTC) in achieving plasma HIV-1 RNA < 50 c/mL in treatment-naive adults at Weeks 48, 96 and 144. We present a secondary endpoint analysis of efficacy at Week 144 by demographics and baseline characteristics.

Methods: GEMINI-1/-2 are identical, global, double-blind, multicentre phase 3 studies. Participants with screening HIV-1 RNA ≤ 500,000 c/mL and no major viral resistance mutations to NRTIs, NNRTIs or PIs were randomised to once-daily DTG + 3TC or DTG + TDF/FTC, stratified by plasma HIV-1 RNA and CD4+ cell count. The primary endpoint was proportion of participants with plasma HIV-1 RNA < 50 c/mL at Week 48 (Snapshot algorithm). For the overall population, estimates and confidence intervals were based on stratified analysis using Cochran-Mantel-Haenszel weights.

Results: 714 and 719 adults were randomised and treated in GEMINI-1/-2, respectively. Using a 10% non-inferiority margin, DTG + 3TC was non-inferior to DTG + TDF/FTC at Week 144 in GEMINI-1/-2 and the pooled analysis. Response rates across baseline HIV-1 RNA subgroups were high and similar in both arms in the pooled analysis, including in subgroups by age, sex, race, baseline HIV-1 RNA (≤ 100,000 or > 100,000 c/mL) or baseline CD4+ cell count (≤ 200 or > 200 cells/mm3). Results were also generally consistent regardless of age, sex or race. While response rates remained lower in DTG + 3TC vs DTG + TDF/FTC participants with CD4+ ≤ 200 cells/mm3, differences were smaller than at Weeks 48 and 96; most reasons for non-response were unrelated to virologic efficacy or treatment regimen. Twelve participants on DTG + 3TC and 9 on DTG + TDF/FTC met confirmed virologic withdrawal (CVW) criteria through Week 144; none had treatment-emergent INSTI or NRTI resistance mutations. One non-CVW DTG + 3TC participant with reported non-adherence developed M184V at Week 132 and R263R/K at Week 144, conferring a 1.8-fold change in DTG susceptibility.

Conclusion: In GEMINI-1/-2, DTG + 3TC was non-inferior to DTG + TDF/FTC in treatment-naive adults at Week 144, demonstrating durable efficacy. Subgroup efficacy results at Week 144 were generally consistent with overall study results and further support DTG + 3TC as an effective initial treatment for people with HIV-1 across disease characteristics and patient populations.

P47

Week 96 efficacy and safety of cabotegravir + rilpivirine every 2 months in ATLAS-2M phase IIIb study

H Jaeger[1]; ET Overton[2]; G Richmond[3]; G Rizzardini[4]; JF Andrade-Villanueva[5]; R Mngqibisa[6]; A Ocampo Hermida[7]; A Thalme[8]; PD Benn[9]; Y Wang[10]; KJ Hudson[9]; DA Margolis[9]; C Talarico[9]; K Vandermeulen[11]; F Zellweger[9]; WR Spreen[9]
[1] MVZ Karlsplatz; [2] University of Alabama at Birmingham; [3] Nova Southeastern University; [4] Fatebenefratelli Sacco Hospital; [5] Hospital Civil “Fray Antonio Alcalde”; [6] Enhancing Care Foundation; [7] Complexo Hospitalario Universitario de Vigo; [8] Karolinska University Hospital; [9] ViiV Healthcare; [10] GlaxoSmithKline; [11] Janssen Research & Development

Aims
Cabotegravir (CAB) and rilpivirine (RPV) long-acting (LA) administered every 1 or 2 months may address challenges associated with daily oral antiretroviral therapy (ART). The ATLAS-2M (NCT03299049) study demonstrated noninferiority of CAB + RPV LA administered every 8 weeks (Q8W) vs every 4 weeks (Q4W) at Week 48.

Methods
ATLAS-2M is an ongoing, randomized (1:1), multicenter, phase IIIb study of CAB + RPV LA administered Q8W vs Q4W to virologically suppressed individuals previously receiving CAB + RPV LA Q4W (ATLAS [NCT02951052] study rollover) or oral standard-of-care ART. The primary endpoint was proportion of participants with plasma HIV-1 RNA ≥ 50 c/mL at Week 48 (US Food and Drug Administration Snapshot, intention-to-treat–exposed; 4% noninferiority margin). Week 96 endpoints were proportions with plasma HIV-1 RNA ≥ 50 and < 50 c/mL, incidence of confirmed virologic failure (CVF; 2 consecutive measurements ≥ 200 c/mL), safety, and tolerability.

Results
1045 participants received CAB + RPV LA (Q8W, n = 522; Q4W, n = 523); 27% were female; 73% were white. At Week 96, 2.1% (n = 11; Q8W) and 1.1% (n = 6; Q4W) of participants had HIV-1 RNA ≥ 50 c/mL (adjusted difference, 1.0; 95% CI, −0.6 to 2.5), consistent with Week 48 results (1.7% vs 1.0%; adjusted difference, 0.8; 95% CI, −0.6 to 2.2). At Week 96, ≥ 90% of participants maintained HIV-1 RNA < 50 c/mL in both groups. There were 9 (1.7%) CVFs in the Q8W group and 2 (0.4%) in the Q4W group through Week 96; 1 occurred after Week 48 in a Q8W participant with baseline RPV resistance-associated mutation Y181C. Safety profiles were comparable between groups; no new safety signals were identified after Week 48. Injection site reactions (ISRs) were the most common adverse event and led to 1 withdrawal after Week 48 (Q8W group). Most ISRs were mild or moderate (98.6%); median duration was 3 days. ISR frequency decreased over time (Week 48: Q8W, n = 115/493 [23%]; Q4W, n = 100/488 [20%]; Week 96: Q8W, n = 74/473 [16%]; Q4W, n = 54/468 [12%]).

Conclusion
Efficacy of CAB + RPV LA Q8W continued to be non-inferior to Q4W at Week 96, with both regimens maintaining high levels of virologic suppression. These longer-term efficacy, safety, and tolerability data further support the therapeutic potential of CAB + RPV LA.

P48

Cabotegravir + rilpivirine long-acting as HIV-1 maintenance therapy: ATLAS Week 96 results

S Swindells[1]; T Lutz[2]; L Van Zyl[3]; N Porteiro[4]; P Benn[5]; JO Huang[6]; CM Harrington[5]; K Hove[6]; SL Ford[6]; CL Talarico[5]; V Chounta[5]; H Crauwels[7]; R Van Solingen-Ristea[7]; S Vanveggel[7]; DA Margolis[5]; KY Smith[5]; K Vandermeulen[7]; S Charbon[5]; WR Spreen[5]
[1] University of Nebraska Medical Center; [2] Infektiologikum; [3] Syzygy Clinical Research Services; [4] Fundación IDEAA; [5] ViiV Healthcare; [6] GlaxoSmithKline; [7] Janssen Research and Development

Aims
Long-acting (LA) injectable therapies have potential to address some challenges of daily oral ART (eg, pill fatigue, drug/food interactions, stigma, suboptimal adherence). ATLAS (NCT02951052) is a phase III, multicenter, open-label study. W48 data demonstrated switching to monthly injectable cabotegravir (CAB) + rilpivirine (RPV) LA was noninferior to continuing 3-drug daily oral ART (CAR) for adults with HIV-1.

Methods
Virologically suppressed ART-experienced participants were randomized (1:1) to continue CAR or switch to LA therapy for a 52-wk Maintenance Phase (MP). After completion, participants could withdraw, transition to ATLAS-2M (NCT03299049; investigating CAB + RPV LA Q8W vs CAB + RPV LA Q4W) or enter an Extension Phase (EP). Participants entering the EP at W52 continued LA therapy (LA arm) or switched from CAR to CAB + RPV LA (Switch arm). Endpoints assessed at W96 were plasma HIV-1 RNA < 50 c/mL and ≥ 50 c/mL, confirmed virologic failure (CVF; 2 consecutive HIV-1 RNA ≥ 200 c/mL), safety, tolerability, and patient-reported outcomes.

Results
Most participants completing the MP transitioned to ATLAS-2M (88%, 502/572), leaving 52 in ATLAS for inclusion in the W96 data analysis. Of these, 100% (23/23) and 97% (28/29) in LA and Switch arms maintained virologic suppression at W96 data analysis, respectively. No participants had CVF during the EP. Safety and tolerability data for LA and Switch arm participants were comparable, similar to data reported during the MP. Most common drug-related adverse events were injection-site reactions, which were generally mild/moderate (> 99%, 389/392) and of short duration (median duration, 3 days). All Switch arm participants responding to the questionnaire at W96 (100%, 27/27) preferred LA to their previous daily oral regimen.

Conclusion
CAB + RPV LA maintained virologic suppression in most participants who entered the EP and were present at the W96 data analysis, with no CVFs or new safety signals identified. These longer-term efficacy/safety data as well as patient preference data support the therapeutic potential of CAB + RPV LA.

P49

Predicting COVID19 related hospital occupancy amid uncertainty: an “ensemble” modelling approach for the Inselspital

L Salazar-Vizcaya; A Atkinson; C Mugglin; A Rauch; J Marschall; U Mosimann
Inselspital - Universitätsspital Bern

Aims
COVID19 transmission is driven by human behaviour under the pressure of changing public health interventions. Hospitals are in urgent need of timely projections that provide benchmarks for planning COVID19 related bed and ventilator occupancy. This was particularly complex soon after the onset of the pandemic, because projection uncertainty arises from model parameterisations and assumptions based on short run data. Moreover, differences across regions including health care systems, contact structures and courses of transmission, limit the robustness of modelling frameworks from outside the specific locality. We aimed to produce timely projections of hospital occupancy by means of the step-wise implementation of three transmission models (m1-m3) with increasing flexibility and accuracy.

Methods
We ensembled m1-m3 fitted to data from the hospital and from the Canton of Bern. We started off with m1, and as more flexible models able to take into account public health and hospital interventions became available, these successively replaced the existing approach (hence model m1 then m2 followed by m3). M3 has subsequently been modified to suit the modelled system and to incorporate information (e.g. vaccination patterns, regulations to prevent transmission and age structure). M3 further included the development of a dynamic model for patient flow within the hospital .Outcomes were COVID19 related numbers of hospitalised and ventilated patients. Predictions reflect potential transmission scenarios (“Optimistic”, “Pessimistic”, and “Status quo”).

Results
Model m1 resulted in accurate predictions until the first peak of hospital occupancy (April 2020), but failed to capture the subsequent decline with overestimated hospitalised and ventilated patients. Model m2 captured the decline in number of ventilated patients until mid-May 2020 successfully. At this point, our inhouse developed model m3 became available, and this was used for all subsequent predictions. When assuming a pessimistic scenario until the end of April 2021, m3 projects that hospitalisation could reach levels comparable to those observed during the second wave, and that the hospital would be able to cope with the demand for ventilators.

Conclusion
This ensemble approach where existing models were replaced to gain flexibility, accuracy and local applicability, provided a reliable tool for planning COVID19 related hospital occupation.

P50

The Adjuvanted Recombinant Zoster Vaccine (RZV) Confers Long-term Protection Against Herpes Zoster: Interim Results of an Extension Study (ZOSTER-049) of Two Clinical Trials (ZOE-50 and ZOE-70)

C Boutry[1]; A Hastie[2]; M Shi[2]; J Diez-Domingo[3]; JC Tinoco[4]; C Yu[5]; P Pirrotta[2]; G Kalema[6]; A Schuind[2]
[1] Aixial; [2] GSK GlaxoSmithKline; [3] FISABIO; [4] Hospital General de Durango; [5] National Taiwan University Hospital; [6] Keyrus Biopharma

Aims
Two large-scale phase 3 clinical trials (ZOE-50 [NCT01165177] and ZOE-70 [NCT01165229]) demonstrated that, in adults ≥ 50 years of age followed over a mean period of 3.2 and 3.7 years respectively, the adjuvanted recombinant zoster vaccine (RZV) was highly efficacious in preventing herpes zoster (HZ, ZOE-50: 97.2%, ZOE-70: 89.8%) and post herpetic neuralgia (PHN, pooled ZOE-50/-70: 91.2% for ≥ 50 years of age and 88.8% for ≥ 70 years of age) and had a clinically acceptable safety profile.1,2 In this extension study (ZOSTER-049 [NCT02723773]), RZV-induced immunogenicity persistence and long-term vaccine efficacy (VE) against HZ were evaluated; we report interim results after at least 2 years of follow-up (starting and ending ~5.1 and 7.1 years, respectively, after initial vaccination during the parent studies).

Methods
Primary objective: VE against HZ over the ZOSTER-049 study. Secondary objectives: VE against HZ from 1 month post-dose 2 in ZOE-50/-70 until the end of observation for year (Y)2 of ZOSTER-049, persistence of vaccine-induced humoral immunogenicity (HI) in terms of anti-gE antibody concentrations (by ELISA) and cell-mediated immune (CMI) response in terms of frequency of gE-specific CD4+ T-cells (by intracellular cytokine staining).

Results
Of the 7,413 participants enrolled in ZOSTER-049, 7,277 were included in the VE analysis and 6,972 reached Y2 of this study. The overall VE against HZ during at least 2 years of follow-up in ZOSTER-049 was 84.0% (95% confidence interval [CI]: 75.9–89.8%). From 1 month post-dose 2 in the ZOE-50/-70 studies until the end of observation for Y2 of ZOSTER-049, the overall VE was 90.9% (95% CI: 88.2–93.2%). Anti-gE antibody concentrations persisted ~6 times above pre-vaccination levels up to Y8 after vaccination and the frequency of gE-specific CD4[2+] T-cells remained above baseline from Y6 to Y8 after vaccination (i.e. until the end of observation for Y2 of ZOSTER-049).

Conclusions
RZV demonstrated high VE against HZ until the end of the observation period for this Y2 interim analysis. The HI and CMI responses remained stable and high until the end of observation (i.e. 7.1 years after initial vaccination).

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P51
Scabies Management in children in Switzerland

A Stebler; M Buettcher[1]; M Pfister[2]
[1] Children's Hospital Lucerne, Switzerland; [2] University Children's Hospital Basel, Switzerland

Background
Scabies is a neglected disease with major global health concern, particularly in young children. Highest incidences occur in developing countries, however scabies is encountered globally. Management guidelines are rare and availability of therapeutic agents differ by region. Ivermectin is not licensed in children (< 15kg). We reviewed management in Switzerland among different specialties (paediatricians (P), general practitioners (GP), dermatologists (D), paediatric dermatologists (PD), tropical medicine (TM), paediatric ID (PID)).

Methods
A total of 237 physicians including P (n = 141), GP (n = 28), D (n = 45), PD (n = 6), TM (n = 7), PID (n = 10) completed the national online survey (05 to 08/2020; 36 questions; 15 minutes) asking management, approximate cases seen and research priorities.

Results
Distribution Swiss vs. migrant were equal. Diagnostic criteria were diverse: 84% of P and 65% of GP rely on history and visual skin examination alone. 83% of PD use at least dermoscopy. D (47%) use laboratory diagnostics. 37%, 44%, 40% and 30% of P, D, PD and TM respectively will not use Ivermectin in < 15kg as it is off-label. GP (53%) fear adverse reactions. Improved diagnostic tools are important research priorities for 68% and 47% of the P (incl. PID) and GP respectively. Reviewing Ivermectin in < 15kg would be priority for 83% of PD, 64% of D and 42% of GPs. 54%, 58% of D (incl. PD) and P (incl. PID) respectively prioritize optimized dosing and treatment protocols.

Conclusion
Relevant scabies cases occur in migrant and Swiss populations equally. Management is heterogeneous as non-dermatologists use Ivermectin reluctantly. Research priorities include convenient diagnostic tools, a child-appropriate, oral Ivermectin formulation and optimized dosing and treatment protocols.

P52

Maraviroc Reduces Hippocampal Apoptosis in Experimental Pneumococcal Meningitis

ND Le; M Steinfort; D Grandgirard; SL Leib
Neuroinfection Laboratory, Institute for Infectious Diseases, University of Bern

Background
Pneumococcal meningitis (PM) is associated with excessive neuroinflammation causing damage to the brain including the cortex and the hippocampus, the latter being a brain structure critically involved in learning and memory. Especially when acquired during infancy or childhood, the permanent neurofunctional sequelae such as cognitive impairment severely affects the development of the patient. Maraviroc (MVC), a CCR5 antagonist, was reported to dampen the inflammatory reaction within the central nervous system by attenuating activation of brain-resident immune cells and infiltration of inflammatory cells. This study aims to assess the anti-inflammatory and neuroprotective effects of MVC in experimental PM.

Materials/methods
Eleven-day old Wistar rats were infected intracisternally with 7.8 ± 1.3 x 10^3 CFU S. pneumoniae (n=38) or saline (n=16) and treated with MVC (100mg/kg) plus ceftriaxone (n=27) or vehicle plus ceftriaxone (n=27) at 18 hours post infection (hpi). Cortical damage and hippocampal apoptosis were evaluated histomorphometrically at 42 hpi. Levels of inflammatory cytokines and chemokines, matrix metalloproteinase 9 (MMP-9) and myeloperoxidase (MPO) in the cerebrospinal fluid (CSF) were analyzed at 18, 24 and 42 hpi using magnetic multiplexing system, gel zymography and MPO assay, respectively.

Results
MVC treatment did not affect survival or weight of animals treated with MVC compared to those treated with vehicle only. MVC treatment significantly ($p < 0.0001$) reduced the number of infected animals exhibiting histomorphological evidence of cortical necrosis compared to those receiving vehicle only. Infected animals treated with MVC revealed significant ($p=0.0033$) less hippocampal apoptosis compared to infected animals receiving vehicle only. MVC treatment did not reduce the CSF levels of inflammatory cytokines and chemokines (IL-1β, IL-6, IL-10, TNF-α, RANTES, MIP-1α), MMP-9 and MPO compared to treatment with vehicle only.

Conclusions
MVC treatment reduced the occurrence of cortical brain damage and exerted a neuroprotective effect on hippocampal brain damage by significantly reducing apoptosis. This effect was independent of the modulation of inflammation in the CSF which represents a potential new therapeutic strategy to attenuate neurofunctional deficits. Further investigations are planned to assess whether chronic MVC treatment improves functional outcome including learning and spatial memory.

P53

Acute liver failure due to herpes-simplex virus hepatitis in immunocompetent patients - lessons from a case series

S Kuster[1]; C Keerl[1]; RC Sutter[1]; A Hollinger[1]; R Stoll[2]; HH Hirsch[3]; L Fourie[1]; LM Terracciano[1]; C Bernsmeier[1]; V Bättig[1]
[1] Universitätsspital Basel; [2] Kantonsspital Baselland, Liestal; [3] Universität Basel & Universitätsspital Basel

Background
Commonly, herpes simplex virus (HSV) infection presents as a self-limiting disease with mucocutaneous lesions. However, disseminated infections complicated by concomitant viral hepatitis have been reported, predominantly in immunocompromised patients. In our case series we describe the clinical course of three immunocompetent patients with fulminant HSV related hepatitis after surgery.

Cases
Patient 1
Four days after laparoscopic appendectomy, a 50-year-old male developed fever, which was explained by an intra-abdominal abscess. Surgical evaluation revealed additional micro-abscesses on the liver surface. Biopsy showed acute hepatitis with necrosis, immunohistochemistry was positive for HSV. Accordingly, 431 million copies/ml of HSV type 1 and positive IgM antibodies were detected in the blood. The further course was complicated by septic encephalopathy and hemophagocytic lymphohistiocytosis. The patient survived with no sequelae.

Patient 2
A 71-year-old male presented 17 days after aorto-coronary bypass surgery with fever and elevated liver enzymes. A liver biopsy revealed hepatitis with confluent necrosis, immunohistochemistry confirmed HSV infection. In the blood, 800 million copies/ml of HSV type 1 and positive HSV IgM antibodies were detected. Disseminated infection was proven by colon biopsy and lumbar punction. After several complications such as kidney failure and respiratory insufficiency, treatment was discontinued and the patient died 51 days after diagnosis of HSV hepatitis.

Patient 3
A 57-year-old male underwent robotic-assisted prostatectomy. Postoperatively he presented with fever and elevated liver enzymes. Liver biopsy revealed extended areas of necrosis Immunohistochemistry was positive for HSV. Additionally, 1.4 billion copies/ml of HSV type 1 were detected in the blood with positive HSV IgM antibodies. Multiple organ failure including hepatic, cardiac, and respiratory failure occurred. He recovered well and was discharged to a rehabilitation centre two months after diagnosis of HSV hepatitis.

All patients were treated with aciclovir until the liver enzymes normalised.

Conclusions
Even though HSV hepatitis is a rare entity of acute liver failure diagnosis should not be delayed. Since HSV hepatitis is one of the few treatable causes of acute liver failure, treatment with aciclovir should be initiated as soon as possible if HSV hepatitis is suspected because of the high mortality rate.

P54

HIV with Transmitted Drug Resistance Is Durably Suppressed by B/F/TAF at Week 144

R Acosta[1]; S Chang[1]; R Martin[1]; X Wang[1]; H Huang[1]; D Brainard[1]; J Hindman[1]; S Collins[1]; H Martin[1]; C Oberle[2]; K White[1]
[1] Gilead Sciences; [2] Gilead Sciences Sàrl

AIMS
Two phase 3, randomized, double-blind, active-controlled studies of initial HIV-1 treatment demonstrated that bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) was non-inferior to dolutegravir/abacavir/lamivudine (DTG/ABC/3TC, Study 1489) or to DTG+F/TAF (Study 1490) through 144 weeks. In both studies, there was no emergent resistance to study drugs. Here, we describe the effect of baseline transmitted drug resistance (TDR) on treatment response over 3 years.

METHODS
Population sequencing of HIV-1 protease and reverse transcriptase (RT) was performed at screening; resistance to study nucleos(t)ide reverse transcriptase inhibitors (NRTIs) was excluded. Retrospective baseline next generation sequencing of protease, RT, and integrase (IN) was analyzed at a ≥ 15% cutoff. Treatment outcomes were assessed at Week 144 using last on-treatment observation carried forward (LOCF). Resistance analyses were performed on participants with confirmed viral rebound of HIV-1 RNA ≥ 200 copies/mL through Week 144 or last visit who did not resuppress to < 50 copies/mL while on study drug.

RESULTS
Of 1421 PLWH screened for both studies, only 3 (0.2%) were excluded due to TDR to FTC, TAF, ABC, or 3TC. TDR was present in 19.5% (248/1274) of enrolled participants and consisted of INSTI resistance (-R) in 1.3% (17/1270 with data), NRTI-R in 2.7% (35/1274), NNRTI-R in 14.1% (179/1274), and PI-R in 3.5% (44/1274). Treatment outcomes by LOCF at Week 144 of participants with or without TDR were comparable (98% of those with primary TDR had HIV RNA < 50 copies/mL vs. 97% of those without TDR) (Table), indicating preexisting TDR did not affect treatment outcomes. One participant had preexisting Q148H + G140S in IN and K70R and K103N in RT at baseline. This participant was randomized to B/F/TAF, had HIV-1 RNA < 50 copies/mL at Week 4 and maintained HIV-1 RNA < 50 copies/mL through W 144. In total, 21 participants qualified for post-baseline resistance testing (1.3% [8/634] B/F/TAF; 1.9% [6/315] DTG/ABC/3TC; 2.2% [7/325] DTG+F/TAF); of those, 2/8 B/F/TAF, 6/6 DTG/ABC/3TC, and 4/7 DTG+F/TAF participants had multiple confirmed virologic rebounds during the studies. No participant had emergent resistance to study drugs.

CONCLUSIONS
Initial HIV-1 treatment with B/F/TAF, DTG/ABC/3TC, or DTG+F/TAF achieved high, durable rates of virologic suppression. The presence of TDR did not affect treatment outcomes, and there was no treatment-emergent resistance through 144 weeks.

P55

Potent Antiviral Activity of Lenacapavir in Phase 2/3 in Heavily ART-Experienced PWH

S Segal-Maurer[1]; A Castagna[2]; M Berhe[3]; G Richmond[4]; P Ruane[5]; G Sinclair[6]; K Siripassorn[7]; Y Liu[8]; N Margot[8]; H Dvory-Sobol[8]; R Hyland[8]; M Rhee[8]; J Baeten[8]; T Grabinger[9]; D Brainard[8]
[1] New York Presbyterian Queens; [2] IRCCS Ospedale San Raffaele; [3] North Texas Infectious Disease Consultants; [4] Gary J Richmond, MD; [5] Ruane Clinical Research Group; [6] PrismHealth North Texas; [7] Bamrasnaradura Infectous Diseases Institute; [8] Gilead Sciences; [9] Gilead Sciences Switzerland Sàrl

AIMS
Lenacapavir (LEN, GS-6207), the long-acting first-in-class HIV capsid inhibitor, is in clinical development for the treatment and prevention of HIV-1 infection. With its novel mechanism of action, LEN is fully active in vitro against HIV-1 strains resistant to the major antiretroviral (ARV) classes.

METHODS
We conducted a Phase 2/3, randomized, double-blind, placebo (PBO)-controlled study in heavily treatment-experienced (HTE) people with HIV (PWH) failing their current regimen with HIV-1 RNA (VL) ≥ 400 c/mL and documented resistance to ≥ 2 agents from ≥ 3 of the 4 major ARV classes. Participants were randomized (2:1) to add LEN or PBO to their failing regimen for 2 weeks. During this functional monotherapy period, LEN or PBO was given orally (600 mg on Day [D] 1 and 2 and 300 mg on D 8). The primary efficacy endpoint was the proportion of participants with at least 0.5 log10 c/mL decline in VL by D 15. At D 15, those on oral LEN received subcutaneous (SC) LEN 927 mg every 6 months (Q6M), while those on PBO started the LEN 2-week oral lead-in, followed by Q6M SC. All participants initiated an investigator-selected, optimized background regimen (OBR) at D 15. Here we report complete data for the functional monotherapy period and preliminary data for the LEN + OBR period.

RESULTS
36 participants were randomized: 28% were female and 46% Black. Median age was 54 years. Mean baseline VL was 4.27 log10 c/mL. At D 15, 88% of participants on LEN (21 of 24) had at least 0.5 log10 c/mL decline compared to 17% on PBO (2 of 12) (difference: 71%, 95% CI 35 to 90%, $p < 0.0001$). The median (range) change in VL (log10 c/mL) was -2.00 (-3.29 to 0.29) vs -0.08 (-1.93 to 0.31). During the LEN + OBR period at 4 weeks after SC dosing, 58% (21 of 36) had VL < 50 c/mL. The median (range) duration of follow up on LEN was 26 (7-46) weeks. There were no serious adverse events (AEs) related to study drug, discontinuations due to AEs, or deaths. The most frequent AEs (any grade) were injection site swelling (28%) and nodule (25%). Injection site reactions related to LEN (50%) were all mild or moderate. Longer term data will be reported.

CONCLUSION
LEN led to a rapid and clinically relevant decline in VL when added to a failing regimen in HTE PWH. LEN was generally safe and well-tolerated. These results support the ongoing evaluation of LEN for the treatment and prevention of HIV-1 infection.

P56
Four Year Outcomes of B/F/TAF in Treatment-Naïve Adults

K Workowski[1]; C Orkin[2]; P Sax[3]; D Hagins[4]; E Koenig[5]; J Stephens[6]; S Gupta[7]; H Huang[8]; R Acosta[8]; J Hindman[8]; D Brainard[8]; S Collins[8]; T Grabinger[9]; H Martin[8]
[1] Emory University; [2] Barts Health NHS Trust; [3] Brigham and Women's Hospital/Harvard Medical School; [4] Coastal District Care Clinic; [5] Instituto Dominicano de Estudios Virologicos; [6] Mercer Univerity; [7] Indiana University / University of Minnesota; [8] Gilead Sciences; [9] Gilead Sciences Switzerland Sàrl

AIMS
Bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) is a guidelines-recommended single-tablet regimen for people with HIV-1 (PWH). We present cumulative outcomes from open-label extension (OLE) that followed 144 Weeks (W) of blinded treatment in phase 3 studies in treatment-naïve PWH.

METHODS
We conducted 2 randomized, double-blind, phase 3 studies of B/F/TAF in treatment-naïve adults – Study 1489: B/F/TAF vs dolutegravir/abacavir/lamivudine (DTG/ABC/3TC) and Study 1490: B/F/TAF vs DTG+F/TAF. After completing 144 W of blinded treatment, participants were offered to continue on B/F/TAF for 96 W in the OLE. Efficacy was assessed as the proportion with HIV-1 RNA < 50 copies/mL at each visit after starting B/F/TAF using missing = excluded (M = E) analysis; safety by adverse events (AEs) and laboratory results. Bone mineral density (BMD) in OLE was measured in those randomized to B/F/TAF in Study 1489. We present cumulative results for all participants treated with B/F/TAF in the randomized or OLE phases through a maximum of 192 weeks of follow up (i.e. OLE W 48). The final phase of this study will complete once all participants reach a total of 240 weeks (i.e. OLE W 96).

RESULTS
In Study 1489, 314 participants were randomized to B/F/TAF and 315 to DTG/ABC/3TC; 252 and 254 entered the OLE. In Study 1490, 320 were randomized to B/F/TAF and 325 to DTG+F/TAF; 254 and 265 entered the OLE. Efficacy was > 98% after W48 at each study visit through W 192 in both studies. Across both studies, only one participant experienced an AE that led to drug discontinuation during the OLE analysis window. Grade 3 or 4 drug-related AEs were rare. There were no discontinuations due to renal AEs. In participants initially randomized to B/F/TAF, the median change in weight from baseline to W 192 was 4.6 kg in Study 1490 and 5.0 kg in Study 1490. The mean percent changes (SD) in hip and spine BMD through W 192 were -1.5% (4.9) and -0.9% (5.2), respectively. 13% of participants with baseline osteopenia in hip and 3% with osteopenia of the spine improved to normal at W192, 4% with normal baseline hip and 6% with normal baseline spine BMD progressed to osteopenia and none developed osteoporosis.

CONCLUSION
Over 4 years of follow-up in treatment-naïve participants, B/F/TAF was safe and highly efficacious. Similar outcomes were demonstrated in participants who switched from DTG-containing regimens to B/F/TAF. These results confirm long term safety and efficacy of B/F/TAF.

P57

Clinical considerations of isavuconazole administration in high-risk hematological patients: a single center 5-year experience

I Kronig[1]; S Masouridi-Levrat[1]; Y Chalandon[1]; E Glampedakis[2]; N Vernaz[1]; C van Delden[1]; D Neofytos[1]
[1] University Hospital of Geneva; [2] Centre Hospitalier Universitaire Vaudois

Aims
There are limited real-life data on isavuconazole prophylaxis and treatment of invasive fungal infections (IFI) in hematological patients and allogeneic hematopoietic cell transplant (HCT) recipients. Primary objective was to describe the indications of real-life isavuconazole administration at a university-hospital. Secondary objectives included the description of liver function tests and QTc interval between baseline and end of treatment (EOT), clinical outcomes and breakthrough IFI by the EOT.

Methods
This was a 5-year single-center retrospective study of all adult patients with acute myeloid leukemia and/or allogeneic HCT recipients who received isavuconazole as prophylaxis and/or treatment between 01.06.2016 and 31.07.2020.

Results
Amongst 30 identified patients, the indications for isavuconazole administration were adverse events associated with prior antifungal treatment (N : 18, 60%: hepatotoxicity, renal insufficiency, long QTc-interval, neurotoxicity, and potential drug-drug interactions in 6, 4, 3, 1, and 4 patients, respectively), clinical efficacy (N : 5, 16.6%), and other reasons (N : 10, 33.3%; 5/10 patients treated with isavuconazole to facilitate hospital discharge with orally administered appropriate treatment). Alanine aminotransferase significantly decreased from baseline (mean : 129 IU/L, range : 73, 202) to a mean of 48 IU/L (range : 20, 80) by day 14 (p = 0.02), 23.5 IU/L (range : 20, 27) by day 28 (p = 0.03), and 16.5 IU/L (range : 16, 17) by day 42 (p = 0.009). The QTc-interval decreased from baseline (mean : 456.8 msec, range : 390, 533) to EOT (mean : 433.8 msec, range : 400, 472; p = 0.03). The mean isavuconazole plasma concentration was 2.9 mg/L (range : 0.9, 6.7). There were no breakthrough IFI observed.

Conclusion
Isavuconazole is a safe and reliable antifungal agent in complex hematological patients, with relatively low hepatotoxicity and QTc interval shortening properties.

P58

Invasive mold infections in allogeneic hematopoietic cell transplant recipients in 2020: a 10-year cohort study

R Roth[1]; S Masouridi-Levrat[2]; C Yves[2]; C Van Delden[1]; A Riat[1]; A Fischer[1]; E Glampedakis[3]; V Erard[4]; L Kaiser[1]; D Neofytos[1]
[1] University Hospital of Geneva; [2] University Hospital of Geneva and Faculty of Medicine; [3] University Hospital of Lausanne (CHUV); [4] Cantonal Hospital of Fribourg

Aims
Invasive mold infections (IMI) are a leading cause of mortality in allogeneic hematopoietic stem cell transplant recipients (allo-HCTr). We describe the incidence, risk factors, and mortality of proven and probable IMI in a cohort of allo-HCTr.

Methods
This was a retrospective, single-center cohort study of all adult allo-HCTr from 01.01.2010 through 01.01.2020 with a minimum 1-year follow-up.

Results
Among 515 allo-HCTr, 48 (9.3%) patients developed 51 proven/probable IMI. The most frequently identified IMI was invasive aspergillosis (IA; 34/51, 67%), followed by mucormycosis (9/51, 18%) and other molds (8/51, 15%). Overall 35/51 (68.6%) cases were breakthrough IMI (bIMI), including 22/34 (65%) IA and 13/17 (76.5%) non-IA IMI. One-year cumulative incidence of IMI was 7%: 4.9% and 2.1% for IA and non-IA IMI, respectively. The number of IMI/year did not significantly change through the 10-year study-period. Overall, 15 (31.2 %), 3 (6.3%), 19 (39.6%) and 11 (22.9%) patients were diagnosed with an IMI during the first 30, 31-100, 101-365 and >365 days post-HCT, respectively. Risk factors for IMI included: prior allo-HCT (adjusted hazard ratio, aHR: 4.06, p = 0.004) and ≥ grade 2 acute graft-versus-host disease (GvHD; aHR: 3.52, p < 0.001). All-cause 1-year mortality was 33% (170/515): 48% (23/48) and 31.5% (147/467) for patients with and without a proven/probable IMI (p = 0.02). Mortality predictors included: post-HCT disease relapse (aHR: 7.47, p < 0.001), acute GvHD (aHR: 1.51, p = 0.001), CMV-serology-positive recipients (aHR: 1.47, p = 0.026), and proven/probable IMI (aHR: 3.94, p < 0.001). All-cause 12-week mortality for patients with a proven/probable IMI was 35.4% (17/48): 32.4% (11/34) and 42.9% (6/14) for IA and non-IA IMI, respectively (p = 0.52). At 1-year post-IMI diagnosis 70.8% (34/48) of patients were dead. There were no significant differences in all-cause mortality in patients with proven versus probable IMI and bIMI versus not.

Conclusion
We report a relatively stable and low incidence of proven/probable IMI post-allo-HCT. Despite high-rates of bIMI, our real-life study results confirm 12-week survival rates for IA, as reported in pivotal clinical trials in the last 2 decades. Improved survival in non-IA IMI compared to prior series was observed. The 1-year high mortality in allo-HCTr with IMI requires further studies and actions.

P59

Severe influenza infection and influenza-associated aspergillosis in Swiss intensive-care units – a retrospective multicenter surveillance study

F Waldeck[1]; F Boroli[2]; S Zingg[3]; LN Walti[4]; PD Wendel-Garcia[5]; A Conen[6]; J Pagani[7]; K Boggian[8]; M Schnorf[7]; M Siegemund[3]; S Abed-Maillard[7]; M Michot[6]; M Maggiorini[5]; Y Que[4]; V Bättig[3]; N Suh[2]; G Kleger[8]; W Albrich[8]
[1] Universitätsklinikum Schleswig-Holstein, Campus Lübeck; [2] Geneva University Hospitals; [3] University Hospital Basel; [4] Inselspital - Universitätsspital Bern; [5] University Hospital Zurich; [6] Cantonal Hospital Aarau; [7] University Hospital Lausanne; [8] Cantonal Hospital St. Gallen

Aim
Influenza infection represents a risk factor for invasive fungal diseases, including aspergillosis in intensive-care unit (ICU) patients. We aimed to describe predictors for influenza-associated aspergillosis (IAA) and prognostic factors for poor outcome in critically-ill patients with influenza in Swiss ICUs.

Methods
We conducted a retrospective surveillance at seven tertiary hospitals in Switzerland during the 2017/18 and 2019/2020 influenza seasons. All adult patients with influenza confirmed by polymerase chain reaction and ICU length of stay (ICU-LOS) for more than 24 hours were included. IAA was defined by mycological, radiological and clinical criteria. We analysed predictors of IAA, mortality and poor outcome which was a composite of hospital mortality, ICU- LOS > 7days need for extracorporeal membrane oxygenation and need for invasive mechanical ventilation > 7days. Uni- and multivariate analyses were performed. ICU-LOS was analysed using a competing risk approach including death in the ICU vs. discharged alive.

Results
Of 138 included patients with influenza, 15 (10,8%) developed IAA. IAA patients were male in 60% (p=0.42), with a median age of 58 years (interquartile range (IQR): 50–73) vs. 65.5 years (IQR: 56-63) and had a higher ICU-mortality (40% vs. 14%, p=0.03) compared to influenza patients without IAA. Asthma (odds ratio (OR): 17.4, 95% confidence interval (CI): 2.1- 179.8), secondary respiratory infection (OR: 8.2, 95%CI: 1.8-67.2) and duration of intubation in days (OR: 1.1, 95%CI: 1.0-1.2) were independently associated with IAA. Bad outcome was independently associated with younger age (OR: 0.9, 95%CI: 0.9-1.0), higher SAPSII-score (OR: 1.1, 95%CI: 1.0-1.1), influenza A (OR: 2.6, 95%CI: 0.7-7.7), secondary respiratory infection (OR: 4.8, 95%CI: 1.7-14.6), bacteraemia (OR: 7.8, 95%CI: 1.3-151.8) and IAA (OR: 13.0, 95%CI: 1.9- 267.1). In competitive risk analysis IAA was associated with a longer ICU-LOS (sub-distribution hazard ratio (sHR) 0.46, $p < 0.01$) and a numerically higher ICU-mortality (sHR 1.52, $p = 0.13$).

Conclusions
IAA was a common complication of critically-ill patients with influenza in Swiss ICUs. IAA was associated with worse outcome and with a prolonged stay in the ICU in the surviving group. Increased awareness of secondary aspergillosis in severe influenza infection is urgently needed, particularly in patients with predisposing factors such as asthma and prolonged invasive mechanical ventilation.

P60

Computer-aided medical microbiology monitoring tool: a strategy to adapt to the SARS CoV-2 epidemic and that highlights RT-PCR consistency

L Mueller; V Scherz; G Greub; K Jaton; O Opota
CHUV Centre Hospitalier Universitaire Vaudois (CHUV)

Aims
Since the beginning of the COVID-19 pandemic, our diagnostic laboratory faced a rapid increase in the number of SARS-CoV-2 RT-PCR. To maintain a rapid turnaround time, we moved from a case-by-case validation of RT-PCR results to an automated validation and immediate transmission to clinicians. A quality-monitoring tool based on a homemade algorithm coded in R was developed, to preserve high quality and to track possible aberrant results.

Methods
The quality-monitoring tool was based on a homemade algorithm coded in R. We applied this quality-monitoring tool to 35,137 RT-PCR results corresponding to 30,198 patients.

Results
Patients tested several times led to 4,939 pairwise comparisons: 88% concordant and 12% discrepant. The algorithm automatically solved 428 out of 573 discrepancies. The most likely explanation for these 573 discrepancies was related for 44.9% of the situations to the clinical evolution of the disease, 27.9% to preanalytical factors, and 25.3% to stochasticity of the assay. Finally, 11 discrepant results could not be explained, including 8 for which clinical data was not available. The algorithm also identified patients with sustained RT-PCR positive results. For patients repeatedly tested on the same day, the second result confirmed a first negative or positive result in 99.2% or 88.9% of cases, respectively.

Conclusions
The automatic algorithm was capable of finding discrepant results and attributing them to corresponding testing phases. This computer-aided methodology outlined that besides the expected evolution of the disease, most of discrepant results are compatible with preanalytical factors.
The implemented quality-monitoring strategy allowed to: i) assist the investigation of discrepant results ii) focus the attention of medical microbiologists onto results requiring a specific expertise and iii) maintain an acceptable turnaround time.
This work highlights the high RT-PCR consistency for the detection of SARS-CoV-2 and the necessity for automated processes to handle a huge number of microbiological results while preserving quality.

P61

Evaluation of the aquatic toxicity of a glucoprotamine-based biocide and its effect on behavior at sub-lethal concentrations in Zebrafish larvae

ND Le; FL Leib; D Grandgirard; SL Leib
Neuroinfection Laboratory, Institute for Infectious Diseases, University of Bern

Aim
Disinfection of organism-containing liquid waste by chemical inactivation and its disposal via wastewater is common practice. Incidin Plus (ECOLAB), a disinfectant containing the biocide glucoprotamine, is used in hospitals and labs for disinfection. If leaked into the aquatic environments, it may have detrimental effects. Zebrafish (ZF) larvae are often used to identify chemicals that can cause acute toxicity in aquatic environments. This study aims to determine the effect of Incidin exposure on the lethality and behavior of ZF larvae.

Materials/methods
Two days old post fertilization wild-type ZF larvae were exposed to 0.1-100 mg/l of glucoprotamine (Incidin Plus) or to E3 medium (control) for 72 h. Lethality was determined for each concentration and the 50 % lethal concentration (LC50) calculated using simple logistic regression analysis. For the behavioral testing, larvae were exposed to LC50 and two sublethal concentrations of glucoprotamine. After 72 h, control (n=60) and treated larvae (n=22-24 larvae per concentration) were placed in 96-well plate and transferred into the behavioral testing chamber (DanioVision®, Noldus). Larvae were acclimatized in dark for 1 h before recording. The tracking protocol consisted of a 20 min dark period followed by a 10 min light period and a second dark period of 20 min.

Results
LC50 of glucoprotamine was determined at a range of 3-3.5mg/l. The basal locomotor activity (BLA), defined as the distance moved by the larvae in the first dark period of 20 min, was significantly reduced in larvae treated with 3.5mg/l compared to controls ($p=0.0003$). Larvae exposed to 3, 2 and 0.1mg/l exhibited significantly increased BLA compared to controls ($p < 0.05$). During dark-light transition, larvae exposed to 2 and 0.1mg/l revealed significantly higher activity compared to control ($p < 0.01$), whereas larvae treated with 3.5 but not 3mg/l showed a trend towards decreased activity ($p=0.06$). The visual motor response (VMR), a hyperactivity period evoked by sudden decreased light intensity (light-dark transition), was significantly reduced in larvae exposed to 3.5 and 3mg/l.

Conclusion
Based on our data, we estimate the LC50 of glucoprotamine at a range of 3-3.5mg/l and conclude that sublethal concentrations of Incidin significantly affect the behavior of ZF larvae by increasing their BLA and their response to dark-light transition. Further investigations are needed to better understand the mechanism of these observations.

P62

Resistance and escape of SARS-CoV-2 variants from neutralization by sera from naturally infected patients

M Bekliz; K Adea; B Meyer; I Eckerle
University of Geneva (UNIGE)

In late 2019, the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) emerged in China causing a pandemic and an unprecedented international health crisis of unknown outcome.
Since the end of 2020, new variants of concern (VOC) SARS-CoV-2, B.1.1.7, B1.351 and B1.128 (P1 and P2), emerged in different parts of the world. These variants include multiple substitutions and deletions in the major neutralizing antigen, the spike glycoprotein.
Given these concerns, here, we evaluated the neutralizing potency of a panel of authentic sera from early in the pandemic, including sera from convalescent plasma donors and infected persistence patients against a live infectious SARS-CoV-2 virus (B.1.1.7, B1.351, B1.128 (P1 and P2) isolates and an early Wuhan-related isolate from the first wave) using the plaque reduction neutralization test (PRNT) which has been recently established showing promising performance.
Our data show moderate to substantially diminished neutralizing potency of sera against B.1.1.7 SARS-CoV-2 variant. However, neutralization of B1.128 (P2) by sera from naturally infected patients is significantly reduced, leading in some cases to a complete inability to neutralize this variant. There is evidence of widespread escape from mAbs.

P63

Combined Bacteriophage and Antibiotic Treatment Prevents Pseudomonas aeruginosa Infection of Wild Type and cftr- Epithelial Cells

A Luscher[1]; T Köhler[1]; C van Delden[2]
[1] University of Geneva (UNIGE); [2] HUG Hôpitaux Universitaires Genève

With the increase of infections due to multidrug resistant bacterial pathogens and the shortage of antimicrobial molecules with novel targets, interest in bacteriophages as a therapeutic option has regained much attraction. Before the launch of future clinical trials, in vitro studies are required to better evaluate the efficacies and potential pitfalls of such therapies. Here we studied in an ex vivo human airway epithelial cell line model the efficacy of phage and ciprofloxacin alone and in combination to treat infection by Pseudomonas aeruginosa. The Calu-3 cell line and the isogenic CFTR knock down cell line (cftr-) infected apically with P. aeruginosa strain PAO1 showed a progressive reduction in transepithelial resistance during 24 h. Administration at 6 h p.i. of single phage, phage cocktails or ciprofloxacin alone prevented epithelial layer destruction at 24 h p.i. Bacterial regrowth, due to phage resistant mutants harboring mutations in LPS synthesis genes, occurred thereafter both in vitro and ex vivo. However, co-administration of two phages combined with ciprofloxacin efficiently prevented PAO1 regrowth and maintained epithelial cell integrity at 72 p.i. The phage/ciprofloxacin treatment did not induce an inflammatory response in the tested cell lines as determined by nanoString® gene expression analysis. We conclude that combination of phage and ciprofloxacin efficiently protects wild type and cftr- epithelial cells from infection by P. aeruginosa and emergence of phage resistant mutants without inducing an inflammatory response. Hence, phage-antibiotic combination should be a safe and promising anti-Pseudomonas therapy for future clinical trials potentially including cystic fibrosis patients.

P64

Prevalence of specific SARS-CoV-2 antibodies among Swiss healthcare workers at baseline and after 6 months – results of a prospective multicentre cohort

P Kohler[1]; T Egger[1]; B Babouee Flury[1]; OB Leal-Neto[2]; A Brucher[3]; D Flury[1]; S Güsewell[1]; E Lemmenmeier[4]; C Möller[5]; P Rieder[6]; M Rütti[7]; R Stocker[6]; D Vuchard-Gysin[8]; B Wiggli[9]; U Besold[10]; S Kuster[11]; A McGeer[12]; L Risch[13]; M Schlegel[1]; A Friedl[9]; P Vernazza[1]; C Kahlert[14]
[1] Kantonsspital St. Gallen; [2] Epitrack / Universität Zürich; [3] Psychiatrie-Dienste Süd; [4] Clienia Littenheid AG; [5] Rehaklinik Zihlschlacht AG; [6] Klinik Hirslanden AG; [7] Spitalregion Fürstenland Toggenburg; [8] Spital Thurgau AG; [9] Kantonsspital Baden AG; [10] Geriatrische Klinik St. Gallen; [11] BetterTogether Healthcare Consulting GmbH; [12] Mount Sinai Hospital; [13] Labormedizinisches Zentrum Dr Risch Ostschweiz AG; [14] Ostschweizer Kinderspital St. Gallen

Aims: Healthcare workers (HCW) are at the frontline of the Coronavirus Disease 2019 (COVID-19) pandemic. We present results of our prospective HCW cohort, where specific antibodies against Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) are repetitively measured.

Methods: Between June and September 2020 (after the first COVID-19 wave), we recruited HCW from 10 healthcare networks (23 sites) in Eastern and Northern Switzerland and performed baseline serologies using the Roche Elecsys electro-chemiluminescence immunoassay (ECLIA) which detects anti-nucleocapsid antibodies with high sensitivity and specificity. After enrolment, participants reported results of PCR and rapid antigen test (RAT) for SARS-CoV-2 on a weekly basis. In January and February 2021, follow-up serologies were performed in the same institutions using the same test. We compared seroprevalence at baseline and at follow-up on the network level. Also, the proportion of individuals with positive PCR (or RAT) and negative follow-up serology, and those with conversion to a seronegative status from baseline to follow-up was calculated.

Results: At baseline, seroprevalence among the 5083 included participants was 2.7% (n=139). Preliminary results of follow-up serologies showed an increase to 18.5% (665 positive among 3588 individuals). At follow-up, seroprevalence on the network level ranged from 11.6% (psychiatric institutions) to 37% (acute care institutions). Acute care networks from Eastern Switzerland had a significantly higher prevalence than those from Northern Switzerland (24.4% vs. 13.6%, $P < 0.001$). During follow-up, 376 participants reported a positive PCR, whereof 332 (88%) had a positive, 13 (3%) an inconclusive, and 31 (9%) a negative follow-up serology. A total of 3419 participants had both baseline and follow-up serologies. Among these, 8 of 107 (7.5%) with a positive result at baseline had a negative follow-up serology, suggesting waning immunity over time.

Conclusion: These preliminary data show a steep increase in seroprevalence among Swiss HCW over a period of 6 months. Up to 10% of participants with positive PCR did not show any seroconversion. Seroprevalence was significantly different between different type of institutions and different geographic regions. More in-depth analyses will reveal which individual participant factors contribute to the observed differences as well as to the loss of humoral immunity over time.

P65

Antimicrobial resistance in Mycoplasma genitalium in Switzerland – a nested project of the STAR Trial

J Notter[1]; M Ritzler[2]; N Wohlwend[2]; CV Hauser[3]; N Low[4]; M Risch[2]; L Risch[2]; P Vernazza[1]; AJ Schmidt[1]
[1] Kantonsspital St. Gallen; [2] Labormedizinisches Zentrum Dr. Risch; [3] Inselspital Bern; [4] Universität Bern

Aims
Mycoplasma genitalium (MG) is recognized as an emerging STI causing urethritis, cervicitis, pelvic inflammatory disease and proctitis and is responsible for 10–35% of non-gonococcal, non-chlamydial urethritis in men. Clinical management is challenging due to increasing antimicrobial resistance. The rate of resistance varies between countries and is unknown for Switzerland. We examined the prevalence and risk factors for asymptomatic infections with macrolide and fluoroquinolone (FQ) resistant MG in multi-partner individuals.

Methods
Repeated free STI testing was offered to men and women with multiple sexual partners (≥ 3 in the previous year) within the STAR trial [1, 2]. Information on demographics and sexual behavior was collected with an anonymous questionnaire as self-reported data. Pooled swabs (pharynx, urethra/vagina, anus) were obtained from all participants and tested for various STIs including MG. Macrolide and FQ resistance in MG-positive samples was evaluated by Sanger sequencing (23S rRNA gene, gyrA and parC gene).

Results
Among 2138 specimens orverall, 102 samples (4.8%) tested positive for MG. 77 samples could be successfully amplified. Genotypic resistance to macrolides or FQ was found in 33.8% and 5.2%, respectively (26 and 4/77, with an overlap of 1/77). At baseline, 81/1453 participants (5.5%) were found to be MG-positive; individuals (i.e., MSM) with known HIV infection were over-represented (p = 0.006). Incidence among MSM, after excluding men MG-positive at baseline (to control for persistent infections) was 4.3% (95% confidence interval 2.5%–7.1%). In univariable analyses, the odds ratios for any MG resistance was 8.8 in MSM (2.8–27.6) — in this group 57.9% of all tested specimen showed resistance — and 4.0 in individuals reporting prior diagnosis of gonorrhea/chlamydia (4.0; 1.4–11.5).

Conclusion
This study provides the first data on the epidemiology of MG infections and macrolide and FQ resistance in MG in individuals at high STI risk in Switzerland. In Swiss MSM tested 2016–2017, asymptomatic MG infections were common, and the majority of MG had macrolide resistance, likely due to previous exposure to macrolides for the treatment of gonorrhoea/chlamydia. Given the high level of resistance, the benefit of routine screening for and antibiotic treatment of asymptomatic MG infections may be questioned critically. Our results will help the development of guidelines for the clinical and diagnostic management of MG infections.

P66

Frequency of COVID-19 symptoms and of SARS-CoV-2 positive nasopharyngeal swabs among healthcare workers according to serostatus at baseline: a prospective multi-centre cohort

P Kohler[1]; S Güsewell[1]; T Egger[1]; M Schlegel[1]; O Leal Neto[2]; A Brucher[3]; E Lemmenmeier[4]; C Möller[5]; P Rieder[6]; R Stocker[6]; D Vuichard-Gysin[7]; B Wiggli[8]; A Friedl[8]; U Besold[9]; S Kuster[10]; A Mcgeer[11]; L Risch[12]; M Ruetti[13]; D Flury[1]; P Vernazza[1]; CR Kahlert[14]
[1] Kantonsspital St. Gallen; [2] University of Zürich; [3] Klinik St.Pirminsberg; [4] Clienia AG; [5] Rehaklinik Zihlschlacht AG; [6] Hirslanden AG; [7] Kantonsspital Münsterlingen; [8] Kantonsspital Baden; [9] Geriatrische Klinik St. Gallen; [10] Bundesamt für Gesundheit BAG; [11] Mount Sinai Health System; [12] labormedizinisches zentrum Dr Risch; [13] Spitalregion Fürstenland Toggenburg; [14] Ostschweizer Kinderspital

AIMS: Few data exist as to whether the presence of specific antibodies against Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) protects against reinfection. We performed baseline serologies and analysed digital surveillance data from a cohort of healthcare workers (HCW).

METHODS: We recruited HCW from 23 healthcare institutions in Eastern and Northern Switzerland between June and September 2020 and performed baseline serologies with the Roche Elecsys electro-chemiluminescence immunoassay (detecting anti-nucleocapsid antibodies). During follow-up, a personal link to an electronic questionnaire was sent by email or text message to participants on a weekly basis. Participants indicated which symptoms compatible with Coronavirus Disease 2019 (COVID-19) they experienced during the previous week as well as the date and results of nasopharyngeal swab tests (PCR or rapid antigen tests) performed during that week. Following general practice in Switzerland, participants were requested to undergo SARS-CoV-2 testing if they experienced relevant symptoms. We compared the proportion of seropositive and seronegative participants who reported a particular symptom or a positive test result at least once using Fisher's exact test.

RESULTS: We included 4731 participants; seroprevalence at baseline was 3.0% (142/4731). We analysed 76’216 questionnaires up to January 5th 2021, equalling a median follow-up of 5.9 months. The median number of submitted questionnaires was similar between seropositive and seronegative participants (17 vs. 18 per person, Wilcoxon rank sum test, P=0.58). COVID-19 specific symptoms such as impaired olfaction/taste (OR 0.30, 95%-CI: 0.09-0.72, P=0.002) and limb/muscle pain (OR 0.63 95%-CI: 0.39-0.97, P=0.04) were less frequent among initially seropositive participants. Fever, dyspnoea, cough and sore throat were not significantly different. Among those with specific antibodies at baseline, 0 out of 48 tested individuals (0%) reported a positive nasopharyngeal swab result during follow-up, whereas among those without specific antibodies, 463 out of 2202 tested individuals (21%) reported a positive result ("P < 0.001").

CONCLUSIONS: Based on the lower frequency of positive PCR and of COVID-19 specific symptoms among seropositives, we conclude that specific SARS-CoV-2 antibodies protect against SARS-CoV-2 reinfection for a period of at least 6 months.

P67

SARS-CoV-2 and hCoV-OC43 specific T-cell responses in seronegative household contacts exposed to symptomatic COVID-19

CR Kahlert[1]; S Nigg[2]; T Egger[3]; P Vernazza[4]; P Kohler[4]
[1] Ostschweizer Kinderspital; [2] Kantonsspital St.Gallen; [3] Kantonsspital St. Gallen,;
[4] Kantonsspital St. Gallen

AIMS
Besides SARS-CoV-2 specific neutralising antibodies, specific T cells as well as cross-reacting T cells with specificity against endemic betacoronaviruses contribute to immunity against COVID-19. We here assess T cell immunity in seronegative household contacts (CASES) of persons with confirmed COVID-19 in comparison to a control group of single households with low exposure risk (CONTROLS).

METHODS
Convenience sample of Swiss healthcare workers including their household contacts which all tested seronegative for SARS-CoV-2 at inclusion. Enzyme Linked Immuno Spot Assay (ELISpot) was performed on freshly isolated peripheral blood mononuclear cells (PBMCs). PBMCs were stimulated with overlapping peptides of SARS-CoV-2 spike (S)- and nucleocapsid (N)- as well as HCoV-OC43 spike proteins (OC43). Spot forming cells (SFC), i.e. cells responding to specific stimulation with IFNgamma production, were measured. Information on household exposures were collected using an electronic questionnaire sent to participants.

RESULTS
Between October and December 2020, 28 CASES and 14 CONTROLS were included. All tested SARS-CoV-2 seronegative. At a cut-off of >50 SFC, 10/28 (35%) of CASES had either S- or N- specific T cells compared to 7/14 (50%) of CONTROLS ($p = 0.9$). In terms of HCoV-OC43 responses, PBMCs from 15/58 (54%) of CASES and 11/14 (79%) CONTROLS exhibited SFC above the cut-off ($p = 0.7$). 8/28 (29%) of CASES and 3/14 (21%) of CONTROLS had no SFC after stimulation with peptides.

CONCLUSION
About 35-50% of seronegative participants who were either household exposed or unexposed to COVID-19 showed SARS-CoV-2 specific T cells. More than half of all participants had HCoV-43 specific T cells. There was no difference between CASES and CONTROLS, so “silent” immunisation against SARS-CoV-2 cannot be demonstrated in the CASES. However, the results suggest the presence of a background T-cell immunity to the current pandemic coronavirus, which may contribute to protection against severe COVID-19 infection.

P68

Novel ERG11 and TAC1b mutations associated with azole resistance in Candida auris

J Li; AT Coste; L Maroussia; D Bachmann; D Sanglard; F Lamoth
CHUV - Hôpital universitaire

Aims
Candida auris is a novel Candida spp. that has spread in all continents causing nosocomial outbreaks of invasive candidiasis. C. auris has the ability to develop resistance to all antifungal drug classes. Notably, most C. auris isolates are resistant to the azole drug fluconazole, a standard therapy of invasive candidiasis.
Azole resistance in C. auris can result from mutations in the azole target gene ERG11 and/or overexpression of the efflux pump Cdr1. TAC1 is a transcription factor controlling CDR1 expression in C. albicans. The role of TAC1 homologs in C. auris (TAC1a and TAC1b) remains to be better defined.

Methods
In this study, we compared sequences of ERG11, TAC1a and TAC1b between a fluconazole-susceptible and five fluconazole-resistant C. auris isolates of clade IV. We effectuated gene manipulation by CRISPR-Cas9: we deleted TAC1a/TAC1b and introduced mutations of TAC1b or ERG11. Azole susceptibility of wild-types and mutants was determined by the procedure of the Clinical and Laboratory Standards Institute(CLSI) or spotting assay. CDR1 expression was detemined by Quantitative reverse transcription PCR (RT-qPCR).

Results
Among four of the fluconazole-resistant isolates, we identified a similar genotype with concomitant mutations in ERG11 (F444L) and TAC1b (S611P). The simultaneous deletion of tandemly arranged TAC1a/TAC1b resulted in a significant decrease of minimal inhibitory concentration (MIC) for fluconazole. Introduction of the ERG11 and TAC1b mutations separately and/or combined in the wild-type azole susceptible isolate resulted in a significant increase of azole resistance with a cumulative effect of the two combined mutations. Interestingly, CDR1 expression was not significantly affected by TAC1a/TAC1b deletion or by the presence of the TAC1b S611P mutation, suggesting the existence of Tac1-dependent and Cdr1-independent azole resistance mechanisms.

Conclusion
We demonstrated the role of two previously unreported mutations responsible for azole resistance in C. auris, which were a common signature among azole-resistant isolates of clade IV.

P69

Questionable positive predictive value of COVID-19 rapid antigen test: a real life experience

R Thoma[1]; P Kohler[1]; J Sumer[1]; M Schlegel[1]; G Dollenmaier[2]; O Nolte[2]
[1] Kantonsspital St. Gallen; [2] Center for Laboratory Medicine

Background and Aims
The use of rapid antigen tests (RAT) for the diagnosis of COVID-19 has been questioned because of their lower sensitivity compared to PCR, test specificity is less of an issue. Shortly after introduction of the Roche/SD Biosensor SARS-CoV-2 RAT in our tertiary care centre in October 2020, we observed discordant (RAT+/PCR-) test results in several patients. We aimed to assess the positive predictive value (PPV) and to identify patient- and laboratory factors associated with discordant results.

Methods
From November 8th to December 20th 2020, we prospectively collected all positive RAT results and performed a control-PCR on the same sample. Patient records and clinical status were evaluated and, whenever possible, a second pair (RAT and PCR) of nasopharyngeal samples was taken in patients with a discordant result. Additionally, SARS-CoV-2 serology was performed in these patients when feasible, at least 2 weeks after symptom onset or positive testing, whichever came first. Antigen-testing was performed according to the manufacturers instructions. RT-PCR targets were sequences of the SARS-CoV-2 E-, RdRP- and the human RNAse P gene based on published protocols by Corman et al. (2020).

Results
We performed 1230 RATs in the described time period, whereof 160 (13%) were positive. Thereof, 45 patients revealed a negative PCR result on the same sample, whereof 2 were considered false negative. Among the other 43 patients, 19 had a follow-up sample within 7 days, all of which were negative. All SARS-CoV-2 serologies (n = 11) remained negative. Factors associated with a discordant test result were younger age, pregnancy, being asymptomatic and diagnosis upon hospital admission. No differences in turnaround time between concordant (RAT+/PCR+, n = 34) and discordant (RAT+/PCR-, n = 31) test results were detected. PPV of the RAT was 80% in symptomatic- and 27% in asymptomatic patients.

Discussion
A considerable proportion of RAT was false positive in our hospital. We suspect this is mostly due to screening of asymptomatic patients which is not recommended by the manufacturer. False positive results lead to unnecessary isolation of patients putting further strain on the healthcare system and society.

P70

Tick-borne encephalitis affects sleep-wake behavior and loco-motion in infant rats

G Chiffi[1]; D Grandgirard[1]; S Stöckli[1]; L Valente[1]; A Adamantidis[2]; C Bassetti[2]; S Leib[1]
[1] Institute for Infectious Diseases, University of Bern, Bern, Switzerland; [2] Department of Neurology, Inselspital, Bern University Hospital, University of Bern, Switzerland

Background/Aims
Tick-borne encephalitis (TBE) is a disease affecting the central nervous system. Over the last decade, the incidence of TBE has dramatically increased in Switzerland despite the availably of effective vaccines. Up to 50% of patients after TBE suffer from post-encephalitic syndrome that may develop into long-lasting morbidity. Altered sleep-wake functions, are reported by patients after TBE. The mechanisms causing these disorders in TBE are largely unknown to date. In the present study, we determined parameters of locomotor functions and sleep structure in an established infant rat model of TBE.

Methods
13 days old Wistar rats were infected with 1 x 10^6 FFU Langat virus (LGTV). At day 4, 9 and 21 post infection, Rotarod (balance and motor coordination) and open field tests (general locomotor activity) were performed three times at each time point. At these different timepoints, subgroups of animals were euthanized, and brains were collected. At day 28 the animals were implanted with a wireless EEG/EMG system (Kaha Science). Sleep recording was continuously performed for three consecutive days starting at day 38 post infection and visually scored for Wake, NREM and REM in 4 seconds epochs.

Results
The infection with the LGTV was confirmed by rt-qPCR in the forebrain, the midbrain as well as the cerebellum of the infected animals. LGTV-infected animals showed a reduced rotarod performance ability at day 4 (n_Inf= 28, n_Cont= 27; p = 0.0039) and day 9 (n_Inf= 22, n_Cont= 20; p = 0.0055) and day 21 (n_Inf= 14, n_Cont= 15; p = 0.0037). A lower locomotor activity was also seen at day 4 (n_both= 24, p = 0.029), day 9 (n_both = 20, p = 0.0013) and day 21 (n_Inf = 14, n_Cont = 14; p = 0.049). Furthermore, infected animals (n= 10) showed a significant larger percentage of time spend awake during the dark phase and less NREM and REM compared to the control animals (n = 8, $p < 0.01$ for all comparisons).

Conclusion
Our data show that experimental TBE in infant rats leads to decreased spontaneous locomotor-activity, impaired moto-coordinative function and affects sleep macrostructure.

P71

Performance of anti-SARS-CoV-2 antibody titers and kinetics in predicting the severity of COVID-19 outcomes.

A Kritikos[1]; S Gabellon[2]; J Pagani[3]; M Monti[4]; P Bochud[2]; A Coste[5]; A Croxatto[5]; F Lamoth[1]
[1] Infectious Diseases Service and Microbiology Institute of Lausanne University Hospital (CHUV); [2] Infectious Diseases Service of Lausanne University Hospital (CHUV); [3] Intensive Care Unit, Lausanne University Hospital (CHUV); [4] Service of Internal Medicine, Lausanne University Hospital (CHUV); [5] Microbiology Institute of Lausanne University Hospital (CHUV)

Background
Coronavirus disease 2019 (COVID-19) due to SARS-CoV-2 is associated with a wide spectrum of disease, ranging from asymptomatic infection to acute respiratory distress syndrome. Some biomarkers may predict disease severity. Among them, the importance of the anti-SARS-CoV-2 antibody response has been suggested as an indicator of severe disease. The aim of this study was to assess the correlation between anti-SARS-CoV-2 serological response and COVID-19 outcome.

Methods
Demographic, clinical and biological data from nasopharyngeal-PCR confirmed COVID-19 hospitalized patients have been prospectively collected between april and august 2020 in our institution. All patients had serial weekly serology testing starting from the day of inclusion and up to 14 days from admission or hospital discharge, using the chemiluminescent Liaison® XL (Diasorin, Italy) IgG kit. Kinetics of the serological response and correlation between antibody titers and outcome (i.e. requirement of invasive mechanical ventilation versus no) was assessed.

Results
Among the 70 patients enrolled in the study, 22 required invasive ventilation (11 of them admitted directly or already intubated on admission), 29 required non-invasive ventilation or oxygen supplementation and 19 did not require any oxygen supplementation. The average duration of symptoms upon admission for the three groups were 13, 9 and 8 days respectively. The sensitivity of IgG response within the first 15 days from symptom onset was 66% (95% CI 54-77), rising to 92% (95% CI 64-99) in patients presented after 15 days of symptoms. A significant increase of antibody response was observed within the first 3 weeks from symptom onset in patients requiring invasive mechanical ventilation or oxygen supplementation, but not among patients without oxygen requirement. (figure 1). Antibody titers on admission were significantly higher in critically ill patients (figure 2) and could predict the need of invasive mechanical ventilation with an area under the curve (AUC) of 0.8 (95% confidence interval: 0.64-0.9). An IgG threshold of 46.8UA/ml showed sensitivity, specificity, positive and negative predictive values of 82%, 82%, 78% and 85% for predicting the subsequent need of invasive mechanical ventilation.

Conclusion
Serology testing at admission and in follow-up may be a good indicator to identify severe COVID-19 patients who will require invasive mechanical ventilation.

P72

Increasing Morbidity and Mortality of Candidemia over Two Decades in a Swiss University Hospital

J Battistolo[1]; E Glampedakis[1]; L Damonti[1]; J Poissy[2]; B Grandbastien[1]; L Kalbermatter[1]; J Pagani[1]; P Eggimann[1]; P Bochud[1]; T Calandra[1]; O Marchetti[3]; F Lamoth[1]
[1] CHUV Centre hospitalier universitaire vaudois; [2] University Hospital Centre, Lille University; [3] Ensemble Hospitalier de la Côte

Aims
Candidemia is the most frequent nosocomial fungal infection. Its epidemiology is evolving with raising concern about the emergence of intrinsically resistant non-albicans Candida species and acquired antifungal resistance. Most candidemia surveys are based on microbiological databases. Epidemiological studies including demographic and clinical data are needed to assess the impact of candidemia on morbidity and mortality. The aim of this study was to assess the clinical and microbiological trends of candidemia in a Swiss university hospital over two decades.

Methods
This single-center retrospective study compared the incidence of candidemia, Candida species distribution, antifungal resistance profiles, clinical characteristics, and outcomes between two periods separated by one decade.

Results
170 candidemic episodes were included (68 from period 1, 2004-2006, and 102 from period 2, 2014-2017). Incidence of candidemia (0.9 to 1 episode/ 10000 patient-days), Candida species distribution (C. albicans 57% to 55%) and antifungal resistance rates (< 3%) remained unchanged over time. However, a significant demographic evolution was observed in period 2 with candidemia occurring more frequently in older patients and in the intensive care units (ICU). The impact of candidemia on morbidity and mortality also evolved with higher proportions of patients with septic shock (23% vs 7%, $p = 0.01$), subsequent need for ICU admission (42% vs 12%, $p < 0.01$) and in-hospital mortality (34% vs 18%, $p = 0.03$) in period 2 compared to period 1.

Conclusion
Despite stable incidence, species distribution, and antifungal resistance of candidemia over two decades, the shift towards older and critically ill populations resulted in increased morbidity and mortality.

P73 - Abstract withdrawn

P74

Sensitivity of rapid antigen testing and RT-PCR performed on nasopharyngeal swabs versus saliva samples in COVID-19 hospitalized patients: results of a prospective comparative trial (RESTART).

A Kritikos[1]; G Caruana[1]; R Brouillet[1]; J Miroz[2]; S Abed-Maillard[2]; G Stieger[2]; O Opota[1]; A Croxatto[1]; P Vollenweider[3]; P Bart[3]; J Chiche[2]; G Greub[1]
[1] Institute of Microbiology, Department of Laboratory Medicine, Lausanne University Hospital (CHUV); [2] Intensive Care Unit, Lausanne University Hospital (CHUV); [3] Service of Internal Medicine, Lausanne University Hospital (CHUV)

Background
During the current SARS-CoV-2 pandemics, huge number of tests have been performed. Rapid antigen testing (RAT) might help to mitigate the shortage of reagents sporadically encountered with RT-PCR while saliva sampling could serve as an alternative noninvasive sample. In the RESTART study we compare antigen and RT-PCR testing methods on nasopharyngeal (NP) swabs and salivary samples.

Methods
We conducted a prospective observational study among COVID-19 hospitalized patients between 10th December 2020 and 1st February 2021. Paired saliva and NP samples were investigated by RT-PCR (Cobas 6800, Roche) and by two rapid antigen tests: One Step Immunoassay Exdia COVID-19 Ag (Precision Biosensor, Korea) and Standard Q® COVID-19 Rapid Antigen Test (Roche – Switzerland). Sensitivities of the above-mentioned tests were compared to a gold standard considering a positive result on either NP swab or saliva sample.

Results
A total of 58 paired NP-saliva specimens were collected. Thirty-two of 58 (55%) patients were hospitalized in the intensive care unit and the median duration of symptoms was 11 days (IQR 5-19). NP and salivary RT-PCR exhibited sensitivity of 98% and 69% respectively whereas the specificity of these RT-PCRs assays were of 100% (Table 1). Interestingly, the viral load measured by RT-PCR from NP specimens was significantly higher than that detected on salivary swabs for up to 20 days since symptoms onset (Figure 1). RAT exhibited much lower diagnostic performances with sensitivities of 41% and 35% for the Exdia and Standard Q assays, respectively in hospitalized patients when a wet-swab approach was used (i.e when the swab was diluted in the viral transport medium (VTM) before testing). Noteworthy, the sensitivity of the dry-swab approach was slightly better, suggesting that the dilution in the VTM is not fully compensated by a better release of viral particles from the swab. These antigen tests exhibited very low sensitivity of 8% and 4% for Exdia and Standard Q assays, respectively, when applied to salivary swabs.

Conclusions
Nasopharyngeal RT-PCR is the most accurate test for COVID-19 diagnosis in hospitalized patients. RT-PCR on salivary samples may be used when nasopharyngeal swabs are contraindicated. RAT are not appropriate for hospitalized patients.

P75

A simple phage – antibiotic synergy testing assay against Klebsiella pneumoniae

R Sierra[1]; M Roch[2]; J Prados[2]; W Brasileiro Martins[3]; D Andrey[1]
[1] Geneva University Hospitals and Medical School; [2] Université de Genève; [3] Cardiff University

Aims
Carbapenem-resistant Klebsiella pneumoniae is a leading cause of healthcare-related infections with crude mortality rates for bacteremia reaching 50% [1,2]. K. pneumoniae high-risk clones (ST258/512, ST11, ST37, ST307, ST101 or ST15), often producing carbapenemases, have become endemic worldwide[3-5]. In this context phage therapy has regained a strong interest [6-8]. Only limited examples of phage therapy against K. pneumoniae infections are reported [9, 10], very few being clinical trials [11-13]. Since phage-resistant K. pneumoniae emergence under phage treatment is likely, phage-antibiotics combinations seem warranted [14,15]. The optimal modalities of phage-antibiotic administration remain unclear and need to be studied to address potential antagonisms or synergisms effects, between phage and antibiotics [16]. Here we propose an assay to test phage-antibiotics combinations in vitro.

Methods and Results
We developed a simple phage-antibiotic synergism (Φ:Ab Synergism) in vitro assay, performed in 96-well plates where Klebsiella is challenged against phages (1:10) and antibiotics (1:2) serial dilutions. Growth curve data, obtained on a plate reader, are analysed to obtain the AUC and thus determine the synergic potential. Different bacterial inoculum and phage concentrations were tested. We opted for a bacterial concentration of 2 MacFarland, with growth curves showing an initial drop in O.D., due to (phage infection and progeny release), generally followed by a take-over of bacterial growth. Three phage concentrations were selected. AUC's were preferred over final OD to account for the full growth dynamic. This analysis leads to classify the combination as: (1) neutral: no effect or lack of effectiveness by both agents, (2) additive: the sum of their individual effects is equal to their combinatorial efficacy, (3) synergistic: their combinatorial efficacy is greater than their individual effects, and (4) antagonistic: one agent interferes with the other.

Conclusion
As an example, phage PWKp9B (Drulisviridae), showed lytic activity against the ST16 K. pneumoniae strain HSP80, colistin-resistant (MIC 64mg/L), KPC-producing (meropenem MIC 128 mg/L), harbouring capsule type KL51. A synergic effect when challenged with colistin was observed, reducing colistin MIC by 6 two-fold dilutions. We believe this pre-clinical information might become of paramount importance to guide the clinician at the time of (experimental) phagotherapy.

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Using the WHO verbal autopsy instrument to facilitate routine cause of death monitoring in the Context of COVID-19.

A Di Pasquale[1]; J Leitao[2]; E Nichols[3]
[1] Swiss TPH; [2] WHO; [3] Centers for Disease Control and Prevention

Introduction
Verbal autopsy (VA) is a systematic approach for determining individuals' causes of death in populations without a complete vital registration system. It consists of lengthy interviews to collect information about the signs, symptoms, and other characteristics of a deceased person.

Aim
Our objective here is to describe the process used to implement, and standardise the WHO VA instrument using an electronic data collection system in the Context of COVID-19.

Methods
Mobile devices used for electronic data collection (EDC), and adoption of data management best practices using ODK survey software have the potential to resolve many of the major shortcomings of running a paper data collection (PDC) surveys. The WHO 2016 VA instrument (compatible with publicly available analytical software for assigning the cause of death) was translated in EDC format and used in different countries and settings to collect the data requested using Android devices through the ODK software. ODK allowed the implementation of skips logic, relevancies and constraints needed to ensure the robustness of the instrument and the easy use of it from non IT skilled fieldworkers. ODK allows the possibility to localize the instrument (e.g. language, country specific variables), maintaining core questions and functionality of the master VA instrument. After data collection, we assessed the time required for data collection and the completeness of the data feeding the analytical software for analysis available. A set of questions to identify COVID-19 deaths has been included in the ODK 2016 WHO VA instrument, and guidance on the new questions added in the VA Field Interviewer Manual). Additionally, considerations for the use of VA in the context of COVID-19 have been added to the WHO VA standards manual.

Results
Time to availability of a record is reduced with ODK on average 20 minutes for a questionnaire than with paper forms. It is possible to estimate COVID 19 evolution in countries where the structure of the health system is not able to obtain data from remote areas.

Conclusion
EDC addresses some problems posed by PDC through validation at data collection time, near real time data to the central database, automated review protocols, reports for managers allowing near real time review and processes. EDC can improve quality, timeliness, and costs. VA can fill a critical gap in measuring the mortality from COVID-19 for deaths which occur outside of a healthcare setting.

P77

Trained immunity confers prolonged protection against systemic listeriosis

T Roger; T Heinonen; E Ciarlo; C Théroude; I Schrijver; F Pralong; M Reverté Royo; D Leroy
Lausanne University Hospital and University of Lausanne, Switzerland

Background
Trained immunity characterizes the capacity of memory of the innate immune system. Induction of trained immunity is associated with epigenetic, metabolic and functional reprograming of innate immune cells as well as hematopoietic stems cells (HSCs). We reported that trained immunity protects from lethal bacterial sepsis (Ciarlo, JID 2020), but the length of the protection remains unknown.

Aim
To determine whether trained immunity confers prolonged protection from lethal infection.

Methods
Mice (n=8-9/group) were trained with b-glucan and challenged 9 weeks later with Listeria monocytogenes. Mice were analyzed by bioluminescence imaging. Blood, bone-marrow, liver and spleen were collected to quantify HSCs, leukocytes (flow cytometry), bacteria, metabolic and antimicrobial activity (SeaHorse and killing assay), and injury (histological examination).

Results
Control mice were bacteremic and died from listeriosis, while mice trained 9 weeks earlier controlled bacterial burden and survived infection ($P < 0.001$). Trained mice showed lower inflammation (bioluminescence imaging, systemic cytokines) and liver injury. Listeriosis induced the depletion of blood leukocytes, which was counterbalanced by trained immunity. Trained mice had increased myelopoiesis, and their blood contained 2-fold more Ly6Chigh monocytes and neutrophils ($P < 0.001$), produced more G-CSF, IFNγ, IL-1α, IL-1β, IL-6, IL-10, TNF and CXCL2 in response to LPS, and controlled better the growth of L. monocytogenes. Monocytes and neutrophils showed enhanced glycolytic activity.

Discussion
These results suggest long-lasting protection afforded by trained immunity against lethal listeriosis. We are running experiments to better define the window of protection conferred by trained immunity.

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Clinic attendance, incidence of STIs and attendee's satisfaction in a non-risk-group focused anonymous STI testing site in Switzerland

D Bigler[1]; C Hauser[2]; B Surial[1]; T Konrad[1]; H Furrer[1]; A Rauch[1]; K Aebi-Popp[1]
[1] Inselspital - Universitätsspital Bern; [2] Praxis / Lindenhofspital

Introduction
In Switzerland, the best known locations for anonymous STI testing are checkpoints focusing on MSM. Many people with STI risk behaviors do not attend if asymptomatic. The Bern University Hospital offers since 2016 anonymous STI testing not focused on specific risk groups. We report prevalence of attendance, incidence of STIs and our attendees' service preferences according to a satisfaction questionnaire.

Methods
Between Jan 1st 2016 and Dec 31st 2019, 5402 women and men aged 17–82 (median 33.5) years attended our sexual health clinic. Participants were interviewed with computer-based self-completion questionnaires. Pooled (oral, genital, anal) swabs were tested for Chlamydia trachomatis, Neisseria gonorrhoeae, blood samples were tested for Syphilis (TPHA, VDRL) and HIV (4th Gen. Ab/Ag Test). We describe numbers of visits per year, number of STIs in relation to demographic and behavioral factors and explore client satisfaction by a questionnaire filled in by 175 clients.

Results
Overall, attendance/visit number has increased by 36% from 2017 to 2018 and by 12.9% from 2018 to 2019, and was highest among young clients (47.2% 25-34 years) and heterosexuals (58%). Two third of clients were seeking STI testing because of a new partnership or as routine screening, and 44% (2392/5402) reported unprotected sex or condom failure in the last 6 months. 5044 participants provided swabs and blood samples. Over 3 years, 191 infections with Chlamydia were diagnosed (3.8%) in 89 women (46.6%) and 101 men (52.9%). Gonorrhea was diagnosed in 54 individuals (1.1%), of whom 81.5% were men and 18.5% women. One third of all individuals with gonorrhea were heterosexual.
52/5125 (0.8%) had an active Syphilis infection requiring antibiotic treatment, 71% of those identifying as MSM. Higher number of partners, a history of a bacterial STI and sex without condoms were risk factors for an asymptomatic STI. Overall, 4 clients (4/7123, 0.06%) were newly diagnosed with HIV (3 females, 1 male, all heteroxexual).
The most important factor for client satisfaction was a low threshold offer for STI testing via website and individual counseling about pathogens and risk factors during their appointment.

Discussion
Particularly younger clients and heterosexuals were using our sexual health service. Easily accessible, low threshold service provision is needed to engage clients and ensure that they can attend services appropriate to their needs.

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Impact of 2020 EUCAST criteria on meropenem prescription for the treatment of Pseudomonas aeruginosa infections: an observational study in a university hospital

A Munting[1]; J Regina; J Damas[2]; L Lhopitallier[3]; A Kritikos[2]; B Guery[4]; L Senn[5]; B VIALA[6]
[1] CHUV Centre Hospitalier Universitaire Vaudois (CHUV); [2] Lausanne University Hospital (CHUV) and University of Lausanne (UNIL); [3] Centre Hospitalier Universitaire Vaudois (CHUV); [4] Lausanne University Hospital (CHUV); [5] CHUV Centre hospitalier universitaire vaudois; [6] CHUV - University Hospital

Objectives
We aim to evaluate the impact of the 10th version of European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints table, where most antipseudomonal drugs but meropenem are now categorised as “Susceptible, increased exposure” and labelled I, on meropenem prescriptions for Pseudomonas aeruginosa infections.

Methods
In this retrospective single-centre observational study, we analysed antimicrobial therapies prescribed after susceptibility testing in all consecutive adult patients treated for P. aeruginosa infections between 01.08.2019 and 30.07.2020 in Lausanne University Hospital, Switzerland. We collected epidemiological, microbiological, clinical data, antimicrobial therapy, and infectious diseases specialists (IDS) consultations data.
The primary outcome was the prescription of meropenem to treat P. aeruginosa infections after release of susceptibility testing results. Secondary outcomes were: the use of increased dosage for non-meropenem anti-pseudomonal drugs, and IDS consultations rates after susceptibility testing was made available.

Results
Among the 264 patients included, 40 (15.2%) received meropenem, 3.4% (5/148) before EUCAST update versus 30.2% (35/116) after ($p<0.001$). Multivariate regression showed that new EUCAST criteria might be associated with increased odds of meropenem prescription (odds ratio 22.12, 95% CI [7.96 - 79.52], $P<0.001$), whereas, IDS consultation seemed to be associated with decreased odds of meropenem prescription (odds ratio 0.20, 95% CI [0.07 - 0.49], $P=0.001$).

Conclusions
The change to 2020 EUCAST criteria might be associated with increased odds of meropenem prescription for the treatment of P. aeruginosa infections. IDS consultations seemed to be associated with lower proportion of meropenem prescriptions.

P80

Early mortality prediction of COVID-19 patients: clinical scores, biomarkers or both?

M Van Singer[1]; T Brahier[2]; M Brochu Vez[1]; H Gerhard Donnet[1]; O Hugli[1]; N Boillat Blanco[3]
[1] University Hospital of Lausanne, Switzerland; [2] Hôpital Neuchâtelois; [3] Lausanne University Hospital, Switzerland

Aims
COVID-19 has been overwhelming health care system over the world. Identification of patients at risk of death can support allocation of medical resources to the right patients. We sought to assess the predictive accuracy of clinical scores and biomarkers at clinical presentation to the emergency department (ED) for early mortality.

Methods
Prospective observational study of PCR-confirmed COVID-19 patients in the ED of a Swiss hospital. Clinical parameters and concentration of pancreatic stone protein (PSP) and C-reactive protein (CRP) were determined at admission. We evaluated the accuracy of a clinical severity score (CRB-65), biomarkers and their combination in predicting 7-day mortality by calculating the area under the receiver-operating characteristic curve (AUROC) and by classification and regression tree analysis (CRT).

Results
Of the 173 patients included, 12 (6.9%) died by day 7. The predicting accuracy of CRB-65 (AUROC 0.87; CI 0.79 – 0.95), CRP (AUROC 0.83; CI 0.79 – 0.93) and PSP (AUROC 0.83; CI 0.74 – 0.92) for 7-day mortality were excellent and did not differ significantly. Combining CRP and PSP did not improve the performance (AUROC 0.90; CI 0.84-0.97). Combination of CRB-65 and PSP performed better than the clinical score or biomarker alone (AUROC 0.95; CI 0.91-0.98; p=0.03 and p=0.01, respectively). Combination of CRB-65 and CRP (AUROC 0.95; CI 0.90-0.99) had a similar performance.
An algorithm generated by CRT based on CRB-65 (≥2 points) and CRP (≥134 mg/l) predicted mortality with a sensitivity of 67% (95%CI 35%-90%), specificity of 98% (94%-99%), and positive/ negative predictive value of 67% (41%-85%) and 98% (95%-99%), respectively. CRB-65 (≥2 points) alone had a sensitivity of 75% (43%-95%), specificity of 89% (82%-92%) and a positive/ negative predictive value of 33% (22%-46%) and 98% (95%-99%), respectively.

Conclusion
CRB-65, CRP and PSP in the ED have an excellent and similar predictive accuracy for early mortality in COVID-19. The accuracy is improved by combining the score and a biomarker. However, there is no added value of a clinical score-biomarker combination over a clinical score alone for the use as a triage tool as the negative predictive value is excellent in both cases.

P81

Surveillance des eaux de dialyse lors de la délocalisation du Service de dialyse aigue du CHUV en période Covid

A Lacot
CHUV Centre hospitalier universitaire vaudois

Introduction / objectif
Lors des 2 premières vagues de Covid-19, l'augmentation importante des patients admis aux urgences, dans le service de médecine intensive et en médecine interne a nécessité une restructuration de tout l'hôpital avec la création de nouvelles unités. Dans ce contexte, par 2 fois, le service de dialyse aigue a dû libérer ses locaux habituels. Nous nous sommes intéressés à la qualité de l'eau de dialyse dans le nouveau secteur attribué à la dialyse aiguë lors du mois de novembre 2020.

Méthodes
Si le secteur d'accueil provisoire de l'activité de dialyse aiguë disposait d'une boucle d'eau osmosée, celle-ci était insuffisante pour l'activité et a été complétée par des osmoseurs mobiles. Conformément aux Bonnes Pratiques Européennes en Hémodialyse qui recommandent une surveillance mensuelle, l'eau de dialyse sur chacune des arrivées de la boucle et de chaque osmoseur mobile a été contrôlée pour vérifier ses qualités chimiques (concentrations maximales en Ca, Mg, K et Na, présence d'éventuels toxiques) et microbiologiques (endotoxines, flore mésophile).

Résultats
Les prélèvements effectués le 03.11.2020 ont montré que la boucle fixe fournissait de l'eau purifiée dont la qualité était dans les normes européennes exigées pour l'hémodialyse (germes mésophiles : < 0.05 cfu/ml [norme : < 100 cfu/ml], endotoxine : 0.007 EU/ml [norme : < 0.25 EU/ml]). Par contre, l'eau n'était pas de qualité suffisante pour l'HDF (1.55 cfu/ml sur une des sorties [norme : < 0.1 cfu/ml]). Un des osmoseurs mobile, connecté à 3 postes de dialyse s'est avéré être également non conforme.

Conclusion
Le déménagement d'un secteur de dialyse aiguë est une opération à risque. Elle nécessite une parfaite connaissance de la distribution d'eau et un contrôle a priori de ses qualités chimiques et microbiologiques. L'usage éventuel d'osmoseurs mobiles exige le même niveau de surveillance.
Les difficultés rencontrées à cette occasion militent pour que le service de dialyse soit le moins possible impacté par les réorganisations de l'hôpital en situation de crise Covid. Les non-conformités ont eu un impact significatif sur l'organisation des dialyses et sur les ressources humaines dans une période déjà fortement impactée par la pandémie.

P82

Plasmid transmission in patients colonized with more than one bacterial species harboring extended spectrum beta-lactamases

L Aguilar-Bultet[1]; L Maurer Pekerman[1]; R Schindler[1]; R Stadler[1]; I Vock[1]; T Stadler[2]; A Egli[1]; S Tschudin-Sutter[3]
[1] University Hospital Basel; [2] ETH Zurich - Basel; [3] University Hospital Basel and University of Basel

Aims
Horizontal gene transfer by plasmid transmission is common between bacteria occupying similar ecological niches. The chance of plasmid transfer increases among bacteria belonging to closely related phylogenetic groups. Knowledge on the frequency of plasmid-transfer occurring within patients colonized with Extended-Spectrum Beta-Lactamase (ESBL)-producing Enterobacterales (ESBL-PE), remains elusive, despite its importance for understanding the current epidemiology of ESBL-PE and for tailoring infection prevention and control strategies. We therefore sought to identify ESBL-plasmid transmission events between different bacterial species among hospitalized patients colonized with ESBL-PE.

Methods
Patients hospitalized at the University Hospital Basel, Switzerland from 01/2004-05/2019 and colonized with more than one bacterial species of ESBL-PE were eligible for study inclusion. All isolates underwent whole genome sequencing by Illumina NextSeq500/550, and putative plasmid transmission was assessed based on the presence of the same replicon types and common resistance genes. At least two elements (one being an ESBL gene) needed to be present in two different species to be tagged as a putative ESBL transmission case. ESBL-transmission was considered “likely”, when confirmed by the analysis of the long-read sequencing data obtained for one of the isolates of each patient by Oxford Nanopore Technologies (GridION).

Results
Among 1572 consecutive patients, 103 were colonized with more than one species of ESBL-PE. Based on short-read sequencing data, we identified 31 putative ESBL plasmid transmission events. The presence of the same plasmid was corroborated in 19 cases by long-read sequencing of one of the isolates and mapping the contigs to it. This accounts for 18.4% of all patients carrying multiple bacterial species. In five cases the ESBL-genes were likely located on the chromosome, ruling out ESBL-plasmid transmission despite the presence of the same ESBL-gene in the other colonizing ESBL-PE-species. Plasmid-transmission most commonly occurred between Escherichia coli and Klebsiella pneumoniae and most frequently involved IncF-like plasmids and CTX-M-15 gene.

Conclusions
ESBL-plasmid transmission may have contributed to colonization with different ESBL-PE species in up to fifth part of patients, enhancing the likelihood of plasmid persistence in the host, as well as subsequent spread.

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Les établissements médico sociaux sont-ils des milieux à risque de transmission de Staphylococcus aureus méticilline résistant ?

F Battistella
CHUV Centre hospitalier universitaire vaudois

Introduction/Objectif du travail
La présence du Staphylocoque aureus résistant à la méticilline (SARM) dans les établissements Médico Sociaux (EMS) est directement lié aux comorbidités des résidents et à l'utilisation fréquente d'antibiotiques.
La promiscuité entre résidents dans les EMS et le manque d'observance du personnel aux Précautions Standard (PS) peuvent être à l'origine de la propagation des bactéries multi résistantes.
Une étude menée en 2010-2011 par l'UHPCi avait permis de démontrer que l'observance aux PS était suffisante pour limiter le risque de transmission du SARM dans les EMS et de nouvelles recommandations de prise en charge basées sur l'application des PS ont été émises par l'UHPCI. Conjointement à ces nouvelles recommandations, une surveillance de ce germe a été instaurée à l'admission en soins aigus des résidents provenant des EMS. En 2019, on observe une augmentation du nombre de nouveaux cas de SARM chez les résidents à l'admission en soins aigus. L'objectif de ce travail est d'analyser tous les nouveaux cas SARM provenant des EMS et admis en soins aigus

Matériels et méthodes
Tous les prélèvements positifs pour SARM (frottis nez, gorge et plis inguinaux, ou autre prélèvements cliniques) nous sont systématiquement signalés (alerte automatisée) par les laboratoires du CHUV. Une revue du dossier du patient à la recherche de facteurs de risque (lieu de résidence du patient, hospitalisations antérieures, comorbidités, présence d'une infection, sexe, âge) est effectuée.

Résultats
Un collectif de 35 nouveaux cas SARM ont été recensés sur une période de 27 mois, dont 23 les 12 premiers mois, 7 les 12 mois suivants et 5 les 3 derniers mois. Dans 6% (2/35) des cas : présence d'une infection à SARM à l'admission.
Comme facteurs de risque : 1 dialysé ; 5 porteurs de sonde vésicale ; 5 avec des plaies chroniques et 14 avec plus de 2 hospitalisations dans l'année précédente. Comme lieu de provenance : 11 EMS avec 1 seul résident SARM positifs, 5 EMS avec chacun 2 résidents SARM positifs et 3 EMS respectivement 3, 4 et 6 résidents SARM positifs.

Discussion/conclusion
Dans notre petit collectif, la présence de résidents porteurs de SARM dans l'EMS n'est pas un facteur de risque significatif d'acquisition du SARM dans ce type de milieu. Cependant, au vu du petit collectif, cette surveillance doit être poursuivie pour confirmer notre observation.

P84

New mode of transmission of healthcare-associated pathogens by the shoes of healthcare workers? A prospective cohort study.

AC Büchler; M Wicki Jauslin; R Frei; V Hinic; HM Seth-Smith; A Egli; AF Widmer
University Hospital Basel

Background
The aim of this study was to evaluate the potential of transmission of toxigenic Clostridioides difficile (C. difficile) and vancomycin-resistant enterococci (VRE) by contaminated shoe soles of healthcare workers (HCWs) on general hospital wards.

Methods
We conducted a prospective cohort study at a university tertiary care center in Switzerland. From October 2019 to July 2020, HCWs' shoe soles were cultured for C. difficile or VRE twice per shift while taking care of a patient infected or colonized with one of those two study microorganisms. Additional risk factors were assessed by interviewing the HCWs. Patient's samples were analyzed by routine microbiological methods. Similarity of the HCWs' and patients' isolates was analyzed by whole genome sequencing (WGS).

Results
137 HCWs exposed to 47 hospitalized patients participated in the study, providing 274 samples. Contamination of shoe soles with C. difficile was detected in 37/206 samples (17.8%) of HCWs taking care of patients infected with C. difficile and with VRE in 9/68 samples (13.2%) of HCWs taking care of patients colonized with VRE. Matching strains from patients' and HCWs' isolates were confirmed by WGS in 26/35 isolates (74.3%, two samples not analyzed) with C. difficile and 4/9 isolates (44.4%) with VRE.

Conclusions
Our results demonstrate proof of concept of transmission of C. difficile and VRE by contaminated shoe soles with epidemiological link and supported by matching strains confirmed by WGS. These results should prompt a larger prospective clinical study to estimate the importance of this transmission mode in the epidemiology of healthcare-associated pathogens.

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Outbreaks of seasonal OC43 Coronavirus with nosocomial transmission during COVID-19 pandemic setting: when a coronavirus hides another.

E Moulin; E Kampouri; E Glampedakis; M Gyger Wanzenried; E Gilles de Pélichy; O Opota; L Senn
CHUV Centre Hospitalier Universitaire Vaudois (CHUV)

Aims
To describe control measures and investigations applied over 2 consecutive clusters of patients presenting suspect symptoms of Covid-19 in a 19-bed psychogeriatric unit, hosting concomitantly 2 patients with SARS-CoV-2 infection confirmed by RT-PCR on nasopharyngeal swabs (lineage B.1.1.7, viral loads of 6.9E+8 and 8.0E+7 copies/ml, respectively) among whom one was a nosocomial case with severe clinical course and persistence of a high viral load at day 14 (8.9E+6 copies/ml).

Methods
After identification of the SARS-CoV-2 cases on 26 February, epidemiological measures were promptly applied, including the isolation with Droplet Precautions among the infected patients and investigation of contacts. During the following weeks (early and late March), the clinicians of the ward additionally reported 2 clusters of 3 patients with suspect symptoms, including rhinitis, sore throat and asthenia. All of these additional suspect cases were isolated with Droplet Precautions and were investigated by a nasopharyngeal swab for SARS-CoV-2 testing. If the first SARS-CoV-2 RT-PCR was negative, a second test was performed within 24 hours. Additionally, we proposed to complete investigations by an extended respiratory multiplex RT-PCR, to allow a better adjustment of preventive measures, as adhesion to isolation remain challenging among psychogeriatric patients.

Results
Among the 6 symptomatic patients, all had 2 consecutively negative SARS-CoV-2 RT-PCR. The respiratory virus panel test revealed a positive PCR for OC43 coronavirus in 5/6 patients, with viral load ranging from 3E+5 to 3E+9 copies/ml, confirming a nosocomial outbreak of a seasonal coronavirus. For the remaining patient, infection by OC43 coronavirus was considered possible, regarding the close contacts with positive cases during the hospital stay.

Conclusion
Even if the worldwide actual Covid-19 epidemic setting and more particularly a local suspicion of nosocomial transmissions should imperatively conduct to promptly research a SARS-CoV-2 infection in symptomatic patients, this report highlights the possibility of co-circulation of different respiratory virus within the same ward. More extended microbiological investigations with specific RT-PCR analysis in symptomatic patients repeatedly tested negative for Covid-19, can conduct to a better understanding and management of nosocomial outbreaks. Sometimes a coronavirus can hide another!

P86

Whole genome sequencing excluded the environment as the source of infection of Pseudomonas aeruginosa in a neonatal intensive care unit

D Blanc; L Senn; I Federli; I Koenig; E Giannoni; F Legault; M Roth-Kleiner; B Grandbastien
Centre Hospitalier Universitaire Vaudois

Introduction
Pseudomonas aeruginosa is a rare pathogen in neonatal intensive care unit (NICU). Following P.aeruginosa bacteremia in two NICU patients hospitalized in two different rooms with dedicated nurses, we performed an epidemiological investigation to find environmental sources and routes of transmission.

Methods
All humid environments were screened for P.aeruginosa. This included tap water, faucets, sink traps, water reservoirs of incubators, cosmetics, and disinfectants. Sink traps were dismantled and 10 samples were done at different sites of each sink trap. Isolates were first typed by double locus sequence typing (www.dlst.org/Paeruginosa) and all isolates identical to the three patient's isolates (DLST 28-77), were further analysed by whole genome Multi Locus Sequence Typing (wgMLST, BioNumerics v.7.6.3). As control, we analysed 15 isolates of DLST 28-77 not related to the outbreak.

Results
Among the 287 environmental samples analysed for the presence of P.aeruginosa, 99 were positive, mostly from sink traps. Typing revealed 35 isolates belonging to DLST 28-77. Whole genome sequencing revealed that all DLST28-77 isolates (N=53) belonged to the MLST ST395. wgMLST analysis showed differences of 0 to 180 loci between all isolates. Only 0 to 2 loci differences were observed between the three isolates from the two NICU patients. The closest environmental isolates from the two NICU patients had >70 loci differences and the closest patient isolate had 27-30 loci difference. The later was recovered from a patient in the adult ICU with no link with the NICU.

Conclusions
The thorough investigation of the environment of our NICU showed that sink traps were the main reservoir of P.aeruginosa. However, none of the environmental isolates was genetically close enough to be considered as the source of infection. The sole use of standard molecular typing (DLST) would have lead us to a false conclusion that sink traps were the source of infection.

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Rôle et importance de l'équipe de Prévention et Contrôle de l'Infection dans un service d'urgences universitaires au cours de la pandémie Covid-19

A Vital--Heilbronn
CHUV - Hôpital universitaire

Introduction
En février 2020, les urgences ont été confrontées à une modification majeure de leur patientèle avec un afflux exponentiel d'infections à SARS-CoV-2 dans un contexte d'incertitudes face à ce nouveau pathogène. En octobre 2020, la deuxième vague de COVID s'est surajoutée à l'activité usuelle. Ces deux vagues ont conduit le service des urgences à se réorganiser complètement en implémentant des stratégies d'isolement distinguant les flux COVID et non-COVID.
L'objectif de ce retour d'expérience est de décrire l'implication de l'équipe de Prévention et Contrôle de l'Infection (PCI) en support des urgences pour garantir la protection optimale des patients et du personnel.

Méthode
L'équipe PCI est intervenue à la fois dans la planification, le pilotage de ces changements et dans l'accompagnement auprès des équipes.

Résultats
La procédure institutionnelle décrivait le chemin clinique des prises en charge aux urgences ; elle a tenu compte de l'évolution rapide des connaissances et des recommandations (17 versions successives). L'infrastructure s'est adaptée aux besoins : libération de locaux pour les soins intensifs ; création de nouveaux secteurs hors murs (tente) ou non permettant de doubler la capacité d'accueil (jusqu'à 82 places), signalétique et équipements appropriés (distributeurs de SHA)Des filières de dépistage ont été créés, hors des urgences, afin de protéger l'hôpital. L'activité est restée soutenue en 2020 (38031 admissions) avec une proportion d'isolements respiratoires de 17.4% (vs 3.7% en 2019, $p < 10\text{-}4$) en l'absence de circulation des virus grippaux. En 2020, 1607 patients ont été identifiés Covid-19 positifs aux urgences.
L'équipe PCI est intervenue pour diffuser les recommandations les plus actualisées, dispenser des formations et informations initialement quotidiennes à destination des personnels, préciser les conditions de dépistage et d'isolement, évaluer l'implémentation des mesures/recommandations et participer à l'aménagement de nouveaux locaux.
Le pilotage a reposé sur des cellules de conduite impliquant également les directions, les fonctions supports et l'équipe PCI.

Discussion/conclusion
Cette démarche a permis de répondre aux multiples questionnements des équipes, des procédures très rapidement évolutives et nombreuses modifications par rapport aux pratiques usuelles (i.e. masques). L'équipe des urgences a montré une flexibilité et adaptabilité en coordination avec l'équipe PCI, référence « hygiène » dans c

P88

Sind UV Desinfektionsboxen ein taugliches Hilfsmittel im klinischen Einsatz?

W Steiger; W Steiger; T Thalmann; M Laguardia; J Marschall
Insel Gruppe AG, Inselspital

BACKGROUND
Viele Gegenstände im klinischen Alltag lassen sich mit den gängigen Methoden nicht oder nur sehr schwer aufbereiten. Zunehmend werden auch Smartphones und Tablet PC zur Dokumentation und Datenerfassung wie dem Führen des elektronischen Patientendossiers am Patientenbett eingesetzt. Diese Geräte reagieren empfindlich auf Feuchtigkeit und Chemikalien.

ZIEL
Gesucht wurde eine einfache und sichere Methode zur Aufbereitung von nicht- oder unkritischen Medizinprodukten wie Smartphones, Tablet PC, schnurlose Telefone, Handschuhboxen, Badges, Schlüssel, Brillen und auch Gegenstände wie Stethoskope, Reflexhammer, Materialien aus Isolationszimmern z.B. steril verpackte Einwegprodukte usw.

METHODE
Auf dem Markt sind eine unübersichtliche Anzahl von UV C Desinfektionsboxen erhältlich, aber diese sind allenfalls für den Consumer-Market geeignet. Geräte für den medizinischen Gebrauch sind rar und kommen erst jetzt im Zuge der Pandemie langsam auf den Markt.
Zwei Geräte entsprachen unseren Vorstellungen: 1. UVsmart D25 und 2. CleanslateUV Sanitizer.
Die Wirksamkeit dieser Geräte ist durch Gutachten bestätigt worden. Zur Kontrolle wurde die Wirksamkeit der Desinfektionsleistung aber mittels Abklatschuntersuchungen überprüft. Es wurden zwei Cleanslate und fünf UVsmart D25 beschafft und versuchsweise für eine dreimonatige Testphase in ausgewählte chirurgische und medizinische Abteilungen gegeben. (2 in Covid-Stationen, 2 in Intensivstationen, sowie je 1 in einen OP Bereich, Viszeralchirurgie und Onkologie).

RESULTATE
Die Leistung der Geräte konnte durch eigene Abklatschuntersuchungen sowie externe Studien belegt werden, in den Testabteilungen unseres Spitals fanden die Geräte gemäss der ausgefüllten Fragebögen eine breite Akzeptanz. Gemäss Rückmeldungen wurden die Geräte vor allem zur Desinfektion vom medizinischen Gerätschaften wie Stethoskopen, Fiebermessern, steril verpacken Einwegprodukten sowie von Alltagsgegenständen wie Schlüssel, Smart Phones, Telefone, Badge, Sucher, Brillen, und Schreibmaterialien verwendet.
Allerdings erwies sich das UVsmart Gerät als störungsanfällig; mehrere Defekte in der Testphase betrafen das Verschlusssystem und die Steuerung.

DISKUSSION
UV Desinfektionsgeräte können im klinischen Alltag eine hilfreiche und willkommene Unterstützung darstellen. Sie sind einfach zu bedienen und der Zeitaufwand pro Desinfektion ist mit 20-25s überschaubar. Die Technik scheint aber im Moment je nach Produkt noch nicht ausgereift zu sein.

P89

The golden jackal (Canis aureus): A new host for Echinococcus multilocularis and Trichinella britovi in Switzerland

CF Frey[1]; WU Basso[1]; S Zürcher-Giovannini[2]; I Marti[2]; S Borel[2]; S Guthruf[2]; D Gliga[1]; B Lundström-Stadelmann[1]; FC Origgi[2]; M Ryser-Degiorgis[2]
[1] Institute of Parasitology, Vetsuisse Faculty, University of Bern, Switzerland; [2] Centre for Fish and Wildlife Health, Vetsuisse Faculty, University of Bern, Switzerland

Aim
The golden jackal (Canis aureus) is a wild canid new to Switzerland. It is an officially monitored species and therefore all dead individuals are submitted to postmortem examination to collect baseline health data. The procedure includes an assessment of parasites, with an emphasis on zoonotic, reportable infections, such as those caused by Trichinella spp. or Echinococcus spp.

Methods
From 2016 to 2021, five golden jackals (cases 1-5) originating from four different Swiss cantons were submitted. In one case (case 2), only organ samples were available and therefore parasitological examination was not possible. Parasite stages recovered during necropsy as well as by routine coproscopical techniques were morphologically identified. Taeniid eggs and adult tapeworms were processed for molecular species identification. Additionally, tongue and diaphragm were analysed for Trichinella spp. by the artificial digestion technique followed by multiplex-PCR in positive cases.

Results
Case 1 was culled because of severe debilitation, case 2 was mistaken as a red fox (Vulpes vulpes) and shot by a hunter, case 3 was presumably attacked by a wolf (Canis lupus), and cases 4 and 5 were traffic-killed. Of the four jackals analysed for parasites (cases 1, 3-5), hookworm eggs were detected in one animal (case 1), no parasites were found in case 3, and Echinococcus multilocularis both adult worms and eggs were present in case 4. In case 5, eggs of E. multilocularis as well as eggs of Toxocara canis and sporocysts of Sarcocystis sp. were detected in the intestinal content, and Trichinella britovi larvae were found in the muscle samples.

Conclusions
The health monitoring program in place for protected carnivores in Switzerland allowed us to add the golden jackal to the list of hosts for the endemic zoonotic parasites E. multilocularis and T. britovi in this country. Hunters, farmers and other persons coming in contact with golden jackals should be aware of this and treat faeces and carcasses with caution.

P90

Eco-bio-social determinants of Aedes aegypti larval breeding and susceptibility to insecticides in arbovirus foci in Abidjan, Côte d'Ivoire

J Zahouli[1]; B Koudou[1]; P Müller[2]; J Utzinger[2]
[1] Centre Suisse de Recherches Scientifiques en Côte d'Ivoire, Abidjan, Côte d'Ivoire;
[2] Swiss Tropical and Public Health Institute & University of Basel, Basel, Switzerland

Aim
We assessed the ecological, biological and social (eco-bio-social) factors of Aedes aegypti larval breeding, dengue and yellow fever transmission risk indices and larvae insecticide susceptibility in the large city of Abidjan, Côte d'Ivoire.

Methods
We sampled Ae. aegypti immatures (larvae and pupae) and breeding containers, and household socio-ecological data in six clusters in Abidjan, Côte d'Ivoire from September to October 2020. We calculated Stegomyia indices (container index: CI, household index: HI and Breteau index: BI), and pupal counts (pupae/container: PC, pupae/house: PH and pupae/person: PP). Moreover, Ae. aegypti larvae were tested against the insecticides deltamethrin, DDT, bendiocarb and malathion, and a biolarvicide Bacillus thuringiensis var israelensis (Bti). We then determined the insecticide resistance ratio (RR50 and RR90) and the lethal concentration (CL50 and CL90).

Results
The most productive Ae. aegypti breeding sites were outdoor water-holding containers; tires (53.7%), discarded cans (25.3%) and uncovered potable water receptacles (17.6%). CI, HI and BI were estimated at 77.2%, 57.1% and 137.2, and PC, PH and PP were of 2.31, 1.45 and 0.93, respectively. Ae. aegypti larval infestation and pupal counts were correlated with complex community behaviors related to water and waste management. Breeding sites' positivity and productivity were associated with unmanaged waste, water supply interruptions and long water storage duration. Domestic areas were more favorable for immature production compared with commercial and public spaces, and then schools and religious facilities. The local communities did not know the larvae and larval breeding sites of Ae. aegypti. The respondents reported that they were not using insecticides to control Ae. aegypti larvae. Ae. aegypti larvae were susceptible to deltamethrin, malathion, bendiocarb, and Bti, but resistant to DDT.

Conclusion
In Abidjan, Côte d'Ivoire, local Ae. aegypti larval breeding patterns, arbovirus transmission risk indices and insecticide resistance were correlated with socio-ecological determinants. The risks of transmission of dengue and yellow fever viruses were above the World Health Organization (WHO)-established epidemic thresholds. However, Ae. aegypti larvae were susceptible to insecticides. Integrated community-based vector control programs including larviciding are recommended to achieve effective Ae. aegypti vector control and arboviral disease prevention.

P91

Efficacy of CDC light trap and human decoy trap (HDT) compared to human landing catch (HLC) for estimating malaria vector biting rates in rural Tanzania

I Namango[1]; C Marshall[2]; F Tenywa[3]; O Odufuwa[3]; G(Ligema[3]; H Ngonyani[3]; I Matanila[3]; N Makungwa[3]; J Bharmal[4]; J Moore[3]; D Kaftan[5]; A Saddler[6]; A Ross[1]; S Moore[3]; M Hetzel[1]
[1] Swiss Tropical and Public Health Institute / University of Basel; [2] BC Centre for Excellence in HIV/AIDS; [3] Ifakara Health Institute; [4] Innovative Vector Control Consortium; [5] Marquette University; [6] Telethon Kids Institute

The human landing catch (HLC) is considered the best trap for biting mosquitoes, yet there are concerns about safety for its extensive use. We compared the numbers of mosquitoes caught by the CDC light trap, the human decoy trap (HDT) and HLC in Tanzania in 2017 and 2019.
We collected the mosquitoes as part of an exercise to evaluate the impact of indoor residual spraying (IRS) products in a rural malaria-endemic setting. We conducted CDC light trap surveys indoors, the HDT outdoors and the HLC both indoors and outdoors. We used negative binomial mixed-effects models to compare nightly catches of the CDC light trap to the indoor HLC and of the HDT to the outdoor HLC.
Overall, we trapped 14,606 Anopheles arabiensis, 66,807 An. funestus and 75,248 Culex spp adult female mosquitoes. We observed consistently higher numbers of Culex spp than An. funestus and higher numbers of An. funestus than An. arabiensis across all traps. Compared to indoor HLC, we found that the CDC light trap caught about half as many An. arabiensis, (RR = 0.42 (0.31 - 0.58), p < 0.0001), over two thirds of An. funestus, (RR = 0.64 (0.50 - 0.83), p = 0.0008), and an approximately equal number of Culex spp, (RR = 0.93 (0.74 - 1.18), p = 0.57). We found that HDT caught just about a tenth of both An. arabiensis, (RR = 0.07 (0.01 - 0.31), p = 0.0006) and An. funestus, (RR = 0.10 (0.06 - 0.18), P < 0.0001) and a third of Culex spp, (RR = 0.29 (0.17 - 0.50), P < 0.0001) caught by the reference trap. Differences between the CDC light trap and the indoor HLC did not appear to vary greatly depending on mosquito density. The CDC light trap may be used for regular indoor malaria vector monitoring as long as a correction factor is applied to match mosquito catches of the HLC gold standard trap. Due to low mosquito numbers caught by HDT in this study, we recommend further investigations with a more robust study design to reassess its efficacy and potential use as an alternative to outdoor HLC.

P92

Beyond immune escape: a Trypanosoma brucei VSG that causes drug resistance

P Mäser
Swiss Tropical and Public Health Institute

VSG is the variant surface glycoprotein that protects African trypanosomes from their mammalian hosts' immune responses. The genome of Trypanosoma brucei contains over 1000 VSG genes, only one of which is expressed at a time in bloodstream-form parasites. The VSG proteins are GPI-anchored and form a dense coat on the trypanosomes' surface that is rapidly recycled by endocytosis. We have discovered a surprising link between antigenic variation in T. brucei and drug resistance: expression of a particular VSG, termed VSG-Sur, correlated with resistance to the drug suramin in laboratory-selected mutants (Wiedemar et al., 2018). Reverse genetic experiments with T. brucei bloodstream forms provided proof that expression of VSG-Sur is sufficient to reduce suramin sensitivity by about 60-fold (Wiedemar et al., 2019). Expression of VSG-Sur also caused a strong reduction in the receptor-mediated uptake of transferrin and low-density lipoprotein, but it did not affect the growth of the trypanosomes (Wiedemar et al., 2019). By solving the crystal structure of VSG-Sur in complex with suramin, the labs of Erec Stebbins and Nina Papavasiliou in Heidelberg have shown that VSG-Sur binds suramin with high affinity (Zeelen et al., 2021). Suramin is an old drug that is still being used for the treatment of Nagana in cattle and Surra in camels. Suramin resistance is a serious problem in the control of these diseases. At present, we do not know whether the newly discovery mechanism of suramin resistance via VSG-Sur is relevant in the field. But certainly it provides a new angle to the phenomena of drug uptake and vesicular trafficking in African trypanosomes.

P93

Genetic diversity and structuring of Schistosoma from cattle in Côte d'Ivoire

J Giovanoli Evack[1]; JN Kouadio[2]; LY Achi[3]; B Bonfoh[4]; EK N'Goran[5]; J Zinsstag[1]; J Utzinger[1]; O Balmer[1]
[1] Swiss Tropical and Public Health Institute / University of Basel; [2] Swiss Tropical and Public Health Institute / University of Basel / Centre Suisse de Recherches Scientifiques en Côte d'Ivoire / Unité de Formation et de Recherche Biosciences, Université Félix Houphouët-Boigny; [3] Centre Suisse de Recherches Scientifiques en Côte d'Ivoire / Ecole d'élevage et des métiers de la viande de Bingerville; [4] Centre Suisse de Recherches Scientifiques en Côte d'Ivoire; [5] Centre Suisse de Recherches Scientifiques en Côte d'Ivoire / Unité de Formation et de Recherche Biosciences, Université Félix Houphouët-Boigny

Schistosoma is a genus of parasitic blood fluke that causes the neglected tropical disease (NTD), schistosomiasis. There are over twenty known Schistosoma species, which infect a variety of mammals, such as humans, primates, rats and livestock in tropical and sub-tropical regions. Schistosoma spp. can be zoonotic and cause considerable human morbidity and economic loss to the livestock industry. Currently, the WHO NTD roadmap aims for elimination of schistosomiasis as a public health problem by 2030, but the potential of zoonotic transmission and the implications of zoonotic reservoirs threaten the success of prevention and control programmes. Understanding schistosome epidemiology and population genetics in non-human hosts is essential to reach this goal.

This study aimed to provide molecular species identification of specimens and describe genetic diversity and structuring of Schistosoma spp. populations from cattle in Côte d'Ivoire.

Flukes from slaughtered cattle and miracidia from feces of live cattle were sampled from abattoirs and farms across six sites in Côte d'Ivoire. Polymerase chain reaction of microsatellites, cox1 and ITS1/2 loci were performed on DNA from flukes and miracidia in order to identify species and determine genetic diversity and gene flow using population genetics methods.

All flukes (371/400) and miracidia (101/114) that produced bands displayed the Schistosoma bovis or Schistosoma curassoni genotype in the mitochondrial cox1 gene. Of the 101 flukes and 4 miracidia further subjected to nuclear ITS1/2 sequencing, all were consistent with the pattern for S. bovis, indicating that cattle in Côte d'Ivoire appear to be infected with S. bovis only at this time. Genetic diversity indices revealed a deficiency of heterozygotes and signals of inbreeding across all sites, while structure analyses displayed little structuring and differentiation.

Ivorian cattle appear to be infected with only S. bovis, despite the high prevalence of Schistosoma haematobium x S. bovis hybrids in Ivorian humans. This suggests separate transmission cycles in each host species, with occasional spill-over events from cattle to humans. Cattle, or perhaps other animal hosts, therefore likely play a role in human infection. Determining the contribution of non-human hosts to human schistosome transmission cycles is imperative in order to reach control programme goals.

P94

Private clinics play an important role in the treatment of suspected severe malaria in children who first seek care from a community-based provider in Uganda

T Lee[1]; J Kimera[2]; N Brunner[1]; G Delvento[1]; P Athieno[2]; G Tumukunde[2]; M Lambiris[1]; A Signorell[1]; C Burri[1]; C Lengeler[1]; M Hetzel[1]; P Awor[2]
[1] Swiss Tropical and Public Health Institute / University of Basel; [2] Makerere University School of Public Health

In Uganda, private clinics are an important point of care for children with suspected severe malaria. Considering the importance of seeking prompt and appropriate treatment for this potentially life threatening condition, it is important to understand the role of private clinics in the continuum of care and the quality of care they offer. Data was collected as part of the multi-country Community Access to Rectal Artesunate for Malaria (CARAMAL) study. In Uganda, 1,853 children with suspected severe malaria were enrolled while attending community-based healthcare providers between April 2019 and July 2020. All children were followed up 28-days after enrolment. Caregiver interviews were conducted about the history of care-seeking and treatment. Among children who first visited a community-based healthcare provider (community health worker or primary health centre), 6% were referred to a private clinic at some stage during care-seeking. Common reasons for referral to private clinics were due to no treatment being available (55%) and the given treatment requiring follow-up treatment (50%). Even though few public providers referred to private clinics, 32% of community enrolments subsequently visited a private clinic as the second (90%) or third (10%) point of care. For 99% of all community enrolments who went to a private clinic, the clinic was the last provider from which they sought treatment. In private clinics, 59% (95% CI: 55 – 62) of children received a malaria rapid diagnostic test (mRDT), and 68% (95% CI: 61 – 74) of the mRDT positive children received artemether-lumefantrine. Use of private clinics after entering the public healthcare system was common even though public providers rarely refer to private clinics. These practices demonstrate that care for severe malaria does not always follow official treatment pathways that focus on the public sector. As private clinics appear to play a critical role in the management of children with severe malaria, it is important to understand their treatment practices and consider these providers in efforts to improve quality of care.

P95

Whole genome nanopore sequencing of Theileria annulata identifies novel parasite proteins exported into the host cell

K Woods[1]; F Brühlmann[1]; M Maurizio[1]; M Schmid[2]; P Capewell[3]; W Weir[3]; P Olias[1]
[1] University of Bern; [2] MWSchmid GmbH; [3] University of Glasgow

Theileria are tick-borne Apicomplexan parasites that modify the phenotype of their infected host cell to a remarkable extent. Following invasion of a bovine leukocyte by infective sporozoites, Theileria develops within the cytoplasm of the host cell into a multinucleated syncytium termed a schizont. Within a few days of infection, the cells acquire a transformed phenotype comprising uncontrolled proliferation, resistance to apoptosis, immortality and increased invasiveness. During host cell division, the schizont interacts closely with host microtubules and the mitotic spindle, ensuring its distribution to both daughter cells, and the clonal expansion of parasitized cells. Extensive changes in bovine kinase and transcription factor activity have been reported, and we present RNA sequencing gene expression analyses that reveal for the first time the extent of gene expression changes between primary macrophages and cells freshly transformed by Theileria. The mechanism by which Theileria induces these phenotypes remains poorly understood, and in particular, very few Theileria effector proteins that interact with the host cell have been characterized. We decided to use a comparative bioinformatics approach to identify putative Theileria-encoded effector proteins that are expressed on the schizont surface or secreted into the host cell cytoplasm or nucleus. To date only one published T. annulata genome, generated by random shotgun sequencing more than 15 years ago, is available. Therefore, we performed nanopore and Illumina whole genome sequencing on seven Theileria annulata clones isolated from different geographical regions. Bioinformatic analysis of features such as selective pressure and protein structure allowed us to identify and validate a number of novel Theileria proteins that are exported into host cell compartments, demonstrating the value of this extensive data set.

P96

Cardiovascular Disease in the Peruvian Highlands: Local Perceptions, Barriers, and Paths to Preventing Chronic Diseases in Andean Adults

G Sanchez Samaniego[1]; S Hartinger Peña[2]; P Skye Tallman[3]; D Mäusezahl[4]
[1] Swiss Tropical and Public Health Institute, University of Basel; [2] Universidad Peruana Cayetano Heredia, Swiss Tropical and Public Health Institute, University of Basel; [3] The Field Museum of Natural History; [4] Swiss Tropical and Public Health Institute

Aims
Public health interventions can be improved by understanding peoples' explanatory models of disease. We explored the awareness and perceptions of cardiovascular diseases (CVD) and options for preventive actions in young rural adult highlanders.

Methods
We used purposive sampling to select participants. A total of 46 participants (37 women and 9 men) partook in the eight focus group discussions. We purposively invited 46 men and women from communities in Cajamarca to participate in eight focus groups. The focus group discussion guide was based on the six constructs of the Health Belief Model; perceived susceptibility, perceived severity, perceived benefits, perceived barriers, cues to action, and self-efficacy. We complemented this framework by adding three additional sections on patterns of distress, perceived causes, and gendered differences.

Results
Fresh foods, physical activity, unpleasant emotions, and healthcare access were cited as important determinants of healthy lifestyles. Barriers to healthy diets included lacking nutritional knowledge, fluctuating food prices, and limited access to foodstuffs. Women felt particularly vulnerable to cardiovascular diseases and identified gendered barriers to manage stress and engage in leisure sports. Low health literacy, distance and poor doctor-patient relationships prevented participants from fully accessing healthcare.

Conclusions
Cardiovascular disease prevention should consider local knowledge of these diseases and of healthy lifestyles and harness ongoing programmes that have successfully promoted good nutrition in children and pregnant women. In concert with public-private partnerships, governments should include health prevention for the entire family

P97

Assessment of sensitivity and specificity of a rapid immunchromatographic test (Schistosoma ICT IgG-IgM) for Schistosomiasis in endemic and non-endemic populations

J Hörmann[1]; E Kuenzli[1]; P Odermatt[1]; S Sayasone[2]; C Schäfer[1]; A Neumayr[1]; B Nickel[1]
[1] Swiss Tropcial and Public Health Institute Basel & University of Basel, Basel, Switzerland; [2] Lao Tropical and Public Health Institute, Vientiane, Lao People's Democratic Republic

Objective
Schistosomiasis, an infectious disease caused by human pathogenic Schistosoma species, is a neglected tropical disease affecting more than 200 million people worldwide. For diagnosis of schistosomiasis stool and urine microscopy for detection of eggs is still regarded as gold standard, however with limited sensitivity. In previous years, serological tests have gained more attention. This study examines the sensitivity and specificity of a rapid diagnostic test based on immunchromatography (Schistosoma ICT IgG-IgM, LD Bio, Lyon, France) for detection of specific antibodies in endemic and non-endemic populations.

Methods
We used frozen banked serum samples of patients with proven schistosomiasis, patients with other helminth infections, patients with rheumatoid factor positive rheumatoid arthritis and healthy blood donors to assess the sensitivity and the specificity of the test.

Results
We found a sensitivity of 100% in patients with parasitologically confirmed schistosomiasis, irrespective of the species (S. mansoni, S. haematobicum, S. japonicum, S.mekongi). In healthy blood donors and patients with rheumatoid factor positive rheumatoid arthritis from Europe, specificity of the test was 100%. However, with 75%, specificity was considerably lower in people with other helminth infections.

Conclusion
With its high sensitivity, the Schistosoma ICT IgG-IgM appears to be a good screening test for detection of antibodies. However, in populations with a high risk for co-infection with other tissue helminths, positive results should be confirmed with other tests due to lower specificity of the rapid diagnostic test.

P98

High proportion of additional resistances in extended-spectrum β-lactamase-producing Enterobacteriaceae colonizing international travellers

L Gygax[1]; JA Vlot[2]; F Schaumburg[3]; T Lääveri[4]; LG Visser[2]; A Kantele[4]; E Kuenzli[1]
[1] Swiss Tropical and Public Health Institute Basel & University of Basel ; [2] Leiden University Medical Center; [3] University Hospital Münster; [4] University of Helsinki and Helsinki University Hospital

Aims
Travelling is a known risk factor for intestinal colonization with extended-spectrum β-lactamase-producing Escherichia coli. Up to 90% of European travellers returning from (sub)tropical countries are known to be colonized on an intestinal level. Colonization and the associated spread of ESBL producing E. coli from high to low endemic settings through travellers is worrisome enough on its own. However, matters are made worse by evidence showing that not only asymptomatic carriage but also community-acquired infections with ESBL-producing E. coli are associated with international travel. To ascertain adequate empiric treatment in these patients, more information on additional resistances in ESBL-producing E. coli acquired while travelling is needed.

Methods
We analysed data on antibiotic resistance in ESBL-producing E. coli pooled from four prospective studies conducted between 2009 and 2018 in four European travel clinics.

Results
This joint analysis combined data from 382 travellers colonized with ESBL-producing E. coli. Sixty-three participants carried more than one E. coli morphotype, adding up to a total of 448 morphotypes. Resistance against fluoroquinolones and folate pathway inhibitors was found in 46.3% and 45.2% of the morphotypes, respectively. Resistance against carbapenems and polymyxins was below 1%. Resistance to sulphonamides, namely nitrofurantoin, commonly used to treat uncomplicated cystitis in women, was found in 12.9% of morphotpyes. There was no statistically significant difference in resistance rates according to travel destination.

Conclusions
Resistance against additional antibiotics besides extended-spectrum cephalosporins is common in ESBL-producing E. coli colonizing returning travellers. These information needs to be taken into account when choosing empiric antibiotic treatment in patients with a recent history of international travel.

Keyword 1
extended-spectrum beta-lactamase
Keyword 2
antibiotic resistance
Keyword 3
travel

P99

Feasibility and safety of rVSV-ZEBOV vaccination of humanitarian health workers against Ebola virus disease: an observational study .

L Carnino[1]; P Vetter[1]; F Chappuis[1]; G Eperon[1]; N Peyraud[2]; S Aebischer-Perone[1]; A Huttner[1]; L Kaiser[1]
[1] University Hospital Geneva; [2] Doctors without border

Aim
Geneva University Hospitals was granted a temporary authorization to administer the rVSV-ZEBOV (Ervebo®) vaccine to expatriate humanitarian frontline workers (FLW) prior to mission deployment. Our aims were to assess feasibility of FLW vaccination before deployment and to report adverse events (AEs).

Methods
Frontline workers received a single-injection of rVSV-ZEBOV (>7.2E7 pfu) along with other necessary vaccines during their pre-deployment medical check-up at the Travel Medicine Clinic of the Geneva University Hospitals (day 0); they were advised to remain in Geneva for at least two days following injection. A questionnaire regarding potential adverse events was emailed to all FLW on days 3 and 21. Doctors and nurses were in charge to collect the answers and report the adverse effects. Early and delayed AE were those starting within 3 or 21 days of vaccination, respectively. Thereafter, vaccinees were asked to report AEs by contacting the vaccination team. Serious adverse events were reported by the local pharmacovigilance team to Swiss authorities, and by the program manager to the vaccine manufacturer.

Results
Between August, 1st 2019 and June 30th, 2020, 124 FLWs received the rVSV-ZEBOV vaccine. Eighty-six volunteers (86/124; 69%) received a concomitant vaccine. The response rate to the follow-up questionnaire was 88% and 55% at days 3 and 21, respectively. Most respondents (n=105/109; 96.3%), experienced at least one AE, with a mean of three (+-SD 1.75) AEs per person. The most common AE was pain at the injection site, followed by fever (53 / 109; 48.6 %), fatigue (51 / 109; 46.7%) and myalgia (49 / 109; 44.9 %). Most early AEs (360 / 377; 95.4 %) resolved within 3 days, reflecting vaccine reactogenicity. Delayed AEs were reported by 6 / 69 (7.2 %), and were mostly osteoarticular (3 / 6; 50 %). Two cases of high grade fever, one rash, and one case of arthritis likely attributed to the vaccine, were considered as serious and resolved spontaneously. Among two suspected unexpected serious adverse reactions (SUSARs), one was a persistent neurological AE considered possibly related to the vaccine, the other was a visual disturbance later classified as presbyopia and thus deemed unrelated to the vaccine.

Conclusion
Though common, adverse events were transient and well tolerated. Pre-deployment rVSV-ZEBOV vaccination in FLW is feasible and can be integrated into the general pre-mission check-up .

P100 - Abstract withdrawn