ABSTRACTBOOK

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O01

Etude de faisabilité d'une prévalence ponctuelle des infections associées aux soins et des traitements antibiotiques dans les EMS vaudois

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Introduction
Dans le cadre de sa stratégie nationale de surveillance, prévention et lutte contre les infections associées aux soins (IAS) dans les hôpitaux et les établissements médico-sociaux (EMS), l'équipe de projet Stratégie NOSO et CURAVIVA ont exprimé le désir d'évaluer le risque d'IAS dans les EMS suisses.
L'organisation d'une étude de faisabilité d'une enquête de prévalence des IAS a été confiée à l'Unité Cantonale HPCI Vaud (Unité HPCI) pour 2018.

Objectif
Évaluer la faisabilité d'une enquête de prévalence des IAS dans les EMS vaudois (ressources humaines et qualité des données) en comparant les données récoltées par du personnel formé en PCI à celles récoltées par le personnel de l'EMS.

Methode
Utilisation de la méthodologie proposée par ECDC 2016.
Le recueil de données par questionnaire concerne la structure et l'organisation des EMS, les résidents et leur exposition aux procédures invasives. L'enquête cible aussi les IAS actives et les traitements antibiotiques en cours le jour de l'enquête.
Dans chaque EMS, le recueil de données est réalisé simultanément par une équipe interne à l'EMS composée d'un infirmier répondant en hygiène et/ou d'un infirmier responsable et par l'équipe externe d'infirmier en hygiène prévention et contrôle de l'infection (HPCI).
Une formation a été dispensée aux deux équipes d'enquêteurs par les coordinateurs de l'enquête.

Resultats
L'enquête se déroule entre le 12 avril et le 14 juin 2018, un jour donné.
Cette enquête concerne un échantillon de 8 EMS volontaires et représentatifs, sélectionnés de manière aléatoire et afin d'inclure au minimum 500 résidents.
Les 2 équipes d'enquêteurs ont inclus tous les résidents de l'EMS présent à 8h le jour de l'enquête.
Les données des résidents avec une IAS ou un antibiotique sont validées par un médecin coordinateur de l'Unité HPCI pour évaluer la qualité des données.

Conclusion
Cette étude nous permet d'identifier les éléments nécessaires à la mise en place d'une enquête de prévalence des infections dans les EMS vaudois (personnel PCI vs personnel de l'EMS). L'étude de faisabilité permet également d'estimer le temps nécessaire à l'enquête.

Informations supplémentaires
European Centre for Disease Prevention and Control (ECDC). Protocol for validation of point prevalence surveys of healthcare-associated infections and antimicrobial use in European long-term care facilities. Stockholm: ECDC. 2016.

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O02

Development and Validation of a Semi-Automated Surveillance System for non-ventilator-associated Hospital Acquired Pneumonia (nvHAP)

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Aims
Surveillance of non-ventilator-associated hospital-acquired pneumonia (nvHAP) using HELICS criteria (Hospitals in Europe Link for Infection Control through Surveillance) is very resource intensive. We developed and validated a semi-automated surveillance system for nvHAP and describe nvHAP incidence.

Methods
We included all inpatients from the year 2017 of the University Hospital Zurich, Switzerland. We applied an automated classification algorithm mirroring radiologic and systemic criteria of the HELICS-definition to distinguish 'not at risk' and 'at risk'-patients for nvHAP. 'At risk'-patients were manually screened for nvHAP. For validation, we applied the reference standard of full manual evaluation on a random sample of 700 patients to calculate negative predictive value and accuracy. To assess sensitivity, the algorithm was applied on 62 patients with known nvHAP from the year 2016.

Results
Of 39'519 inpatients, the algorithm identified 2408 'at risk'-patients, reducing the number of medical records to manually screen by 93.9%. NvHAP was detected in 251 patients (0.64%, 95% CI: 0.57 – 0.72%). The overall incidence rate was 0.94/1000 patient days (95% CI: 0.82 – 1.06), with highest rates on hematology, gastroenterology, and internal medicine. The semi-automated surveillance had a negative predictive value of 100% (95% CI: 99.5 – 100%) and an accuracy of 100% (95% CI: 99.5 – 100%). Sensitivity of the algorithm was 100% (95% CI: 94.2 – 100%).

Conclusions
Our classification algorithm reduced the number of patients for manual evaluation substantially, making continuous surveillance of nvHAP feasible. Also, the semi-automated surveillance proved to be accurate in identifying patients with nvHAP.

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O03

progress! Safe Urinary Catheterization - Results of a National Improvement Programme

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Aims
The aim of this national improvement programme was to reduce the use of indwelling urinary catheters (IUC) in acute care hospitals by implementing an evidence-based intervention bundle. As IUCs may lead to catheter-associated infections (CAUTI) and non-infectious complications, reducing IUC use is a prerequisite to prevent catheter harm. Part of the programme was a campaign that aimed at raising awareness among health care workers and promoting safe catheter handling.

Methods
The programme was conducted between 2015 and 2018 and consisted of the campaign and an intervention in 7 hospitals. Within the campaign, we published recommendations on safe IUC use in acute care hospitals. The intervention focused on the implementation of an intervention bundle consisting of an indication list for urinary catheterisation, daily evaluation of continued IUC need and staff education for proper catheter insertion and maintenance. The primary outcome urinary catheter utilisation was measured during two 3-month periods, one before implementation of the intervention bundle (pre-intervention Aug-Oct 2016) and one afterwards (post-intervention Aug-Oct 2017). CAUTI and non-infectious complications were secondary outcomes. To collect data on staff knowledge, attitudes and behaviour regarding IUC use we conducted a written survey at two time points (pre-intervention Oct 2016 and post-intervention Oct 2017).

Results
Catheter utilization rate dropped from 23.7 % (n = 13,171) to 21.0 % (n = 12,709) (p = 0.001). CAUTI rate remained unchanged at a low level with 0.02 CAUTI per 100 patient days for both surveillance periods (p = 0.983). Non-infectious complications dropped significantly from 0.79 to 0.56 complications per 100 patient days (p < 0.001). The staff survey's response rate was 47 % (pre-intervention (n = 1,579)) and 49 % (post-intervention (n = 1,528)). Staff knowledge improved in all hospitals. The mean of correct answers to 15 questions increased significantly from 10.4 (pre-intervention) to 11.0 (post-intervention) (p < 0.001). Catheter utilisation practices and culture within the organization were perceived more favourably and in regard of their own behaviour, staff showed greater readiness to reduce IUC use and safe catheter handling.

Conclusion
Implementation of an evidence-based intervention bundle in Swiss hospitals is feasible and leads to reduced IUC use. The programme also affects staff perception regarding IUC use and culture within the organisation.

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O04

Implementation of an infection prevention-bundle reduces surgical site infections in cranial neurosurgery

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Background
Surgical site infections (SSI) are a leading cause of nosocomial infections and frequently require reoperations, prolong antibiotic exposure and increase mortality. Infection control interventions including standardized surveillance with immediate feedback and perioperative infection prevention-bundles (IPB) have proven effective in reducing infection rates.

Aims/Methods
Quantify SSI rates after cranial neurosurgery in a tertiary care hospital, identify risk factors for SSI and evaluate the impact of standardized surveillance and an IPB. For this purpose, we compared SSI rates before (2012) and after (2014) the implementation of standardized surveillance and an IPB in 2013. The IPB included standardized patient preparation, perioperative antibiotic/antiseptic use, barrier precautions, coaching of surgeons and the implementation of a specialized operations assistant team.

Results
We evaluated 322 unselected consecutive patients pre and 296 post intervention. Infection rates after 1 year follow-up decreased from 25/322 (7.8%) to 11/296 (3.7%, p=0.03) with no difference in mortality (14.7 vs. 13.8%). The isolated bacteria included S. aureus (42%), P. acnes (22%) and CoNS (14%). Organ/space infections dominated with 67% and mostly consisted of subdural empyemas and meningitis/ventriculitis. Among the 36 SSI, 13 (36%) occurred during hospitalization, 29 (81%) within the first 3 months of follow-up. In multivariable analysis including established risk factors described in the literature, non-CNS neoplasia (OR 3.82, 95% CI 1.39-10.53), postoperative bleeding (4.09, 1.44-11.62), operations performed by or under supervision of a senior physician (0.38, 0.17-0.84) and operations performed after the implementation of standardized surveillance and an IPB (0.38, 0.17-0.85) significantly influenced the infection rate.

Conclusions
The introduction of an IPB combined with routine surveillance and personal feedback was associated with a 53% reduced infection rate down to 3.7%, which is comparable to the 0.5-6.6% described in the literature for cranial neurosurgery. The lower infection rate of senior physicians (despite performing the most difficult surgical procedures) and the strong association between postoperative bleeding and infection underline the importance of surgical experience.

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O05

Creating and testing a prevention bundle for non-ventilator-associated hospital-acquired pneumonia (nvHAP) – a mixed method innovation project protocol

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Aim
Hospital acquired pneumonia (HAP) is divided in two distinct groups, the ventilator-associated pneumonia (VAP) and the non-ventilator-associated HAP (nvHAP). HAP and lower respiratory tract infections were shown to be the most common healthcare-associated infection (HAI). In the European Point Prevalence Study of 2011/2012, HAP constituted a percentage of 26% to all HAI, and 67% were nvHAP. Even though nvHAP is more frequent, was shown to have comparable mortality, and similar costs than VAP, research, prevention guidelines, and prevention efforts almost exclusively focus on VAP. We present a protocol for a project to design, implement, and evaluate a bundle of prevention measures for nvHAP.

Methods
The project comprises five work packages. 1) Designing a bundle of prevention measures - the nvHAP-bundle; 2) Implementation of nvHAP-bundle in high-volume departments; 3) Evaluation of bundle concerning effectiveness to prevent nvHAP; 4) Evaluation of adherence to bundle elements; 5) Qualitative evaluation of implementation success.
This single-centre project at the 900-bed University Hospital Zurich (USZ) will engage the wards of nine departments with substantial nvHAP rates. The implementation strategy will be tested in a pilot-ward. Then, we employ a stepped wedged sequential inclusion of the nine departments. Using a interrupted times series analysis, we will evaluate the effectiveness of the nvHAP-bundle by investigating the primary outcome variable ‘nvHAP/patient discharge’ and the secondary outcome variables ‘in-hospital mortality’, and ‘length of stay’. We will evaluate adherence to nvHAP-bundle by evaluation of documented prevention measures, direct non-participatory observations, and, by questionnaires and/or interviews as appropriate. Last, we will assess implementation success by interviews and/or questionnaires. Interviews will be conducted with involved healthcare providers, with the study and implementation team, and with key individuals in the hospital leadership team to identify barriers and facilitators for implementation success.

Conclusion
This innovative project aims to bridge the knowledge gap in nvHAP prevention, a neglected but major HAI. If successful, this unique and world-first nvHAP-bundle, coming with a validated implementation strategy, will represent face value to increase the safety of patients in the Swiss healthcare system and beyond.

Funding
This project is partially funded by the Federal Office of Public Health, the USZ Innovation pool, and a SNF grant (32003B_149474).

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O06

Gemeinsam stetig besser werden – Steigerung der Grippe-Impfrate der Pflege an einer Zentralschweizer Privatklinik

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Influenza ist der einzige virale respiratorische Infektionserreger, gegen den eine wirksame Impfung existiert. Im Gesundheitswesen führen Grippe-Erkrankungen von Mitarbeitenden nicht nur zu Arbeitsausfällen und damit verbundenen volkswirtschaftlichen Kosten, sondern auch zu potenziellen Übertragungen auf Patienten. Die Zentralschweiz ist bekannt als Region mit einer allgemein sehr tiefen Impfrate und einem hohen Anteil an Impfgegnern. Die Grippe-Impfrate der Pflege in der Zentralschweiz beträgt seit Jahren um 10%.

Ziel
Entwicklung einer Grippe-Impfkampagne zur Steigerung Grippe-Impfrate der Pflege auf > 30%.

Methoden
Entwicklung einer Grippe-Impfkampagne durch das Team Spitalhygiene & Infektiologie der Klinik St. Anna ab der Grippe-Saison 2014/15. Jährliche Anpassungen aufgrund von eigenen Erfahrungen sowie Rückmeldungen der Mitarbeitenden und der Geschäftsleitung. Die über einen Zeitraum von 3 Jahren entwickelte Grippe-Impfkampagne 2017/2018 bestand schlussendlich aus 15 Elementen mit den Schwerpunkten: Befähigerstrategie (Einbezug von Stationsleitungen, Abteilungsleitungen und link nurses als Impf-Botschafter; deren Befähigung durch Wissensvermittlung, Bereitstellen von Unterlagen sowie Unterstützung/Briefings während der Impfsaison), Vereinfachung der Grippe-assoziierten Prozesse (Grippe-Algorithmus, Tröpfchenisolation im Mehrbettzimmer), breit gestreutes Impfangebot, spezielle Motivationselemente (zweiwöchentliche Grippenews mit Informationen rund um die Grippe inkl. aktueller Impfraten, Wettbewerb für bestes Statement zur Grippeimpfung) und einer engen Zusammenarbeit inkl. konstruktiver Feedback-Kultur mit Schlüssel-Stationen (Notfallstation, Intensivstation). Ausserdem prospektive Erfassung der Grippe-Impfrate während der Grippe-Impfsaison resp.- Epidemie mit regelmässigen Zwischenanalysen und bei Bedarf gezielten Interventionen.

Resultate
Die Grippe-Impfrate der Pflege wurde über 3 Jahre signifikant gesteigert von 7.3% (2014/15), über 10.8% (2015/16) und 26.1% (2016/17) auf 41% (2017/18).
Konklusion: Durch jährliche Anpassung der Grippe-Impfkampagne und Fokus auf einer Befähiger-Strategie mit Abgabe eines Teils der Impfverantwortung in die Pflegeteams konnte innert 3 Jahren eine spektakuläre Steigerung der Grippe-Impfrate in der Pflege von 7.3% auf 41% erreicht werden. Diese Impfrate ist immer noch tief, sodass die Aktivitäten zur weiteren Steigerung weiterverfolgt und stetig an aktuelle Bedingungen angepasst werden müssen.

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O07

Concept mapping to reveal healthcare provider mental models of the hand hygiene-related "patient zone"

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Aims
Transmission of pathogens via healthcare provider (HCP) hands plays a major role in the development of healthcare-associated infections. The "patient zone" is a central element in the WHO "My 5 moments for hand hygiene concept", primarily developed to geographically distinguish the area contaminated by flora of a given patient from the "healthcare zone". Infection prevention efforts should aim to prevent the transmission of microorganisms between the zones. Discrepancies in HCP mental models about how the patient zone is defined may lead to lapses in infection prevention measures that may lead to patient harm. To our knowledge there are no studies addressing this issue. Therefore, the aim of this study was to explore HCP mental models of the patient zone.

Method
We conducted a concept mapping study using a card sorting technique to examine HCP's mental models of the patient zone. Using an online-tool, 10 HCP's without speciality training in infection prevention (non-experts) and two infection prevention experts sorted 32 items (e.g. stethoscope, infusion pump, pens, etc.) into categories of "inside" or "outside" the patient zone and verbalised their thought process throughout the activity. We calculated percentage agreement and did a content analysis on qualitative data.

Results
Three participants, including the experts, (25%) reported having received training on the concept and seven (58%) reported being either well- or moderately informed about the patient zone. High agreement (≥90%) was achieved for 13 of 32 items. Medium agreement (89-60%) was achieved for seven items. Low agreement (≤59%) was achieved for 12 items. We observed notable differences between professional groups and between experts and non-experts, driven in particular by varying mental models about how the patient zone is defined. These mental models revealed that certain HCP's defined the patient zone as a function of proximity to the patient (i.e. within 1 meter), demarcation of the physical patient room, and movement between multiple patients. In particular varying mental models resulted in low agreement for the stethoscope, tourniquet, floor, medication trays, partition walls and ultrasound device.

Conclusions
Items with medium-to-low agreement may represent the highest potential for infection prevention lapses. Low agreement is likely related to different mental models about how the patient zone is defined. Interventions should aim to rectify these discrepancies.

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O08

18S sequencing reveals eukaryome differences among geographically diverse African children

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Aims
The primary objective of this study is to analyze the eukaryome of children aged 2-5 years living in two low-income countries, Madagascar and the Central African Republic (CAR). The secondary objective is to link the eukaryome with the country of origin, age and nutritional status of the children.

Methods
Stool and duodenal samples were collected in the context of the AFRIBIOTA project, a translational research project investigating the pathophysiology underlying stunting. DNA was extracted using a commercial extraction kit. DNA samples were subjected to library generation for 18S rRNA amplicon (V4 region) and sequenced using Illumina. Filtering was performed using QIIME and OTU clustering and assignment was performed using Minimum Entropy Decomposition (MED) and the SILVA Database. The 260 fecal and 22 duodenal samples yielded a total of 497,981 filtered eukaryotic reads. For alpha diversity analysis, sample reads were rarefied to 300 sequences. For beta diversity, non-rarefied data data was used considering sequence count as a covariable of the analysis. Analysis was performed on the presence (>5 seqs) or absence (< 5 seqs) of a given taxon. Statistical analysis was performed using R.

Results
Sequencing depth was highly variable (minimum: 2, maximum: 15,881, median. 1,016 sequences). Duodenal samples had few sequences and were excluded from the analysis. A total of 259 fecal samples were analyzed (109 from CAR and 151 from Madagascar). We observed 327 OTUs belonging to unicellular eukaryotes and worms. Alpha and beta diversity differed according to country of origin. The most prevalent genera were Blastocystis (CAR: 74%; Madagascar: 81%), Saccharomyces (62%; 44%), Candida (54%; 11%), Entamoeba (44%; 60%), Pichia (36%; 15%), Giardia (12%; 24%), Ascaris (0%; 23%), Trichuris (0%; 14%) and Toxocara (0%; 13%). The prevalence of Blastocystis, Issatchenkia and Zygotorulaspora was age-dependent. Fungal taxa were more prevalent in the CAR (85% vs. 75%) while helminths were more common in Madagascar (4% vs. 46%).

Conclusion
This is the first detailed description of the eukaryome of children living in Madagascar and CAR and the first study to compare the eukaryome of children with different nutritional stati. While no differences were observed according to nutritional status, the eukaryome differed significantly according to country of origin. More in depth analyses are needed to understand the observed changes and to evaluate their role in gut homeostasis.

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O09

Implementation and Evaluation of a molecular protozoan gastro-panel at Swiss TPH

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Aims

Travelling in tropical or sub-tropical countries can be linked to gastro-intestinal disorders caused by protozoans. The standard method of detection is by microscopy of stool samples, however this method is limited to the expertise of the microscopists and can be time-consuming esp. when involving specific staining i.e. for coccidia or microsporidia. The use of molecular methods to standardize the detection of these parasites has thus evolved as an interesting alternative.

Methods

52 post-travel samples were tested by a protozoan gastro-panel (PGP) developed at the Swiss TPH. Primer were either newly designed or modified from literature to detect the pathogens at the same qPCR conditions. DNA was extracted from 200mg of stool. The PGP simultaneously tests the presence of the following protozoan in human stool by 6 TaqMan qPCR duplex assays: (1) Entamoeba dispar and E. histolytica; (2) Entamoeba polecki and E. moshkovskii; (3) Dientamoeba fragilis and Giardia lamblia; (4) Cystoisospora belli and Cyclospora cayetanensis; (5) Cryptosporidium hominis/parvum and Cryptosporidium spp.; (6) Microsporidia: Enterocytozoon bieneusi and Encephalitozoon spp. with subsequent sequencing.

Results

In a small exploratory study, we found that in 52 patients returning from holidays from a tropical or sub-tropical country, 4% had Giardia lamblia infections, 8% Dientamoeba fragilis and 6% Entamoeba dispar. Additionally an evaluation of the PGP running for months in the routine diagnostics at Swiss TPH detected pathogens that would have been missed by microscopy and yielded interesting results.

Conclusion

The PGP is a valuable tool to complement microscopy. Results are obtained within one day. However, the sensitivity is limited to the presence of the parasite in the fraction of stool used for DNA extraction. The strength of the PGP is in the differentiation of amoebas as well as in the detection of D. fragilis and small protozoans such as Cryptosporidium spp. and Microsporidia sp. within a single run.

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O10

Holistic Care from Start to Finish: The Key to Effectiveness in Community Management of Pediatric Diseases in 3 African Countries

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Integrated Community Case Management (iCCM) is an equity-based approach to childhood illness designed to provide children in remote areas of Africa with access to care for pneumonia, diarrhea, and malaria through Community Health Workers (CHWs).
There is currently little evidence documenting how health outcomes are influenced by differences in iCCM program organization and implementation, or how the contexts of program actors affects these outcomes. This research explores how iCCM programmatic differences in the areas of data systems, supply chain, and social mobilization (CSM), influence effectiveness of iCCM and health outcomes for children in an iCCM program in four sites of Malawi, DRC, and Nigeria.
We analyzed caregiver surveys before and after program implementation to observe how careseeking, testing, treatment and referral had changed. We used routine monitoring data on case management to triangulate this information, and 3000 surveys and 46 focus group discussions with CHWs, supervisors and caregivers, and key informant interviews with ministry, program and local actors.
All iCCM sites demonstrated significant change across all four areas of their trajectories of care in all three disease categories. The greatest area of absolute patient loss is largely that of careseeking, except for Niger State, while treatment and referral adherence demonstrated varying degrees of relative patient loss depending on the site.
The greatest reason for lack of careseeking was due to ineffective CSM strategies that either lacked coherent messages or relied on haphazard transmission schemes diluting information downstream. The typical CSM emphasis on awareness was less effective; successful strategies focusing on relationships and holistic local ownership observed the greatest impact. Gaps in testing and treatment were indicative of not only supply chain failures, but administrative, financial, and data transmission issues. These included CHW residency, infrequent supervision, breakdown in mhealth, inadequate data-transmission schemes, top-down payment mechanisms, among common procurement and distribution issues. Soft issues, such as gender, relationships, power dynamics, and motivation played a strong part in these as well.
A robust CSM strategy, frequent supervision, and a strengthened link between the facility and district are likely the greatest keys to ensuring a comprehensive approach to ensure community-based initiatives are not only effective, but sustainable.

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O11

Coinfections between persistent parasitic neglected tropical diseases and viral infections among migrants from sub-Saharan Africa and Latin America in a Swiss prison.

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Aims
In Swiss prisons, more than 70% of detained people are foreigners, and over one third originate from sub-Saharan Africa or Latin America. These two regions are endemic for various tropical diseases and viral infections, which persist after migration to non-endemic countries. Parasitic infections (schistosomiasis, strongyloidiasis) and co-occurrent viral infections (HIV, hepatitis B (HBV), hepatitis C (HCV)) are especially concerned, but have been neglected in empirical research. These diseases, often remaining silent for years, later cause complications especially if they occur concomitantly. In particular, coinfection between schistosomiasis and chronic viral hepatitis is associated with severer forms of liver disease. Our research aimed to study the prevalence and coinfections of two neglected tropical diseases, namely Strongyloides stercoralis, Schistosoma sp and viral infections among sub-Saharan Africans (SSA) and Latin Americans (LA) in Switzerland's largest pre-trial prison (Champ-Dollon – Geneva).

Methods
We carried out, in 2015, a cross-sectional prevalence study using a standardized questionnaire and serological testing.

Results
Among the 201 participants, 85.6% originated from sub-Saharan Africa and 14.4% from Latin America. We found the following prevalence ratios among participants: 3.5% of HIV (4.1% in SSA, 0% in LA), 12.4% of chronic HBV (14.5% in SSA, 0% in LA), 2.0% of viraemic HCV (1.7% in SSA, 3.4% in LA), and 8.0% of strongyloidiasis (8.1% in SSA, 6.9% in LA). The serological prevalence of schistosomiasis among SSA was 20.3% (not endemic in Latin America). Two infections were simultaneously detected in SSA: 4.7% were coinfected with schistosomiasis and chronic HBV. Four other coinfections were detected among SSA: schistosomiasis - HIV, HIV- chronic HBV, HIV - HCV, and schistosomiasis – strongyloidiasis.

Conclusion
Our study results indicate that a substantial proportion of people from sub-Saharan Africa and Latin America present parasitic infections (schistosomiasis and strongyloidiasis) and/or viral infections (HIV, hepatitis B, hepatitis C) that persist after migration to a non-endemic country.
The high prevalence of persistent viral and parasitic infections and their potential coinfections among detained migrants from sub-Saharan Africa and Latin America reinforces the need to implement control strategies and programs that also reach people in detention centers in non-endemic countries.

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O12

Household-level risk factors for water contamination and antimicrobial resistance in drinking water and childhood illness in rural San Marcos, Cajamarca, Peru.

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Background
Household drinking water has been shown to carry bacterial contamination, including antimicrobial resistant bacteria. Household water treatment (HWT) and storage interventions have achieved mixed impacts, literature addressing drinking water contamination and antimicrobial resistance (AMR) is scarce, and little is known regarding the natural occurrence of AMR in environmental sources in rural Peru.

Methods
This study investigated the association between individual household factors and the prevalence of bacterial contamination and AMR in household drinking water among a cohort of 314 households in rural Cajamarca, Peru using generalized linear models. AMR was determined using Kirby-Bauer disk diffusion.

Results
Boiling of water was associated with a higher level of thermotolerant coliform (IRR=1.15, $p < 0.001$), but this association was no longer significant when the water source was included as a covariate. Certain containers used to provide water samples were associated with greater odds of contamination (OR=4.60, $p < 0.001$ for bucket and OR=2.27, p=0.017 for faucet use). Farm birds, cows, guinea pigs and rabbits, and pigs were associated with increased contamination by multiple metrics, while sheep, ram and goats were associated with lower counts of thermotolerant coliforms, and plough animals were associated with lower CFUs but greater likelihood of the presence of E. coli. For all antimicrobials, the prevalence of AMR in drinking water was lower in homes that boiled water, but the reduction was only significant for ampicillin (OR=0.39, p=0.04) and chloramphenicol (OR=0.20, p=0.02). The prevalence of AMR was higher among pig owners for ampicillin (OR=2.61, p=0.03), trimethoprim-sulfamethoxazole (OR=3.64, p=0.02), tetracycline (OR=2.56, p=0.025), and any antimicrobial tested (OR=2.63, p=0.012); and was higher among families in which a child had recently taken antimicrobials for resistance to trimethoprim-sulfamethoxazole (OR=3.0, p=0.04).

Conclusions
In-home contamination and household animals may play a critical role in drinking water contamination in the Cajamarca region. Boiling does not appear to reduce contamination levels, but may play a role in changing the population of resistant bacteria. More research is needed to understand AMR in the local environment and the factors contributing to bacterial contamination and AMR in drinking water at high altitudes.

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O13

Ethical implications of malaria vaccine development: addressing vulnerability in low-resource settings through integrated communication tools

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Introduction
Recently, through a public-private partnership with PATH Malaria Vaccine Initiate (MVI) and GlaxoSmithKline (GSK), a malaria vaccine candidate (RTS,S) targeting children received positive reviews from European regulators and was recommended by the WHO for pilot-study implementation in three selected countries. These pilot studies will be carried out in Kenya, Malawi and Ghana before broader roll-out can and will be recommended. There are currently no systems in place addressing the implications of this vaccine on malaria epidemiology, delayed acquired immunity, morbidity and mortality – inviting ethical questions pertaining to its research. In recent years there has been accelerated investment in the push for the development of a malaria vaccine. In this study, the ethical aspects of such an endeavor are explored. Through empirical evidence gathered from semi-structured interviews, an ethical framework identifying key ethical concerns is presented.

Methods
We conducted a total of 76 interviews in Uganda, Kenya and Tanzania with parents of children enrolled in a pediatric malaria vaccine clinical trial. The interviews were semi-structured and used elements of grounded theory methodology. The respondents in Tanzania and Kenya were involved in a phase III RTS,S clinical trial. The respondents in Uganda were involved in a phase IIb GMZ2 clinical trial.

Results
Based on the experience of the parents, the respondents shared their perspectives on the malaria vaccine clinical trial their child was enrolled in. The responses allowed for the identification of three broad themes and the role relational ethics played in each 1) informed consent procedures 2) risk vs. benefit communication 3) community engagement

Conclusions
The low-resource setting of research and development for a malaria vaccine enhances the vulnerability of the participants. Mitigation of this vulnerability can be addressed through effective communication tools, rooted in local realities. By working together with the local communities, the utilization of these tools can mitigate context-specific challenges around vulnerability.

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P01

A large outbreak due to Vancomycin Resistant Enterococci: Description of clonal features and management strategies

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Aims
A large outbreak with different clones of vancomycin-resistant enterococci (VRE) affected the Bern University Hospital for several months. The aim of this study was to describe the extent of the outbreak and the infection control measures implemented to control transmission.

Methods
Triggered by two cases of VRE bloodstream infections on our hemato-oncologic ward, an outbreak investigation was started. Microbiological diagnosis of VRE was obtained by culture. Epidemiological links were assessed by meticulous chart review and supplemented with whole genome sequencing (WGS) analyses. Multiple infection control measures were implemented to avoid further transmissions.

Results
Between 29 December 2017 and 21 April 2018, 2877 screening samples were obtained from 1200 patients. 83 patients (6.9%) were found to be colonized with VR Enterococcus faecium. Of those, 76 (91.6%) had a strain carrying vanB, with 70 (84%) isolates virtually identical by cgMLST. The remaining eight patients (9.6%) were colonized with vanA carrying strains belonging to five different STs. Five patients (7%) developed an invasive infection (four bloodstream infections, one abdominal abscess). In order to control the outbreak, a VRE task force was formed and extensive infection control measures were implemented: temporary admission stop, patient isolation and cohorting, staff cohorting, active contact tracing and targeted screening, ward screening of “at risk” wards (irrespective of exposure), reinforcement of hand hygiene compliance, intensified environmental cleaning and proactive communication. By April 2018 the outbreak was contained with these specific measures, which required a substantial effort from the infection prevention team and the involved healthcare workers.

Conclusions
This VRE outbreak was characterized by a rapid spread of the causative clone. Epidemiological analyses supplemented by WGS typing results were essential for the reconstruction of transmission pathways and to guide contact tracing. A multi-faceted infection control led to the containment of the outbreak.

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P02

In vitro metabolomic studies on the Echinococcus multilocularis metacestode

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The metacestode (larval stage) of the tapeworm Echinococcus multilocularis is the causative agent of alveolar echinococcosis (AE), which is a severe and in many cases incurable disease in humans and other mammals. Livelong benzimidazole chemotherapy is often the only option for AE patients. Benzimidazoles can cause substantial side effects and therefore novel therapeutic treatment strategies are urgently needed.
We follow the strategy to discover new treatment options against AE by investigating the host-dependent nutritional requirements of the parasite. Like this, specific factors could be targeted to starve the parasite within the host.
We applied metabolomic profiling by 1H Nuclear Magnetic Resonance (NMR) spectroscopy to investigate the nutritional requirements of the E. multilocularis metacestode in an in vitro model.
Of the unambiguously detected metabolites, six were significantly consumed from the medium and thirteen released into the medium. We confirmed the above-described NMR results by amino acid quantification assays, and specific measurements of the energy metabolism and metabolic products. Several released metabolites are involved in the anaerobic malate dismutation pathway, which could offer a potential drug target, as it is not found in mammals. Among the most consumed metabolites was the amino acid threonine. Metacestode growth in vitro was accelerated in L-threonine enriched medium. Currently, we investigate the threonine pathways of the E. multilocularis metacestode to specifically identify key steps in threonine consumption. Preliminary experiments showed increased parasite respiration upon addition of threonine to E. multilocularis metacestodes, which indicates that threonine could be used as a substrate for the energy metabolism of Echinococcus. This could offer new innovative ways for starving the parasite in the future.

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P03

Pentraxin-3 Polymorphisms and Invasive Mold Infections in Patients Undergoing Myeloablative Chemotherapy for Acute Leukemia

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Aims
Single nucleotide polymorphisms (SNPs) in Pentraxin-3 (PTX3) have been associated with the risk of invasive mold infections (IMIs) in hematopoietic cells (HCT) and solid organ transplant recipients. However, similar associations have not been reported in acute leukemia (AL) patients. The aim of this study was to analyze the role of two PTX3 SNPs on susceptibility for IMIs in AL patients undergoing myeloablative chemotherapy.

Methods
All adult patients hospitalized in the isolation Unit of the Lausanne University Hospital for acute myeloid leukemia (AML), acute lymphoblastic leukemia (ALL), or refractory anemia with excess blast-2 (RAEB-2) between 2007 and 2017 who signed an informed consent for genetic biobanking were included. Clinical data were prospectively collected during complete chemotherapy courses, associating induction, consolidation and potential reinduction cycles for up to 6 months. The association between IMI and PTX3 SNPs was assessed by cumulative incidence (CI) curves and uni/multivariable Cox regression models with censoring on last hospitalization date or upon HCT administration, considering death as a competing risk.

Results
Among 185 patients included, 172 completed a single chemotherapy course (N = 172) and 20 two chemotherapy courses (N = 40), for a total of 212 chemotherapy courses (150 in AML, 45 in ALL and 17 in RAEB-2 patients). A total of 26 IMIs (10 proven and 16 probable) occurred. Homozygosity for rs2305619 and/or rs3816527 was associated with an increased risk of IMI (CI = 21% versus 10%, P = 0.04). After stratification according to the absolute neutrophils count (ANC) at leukemia presentation, the association was significant in patients without pre-existing neutropenia (ANC ≥ 500/mm3, CI = 27% versus 6%, P = 0.006) but not in the other (ANC < 500/mm3, P = 0.6). PTX3 SNPs were independent risk factors for IMIs (HR = 5.06, 95% confidence interval 1.68-15.2, P = 0.004) in the non-neutropenic group. These associations remained significant in multivariable analyses (hazard ratio = 4.0, 95% confidence interval 1.55-10.3, P = 0.004) adjusted for age, sex and type of hematological malignancy.

Conclusions
The new evidence for a robust association between PTX3 SNPs and IMIs among AL patients undergoing myeloablative chemotherapy makes PTX3 one of the most promising markers for novel management strategies, especially in this population which may be particularly well suited for genetically-targeted antifungal prophylaxis.

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P04

Validation of the Management of Aortic Graft Infection Collaboration criteria for the diagnosis of vascular graft infection: results from the prospective Vascular graft cohort study

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Aims

There is still a lack of evidence-based, validated diagnostic criteria for vascular graft infections (VGI), although VGIs cause major morbidity, mortality and economic costs. Recently, a formal case definition has been issued by the multidisciplinary Management of Aortic Graft Infection Collaboration (MAGIC)1. We aimed to validate the proposed diagnostic standard for VGI in the prospective Vascular Graft Infection Cohort Study (VASGRA).

Methods

We investigated participants with VGI, suspicion of VGI and contemporary control patients after vascular graft implantation. Using the MAGIC criteria for evaluation, VGI were defined as diagnosed (two major criteria; one major criterion and one minor criterion from a different category), suspected (one isolated major criterion; at least two minor criteria from different categories) or rejected (no criterion, one minor criterion,). We assessed the diagnostic accuracy of the MAGIC criteria by calculating sensitivity, specificity and the positive (PPV) and negative predictive value (NPV).

Results

We analyzed 202 predominantly male (85%) VASGRA participants with a median age of 68 years (Interquartile range [IQR] 58.5-75). Thereof, VGI was diagnosed by our multidisciplinary group in 103 patients (101 definite, 2 possible) and rejected by consensus in 34 patients. As a control group, we included 65 VASGRA participants undergoing routine vascular surgery. Assuming that patients with possible VGI according to our judgement and suspected VGI according to the MAGIC criteria were actually diseased, a sensitivity of 100% (95% Confidence Interval (C.I.) 97-100%), a specificity of 61% (95% C.I. 50-70%), a PPV 73% (95% C.I. 64-78%), and a NPV 100% (95% C.I. 94-100%) was reached. Counting possible VGI (our rating) and suspected VGI according to the MAGIC criteria as not diseased, the diagnostic accuracy improved with a sensitivity of 95% (95% Confidence Interval [C.I.] 89-98%), a specificity of 92% (95% C.I. 84-96%), a PPV 91% (95% C.I. 84-96%), and a NPV 95% (95% C.I. 88-98%).

Conclusion

The current MAGIC criteria offer a high sensitivity and good specificity for the diagnosis of VGI, and therefore they may be safely used for VGI case definition. Considering some shortcomings of the MAGIC scheme (lack of specificity for possible VGI; lack of consideration of histopathology, molecular diagnostics and serology; rating of PET/CT as minor radiologic criterion) further modifications will be needed in the near future.

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The members of the *VASGRA Cohort Study are (in alphabetical order): A. Anagnostopoulos, B. Hasse (Principle investigator), L. Husmann, B. Ledergerber, M. Lachat, D. Mayer, Z. Rancic, A. Scherrer, A. Weber, R. Weber, R. Zbinden, A. Zinkernagel

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P05

Long-term immune response to yellow fever vaccination in HIV-infected individuals depends on HIV-RNA suppression status: Implications for vaccination schedule

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Background
In human immunodeficiency virus (HIV)–infected individuals, the immune response over time to yellow fever vaccination (YFV) and the necessity for booster vaccination are not well understood.

Methods
We studied 247 participants of the Swiss HIV Cohort Study (SHCS) with a first YFV after HIV diagnosis and determined their immune responses at 1 year, 5 years, and 10 years postvaccination by yellow fever plaque reduction neutralization titers (PRNTs) in stored blood samples. A PRNT of 1: ≥ 10 was regarded as reactive and protective. Predictors of vaccination response were analyzed with Poisson regression.

Results
At vaccination, 82% of the vaccinees were taking combination antiretroviral therapy (cART), 83% had suppressed HIV RNA levels (< 400 copies/mL), and their median CD4 T-cell count was 536 cells/μL. PRNT was reactive in 46% (95% confidence interval [CI], 38%–53%) before, 95% (95% CI, 91%–98%) within 1 year, 86% (95% CI, 79%–92%) at 5 years, and 75% (95% CI, 62%–85%) at 10 years postvaccination. In those with suppressed plasma HIV RNA at YFV, the proportion with reactive PRNTs remained high: 99% (95% CI, 95%–99.8%) within 1 year, 99% (95% CI, 92%–100%) at 5 years, and 100% (95% CI, 86%–100%) at 10 years.

Conclusions
HIV-infected patients' long-term immune response up to 10 years to YFV is primarily dependent on the control of HIV replication at the time of vaccination. For those on successful cART, immune response up to 10 years is comparable to that of non-HIV-infected adults. We recommend a single YFV booster after 10 years for patients vaccinated on successful cART, whereas those vaccinated with uncontrolled HIV RNA may need an early booster.

Conflict of interest
C. S. has received financial support paid to her institution from AbbVie, Gilead, Merck, and ViiV. M. S. has received financial support from AbbVie, Gilead, Janssen-Cilag, MSD, ViiV, and Sandoz. A. C. has received support paid to her institution from AbbV.

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P06

Pseudo-outbreak of a carbapenem-resistant Klebsiella pneumoniae on an intensive care unit potentially linked to a contaminated bronchoscope

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Aim

We report the detection and management of a pseudo-outbreak of carbapenem-resistant Klebsiella pneumoniae (CR-KP) in our surgical intensive care unit (SICU).

Methods

A patient colonized with a CR-KP (index patient) was hospitalized and contact-isolated in our SICU in December 2017. Upon detection of the same CR-KP in a respiratory sample of another SICU patient, an outbreak investigation was started. This included screening for and isolation of secondary cases, observation of work processes, reinforcement of hygiene measures, generation of transmission hypotheses, and environmental screening. Case patients were screened at other body sites for CR-KP colonization and whole-genome sequencing was used to characterize and to compare isolates.

Results

We detected CR-KP in 3 secondary SICU patients with the identical resistance profile as the index case, all in broncho-alveolar lavage (BAL) specimens collected with the same bronchoscope. Multiple rectal, urine (in case of urinary catheter), and follow-up sputum/BAL samples remained negative for all 3 patients; no infections developed. Using whole-genome sequencing, a K. pneumoniae multi-locus sequence type (MLST) 37 harbouring the TEM1B β-lactamase, 2 extended-spectrum β-lactamases (OXA-1, SHV-11), and an AmpC β-lactamase (DHA-7) was detected; cgMLST analysis showed identical isolates without allelic differences. Several steps in the cleaning process of the bronchoscope with potential for improvement were identified, such as suboptimal pre-treatment of instruments; high humidity in the storage room; or spatially close stowing of clean and used bronchoscopes. However, swabs taken from the orifices of the incriminated bronchoscope and cultures of rinsing liquid of both the working and suction channels remained negative, even after sonification was performed. After removal of the instrument, no new cases were detected beyond February 2017.

Discussion

A pseudo-outbreak of a CR-KP in our SICU involving the index and three additional cases was potentially related to a contaminated bronchoscope. Outbreak investigations revealed several breaches of hygiene in the cleaning process and storage of the bronchoscopes, which were addressed and resolved.

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P07

Point prevalence study of antibiotic appropriateness in a Swiss University Hospital to tailor antibiotic stewardship interventions.

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Background
The emergence and spread of bacterial resistance are an increasing public health concern. Epidemiological studies support a close correlation between consumption and bacterial resistance. Proactive antibiotic stewardship interventions are limited in Switzerland, although inappropriate antimicrobial therapies have been reported. In our hospital, we have limited data on appropriateness of antibiotic prescriptions. An evaluation was needed to tailor interventions.

Methods
We conducted a point prevalence study in 31 acute medical and surgical units. Intermediate and intensive care units were excluded. All hospitalised patients receiving antibiotics (treatment or prophylaxis) on the day of evaluation were included. Antibiotic appropriateness, including indication, duration, route of administration, spectrum and dosing was evaluated by an infectious disease specialist based on patients' charts, clinical data, microbiological documentation, local antibiotic guidelines and expert opinion.

Results
A total of 564 patients were reviewed, of whom 186 (33%) received one or more topic or systemic antibiotics: 64 (34%) as a prophylaxis and 122 (66%) as a treatment +/- prophylaxis. Among these latter, 90 (75%) were on iv +/- another route of administration, 30 (25%) on oral route only and 2 (1%) on another route only. 69 (58%) presented at least one episode of microbiologically documented infection and 56 (45%) were followed at least once by the infectious diseases team. 70 patients (58%) presented at least one opportunity of treatment adaptation: 23 (19%) were eligible for treatment interruption, 14 (11%) had no indication for at least one prescribed antibiotic, 12 (10%) could benefit from an iv to oral switch, 10 (8%) could have an adaptation of spectrum, 10 (8%) needed a dosing adaptation and 2 (2%) received antibiotics on an inappropriate oral route. Of patients receiving prophylaxis, 37/64 (58%) had no longer indications for antibiotics.

Conclusion
In our hospital, 58% of patient receiving antibiotics on a given day presented at least one opportunity of treatment adaptation, although most of them had been evaluated by the infectious diseases team during the days before. These results highlight the need of joint efforts together with a dedicated antimicrobial stewardship team to improve antibiotics prescriptions and increase prescribers' awareness of necessary daily reassessment of antimicrobial therapies.

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P08

A simplified dolutegravir monotherapy is non-inferior compared to cART in patients with early ART: a randomized controlled trial

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Background
Patients (pt) who started combination antiretroviral therapy (cART) during acute/recent HIV-1 infection show a smaller HIV-1 reservoir size compared to pt who started cART during chronic infection. Thus, we hypothesized that a smaller HIV-1 reservoir size translates in sustained virological suppression after simplification of cART to dolutegravir (DTG) monotherapy (MT).

Methods
In this randomized, open label, non-inferiority trial, we recruited pt > 18 yr with documented primary HIV-1 infection (PHI) who started cART < 180 days after estimated date of infection (EDI), who were fully suppressed for > 48wks (< 50 cp/mL plasma). Exclusion criteria were previous virological failure (VF) or treatment interruption and major resistance associated mutations (RAM) to integrase inhibitors. We randomly assigned patients in a 2:1 ratio to MT with DTG 50 mg once daily or to continuation of standard cART. The primary endpoint was virological response, defined as HIV-1 RNA < 50 cp/mL plasma at wk 48, in the per-protocol (PP) population, with a non-inferiority margin of 10% (ClinicalTrials.gov, NCT02551523).

Results
Between 11/2015-3/2017, we randomly assigned 101 patients (68 to simplification to DTG MT, 33 to continuation of cART). Median age was 42 yr and 83% were MSM. At week 48 in the PP population, 67/67 (100%) had virological response in the DTG MT group versus 31/31 (100%) in the cART group (difference 0%, 95%-CI [-1, 0.047)], showing non-inferiority at the prespecified level. In the intention-to-treat population, 1 pt in the DTG MT group experienced viral failure at week 36 (viral load 382 cp/mL) and 2 patients in the cART group left the study before wk 48 because they moved abroad. The pt in the MT group who experienced viral failure was found to be chronically infected at the start of first cART and therefore violated entry criteria. Resistance test at time of viral failure revealed no RAMs and he was re-suppressed on cART. Overall, 14 severe adverse events occurred (DTG MT 10 [15%]; cART 4 [12%]), none related to study drugs.

Conclusion
In our randomized simplification trial, MT with once daily DTG was effective, safe, and non-inferior to cART in pt with a documented PHI who initiated cART < 180 days after EDI and were virologically suppressed for at least 48 weeks. Our results suggest that future simplification studies should use a stratification according to time of infection at start of first cART.

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P09

A five-day course of oral antibiotics followed by feacal transplantation to eradicate carriage of multidrug-resistant Enterobacteriaceae: A Randomized Clinical Trial

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Background

Fecal microbiota transplantation (FMT) has been suggested to eradicate intestinal carriage with Extended spectrum beta-lactamase (ESBL-E) and carbapenemase-producing Enterobacteriaceae (CPE).

Materials/methods

This publically funded, multicenter (Geneva [G], Paris [P], Utrecht [U], Tel Aviv [T]) open-label, randomized trial examined whether a 5-day course of oral antibiotics followed by FMT is superior to no intervention for the eradication of intestinal carriage of ESBL-E and/or CPE. Adult, immunocompetent patients with ESBL-E or CPE carriage were eligible. Patients were randomized 1:1 to either 5 days of colistin sulphate 2 million IU per os 4x/day & Neomycin sulphate 500 mg (salt) per os 4x/day for 5 days followed by FMT (either by administration of 15 FMT capsules on two consecutive days [G, P] or by a single administration of 80ml of faecal material via nasogastric tube [U,T]). FMT was obtained from healthy, unrelated donors [G, P, U] or from a stool bank [T]. Stool cultures for ESBL-E/CPE carriage were obtained 8-15 days [V2], 16-28 days [V3], 35-48 days [V4, primary outcome] and 5-7 months [V5] after randomization. The targeted sample size was 16 patients per centre. The primary analysis was “intention-to-treat”. ClincalTrials.gov NCT02472600.

Results

Between 02/2016-06/2017 39 patients were randomized [G=14; P=16; U=7; T=2], 22 to the intervention (21/22 underwent the intervention) and 17 to the control. Recruitment stopped in 06/2017 due to lack of further funding. Median age was 65 years (range 22-89), 20 were female, 36 of 39 patients were colonized with ESBL-E and 11 with CPE (8 had both). Of the 22 patients in the intervention arm, 9 (41%) were negative for ESBL-E/CPE at V4. In the control arm, 4 patients were negative (24%), 12 positive and 1 was lost to follow-up (imputed as negative). The intervention had no significant effect (OR for decolonization; 2.0 [95%CI 0.5-7.6]). Study drugs were overall well tolerated.

Conclusions

While this clinical trial failed to achieve its targeted sample size, the results suggest only a small effect of oral non-absorbable antibiotics followed by FMT on the eradication of intestinal carriage of ESBL-E and/or CPE.

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P10

Patient selection for blood culture sampling: A prospective cohort study to compare a prediction score including biomarkers with non-standardized clinical judgement

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Aim
Although still established as gold standard for detection of bacteremia, blood cultures (BC) have a low diagnostic yield resulting in high diagnostic costs. Guidelines for effective BC sampling (BCS) are lacking. A retrospective study reported a high predictive value for BC positivity when different clinical parameters included in the “Shapiro score” were combined with procalcitonin (PCT).

Methods
This single-center, prospective cohort study was designed to validate the SPA criteria (i.e., “Shapiro score” ≥ 3 points combined with PCT > 0.25µg/l) for positive BC prediction in patients with a systemic inflammatory response syndrome (SIRS) and suspected infection at the emergency ward. Predefined overruling criteria for BCS were severe sepsis, immunosuppression, suspected endocarditis or meningitis. The algorithm was tested against individual doctors’ decisions for BCS. We calculated logistic regression analysis with odds ratios (OR) and area under the receiver operating characteristic curve (AUROC) to study associations of predictors and positive BC.

Results
The overall population in this study included 1438 patients with routine BCS, the diagnostic yield for positive BC was 15% (n=215). In patients with positive SPA criteria, the diagnostic yield of BC increased to 31% (173/555), corresponding to an OR of 9.07 (95%CI 6.34-12.97). In patients with either positive SPA or overruling criteria (n=749) the number of positive BC increased to 194 with a slight reduction in diagnostic yield (26%), corresponding to an OR of 11.12 (95%CI 6.99-17.69). In contrast, the diagnostic yield for positive BC in patients without SPA or overruling criteria was only 3% (21/689) with an OR of 0.09 (95%CI 0.06-0.14). Sensitivity, specificity and AUROC were as follows: SIRS (93%, 35%, 0.640), SPA or overruling (81%, 69%, 0.746), PCT > 0.25µg/l (91%, 42%, 0.667), Shapiro ≥ 3 (91%, 40%, 0.657). In the 21 positive BC missed by the algorithm, two had a symptom onset < 24 h and therefore still low PCT, six pathogens were detected alternatively (3 urine, 1 synovial fluid, 1 vertebral tissue culture, 1 urine pneumococcal antigen test).

Conclusions
Our data validated the high prognostic value of SPA combined with overruling criteria for accurate prediction of positive BC with an increase in diagnostic yield from 15% to 26% compared to usual care. The algorithm allows to reduce BC by 48% while still detecting 202/215 organisms (94%), representing a novel diagnostic stewardship tool.

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P11

Antimicrobial resistance of Salmonella isolated from wild animals and reared grasscutters used as animal source food in Côte d'Ivoire (West Africa)

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Aims
The study aims to contribute to the surveillance of food safety and of antimicrobial resistance (AMR) in wildlife and animal source food by assessing the AMR prevalence of Salmonella spp isolated from wild animals and reared grasscutters and by estimating the frequency of risky consumption.

Methods
The study was conducted in Abidjan, located in South-Côte d'Ivoire (CI). We collected swabs and feces among reared grascutters in farms and swabs of dead wild animals sold in markets. Overall 425 samples have been analyzed for Salmonella spp isolation according the protocol ISO 6579. Biochemical and agglutination tests have been used for confirmation and determination of serogroups of strains isolated and then the susceptibility of Salmonella spp to thirteen antimicrobial agents was determined using the Kirby-Baüer method. In addition, consumption interviews were conducted with hunters, butchers, vendors of wildlife and households in Toumodi (south-central of CI), one of the greatest hub in wild animal meat (bushmeat) traffic.

Results
Salmonella were isolated from 14.6% (CI 95 11.4-18.3) of samples with a significant higher frequency in wild animals (22.4%) compared to the reared grasscutters (7%) (OR = 3.8, CI 95 2 – 7.6). The isolated strains belonged to the serogroups B (39.4%), E or G (29.6%), D (16.9%) and C (14.1%). Resistance to at least on antibiotic agent was found in 63% (CI 95 50.2 - 74.7) of strains. Multi-resistances went up to seven antibiotics. No significant difference of AMR was observed between wild animal and reared animals. The highest rates of resistance are observed for Ciprofloxacin (53.8%), Tobramycin (43%), Gentamicin (23%) and Ceftriaxone (13.8%), whereas we found 100% of sensitivity of strains for the following agents: Amoxicilin + Clavulanic acid, Trimethoprim + Sulfamethoxazole and Chloramphenicol. Data analyses are ongoing.

Preliminary conclusion
People handling wild animals are seemingly 4 times more exposed to Salmonella than those in contact with farmed grasscutters. Infrequent use of antibiotics in grasscutter farms likely explains the limited resistances among reared animals. However, the relative risk for human health exists with regard to high resistances observed for some antibiotics, particularly of Ciprofloxacin which is often used for treating human enteric fever.

Key words
wild animal, grasscutter, antimicrobial resistance, food

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P12

Immunogenicity and Safety of Seasonal Influenza Vaccine with Topical Imiquimod in Immunocompromised Patients: a Randomized Controlled Pilot Trial

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Aim
Application of a cream containing the Toll-like receptor 7 agonist imiquimod before intradermal injection of the influenza vaccine has been shown to significantly increase the vaccine immunogenicity in the immunocompetent host, but the effect in immunocompromised patients is unknown. We aimed to assess the impact of an imiquimod-based vaccination strategy in immunocompromised patients and the effect of imiquimod before intramuscular vaccination.

Methods
Kidney transplant recipients (KT) and HIV infected (HIV+) patients were randomized to receive the intramuscular vaccine alone (IM) or, respectively, the intramuscular (IMI-IM) or the intradermal (IMI-ID) vaccine after topical imiquimod. Anti-influenza antibody titers were measured by hemagglutination inhibition assay before and 3 and 24 weeks after vaccination. Vaccine response was defined as seroconversion (4-fold increase in antibody titer) to at least one viral strain 3 weeks after vaccination, and seroprotection as a titer ≥ 1:40. Predictors of vaccine response were analyzed by logistic regression. Participants were followed for 6 months.

Results
Seventy patients (35 KT and 35 HIV+) received the IM (24), the IMI-IM (22) or the IMI-ID (24) vaccine. Baseline characteristics were comparables between groups. Fourteen (61 %) patients in the IM group, 13 (59 %) in the IMI-IM and 15 (65 %) in the IMI-ID group responded to the vaccine (P = 0.909). Vaccine response was significantly better in HIV+ when compared to KT, regardless of the imiquimod application or route of injection (OR 3.7, 95 % CI (1.3 – 10.3), P = 0.015). After vaccination the majority of the patients were seroprotected to all 3 viral strains without differences between groups (19 / 24 (78 %), 15 / 22 (68 %) and 16 / 23 (70 %) in the IM, IMI-IM and IMI-ID groups, P = 0.657). We did not observe any vaccine-related severe adverse event or episode of acute rejection during the study period. One KT and 1 HIV+ patient (1 in the IMI-ID and 1 in the IMI-IM group) developed laboratory confirmed influenza.

Conclusions
Although safe and well tolerated, topical imiquimod before intradermal or intramuscular injection did not improve the immunogenicity of influenza vaccine in KT and in HIV+. Thus, application of topical imiquimod seems not to be an appropriate strategy to improve the immunogenicity of the influenza vaccine in immunocompromised patients.

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P13

Recommandations pour la prévention et la prise en charge des infections par le virus de la grippe dans les hôpitaux de la Suisse latine

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La grippe circule largement en Suisse entre l'automne et le début du printemps. Certains patients sont à risque de complications (pneumonie, perte d'autonomie, décès). Aucune étude récente n'a comparé les mesures de prévention et contrôle de l'infection pour la grippe.
L'objectif de cette recommandation est d'harmoniser les mesures de prévention et la prise en charge de la grippe dans les hôpitaux de Suisse latine.
En 2017-2018, un groupe de responsables du contrôle de l'infection se réunit à l'initiative et sous la responsabilité de la Conférence des Directeurs médicaux de Suisse latine (VD, GE, FR, NE, VS, JU, BE, TI) dans le but d'harmoniser les pratiques dans les hôpitaux de Suisse latine. Les sujets traités sont les mesures de prévention des infections par la grippe, les mesures de prise en charge des patients atteints par la grippe et de leurs contacts, les mesures complémentaires (personnel soignant et visiteurs avec un syndrome grippal).
Le chapitre de prévention des infections par la grippe met l'accent sur la vaccination annuelle du personnel, en particulier le personnel ayant des contacts < 1m avec les patients. Durant l'épidémie de grippe, le personnel non-vacciné ou vacciné depuis < 2 semaines doit porter un masque lors de contact de < 1m avec le patient. Le statut vaccinal doit être facilement identifiable. La prise en charge des patients atteints sera multimodale (masque pour les patients, hygiène des mains, Mesures Additionnelles Gouttelettes dès la suspicion de grippe et jusqu'à 5 jours après le début des symptômes).
Les patients hospitalisés avec des symptômes grippaux aigus (< 5 jours) doivent être diagnostiqués. Le traitement doit débuter après diagnostic, ou avant, pour les groupes à risque de complications, en l'absence de test diagnostic disponible dans les 6-8h. Le traitement doit être initié dans les 48 premières heures de symptômes, voire au-delà pour les patients à risque de complications. Si un cas de grippe est diagnostiqué en cours d'hospitalisation, une prophylaxie post-expositionnelle sera donnée aux contacts à risque de complications. Le personnel soignant avec des symptômes grippaux et de la fièvre doit s'abstenir de travailler et consulter son médecin. En l'absence de fièvre, il peut travailler avec un masque. Le visiteur avec des symptômes de grippe doit reporter sa visite.
Les réunions d'experts ont permis d'établir une ligne commune en Suisse latine pour la prise en charge de la grippe à l'hôpital.

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P14

Antibiotic-resistant pathogens in different patient settings in Switzerland – a narrative review

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Aims
We aimed to summarize the current evidence on the epidemiology of the most important antibiotic resistant pathogens within different patient settings in Switzerland, to identify surveillance gaps, and to compare these findings with data from neighbouring countries.

Methods
We performed a systematic literature search in the Pubmed, MEDLINE, and Embase databases from January 2000 to May 2017 and searched conference proceedings for studies reporting on carbapenemase-producing Enterobacteriaceae (CPE), extended-spectrum beta-lactamase (ESBL) producers, methicillin-resistant Staphylococcus aureus (MRSA), and vancomycin-resistant Enterococci (VRE) from Switzerland. Studies focussing on microbiological aspects without information on patient settings were excluded. We qualitatively summarized the available evidence and gathered prevalence data stratified by time period and patient settings (i.e. adult and pediatric in- and outpatients, long-term care facilities [LTCF], and healthy population).

Results
We identified 791 references and 1,554 conference abstracts. Full-text review was done on 118 records, 86 (including 21 abstracts) were selected. CPE are increasing and have been reported from hospital outbreaks or targeted acute care admission screenings (prevalence range 1-3%). Prevalence among hospitalized acute care or LTCF patients remains unknown. ESBL-prevalence has been reported from universal (5-8%) or targeted (14-21%) acute care admission screenings and for outpatients (3-7%), with increasing trends over time. Among healthy individuals, the highest ESBL-prevalence has been reported for travellers (68-80%) and refugees (9-24%). For MRSA, universal acute care admission screenings from Western Switzerland have shown prevalences of 5% (2005) and 2% (2008), whereas numbers from targeted admission screenings in the East/German part are lower (1-2%). For LTCFs, MRSA-prevalence has been decreasing between 2010 (9%) and 2015 (5%). Prevalence is high among refugees (16-24%) and has been increasing for pig farmers from 0% (2009) to 12% (2015). For VRE, sporadic cases and presumably unrelated outbreaks have been reported from acute care.

Conclusion
There is a scarcity of AMR surveillance data from LTCFs and the pediatric population in Switzerland, whereas outpatients and healthy individuals are relatively well-studied. In line with data from other European countries, MRSA prevalence is declining, whereas ESBL and CPE numbers are increasing.

Additional information
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P15

Promoting an Action Plan for Devices in the Emergency Department – Does it Impact Catheter Duration?

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Aims

Medical devices such as urinary catheters, central venous catheters (CVC) or arterial lines are frequently placed in emergency departments (ED). However, since many devices are inserted for inappropriate and poorly documented reasons1, 2, physicians of the receiving hospital floors are often unaware of their presence and indication, which can lead to unnecessarily long catheterization3. We assessed whether the explicit documentation of the indication of medical devices in the ED report can shorten the duration of catheterization in hospitalized ED patients.

Methods

We conducted an intervention study where all hospitalized patients with a device placed initially in the ED between July 2016 and June 2017 were included. During the intervention period (April – June 2017), all ED physicians were asked to include in the ED report: (1) the type of device; (2) the indication for its placement; (3) an estimated duration of catheterization. The primary outcome was duration of device placement before and after the intervention. Secondary outcomes were device insertion rates of hospitalized patients and compliance with the intervention requirements.

Results

During the study period, 1346 devices were inserted in ED patients admitted to our hospital, of which 771 (57.3%) were urinary catheters, 528 (39.2%) were arterial lines and 47 (3.5%) were CVC. The median duration before versus after intervention were: 70.5 hours [IQR 36.7 – 140.3] vs. 67.1 hours [32.0 – 127.1] for urinary catheters (p = 0.18); 39.3 hours [20.3 – 744.1] vs. 41.9 hours [22.6 – 86.0] for arterial lines (p = 0.51); and 99.8 hours [48.1 – 169.6] vs. 36.9 [24.1 – 108.5] for CVC (p = 0.15). Although the overall insertion rates did not change over the study period (p = 0.45), we observed an increased use of arterial lines in the intervention period (p = 0.01). During the intervention period, devices were mentioned in 102 ED reports (29.6%), and a complete action plan was present in 35 cases (10.1%).

Conclusion

In this intervention study, we observed no decrease in duration of catheterization or insertion rates after our intervention. However, the uptake of documentation was low with an action plan present in only 10% of all cases. Recommending the inclusion of an action plan in the ED report appears to be insufficient for reducing duration of catheterization. Implementing other measures such as mandatory device plans or daily device rounds on receiving hospital floors may be more promising

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P16

Are there seasonal differences in CLABSI incidence rates – results from prospective surveillance in a central European setting

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Aims
Seasonal variations in incidence of a broad spectrum of infectious diseases have been described. Popular examples include respiratory viral infections, chickenpox or viral gastroenteritis. No data is published on the question, whether central line bloodstream infection (CLABSI) incidence also shows a seasonal pattern. We addressed the question of seasonality of CLABSI using prospectively collected data at the University Hospital Zurich and investigated correlation of CLABSI incidence rates with meteorological parameters.

Methods
In January 2016 a manually supported automatic surveillance system for CLABSI incidence was implemented. This surveillance system continuously extracts source data, i.e. presence of central line, length of hospitalization and microbiology results from the patient data management system into Caradigm Intelligence Platform® (CIP). Within CIP a list of patients with possible CLABSI is generated; based on CDC definitions, a specialized infection control nurse differentiates between bacteremia of another origin and CLABSI. Verified CLABSI data were used to calculate quarterly incidence rates (January-March, April-June, July-September, and October-December).
Meteorological data derived from a public meteorological station (StadtZürich, Sicherheitsdepartment, WetterstationMythenquai, https://www.tecson-data.ch/zurich/mythenquai/).

Results
Over a period of 21 months, highest incidence rates for CLABSI were observed in the third quarters of 2016 and 2017. In 2016, the difference in CLABSI rates of the third quarter compared to other quarters was not significant. In 2017, a significantly higher CLABSI rate in the third quarter (IR 1.73, 95%CI 1.17-2.46) compared to other quarters (IR 0.77, 95% CI 0.51-1.12, p= 0.009) was detected. Pooled data from both years confirmed a higher CLABSI rate in the third quarter (IR 1.88, 95%CI 1.44 –2.42; other quarters IR 1.29, 95%CI 1.05 –1.56, p= 0.036). No correlation was detected between CLABSI incidence rates and temperature, humidity and wind force. We found a borderline significant correlation between CLABSI incidence and precipitation (r= 0.433, p= 0.050).

Conclusions
Prospective surveillance identified highest incidence rates of CLABSI in the third quarter of two consecutive years. Future studies are desirable to confirm seasonality of CLABSI incidence and the potential association with precipitation.

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P17

Storage Time of Flexible Endoscopes Longer than 30 Days is Associated with an Increased Contamination Rate

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Background
The maximum storage time for flexible endoscopes is not well defined. Given the paucity of high-quality data, some guidelines do not address storage time at all, while others set the tolerable maximum anywhere between 12 hours and two month. We aimed to delineate the risk of contamination over time in order to identify an optimal time point for reprocessing.

Materials/methods
Single centre surveillance study between March 2014 and April 2017. We analysed microbiological samples from flexible endoscopes obtained for quality control purposes where the date of last disinfection processing was available. Co-variables were sampled endoscope channel, endoscope type, central versus unit-based processing, endoscope use in a dedicated centre, and storage condition. Contamination was defined as detecting ≥10 CFUs/ml flush medium. We used generalized linear and additive models (GAM) to describe effects predicting endoscope contamination.

Results
1.026 flush samples from 106 flexible endoscopes were included. The co-variables were normally distributed for three different storage periods (0-7; 8-30; >30 days). The contamination rate was higher for storage times >30d than for 0-7d (6% vs 1.2%; OR 5.3; 95%CI, 1.2-17.9; p=0.01). The increase in contamination rate after 30 days was displayed in a GAM (p=0.045) and confirmed by subgroup and sensitivity analysis. None of the co-variables were associated with the outcome of interest.

Conclusions
Storage times over 30 days were the only parameter predicting increased likelihood of endoscope contamination. Contamination risk was not influenced by storage condition or unit-based processing. Our data suggest that endoscopes stored for >30 days should be reprocessed prior to clinical use.

Keywords
flexible endoscopes, microbiologic sampling, storage

Additional information

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P18
Hand hygiene: a new campaign targeting hand jewellery

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Aims
Improving hand hygiene quality by removing obstacles that might limit its efficacy: rings, bracelets, watches, nail artifices and long sleeves using an ongoing campaign.

Methods
Since 2012, our institution focused on hand hygiene (HH) improvement. Starting at 61% of HH compliance at baseline, we reached a level of 85% of compliance throughout an 18-monthes project and maintained this level thereafter. The quality of HH practice has never been prospectively assessed, but observation of various hand artifices on health-care workers was observed and might result in suboptimal HH quality.
Institutional dress code requires bare forearms and hands. Wearing a simple wedding ring only remains tolerated. Pilot observations suggested that compliance with the institutional dress code was suboptimal. After a baseline observation in different hospital units, using culture of hand artifices for illustration purpose, we designed three campaigns in order to challenge health-care workers to remove hand artifices, using advertisements inspired by a previous French-campaign and ward leaders exemplary. One month later, we launched the three-part poster campaign in all hospital wards and used a specific leaflet for health-care workers as reminder of the campaign.

Results
Baseline observation of 252 health-care workers during routine clinical activity revealed 17 persons wearing long sleeves (7%), one with nail polish (0.4%), 13 with hand ring (5%), and 50 with a wedding ring (13%); 24 health-care workers wore a wristwatch (10%) and 7 a bracelet (3%). Alltogether, 190/252 (75%) were in conformity with institutional dress code Follow-up observations and project evaluation by HCW are ongoing.
So far, the campaign was well perceived but we especially encountered resistance regarding wedding rings.

Conclusions
Baseline observation of HH quality regarding hand artifices revealed suboptimal adherence to institutional dress code. Raising health-care workers awareness about the importance of HH quality using a three-part campaign will be further evaluated.

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P19

Introduction of pocket dispensers for hand hygiene: things end differently than you think! – A mixed methods study

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Aims
Hand Hygiene (HH) compliance was shown to be poor in several studies. Increasing the availability of alcohol-based hand rub (ABHR) is a cornerstone for improving compliance successfully. In this single-centre intervention study, we introduced pocket dispensers for ABHR and accompanied this introduction by a mixed-method study with a quantitative and an explanatory sequential qualitative approach.

Methods
This study was performed in the Emergency Department of the University Hospital Zurich. During a five-week baseline period and a seven-week follow-up period after introduction of pocket dispensers, we observed HH compliance, measured consumption of ABHR, and investigated self-reported HH compliance and perceived ABHR availability by questionnaire. Semi-structured interviews were coded inductively to assess barriers and facilitators for use of pocket dispensers.

Results
According to multivariable analysis, the average HH-compliance across all indications did not change after the intervention and was 56% (95% CI: 51-62%) and 64% (95% CI: 59-68%) in the baseline and follow-up period (p=0.22), respectively. Further, no significant changes were observed in self-assessed HH compliance, perceived availability of ABHR, or consumption of ABHR. Only 7.5% of ABHR was consumed by use of pocket dispensers in the follow-up period. Semi-structured interviews identified that pocket dispensers were perceived as unnecessary and that wall-mounted or table-top dispensers were directly available during the vast majority of HH opportunities. Also, usability of the pocket dispensers emerged as a main barrier, especially its bottle top and fastening mechanism. Interviews identified two target groups for pocket dispensers: HCP who do not have, or who leave, their designated working area, and HCP who work on wards sparsely equipped with wall-mounted or table-top dispensers

Conclusion
A single intervention of introducing pocket dispensers does not improve hand hygiene compliance or increase disinfectant consumption in a ward already well equipped with dispensers. Pocket dispensers can be useful as a “fallback solution” in specific situations. For broader acceptance and use, the design of the product should be modified to address HCP needs.

Additional information
We would like to acknowledge the contribution of the health care providers of the Emergency Department of the University Hospital Zurich, Switzerland, who took part in the study.

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Nation-wide survey of screening practices to detect carriers of multi-drug resistant-organisms (MDRO) upon admission to Swiss healthcare institutions

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Background
In 2010, a survey conducted in Swiss ICUs revealed a lack of homogeneous MDRO screening practices. As more MDRO are emerging, an update was deemed necessary.
Objective: To evaluate current MDRO admission screening practices in Swiss hospitals and identify potential barriers against their implementation.

Methods
In early 2018, a nation-wide 34-item questionnaire was sent to every Swiss public and private healthcare institution providing inpatient care. Psychiatric institutions and nursing homes were excluded. Data were entered into a spreadsheet, checked for accuracy, and exported to STATA for descriptive analysis.

Results
139 respondents answered for 180 institutions (response rate, 80%), with 57 % from public institutions and 61 % small-size (< 200 beds), 21 % medium-size, and 18 % large-size institutions (> 500 beds). Most non-responders were small-size institutions. The majority of hospitals (72 %) was located in the Swiss-German part. 83% of institutions had implemented some type of admission screening. Targeted screening included CPEs, ESBLs and MRSA at the institutional level for respectively 78 % (115), 81 % (118) and 98 % (145) of institutions. Respectively, 22 (28 %) and 9 (9 %) of private and public institutions did not perform any MDRO admission screening. Among hospitals with on-admission screening, VRE (44 % of institutions), multi-resistant Acinetobacter baumanii (41 %) and Pseudomonas aeruginosa (37 %) were systematically searched only by a minority of institutions, without differences between small and large institutions. A large diversity of risk factors for targeted screening and some heterogeneity in body sites screened were also revealed by this survey. Admission-screening practices were mostly impeded by a difficulty to identify high-risk patients (44 %) and non-compliance of healthcare workers (35 %). Reimbursement issues were less commonly cited as obstacle (15 %).

Conclusions
The survey revealed good compliance with on-admission MDROs screening practices in larger acute care hospitals, but also important gaps in small and private institutions. A mismatch between the current epidemiologic MDRO situation and screening practices was noticed with a disproportionate focus on MRSA and a possible lack of awareness for possible spread of VRE, Acinetobacter and Pseudomonas by unknown carriers, including patients transferred within Switzerland. These results highlight the need for uniform national MDRO screening standards.

Additional information
This survey has been co-financed by the FOPH

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P21

Adaptation des mesures de prévention de la transmission de bactéries multirésistantes pour les établissements de long séjour

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Introduction

Les bactéries multirésistantes (BMR) représentent une cause de morbidité et de mortalité en milieu de soins aigus. Les concepts de prévention des BMR et IAS (infections associés aux soins) concernent également les établissements de soins chroniques (EMS). L'application des mesures hospitalières ne se justifie pas en EMS, les facteurs de risques y étant plus faibles. L'Unité Hygiène Prévention et Contrôle de l'infection (UHPCi) du Canton de Vaud propose dès 2008 une stratégie de prise en charge des résidents en EMS basée sur l'adaptation des MA aux Précautions Standard (PS) en tenant compte des caractéristiques d'un EMS et des risques d'IAS.

Objectif

Proposer des recommandations pour la prise en charge des BMR adaptées au risque de transmission de BMR et à la mission d'un EMS.

Méthode

En l'absence de recommandations consensuelles d'experts pour les soins chroniques et en se basant sur les résultats des études et surveillances conduites en EMS, l'UHPCi a adapté les recommandations BMR pour les soins aigus de manière à proposer un concept de prévention de BMR adapté aux facteurs de risques d'IAS et qui tienne compte de la mission de ce type d'institution.

Résultats

L'application des PS complétées de mesures spécifiques pour certaines BMR (toilettes dédiées, isolement du site colonisé, MAC lors de soins en chambre) favorisent la prévention de la transmission de BMR en dehors de situations exceptionnelles (épidémies, immunosuppression). La rationalisation des recommandations BMR pour les EMS permet de mieux tenir compte des facteurs tels la promotion d'échanges sociaux, d'activités physiques, la vulnérabilité des résidents tant cognitifs que physiques tout en prévenant le risque de transmission de BMR.

Conclusion

L'adaptation des mesures de prévention de transmission de BMR en tenant compte de la mission et des facteurs de risque des résidents garantissent l'adhésion aux recommandations des professionnels, des résidents et de leurs proches tout en permettant de prévenir les IAS.

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P22

Développement d'un concept de formation PCI à l'intention des professionnels travaillant en soins chroniques et en ambulatoires

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Introduction

La formation en Hygiène Prévention et Contrôle de l'infection (HPCi) est indispensable pour la promotion et l'uniformisation des mesures d'hygiène dans les structures sanitaires. En 2011, l'unité HPCi Vaud (UHPCi) a développé un concept de formation en prévention et contrôle de l'infection pour les soignants travaillant en établissement de soins chroniques (EMS) et en soins à domicile (CMS), en vue d'une mise à niveau des connaissances et afin de favoriser, dès la prise de fonction, l'application des mesures de prévention des infections lors des soins.

Objectifs

Offrir aux soignants des CMS et EMS des notions en HPCi leur permettant l'acquisition d'un langage commun, l'actualisation des connaissances et le développement des compétences nécessaires pour assumer une prise en charge optimale du patient.

Méthode

Décliner le concept des Précautions Standard (PS) pour les EMS et CMS en fonction de la catégorie professionnelle des soignants.
Elaborer des vignettes de soins pour promouvoir l'application optimale des PS.
Encourager la participation des soignants à la formation.
Faire évoluer les supports de formation en tenant compte des évaluations des participants.

Résultats / Discussion

Ce concept de formation a répondu à une demande du terrain et a permis de suppléer à l'absence de formation en HPCi des nouveaux collaborateurs travaillant en EMS et CMS.
Depuis 2013, 714 collaborateurs ont été formés (247 diplômés, 467 non diplômés),
Les bénéfices de la formation en termes d'acquisition de connaissance et d'échanges se traduisent par une augmentation du taux d'observance d'hygiène des mains de 75% à 80% (2012-2016).
L'unité HPCi a revu l'organisation de cette formation en 2017 en vue de sa pérennisation.

Conclusion

La période quinquennale 2013-2017 a permis à 247 collaborateurs diplômés et 467 collaborateurs non diplômés de bénéficier des cours dispensés par l'unité HPCi Vaud. Cette formation est devenue obligatoire pour les nouveaux collaborateurs des CMS. Il faut souligner que la présence de personnel formé dans les structures sanitaires constitue une plus-value en terme de sensibilisation aux différents problématiques liés à la prévention des infections. Le résultat des évaluations et la collaboration multidisciplinaire en EMS et CMS a permis de destiner un cours HPCi aux professionnels d'intendance dès 2017.

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Bactériuries à bactéries multiréistantes en EMS : étendue du problème et prévention

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Introduction

Les infections urinaires dues à des bactéries gram-négatif résistantes aux antibiotiques augmentent y compris en collectivité. Les entérobactéries productrices de béta-lactamase à spectre élargi (BLSE), en particulier les Escherichia coli (E. coli), concernent également les établissements de long séjour (EMS) ce qui complique leur traitement présomptif. L'instauration d'une antibiothérapie ciblée, lors d'infection urinaire, permet de limiter le développement et la diffusion de germes multirésistants.
Pour estimer la situation dans les EMS vaudois et évaluer le taux de portage E. coli producteurs de BLSE dans ces institutions, l'unité HPCi (UHPCi) a initié en 2015 une surveillance des bactériuries en EMS.

Objectif

Evaluer le taux de portage de BLSE en particulier E. coli dans les EMS vaudois.

Méthode/Strategie

Depuis 2015 l'UHPCi surveille les bactériuries dans les EMS vaudois en collaboration avec les laboratoires. La participation des EMS est volontaire. A chaque résultat d'analyse bactériologique d'urine positive, une copie est adressée à l'UHPCI.
Les résultats sont centralisés dans une base de données. Une analyse des microorganismes retrouvés est effectuée.

Résultats/Discussion

La quasi-totalité des EMS vaudois (94%) et 12 laboratoires participent à la surveillance. En 2017, 2,325 résultats ont été récoltés. L'analyse de ces données a mis en évidence pour 2017 : 84% d'entérobactéries dont 74% d'E coli ; pour 2016 : 84% d'entérobactéries dont 75% d'E coli alors qu'en 2015, les entérobactéries représentaient 89% des prélèvements dont 74% d'E. coli. Le taux d'entérobactéries productrices de BLSE était estimé à 12% (16% E. coli), 11% (13% E coli) et 9% (11% E coli) respectivement pour 2017,2016 et 2015.

Conclusions

Nous observons une présence non négligeable d'entérobactéries porteuses de BLSE, en particulier d'E. coli, dans les EMS vaudois. Mais les taux observés sont comparables à ceux de la surveillance européenne et nationale en collectivité.
La pérennisation de cette surveillance permet d'adapter par une bonne connaissance de l'écologie bactérienne locale nos recommandations de prise en charge des résidents infectés

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Antibiotic Resistance in Swiss Long-Term Care Facilities: Analysis of National Surveillance Data over an 11-year Period between 2007 and 2017

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Aims
We evaluated data from nursing home (NH) patient isolates sent to the Swiss centre for antibiotic resistance (ANRESIS). Resistance data for carbapenem-resistant (CR) Gram-negative pathogens, extended-spectrum cephalosporin-resistant (ESC-R) Escherichia coli/Klebsiella pneumoniae, methicillin-resistant Staphylococcus aureus (MRSA), and glycopeptide-resistant enterococci (GRE) were analysed.

Methods
We extracted data from Jan 2007 to Oct 2017. Linear regression was used to estimate the association between resistance and year of surveillance. For ESC-R and MRSA, univariable and multivariable logistic regression were performed to assess factors independently associated with resistance. For every canton, we estimated the coverage rate, defined as number of beds in the dataset from governmentally funded NH who sent at least one isolate in 2014, 2015, and 2016, divided by the total number of funded beds for the respective canton.

Results
From 2007 to 2017, ESC-R E. coli increased from 5.4% to 21.6% (P < 0.0001); isolates originating from East/Central Switzerland (vs. South/West; OR 0.5, 95% CI 0.4-0.7) were less likely, and those from men (vs. women; OR 1.6, 95% CI 1.2-2.1) more likely to exhibit ESC-R. Co-resistances were more common for ESC-R than for ESC-S isolates, with 75% of ESC-R E. coli isolates being resistant to fluoroquinolones. Resistance rates to fosfomycin (6.8%) and nitrofurantoin (8.8%) were low. Among 1'482 isolates of S. aureus, 556 (37.5%) were resistant to methicillin. Prevalence decreased over time from 34% in 2007 to 25.9% in 2017 (P=0.004). Isolates from East/Central Switzerland were less commonly resistant than those from South/West Switzerland (OR 0.1, 95% CI 0.1-0.2, P < 0.0001). Among P. aeruginosa, 9.6% were CR; CR Enterobacteriaceae (0.3%) and GRE (0.4%) were rare. Considering 11'584 samples from governmentally funded NHs, the national coverage rate was 9%. Whereas some cantons did not provide any isolates to ANRESIS, others had coverage rates of up to 58%, with a significant difference between cantons in the South/West (median 13%, IQR 4-43%) and East/Central (median 0%, IQR 0-5%) (P=0.02).

Conclusion
ESC-R among E. coli is emerging in Swiss nursing homes, whereas MRSA show a declining trend. For ESC-R E. coli, fosfomycin and nitrofurantoin remain reasonable treatment options. A minority of Swiss nursing homes is represented in ANRESIS, with a preponderance of institutions from South/Western Switzerland.

Additional information
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Évaluation des pratiques d'une équipe de stomathérapie dans le cadre de l'investigation d'épidémies d'entérocoques résistants à la vancomycine (VRE)

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Introduction
Dans le cadre d'investigations menées suite à 2 épidémies de VRE en 2016/2017 dans un service de chirurgie ayant impliqué 93 patients, dont 23% étaient porteurs d'une stomie, nous avons évalué les pratiques de soins chez ces patients.

Objectif/ Question
Identifier les opportunités d'amélioration des soins de stomies afin de diminuer les risques de transmission croisée de VRE.

Methode
Observations directes par une infirmière PCI de la gestion des stomies par l'équipe de soins, suivies par des entretiens avec l'équipe de stomathérapie pour déterminer l'adéquation des techniques de soins en regard de la gestion sécurisée des excreta.

Résultats/ Discussion
Plusieurs opportunités d'amélioration ont étés relevées concernant la gestion de l'élimination des poches, la désinfection de l'environnement et du matériel et l'hygiène des mains. Cela a amené à réviser la procédure de la gestion des stomies en concertation avec l'équipe de stomathérapie et les cadres de chirurgie. Nous avons créé en collaboration interprofessionnelle des outils didactiques (ateliers, affiche informative spécifique).

Conclusion
Ce travail a permis de montrer l'importance de savoir se repositionner : revoir les pratiques en place et favoriser la collaboration de l'équipe HPCi avec les différents professionnels concernés.
Une gestion plus sécurisée des soins chez les patients avec stomie est une des mesures qui peut contribuer à diminuer le risque de transmission VRE.

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Portage de BMR chez les patients hospitalisés à l'étranger: expérience d'un dépistage systématique dans un centre hospitalier universitaire entre 2014 et 2017

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Introduction / objectif du travail
Les patients rapatriés ou hospitalisés dans les 12 mois à l'étranger sont connus pour être à haut risque de portage de bactéries multirésistantes. Leur prise en charge est encadrée par des recommandations institutionnelles. Notre objectif était de décrire les résultats de la mise en place de dépistages systématiques à leur admission.

Matériels et Méthodes
À partir du système de gestion du laboratoire, une extraction de toutes les recherches de BMR entre le 01.01.14 et le 31.12.17 (N=42753) a été effectuée. Les recherches simultanées dans les 72 premières heures d'hospitalisation d'un pool des 4 BMR (ou familles de BMR) suivantes ont été identifiées : Staphylococcus aureus résistant à la méticilline (MRSA), entérobactérie productrice de béta-lactamase à spectre étendu hors E. coli (ESBL), entérocoque résistant à la vancomycine (VRE) et entérobactéries productrices d'une carbapénémase (EPC). Les informations relatives au motif de réalisation de ces pools (rapatriement, antécédent d'hospitalisation à l'étranger dans les 12 mois ou prise en charge dans le cadre d'un programme humanitaire) ont été recherchées dans le dossier médical informatisé.

Résultats
1202 patients-séjours ont eu un pool de dépistage à l'admission. Parmi eux, 928 (77%) entraient dans les recommandations ; les autres correspondaient à : d'autres motivations de prescription (8%) (suivi de portage déjà connu, extension d'un dépistage qui ne devait cibler qu'une BMR) ; la notion de voyage, de consultations, d'hospitalisations à l'étranger plus anciennes (7%) ou un suivi de patients de programmes humanitaires (7%). Au moins une BMR a été identifiée chez 148 des 928 patients (16%), avec respectivement 83 ESBL, 45 MRSA, 23 EPC et 17 VRE. L'incidence pour les patients transférés ou avec antécédent d'hospitalisation à l'étranger était de 11.6%, vs 27.1% pour les patients inscrits dans un programme humanitaire ($p < 10\text{-}6$). Stratifié selon les régions OMS, la positivité à au moins une BMR était pour l'Afrique de 66/244 (27%) vs 82/684 (12%) pour le reste du monde ($p < 10\text{-}6$). Pour l'Europe, ce taux était le plus bas (44/482 ; 9%).

Conclusion
Ces données confortent l'importance de la recherche des BMR chez les patients ayant eu un contact avec les milieux hospitaliers à l'étranger et justifient la mise en place d'isolements préemptifs.

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Evaluation of antibiotic appropriateness and possibility of early discharge from hospital among patients admitted in a Swiss University Hospital: a point prevalence study

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Background
To decrease the risk of nosocomial complications, reduce cost and accelerate patients' rehabilitation, antibiotic prescription optimization in hospital should be combined with an early discharge plan. Few studies have examined eligibility for early hospital discharge and the need for community follow-up structures among patients on antibiotics. A punctual evaluation was conducted at the University hospital of Lausanne, Switzerland, to evaluate antibiotic appropriateness and patients' suitability for early discharge.

Methods
An evaluation was performed prospectively by an infectious disease specialist in 31 acute medical and surgical units on a given day between March and June 2017. Intermediate and intensive care units were excluded. All hospitalised patients receiving antibiotics (treatment or prophylaxis) on the day of evaluation were included and evaluated for antibiotic appropriateness, including the possibility of antibiotic stop or switch from intravenous to oral route. Suitability for discharge on the day of evaluation was then assessed by a 3-step algorithm: favourable clinical and paraclinical evolution, absence of comorbidities requiring hospitalisation and independence in daily activities on the basis of the medical and nurses observations. Among patients suitable for discharge on the day of evaluation, the real discharge date was recorded to calculate the potential reduction of hospital stay. Finally, the need of additional community support was evaluated.

Results
Among a total of 564 patients reviewed, 120 (21%) received at least one systemic antibiotic treatment: 90 (75%) were on intravenous treatment and 30 (25%) on oral treatment only. Among these 120 patients, antibiotics were no more needed in 30 patients (25%) and 12/90 patients (13%) could have benefited from an intravenous to oral switch on the day of evaluation. Eleven patients (9%) were eligible for discharge, saving potentially a total of 29 bed-days. Seven patients (6%) could have been discharged with community support, including outpatient parenteral antimicrobial therapy (OPAT).

Conclusion
This punctual evaluation using a systematic approach shows that antibiotics could have been stopped or switched from iv to oral in 35% of patients and that 9% of patients were eligible for discharge. Reflexion on a dedicated antimicrobial stewardship team implementation and development of flexible community follow-up structures are needed.

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Clinical presentation, management and outcome of hospitalized patients with seasonal influenza

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Aims
Data on the management and outcome of complicated influenza cases in hospitalized patients is limited. The objective of this study was to describe clinical characteristics, management strategies and outcomes of inpatients with seasonal influenza infection.

Methods
We conducted an observational cohort study of all hospitalized patients with laboratory-confirmed influenza infection in an academic hospital in Bern, Switzerland, during two influenza seasons. Medical records were reviewed retrospectively for the 2015/16 and 2016/17 seasons.

Results
We analyzed data from 265 hospitalized patients, of which 13.2% (n = 35) were healthcare-associated influenza episodes. Median age was 58 years, with a biphasic distribution: More than half (56.6%) were ≥ 65 years and 10.9% were < 5 years. 25.6% (n = 68) of the patients had an underlying chronic pulmonary disease, 54.7% (n = 145) a chronic cardiovascular disease and 49% (n = 130) some form of immunosuppression; most of the latter received either immunosuppressive treatment (19.6%, n = 52) or had an active malignancy (15.5%, n = 41). Mean length of stay was 7.8 days (± 6.3), 2 days longer than the average length of stay (5.8 days) at Bern University Hospital. 46% (n = 121) of the patients were treated with neuraminidase inhibitors. 61% (n = 162) received antibiotics, although 25% of these did not exhibit pulmonary infiltration in imaging studies. 78% (n = 207) of the patients had blood cultures drawn but microbial growth was detected in only 4% (n = 11) of them. 135 (50.9%) patients developed complications during hospitalization, most of them involved the respiratory tract (83.7%, n = 113). Poor outcome was defined as the need of intensive care or death. In our study 47 (17.7%) patients were admitted to the intensive care unit (ICU) and ten (3.8%) died. Independent predictors for poor outcome, were age, longer duration of symptoms at inclusion, chronic cardiovascular or pulmonary disease, ongoing malignancy and pulmonary infiltration in imaging studies.

Conclusion
Hospitalized patients with influenza infection are at increased risk of complications and poor outcome, especially if they are older, have underlying chronic conditions or signs suggestive of bacterial superinfection. These data reinforce the need to monitor hospitalized patients with seasonal influenza regarding disease severity in order to prevent morbidity and mortality.

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Feasibility of prospective influenza surveillance among primary care workers in Switzerland

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Aims
Although primary care practices play a key role during annual influenza epidemics, their role in the transmission chain has rarely been explored. A better understanding of influenza epidemiology among primary care workers could guide future recommendations to prevent transmission in this setting. This pilot study aims at evaluating the feasibility of a work-based online surveillance system for influenza among workers of primary care practices.

Methods
Observational prospective pilot study, conducted between week 40 in 2017 and week 16 in 2018 in one walk-in clinic and two selected primary care practices. Staff working in the practices, aged ≥ 18 years and having a work contract covering the study period, were invited to record symptoms of influenza-like illness (ILI) in a weekly online survey. Patients with symptoms also self-collected a nasopharyngeal swab following written instructions. Samples were tested for influenza A and B viruses by RT-PCR on a weekly basis and, twice during the season, for a panel of respiratory pathogens (FTDresp21). Main outcomes were the adhesion to online survey by primary care workers, the weekly survey response rate and the fully completed questionnaire rate. Secondary outcomes were the assessment of ILI attack rate and the confirmed influenza cases over the entire influenza season as well as the influenza vaccination coverage.

Results
Out of 69 eligible, 39 (56.5%) consented to the study, 19/49 (38.8%) in the walk-in clinic and 20/20 (100%) in both private practices, corresponding to 23 physicians and 16 medical assistants. 36 (92.3%) finally provided data in the online survey, completing a median of 27 weekly questionnaires out of 29 (IQR 23 – 28.5).
Out of 79 symptomatic episodes (mean 2.2 per participant), 10 fitted the ILI case definition (7 participants). Among the 8 swabbed ILI, one was confirmed to be due to influenza A virus H1N1 (AR 2.8%), in addition to 2 rhinoviruses and one coronavirus OC43.
In total, 20 swabs were taken, a median of 3 days after start of symptoms (IQR 1 – 5), and received in the lab a median of 2 days later (IQR 1 – 3). Out of 16 (4 missing data), 7 (43.8%) were autoswabs, mostly done by physicians (85.7%).
Conclusion
The study confirmed the feasibility of a work-based online surveillance system for influenza among primary care practices workers. The attack rate of symptomatic influenza appeared to be low in this population.

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P30

OPTIMAL DETECTION OF COLONIZATION BY COLISTIN-RESISTANT GRAM NEGATIVES WITH THE SUPERPOLYMYXIN MEDIUM

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Background
The recent identification of plasmid-mediated colistin resistance genes (mcr-1 to mcr-5) worldwide revealed that a likely silent dissemination of those colistin resistance detrminants actually occurred those latter years. In this context, the ECDC recommended in 2016 to perform sentinel testing surveys and to ensure the containment of MCR-producers by enhancing control measures.
Recently, a screening medium, the SuperPolymyxin medium was developed to detect colistin-resistant Gram negative rods from clinical samples. The objective of this study was to implement a protocol to screen colistin-resistant Gram negative rods from rectal swab samples with the commercial version of the SuperPolymyxin medium (ELITech MICROBIO, France).

Materials/Methods
In this study, 57 rectal swab samples (41 clinical rectal swabs and 16 spiked rectal swabs) were tested.Clinical rectal swabs were suspended into BD ESwab transport medium. Ten microliters of the medium was transferred and streak onto the SuperPolymyxin plate. An Eosine Methylene Blue plate was streak in parallel with the same protocol. The plates were incubated for 48 hours at 37°C and visually inspected at 24 and 48 hours to evaluate the growth of bacterial isolates. Each aspect of colony growing on the two medium was identified using MALDI-TOF mass spectrometer and colistin MICs were determined by broth microdilution reference method.
Sixteen spiked rectal swab samples were also tested with a collection of enterobacterial isolates carrying mcr-1 to mcr-4 genes. Using an inoculum of ≈108 CFU/ml, serial 10-fold dilutions were made. Spiked rectal swab samples were made by adding 100 µl of each strain dilution to 900 µl of rectal swab transport medium obtained from a healthy volunteer. The plates were streak as indicated above.

Results
The overall sensitivity and specificity of the commercial SuperPolymyxin medium was of 100% and 90.3%, respectively. Noteworthy, the detection of the isolates producing MCR-1, MCR-2, MCR-3 or MCR-4 was excellent with a lowest detection limit of 103 or 104 cfu/ml.

Conclusions
The SuperPolymyxin medium provides a significant improvement for detection of fecal carriage with colistin resistant isolates regardless of the level and the mechanism of colistin resistance.

Conflict of interest
Development of the home-made version of the superpolymyxin medium in our unit.

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P31

Catheter-Related Bloodstream Infections with Coagulase-Negative Staphylococci: Are Antibiotics Necessary if the Catheter is Removed?

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Aims
Catheter-related bloodstream infections (CRBSI) with coagulase-negative Staphylococci (CoNS) are a common source of hospital-acquired bloodstream infections. The main objective of this study was to elucidate the role of systemic antibiotic therapy in the setting of catheter removal in adult patients with CoNS-CRBSI.

Methods
We performed a retrospective cohort study on patients with CoNS-CRBSI between 2008 and 2016 with a follow-up period of up to 12 months. The inclusion criteria for this study were: removed intravascular catheter with a positive quantitative catheter tip culture with CoNS and the same CoNS isolated from a blood culture seven days before to two days after catheter removal. Outcomes were complicated course (presence of prolonged bacteremia or symptoms attributed to CoNS-CRBSI > 2 days after the catheter removal), recurrences, mortality and length of hospital-stay after catheter removal. We compared outcomes between a group with antibiotic treatment prescribed according to current Infectious Diseases Society of America (IDSA) guidelines (≥ 5 days, treatment group) and a “no-treatment” group.

Results
Our study population comprised 184 CoNS-CRBSI episodes. Twenty-seven percent (n = 49) had orthopedic hardware or intravascular prosthetic material in place. Seventy-six percent (n = 145) received antibiotic treatment according to current IDSA guidelines, 17% (n = 32) did not receive any antibiotic therapy. There was no complicated course in the no-treatment group (n = 0). Neutropenia, hematologic cancer and immunosuppression were significantly more frequent in the treatment group. The case-control-subgroup-analysis with 32 matched pairs showed no significant difference in frequency of complicated course (0% no-treatment group vs. 22% treatment ≥ 5 days group, p = 0.06). The remaining outcomes were similar in the two comparison groups.

Conclusions
Our findings indicate that withholding antimicrobial therapy is not associated with either short-term complications or long-term recurrences, even if orthopedic hardware or intravascular prosthetic material remained in place.

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P32

The Link between Poster Campaign and assessed Hand hygiene Compliance during a five-year Surveillance

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Aims
Hand hygiene (HH) became one of the most important preventive measures for hospital acquired infections. It is well known, that training leads to higher level of compliance. However, little is known about keeping a high level compliance in hand hygiene.

Methods
We performed a prospective study of the impact of a poster campaign on HH compliance in a 200-bed hospital. After an initial training according to Swiss Hand Hygiene (SHH) campaign focusing on the 5 moments, a different poster campaign was conducted in each year. The posters were displayed in all working spaces. For the purpose of compliance assessment included the range of HH in 1006 to 1068 opportunities/ 793 to 875 actions a year during a 4 month study period. The compliance was assessed by trained (based on Swiss Hand Hygiene (SHH) campaign) staff who participated in the prevention of hospital infections.

Results
Over the 5 years, a total of 5209 opportunities and 3335 actions were observed. The median overall HH compliance was 82% (range: 77% - 84%). The doctors had a median HH compliance of 84% (72% - 91%), nurses a compliance level at 83% (77% - 84%) and the auxiliary staff 75% (64%-84%). The HCW in surgical wards showed a significant lower HH compliance than HCW in medical wards. The compliance of doctors (median 68% (56% - 91%)) was much lower than the compliance of nurses (median 78% (54% - 95%)) in surgical wards. In contrast, the compliance of doctors (median 99% (93% - 100%)) was better than nurses (median 87% (74% - 98%)) in medical wards. There was no significant change of hand hygiene compliance during the 5 year observation period.

Conclusion
This study shows that poster campaign as a reminder in hand hygiene is an excellent tool to keep high levels of hand hygiene compliance. However, the Hand Hygiene training should be more frequent in HCW in surgical wards.

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P33

UV Dekontaminationsgeräte kritisch beleuchtet: Hype oder Zukunft?

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Background

Hospitalisierte Patienten sind dem Risiko ausgesetzt, sich via Spitalumgebung mit multiresistenten Keimen anzustecken. Da die manuelle Desinfektion Lücken aufweisen kann, wurde in den letzten Jahren bei der Schlussdesinfektion von Krankenzimmern die Wirksamkeit von UV-C Strahlern als ergänzende Massnahme untersucht. Wir wählten zwei in der Schweiz erhältliche Systeme für Praxistests aus. Mittels standardisierten Abklatschuntersuchungen sollte die Wirksamkeit der UV-Desinfektion im Alltag nachgewiesen werden.

Methode

Die Tests wurden mit den Geräten UV-360 von UVDI, einem Singletower mit Rundstrahlung, und Surfacide von Helios, einer Dreiereinheit mit drehenden Säulen und zielgerichtetem UV-Strahl, durchgeführt. Abklatschproben in den Testzimmern wurden vor und nach der Schlussdesinfektion sowie nach der UV-Desinfektion an standardisierten Punkten mit hoher Berührungsfrequenz entnommen.
Die Proben, (Hygicult TPC Slides, Orion Diagnostica), wurden bei 36°C inkubiert und nach 24h und 48h abgelesen. Die Geräte wurden gemäss Herstellerprotokoll im Raum positioniert und gemäss empfohlenen Bestrahlungszeiten eingesetzt. Es wurden pro Gerät je fünf Zimmer geprüft.

Resultate

Mit der manuellen Desinfektion reduzierte sich die durchschnittliche Keimbelastung an den Testpunkten um etwa 60-70%. In der Folge verblieben statt einer Mischflora vielmals aerobe Sporenbildner wie Bacillus cereus. Nach der UV Desinfektion liessen sich an diesen Stellen keine oder sehr wenige Keime nachweisen. Die beiden Systeme erwiesen sich als gleichermassen wirksam.
Im Handling zeigten sich jedoch deutliche Unterschiede: Das Gerät UV-360 lässt sich einfach bewegen, die integrierte Steuerung ist sehr einfach in der Handhabung. Das Gerät Surfacide ist, durch die drei Tower bedingt, etwas anspruchsvoll beim Manövrieren. Die Steuerung erfolgt via Bluetooth und Remote Control.

Diskussion

Der Einsatz von UV-C Strahlern bewirkte eine fast vollständige Inaktivierung der vorhandenen Keimflora in den ausgetesteten Spitalräumen. Es fanden sich Unterschiede punkto Einfachheit des Handlings zwischen den untersuchten Geräten. Für einen künftigen Einsatz im Spital müssen klare Indikationen entwickelt werden.

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Measles: Atypical clinical presentation and transmission to vaccinates healthcare worker

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Background
Indigenous measles are not yet eliminated in Switzerland. Therefore, healthcare-workers (HCW) are still exposed to patients with measles. We describe an atypical clinical presentation of measles in a vaccinated patient, the transmission to a vaccinated HCW and the results of the investigation.

Methods
In this primary-care institution, HCW are considered to be immune in case of i) 2 documented measles vaccines, ii) a documented protective IgG titer, or iii) birth year < 1964. Immunisation is recommended for all non-immune employees. In case of unprotected contacts, examination of the immunity against measles is foreseen in patients and HCW, evaluation of private contacts is done by the cantonal medical service.

Results
A 32-year old man (index patient) presented with acute gastrointestinal symptoms, followed by a maculopapular rash and fever without respiratory symptoms or conjunctivitis. Measles nasopharyngeal PCR was positive and serology showed positive IgM and IgG, suggesting previous vaccination. (no Vaccination status available). Due to the atypical clinical presentation, implementation of isolation precautions where delayed. The evaluation of 31 exposed HCW showed 11 with missing/no information on vaccination (which were all IgG positive in serology testing) and 3 patients born before 1964. Ten days after exposure, an exposed 23-old female nurse developed gastrointestinal symptoms, fever and a papulo-vesicular rash on the forehead, and PCR from the nasopharynx was also positive for measles. She had 1 documented vaccination and an IgG titer of 23 VE (with a cut off of < 9) and was therefore not flagged in the initial HCW screening round. Her unvaccinated 7-month old boy received passive immunization. Contact screening revealed 35 exposed patients (5 born after 1964, all vaccinated twice), 27 HCW with missing/no information on vaccination (5 exposed, all with positive Ig G serology).

Conclusion
This report illustrates that i) the clinical picture of measles in vaccinated patients is often atypical and ii) implementation of isolation precaution is delayed and iii) vaccinated people cannot only acquire measles but can potentially also transmit them . As recommended by the FOPH, all HCW born after 1965 should be documented to be vaccinated twice. Nevertheless isolation precaution should probably be applied by all HCW in care of measles patients irrespective of their immune status. The role of a booster vaccine in adulthood should be evaluated.

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P35

Spitalaufenthalt hinter geschlossenen Türen! Auswirkungen von infektionspräventiven Isolationsmassnahmen auf die psychische Gesundheit - Eine systematische Literaturarbeit

S Passerini
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Ausgangslage

In der Schweiz erleiden jährlich 7–8% der hospitalisierten Patientinnen und Patienten an einer spitalerworbenen Infektion. Werden während dem Spitalaufenthalt Krankheitserreger mit einem erhöhten Übertragungspotential oder erhöhter Gefährlichkeit gefunden, kommen bei Betroffenen sogenannte Isolationsmassnahmen zum Einsatz. Sie werden gebraucht, um Mitpatientinnen und Patienten, sowie das Personal vor einer Infektion zu schützen. Isolationsmassnahmen können jedoch auch negative Auswirkungen haben. Deshalb wurde eine Literaturarbeit durchgeführt mit der Fragestellung: Welche Auswirkungen haben Isolationsmassnahmen zur Infektionsprävention auf die psychische Gesundheit von hospitalisierten erwachsene Patientinnen und Patienten?

Methode

Diese systematische Literaturarbeit wurde durchgeführt anhand der PRISMA Guideline. Die Datenbanken CINAHL, Cochrane Library, Medline, PsychINFO und Web of Science wurden durchsucht für Artikel, publiziert zwischen 2009 – 2017 in Deutscher und Englischer Sprache. Verwendet wurden Schlüsselwörter, die die Bereiche Isolationsmassnahmen, Übertragungs- und Infektionsprävention sowie die psychische Gesundheit abdecken.

Ergebnisse

Neun Studien wurden eingeschlossen. Es wurden positive und negative Patientenerfahrungen mit Isolationen gefunden. Die Massnahme wird in drei Studien als Einschränkung der Geselligkeit und Interaktion mit Mitmenschen wahrgenommen und sind gemäss sechs Studien mit negativen psychologischen Auswirkungen assoziiert, einschliesslich Angst und/oder Depressionen. Dazu kommen gemäss fünf Studien Gefühle wie Wut, Verwirrtheit, Schuld, Stress und Frustration. Andererseits zeigen drei Studien auf, das Patientinnen und Patienten bei Verlegung von einem Mehrbettzimmer in ein Einzelzimmer von der Ruhe und Privatsphäre in einem Einzelzimmer profitieren.

Schlussfolgerung

Aufgrund der möglichen negativen psychischen Auswirkungen von Isolationsmassnahmen sollen Isolationen so kurz wie möglich gehalten werden, z.B. durch schnellen Ausschluss der Verdachtsdiagnose oder modifizierende Faktoren, die das Betreten des Isolationszimmers für Mitarbeitende erleichtert (z.B. keine Handschuhe bei Kontaktisolation). Die individuellen Bedürfnisse von betroffenen Patientinnen und Patienten müssen erkannt werden, um entsprechend – präventiv und proaktiv - emotionale Unterstützung bieten zu können: eine gute Information über die Bedeutung der Isolation, Reduktion von Langweile und Erhöhung der Selbstkontrolle.

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P36

Kennen Pflegefachpersonen den präventiven Nutzen der Mundpflege gegen nosokomiale Pneumonien? – Eine qualitative Studie

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Ziel

Pneumonien bei nicht-intubierten Patienten (non-ventilator-associated hospital-acquired pneumonia, nvHAP) gehören zu den häufigsten spitalerworbenen Infektionen. Zahn- und Mundpflege ist eine wichtige Präventionsmassnahme zur Verhinderung von nvHAP. Primäres Ziel dieser Studie war, den Wissensstand von Pflegefachpersonen bzgl. Mundpflege als Präventionsmassnahme für nvHAP zu ermitteln. Als sekundäres Ziel wurde die persönliche Haltung zur Mundpflege und ihrer Priorisierung in der Pflegepraxis untersucht.

Methode

Diese qualitative Studie wurde am UniversitätsSpital Zürich (USZ) durchgeführt. Wir führten semistrukturierte Interviews mit Pflegefachpersonen durch. Eingeschlossen wurden Pflegefachpersonen mit einer abgeschlossenen Ausbildung oder einem Bachelor in Pflege, welche seit mindestens 12 Monaten am USZ tätig waren. Die Interviews wurden aufgenommen und verbatim transkribiert. Der Interviewinhalt wurde mittels eines induktiven Ansatzes nach Elo & Kyngäs (2008) analysiert.

Resultate

Neun Pflegefachpersonen von verschiedenen Abteilungen des USZ wurden interviewt. Nur zwei von neun Pflegefachpersonen wussten um den nvHAP-präventiven Nutzen der Mundpflege. Diese beiden Pflegenden wurden im Ausland ausgebildet, das Thema Mundpflege als Infektionsprävention war Bestandteil ihrer Ausbildung. Die Mundpflege-Arbeitsanweisung des USZ war den meisten Interviewten nicht bekannt. Aufgrund von begrenzten zeitlichen Ressourcen wird die Mundpflege maximal zweimal täglich durchgeführt und häufig delegiert, gelegentlich sogar an ungelerntes Personal. Der Mundpflege wird eine tiefere Priorität zugeschrieben als medizinaltechnischen Verrichtungen. Pflegefachpersonen haben die Einstellung, dass selbständige Patienten für ihre Mundpflege selber verantwortlich sind und scheuen sich, das Thema mit den Patienten anzusprechen.

Schlussfolgerung

Die meisten Pflegefachpersonen kennen den infektionspräventiven Nutzen von Mundpflege nicht, priorisieren Mundpflege (deswegen?) tief und delegieren sie häufig. Die Wissenslücke basiert auf ungenügender Sensibilisierung während der Ausbildung und auf fehlende Strukturen beim Wissenstransfer im klinischen Alltag. Ein strukturierter Ansatz ist erforderlich, um das Wissen über Mundpflege als präventive Massnahme zu vermitteln.

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P37

Antibiotic prescriptions and prescription profiles delivered through self-dispensing physicians versus pharmacies in the outpatient setting in Switzerland

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Aims
In Switzerland, outpatients mainly get the antibiotics in pharmacies by prescription or directly by self-dispensing physicians. Self-dispensing physicians account for around 32% of all medical practitioners. The objectives were to compare antibiotic prescriptions and prescription profiles in the outpatient setting according to the delivery mode (through self-dispensing physicians versus pharmacies).

Methods
Antibiotics for systemic use (class J01 of WHO ATC system, 2017) were collected over the years 2015-2016. The analysis of antibiotic consumption data was carried out on behalf of the Swiss Federal Office of Public Health through IQVIA database which provides pharmaceutical sales data. Aggregated data were converted into defined daily doses (DDD) and antibiotic use expressed in DDD per 1000 inhabitants and per day (DID).

Results
Global antibiotic consumption (10.3 and 10.2 DID in 2015 and 2016, -1%) was relatively low compared with European countries participating to ESAC-Net (21.9 DID in 2016). 36% of total consumption in Switzerland was prescribed by self-dispensing physicians (59% in the German-speaking part, < 3% in the French- and Italian-speaking parts). It was higher in the French- (0.2 DID by self-dispensing physicians and 13.4 DID by pharmacies) and in the Italian-speaking parts (0.2 and 12.8 DID, resp.) than in the German-speaking part (5.3 and 3.6 DID, resp.). The five-most prescribed antibiotics were amoxicillin-clavulanic acid (37%), amoxicillin (14%), ciprofloxacin (9%), doxycycline (9%) and clarithromycin (8%). Self-dispensing physicians prescribed less amoxicillin (9% vs 16%, $p < 0.0001$) and more clarithromycin (10% vs 6%, $p < 0.0001$).

Conclusion
Compared with European countries, Switzerland has a relatively low global antibiotic consumption. French- and Italian-speaking parts of Switzerland remained higher antibiotic consumers than the German-speaking part. In comparison between prescriptions through self-dispensing physicians and pharmacies in the German-speaking part of Switzerland, we observed higher antibiotic consumption among self-dispensing physicians (when expressed in DID). Prescriptions by antibiotic families was similar between those delivered through self-dispensing physicians and pharmacies. The impact of self-dispensing physicians on prescriptions need to be further investigated. Further analyses should take into account that self-dispensing physicians are not equally distributed across medical specialties.

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P38

Nothing to sneeze at - Isolation precautions for influenza show no impact on work load in single center experience

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Introduction

Isolation precautions are intended to prevent the spread of infectious diseases and are used frequently in inpatients (1). But Isolation requires hospital staff to put on gowns and gloves and surgical masks prior to entering patient rooms and it has been shown that isolation is associated with worse outcome (2). Healthcare workers visit patients on isolation approximately half as frequently as non-isolated patientS (2, 3). During Influenza season almost a fifth of inpatients is experiencing isolation precautions. While it has been shown previously that isolation precautions dont show a worse outcome (4), the notion that caring is worse remains.

Methods

In our 380-bed single center we conducted a retrospective analysis of the influenza-cohort of the 2017/2018 season. We prospectively collected all patients who had been hospitalized with a diagnosis of influenza, irrespective of their main diagnosis. We analysed basic characteristics and demographics of the patients. We also obtained data from the nursing performance-recording-system and analysed for time-with-patient and subjective-workload. We further correlated that data with the beginning and end of the influenza-season, as defined by the national authorities, and compared to a similar time-frame during a summer-period.

Results

During the time-period from 11/2017 to 2018 a total of 100 patients were put under isolation precautions due to influenza, compared to a cohort of 2700 patients from 05/2017 to 09/2017. Mean age in the Influenza group was 69y and 53% were male. In our comparison group, mean age was 63y and 56% male. Mean duration for isolation was 4.8 days and mean duration of hospital stay was 9 days (7.3 days respectively).
Mean duration of patient-contact showed no significant difference and was 242min/d, 238min/d respectively. The subjective-workload was 0.299 and 0.2535 respectively ($p < 0.05$)

Conclusion

In this observational and retrospective study of isolation precautions for influenza we find that, contrary to common believe, there seems to be a tendency to more time and effort spent on patients who are under isolation precautions, whereas subjective workload differs only marginally. This might suggest that conception of and working under isolation precautions might have changed in medical staff.

Additional information

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P39

Ongoing burden of Streptococcus pneumoniae sepsis in children after introduction of pneumococcal conjuguate vaccines

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Background
Recent population-based studies assessing the impact of pneumococcal conjugate vaccines (PCV) on the burden of pneumococcal sepsis in children are lacking. We aimed to define the burden of pneumococcal sepsis in children and assess predictors for severe outcomes following the introduction of PCV-13 in 2011 in a nationwide cohort study.

Methods
The Swiss Paediatric Sepsis Study prospectively recruited children under 17 years of age with blood culture-proven sepsis between September 2011 and December 2015 in Switzerland. We report on patients with Streptococcus pneumoniae sepsis stratified by the presence of meningitis versus any other clinical focus. Admission to the paediatric intensive care unit (PICU) and length of hospital stay (LOS) were defined as outcomes.

Results
From all 1181 sepsis episodes recorded during the 4.3 years period, children with pneumococcal sepsis (n=117) accounted for 10% of all sepsis episodes, and 25% of community- acquired sepsis episodes. 42 (36%) patients required PICU admission resulting in a mortality of 8%. Children presenting with meningitis (29; 25%) were more frequently admitted to PICU (69% vs 25%; $p < 0.001$) and more likely infected by serotypes not included in vaccines (69% vs 31%; $p < 0.001$) than those without meningitis. Pneumococcal serotypes 3, 19A and 7F accounted for 49 (44%) pneumococcal sepsis episodes. From 62 children completely immunised with PCV, of whom 32 were infected with vaccine serotypes , 16 (50%) presented with vaccine failure, of whom 11 were infected with serotype 3. In multivariable analyses children with meningitis (OR 6.8; 95% C.I 2.4-19.3; $p < 0.001$) and those infected with serotype 3 (OR 2.8; 95% C.I 1.1- 7.3; $p =0.04$) were more likely admitted to PICU, and those infected with serotype 3 had a longer hospital stay (Beta coefficient 0.2, 95% CI 0.1-1.1; $p= 0.01$).

Conclusions
The burden of pneumococcal sepsis in swiss children shortly after the introduction of PCV-13 remains important. Meningitis mostly due to serotype 3 and non-vaccine serotypes and were significant predictors of severity.

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P40

Clinical spectrum of lethal infection after solid organ transplantation in the Swiss Transplant Cohort Study

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Background
Infections contribute to fatal outcomes after solid organ transplantation. The current immunosuppressive agents have decreased rejections after transplantation, but infections are now the leading reason for hospitalization. Comprehensive data on infections as a cause of death are missing. The current analysis is based on the Swiss Transplant Cohort Study, which prospectively follows all solid organ transplant recipients since 2008.

Methods
For each death, the underlying and immediate cause of death was recorded by the treating organ specialists, and linked to a separate infectious diseases (ID) event record in case an infection was implied. All consenting patients transplanted between 01.05.2008 and 30.06.2016 and a follow-up till 31.12.2016 were included in a detailed descriptive analysis. Baseline characteristics, transplant characteristics, immunosuppressive regimen, cause of death and if associated with an ID event, type of pathogen and site of infection were retrieved.

Results
In a total of 3480 transplant patients in the STCS, 499 deaths (14.3%) were recorded. In 87 patients (2.5% of all patients, 17.4% of all deaths) an ID event was implied as the underlying cause. Bacteria were the cause in 47.2%, viruses in 17.6%, and fungi in 16.7% of all lethal infections, while in 17.6% the pathogen remained unknown, despite a very strong suspicion of an infection leading to death. The most common bacteria were Enterococcus spp. (12 cases) followed by Escherichia coli (8 cases) and Pseudomonas aeruginosa (7 cases). Most common viral infections were hepatitis C (7 cases) and cytomegalovirus infections(7 cases), the most common fungus Aspergillus fumigatus (9 cases). The respiratory tract (30.6%) was followed by blood (27.8%) as the most commonly involved sites. Demographics, the type of transplanted organ, the type of transplantation (first, re, double), the induction and maintenance immunosuppressive and CMV risk status did not differ between the group with an infection as underlying cause when it was compared to the non-infectious deaths.

Conclusion
Death due to infection is a rare event after SOT but one of the most important causes of death. Bacteria are the leading group of pathogens, while the respiratory tract and the blood are the main sites involved. A more detailed analysis of the respective variables will allow detecting potential different patterns in terms of pathogens and sites involved between the specific transplanted organ groups.

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DETERMINANTS OF HIV-1 RESERVOIR SIZE AND LONG-TERM DYNAMICS UNDER SUPPRESSIVE ART

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The HIV-1 reservoir is the major hurdle to cure. Thus, understanding factors affecting size and decay of this reservoir is crucial for development of cure strategies.

In 1,078 patients (pt) enrolled in the Swiss HIV Cohort Study, who after initiating their 1st triple combination antiretroviral therapy (cART) were fully suppressed for >5 yr (< 50 HIV RNA cp/ml of plasma), we measured total HIV-1 DNA levels at 3-4 time points using droplet digital PCR (in total 3,546 samples). Focusing on the time after the 1st rapid decay of HIV-1 DNA we chose the 1. time point 1.49 yr (IQR=[1.27,1.7], N=1,078) after ART initiation, the 2. time point 2 yr later (IQR=[1.87,2.16], N=1,068) and the 3. time point on average 1.93 yr (IQR=[1.77,2.15], N=1,071) thereafter. Total HIV-1 DNA in a 4th sample was quantified for a subset of pt 4.92 yr (IQR=[3.28,6.02], N=429) later. This extensive data set enabled a systematic investigation of parameters that potentially steer decay dynamics of the HIV-1 reservoir in infected individuals on long-term successful ART.

Total HIV-1 DNA levels significantly decreased between our sampling times with diminishing differences over time. Further, our data identified pre-cART RNA levels, viral subtype, risk group injecting drug user, time to suppression, blips before 1st sample and infection stage at cART start to be independent drivers of the initial total HIV-1 DNA level. Studying decay slopes for each pt, pre-cART CD4 cell count, pre-cART CD4/CD8 ratio, pre-cART viral load and viral blips were significant drivers in the univariate model. The type of treatment (NNRTI vs boosted PI based cART) showed no differential effect on the decay. However, in multivariable analysis a very strong and independent inhibitory effect on total HIV-1 DNA decay was governed by viral blips. To conclude, our data confirm relevant drivers of the establishment and the depletion of the viral reservoir and reflect a highly interesting causal interplay between intermittent replication and dynamics of total HIV-1 DNA of patients on successful therapy.

The size of the viral reservoir as measured by total HIV-1 DNA in this large study is strongly governed by time of cART initiation. Strikingly, the main independent predictor of total HIV-1 DNA decay were viral blips, which had a strong inhibiting effect. Thus, viral blips are of biological relevance for the latent reservoir and this may have implications for cure research.

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Durable Suppression 2 years after switch to DTG+RPV 2-Drug Regimen: SWORD 1&2 Studies

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Background:
Reducing long-term cumulative toxicity becomes more important in an era of near normal life expectancy for PLWHIV. Treatment modalities that reduce long term cumulative ARV exposure in the form of 2-drug regimens (2DR) are an area of active research. At 48 weeks, efficacy of DTG+RPV as a 2DR for maintenance of virologic suppression was non-inferior to 3DRs in SWORD 1&2. Improvements in bone, renal biomarkers and neutral effects on inflammatory biomarkers were demonstrated. We summarize outcomes through week 100.

Methods:
Two identical open-label, global, phase III, non-inferiority studies evaluated efficacy and safety of switching from CAR to DTG+RPV once daily in HIV-1-infected adults, with HIV-1 RNA < 50c/mL (VL < 50c/mL) for >6 months and no history of virologic failure. Participants were randomized 1:1 to switch immediately to DTG+RPV (Early Switch group) or continue CAR. Participants randomised to CAR with confirmed suppression at Week (Wk)48 switched to DTG+RPV at Wk52 (Late Switch group). Secondary endpoints included proportion of participants with VL < 50c/mL at Wk100 using Snapshot algorithm for ITT exposed (ITTe) population and safety evaluations.

Results:
1024 participants were randomized and exposed (DTG+RPV 513; CAR 511), across both studies. At Wk100 in Early Switch group, 456 (89%) had VL < 50c/mL; low rate of snapshot virologic non-response was observed (3%); 6 (1.2%) participants met Confirmed Virologic Withdrawal (CVW) criterion. The Early Switch group demonstrated a stable safety profile consistent with each individual component; 34 participants (7%) experienced AEs leading to withdrawal. At Wk100 in the Late Switch group, 444 (93%) had VL < 50c/mL; 2 (< 1%) participants met CVW criterion. Safety profile of the Late Switch group was comparable to the Early Switch group at Wk48 (Table 1). One participants with RPV resistance at CVW (Early Switch group, Wk100) had pre-existing NNRTI mutations at baseline. No participants developed INSTI resistance.

Conclusions:
The novel once-daily 2DR of DTG+RPV demonstrated durable maintenance of HIV suppression through Week 100, following switch from 3DR in virologically suppressed HIV-1-infected adults. The safety profile of DTG+RPV was consistent with their respective labels. A DTG+RPV 2DR offers potential for reduction in cumulative ARV exposure, without increased risk of virologic failure.

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Group A Streptococcal DNase Sda1 impairs plasmacytoid dendritic cells type I interferon response

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Introduction

In healthy skin, plasmacytoid dendritic cells (pDCs) are rare but increase under pathological conditions. Recognition of pathogens by pDCs occurs through the highly abundant intracellular localized Toll-like Receptors (TLR)-7 and 9. Due to the constitutive expression of IRF7 high amounts of type I interferon (IFN), in particular IFN-alpha, are produced by pDCs. We recently showed that IFN-alpha enhanced clearance of group A Streptococcus (GAS) in human blood despite neutropenia and monocytopenia. The number of severe infections caused by GAS increased over the last decades due to the emergence of a hyper-virulent clone carrying a prophage encoding for the streptococcal DNase Sda1. Sda1 is an important virulence factor that degrades neutrophil extracellular traps and reduces TLR-mediated recognition. It was shown that the danger associated molecule high mobility group box 1 (HMGB1) is able to form complexes with DNA leading to an enhanced type I IFN response by pDCs. HMGB1 were found to correlate with the severity of streptococcal skin infection. We thus aimed to corroborate the influence of the DNase Sda1 on the DNA-HMGB1 mediated type I IFN response in patients and murine NF.

Methods

Tissue biopsies from patients with necrotizing fasciitis (NF) were analyzed for presence of pDCs and compared to tissue from healthy individuals. An in vivo mouse model of NF and an in vitro 3D human skin tissue model were used to further elaborate pDCs and type I IFN involvement.

Results

Tissue from patients with GAS NF had a higher number of pDCs as compared to tissue from healthy individuals. pDCs infiltration was accompanied by a higher expression of the type I IFN induced protein MxA. Using gain- and loss-of function mouse models we showed that higher numbers of pDCs and higher type I IFN levels resulted in smaller skin lesions and lower CFU counts. Additionally, we observed that the streptococcal DNase Sda1 regulated both the type I IFN response as well as pDCs recruitment.

Conclusion

We found increased numbers of pDCs in invasive GAS skin infections in mouse and man. This was associated with enhanced expression of the type I IFN induced protein MxA. Additionally, higher levels of type I IFN at site of infection correlated with enhanced bacterial clearance.

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Phylogenetic clusters of HIV-1 reveal potential viral genetic impact on comorbidities

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Aims
Understanding and addressing comorbidities, co-infections, and AIDS-defining illnesses in HIV-infected patients remains one of the major challenges in managing HIV-infection in the era of highly active antiretroviral therapy. Here we tested at the population level whether viral genetic data can be informative to discern the differences in occurrence of comorbidities respective co-infections based on similarity of viral genomes in addition to demographic and clinical parameters.

Methods
Using HIV-1 pol-sequences of ~11,000 patients of the drug resistance database of the Swiss HIV Cohort Study (SHCS) as well as 240,000 Los Alamos background sequences, we identified phylogenetic clusters of SHCS patients. The occurrence of comorbidities, co-infections and AIDS-defining illnesses in these patients was then analyzed with respect to those demographical and clinical confounders, which revealed a clustering pattern in the HIV-1 transmission network, by applying mixed effects logistic models.

Results
Overall, HIV-related thrombocytopenia, Kaposi's sarcoma and HIV-associated encephalopathy exhibited a significant phylogenetic signal after adjusting for confounders suggesting a potential role of viral genetic factors for these diseases. In addition, the co-infections Hepatitis C, Hepatitis B and Cytomegalovirus revealed a strong phylogenetic clustering after adjusting for confounding suggesting shared transmission routes for these infectious conditions. The phylogenetic signal for diabetes mellitus, cardiovascular diseases, neoplasms, syphilis and candida stomatitis could be explained by the clustering of those demographical and clinical confounders which showed a high within-cluster similarity, such as age, sex, risk group, ethnicity, length of HIV infection and antiretroviral treatment.

Conclusion
This new type of analysis of combining viral sequences and well-defined clinical endpoints could be useful in triggering targeted pathogenesis studies and inform about targeted screening: Most of the studied diseases were not randomly distributed on the HIV-1 transmission network, which is only partly due to the clustering of demographic properties and other well-known risk factors of comorbidities. Such analysis could hence be helpful in identifying additional pathogenesis traits for specific illnesses, such as HIV-associated encephalopathy as found in the current analysis or other comorbidities.

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Cluster analysis reveals important shift of drivers of the HIV epidemic in Swiss MSM

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Transmission clusters in phylogenetic trees constructed from densely sampled HIV-1 sequencing data reflect recent or ongoing transmission and can be used to identify local outbreaks. In this study, we aimed to illustrate methods to identify those phylogenetic clusters relevant for targeted prevention in a real-world clinical setting. We hypothesized that cluster growth in high-risk HIV-1 subpopulations can be predicted using a combination of phylogenetic methods, clinical and behavioral data.

We used HIV-1 pol sequence data from the Swiss HIV Cohort Study (SHCS) and Los Alamos background sequences to construct eight phylogenetic trees including all patients enrolled in the SHCS by the end of the years 2007 to 2014. The SHCS is highly representative of the HIV epidemic in Switzerland and contains sequences for approximately 60% of all ~20'000 patients ever enrolled. We identified HIV-1 transmission clusters of Swiss MSM in eight consecutive years, assigned annual per-cluster infectivity scores as the fraction of cluster members who had a viral load measurement above 1'000 copies/ml and annual per-cluster risk scores as the fraction who reported condom-less sex with occasional partners, and then studied the cluster growth in the subsequent years.

Our analysis revealed that, over the course of the study, the infectivity score became less predictive of new infections within MSM clusters, while the risk score gained predictive power. We quantified the fraction of new infections within pre-existing transmission clusters and compared cluster characteristics of growing and non-growing clusters. Between 2008 and 2014, 35-65% of the newly infected MSM appeared within pre-existing MSM transmission clusters (p for linear trend=0.6). Uni- and multivariate Poisson regressions with per capita growth as outcome and infectivity and risk scores as dependent variables exhibited that infectivity significantly predicted the per capita growth of a cluster from 2007 to 2012, while the risk behavior was only a significant predictor in 2011, 2012 and 2014.

Our results demonstrate the effectiveness of treatment as prevention but also highlight that in recent years there was an epidemiologically important shift from the diagnosed to the undiagnosed population as the driver of the HIV epidemic in Swiss MSM. To achieve a further decrease in infection rates, phylogenetic clusters could be used to identify social networks, in which one should intensify HIV-1 testing.

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Prolonged survival of S. pneumoniae in human cerebral spinal fluid in vitro

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Background and aims
Streptococcus pneumoniae (S. pneumoniae) bacteria cause invasive pneumococcal disease including meningitis and are a common cause of mortality and morbidity. One reason is that the current vaccines only cover a limited number of the over 90 serotypes. Additionally, due to the vaccines there is a shift of serotypes causing disease. This has led to the search for new vaccine targets. For future vaccine design it is therefore important to know which of the emerging serotypes have the highest prevalence and cause the highest disease severity. Understanding the pathophysiology of S. pneumoniae in humans is thus essential.
Currently, most research performed on S. pneumoniae is in lab media such as brain-heart infusion broth (BHI) and using in vivo methods with laboratory animals. In view of the differences between humans and animals the aim of this study was to gain insight into the pathophysiology of S. pneumoniae in humans by first analyzing the growth behaviour in human cerebro-spinal fluid (hCSF).

Methods
Residual CSF from patients undergoing routine lumbar puncture by clinical indication except for infectious disease was used for analyses (ethics approval by Cantonal Ethics Committee Bern, KEK-BE 2017-01369). Growth analysis of S. pneumoniae in hCSF and BHI was performed by measuring the OD_(450 nm) over 50 hours. In a separate experiment, long-term survival of S. pneumoniae was assessed over a prolonged time period by incubating the bacteria in hCSF and BHI respectively at 37°C, plating out and counting colony forming units.

Results
S. pneumoniae was able to survive in hCSF for prolonged time periods. In BHI S. pneumoniae growth is defined by the typical lag phase, followed by an exponential growth and then autolysis which can be observed by a rapid drop in OD. In contrast to this, in hCSF, the typical growth peak and the following drop of OD due to autolysis were not observed. In hCSF, S. pneumoniae growth resembles a linear pattern, stabilizing after 20 hours. After 50 hours, when plated and incubated at 37°C, only plates with S. pneumoniae grown in hCSF formed colonies.

Conclusions
We show that the growth pattern in hCSF differs to that in BHI. This is important to take into account in pathophysiological studies of S. pneumoniae for meningitis. Our results also show that S. pneumoniae is able to survive for prolonged time periods in hCSF.

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IFNL3/4 polymorphisms increases susceptibility to AIDS-related Kaposi's sarcoma

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Background and Aims
Kaposi's sarcoma is the most common AIDS related cancer and represents a major public concern in resource limited countries. Single nucleotide polymorphisms within the Interferon lambda 3/4 region (IFNL3/4) determine the expression, function of IFNL4, and influence the clinical course of a growing number of viral infections. The current study aims at analyzing whether IFNL3/4 variants are associated with susceptibility to AIDS-related Kaposi's sarcoma among men who have sex with men (MSM) from the Swiss HIV Cohort Study.

Methods
The risk to develop Kaposi's sarcoma according to the carriage of IFNL3/4 SNPs (rs8099917, rs12980275) and their haplotypic/diplotypic combinations was assessed by using cumulative incidence (CI) curves and Cox regression models, accounting for relevant co-variables.

Results
Both rs8099917 and rs12980275 were associated with a higher risk of Kaposi's sarcoma (P=0.009 and P=0.01 respectively). Diplotypes predicted to produce the active P70 form (P=0.02), but not the inactive S70 (P=0.7) form of IFNL4, were associated with an increased risk to develop Kaposi sarcoma compared to those predicted not to produce IFNL4. The associations were still significant in a multivariate Cox regression model after adjustment for relevant covariates (P=0.011 for IFLN P70 versus no IFNL4).

Conclusion
This study reported for the first time an association between IFNL3/4 polymorphisms and susceptibility to AIDS-related Kaposi's sarcoma and confirmed the role of IFNL3/4 in immunity against an extended range of viruses.

Additional information
The authors thank all patients from the Swiss HIV Cohort Study (SHCS), as well as collaborators from the clinical, laboratory and data centers and all study nurses.
The members of the SHCS are Anagnostopoulos A, Battegay M, Bernasconi E, Böni J, Braun DL, Bucher HC, Calmy A, Cavassini M, Ciuffi A, Dollenmaier G, Egger M, Elzi L, Fehr J, Fellay J, Furrer H, Fux CA, Günthard HF, Haerry D, Hasse B, Hirsch HH, Hoffmann M, Hösli I, Huber M, Kahlert C, Kaiser L, Keiser O, Klimkait T, Kouyos RD, Kovari H, Ledergerber B, Martinetti G, Martinez de Tejada B, Marzolini C, Metzner KJ, Müller N, Nicca D, Paioni P, Pantaleo G, Perreau M, Rauch A, Rudin C, Scherrer AU, Schmid P, Speck R, Stöckle M, Tarr P, Trkola A, Vernazza P, Wandeler G, Weber R, Yerly S.

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Time to Viral Suppression does not Impact SVR in Patients Treated with Glecaprevir/Pibrentasvir for 8 Weeks

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Aims
The pangenotypic direct-acting antivirals (DAAs) glecaprevir (developed by AbbVie and Enanta) coformulated with pibrentasvir (G/P) are approved as an 8-week (wk) regimen to treat chronic HCV infection for all six major genotypes (GT). Historically, an on-treatment predictor of HCV cure with interferon (IFN)-containing regimens has been viral suppression at treatment wk 4. However, the relevance of viral kinetics as predictors of cure in the era of shortened, 8-wk DAA regimens is unclear, and concerns remain that failure to suppress HCV RNA quickly may lead to relapse. An integrated analysis of patients treated with G/P for 8 wk was performed to investigate factors impacting time to viral suppression, and whether lack of viral suppression by treatment wk 4 was predictive of relapse.

Methods
Data were pooled from five phase 2 or 3 clinical studies, and included patients with HCV GT 1–6 infection without cirrhosis who were either treatment naïve or experienced with IFN or pegIFN with or without ribavirin (RBV) or sofosbuvir and RBV with or without pegIFN. G/P (300 mg/120 mg) was orally dosed once-daily for 8 wk. Patients lost to follow up or with missing SVR12 data (N = 13) were excluded from the analysis since the impact of viral suppression (HCV RNA below lower limit of quantification [LLOQ]) on response cannot be assessed in these patients. Two patients with on-treatment virologic failure were excluded since we sought to determine whether detectable HCV RNA at treatment wk 4 was predictive of relapse.

Results
The analysis included 950 patients; 63 (7%) were black, 171 (18%) had BMI ≥ 30, and 24% had baseline HCV RNA ≥ 6 million. The majority of patients were white, male, and HCV treatment-naïve. Among 942 patients with data, 906 (96%) had HCV RNA < LLOQ at treatment wk 4, and of those, 899/906 (99%; 95% CI 98.4 – 99.6) achieved SVR12. There was no common baseline factor more frequently observed among the 7 seven patients who relapsed other than male sex (5/7; 71%). Of the 36 patients with HCV RNA > LLOQ at treatment wk 4 (median baseline HCV RNA 6.7 log10 IU/mL; range 5.2–7.6 log10 IU/mL), 100% (95% CI 90.4–100.0) achieved SVR12.

Conclusion
In patients treated with G/P for 8 wk, failure to suppress HCV RNA by treatment wk 4 was not predictive of treatment outcome, suggesting that treatment extension in patients eligible for 8-wk regimens based on this milestone is not warranted.

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HIV-1 SUPERINFECTION IN THE SWISS HIV COHORT STUDY: A LARGE SCALE SCREEN

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HIV-1 superinfection (SI) is the infection of HIV-1 infected individuals by another viral strain. SI has been associated with disease progression, viral recombination and immune escape. Identifying SI remains challenging for various reasons: 1. SI strain may outcompete or be outcompeted by the first strain. 2. SI is difficult to discern from co-infection. 3. SI is difficult to prove within viral subtypes, especially if caused by viruses from similar transmission clusters. 4. Sampling frequencies are too low and systematic screens of large populations to date are missing due to lack of needed longitudinal samples in untreated patients. Here we benefit from historic samples of 2 well characterized longitudinal studies; the Zurich Primary HIV Infection Cohort Study (ZPHI, >360 patients with documented PHI) and the Swiss HIV Cohort Study (SHCS, >19,000 HIV infected individuals).

Sequences of the HIV-1 pol gene from 11,738 patients in the SHCS drug resistance database were used for phylogenetic reconstruction. Then, patients with ≥2 longitudinal sequences were kept. From the distribution of our dataset; 2 criteria were used to select HIV-1 superinfected patients: 1. a phylogenetic cluster diversity of at least 20 patients for each individual patient's cluster and 2. a genetic distance ≥5% between a patient's sequences. Finally, to address potential samples mislabelling, patients were categorized on their number of longitudinal sequences and the spatial positioning of these sequences in the phylogeny. Category 1 patients have 2 sequences; categories 2 and 3 patients have >2 sequences and respectively 1 sequence or none spatially away from the others.

Of 4,558 HIV-infected individuals with ≥2 sequences, 330 candidates for HIV-1 superinfection including 7 enrolled in the ZPHI, were found. 111 patients are men having sex with men, 117 heterosexuals and 90 intravenous drug users. In addition, 123 patients show evidence of ≥ 2 viral subtypes. In category 3, mislabelling can be excluded due to patients' sequences clustering pattern corresponding to 31 strong candidates for SI. Based on the 25 patients in category 3 and the 1,224 individuals with ≥ 4 longitudinal sequences, we estimated a minimum rate of SI in our cohorts of 2%.

Our molecular epidemiology approach is the largest screen to identify HIV-1 superinfection using longitudinal samples so far. This work sets the basis to validate and characterize HIV-1 SI using next generation sequencing and our cohorts.

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Is Antifungal Treatment Needed in Non-Candidemic Patients with a Positive Catheter Tip Culture for Candida ? A Multi-Center Cohort Study of the Fungal Infection Network of Switzerland (FUNGINOS)

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Aims
Candidemia is associated with significant morbidity/mortality: antifungal therapy is routinely recommended. Although endovascular catheters are a frequent source of infection, impact of their removal on outcome is matter of debate. Uncertainty remains regarding the benefit of antifungal therapy in non-candidemic patients with a positive catheter tip culture for Candida. The aim of this study was to analyze clinical outcome according to the presence/absence of candidemia and antifungal treatment.

Methods
In this multi-center cohort study over a 3-year period in Swiss university hospitals, demographics, clinical characteristics, and outcome of patients with a positive catheter tip culture for Candida were investigated. Two patients settings were compared: 1) Absence vs. presence of concomitant candidemia. 2) Antifungal treatment vs. no treatment in absence of concomitant candidemia.

Results
Among 212 adult patients with a positive catheter tip culture for Candida, 84 (40%) had candidemia and 128 (60%) were non-candidemic. Patients with concomitant candidemia compared to non-candidemic patients had more frequently infection signs at catheter insertion site (89% vs. 25%, $p < 0.001$) and antifungal therapy (96% vs. 58%, $p < 0.001$). Hospital stay was significantly longer in candidemic patients (median 25 days, IQR 12-42, vs. 16.5, 6-37.5, p=0.05). 100-day mortality (23% vs. 20%, p=0.68) and 12-month rehospitalisation rates (38% vs. 35%, p=0.4) were similar. Among non-candidemic patients, those who received antifungal therapy (n=75, 58%) had more endovascular devices (23% vs. 6%, p=0.04). While a trend to higher rates of insertion site infection (31% vs. 17%, p=0.08), and sepsis/septic shock (15% vs. 6%, p=0.08) was observed, bacterial infection rates were similar (12% vs. 13%, p=0.84), Candida CFU/ml on catheter tip were not different (25, 10-100, vs. 42, 6-100, p=0.99). Time to discharge was significantly longer in those who were treated (21 days, IQR 21-44 vs. 9, 3-30, p=0.001). 100-day mortality (23% vs. 17%, p=0.43) and 12-month rehospitalisation rates (31% vs. 41%, p=0.2) were similar.

Conclusion
Mortality is not different in patients with a positive endovascular catheter culture for Candida with/without concomitant candidemia. In non-candidemic patients, mortality is similar in those who receive or not receive antifungals: signs of infection, severity criteria and risk for endovascular complications probably guide the decision to start therapy.

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P51

APOBEC3G shapes viral diversification and adaptation to antiviral monotherapy in humanized mice

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Aim
Genetic diversification of HIV is essential for viral evolution, adaptation and escape from immune surveillance and antiretroviral therapy (ART). In patients, viral diversification is associated with increased pathogenicity and underlies the rapid emergence of drug resistant HIV strains. HIV's extensive sequence variation is attributed to the low fidelity of the viral reverse transcriptase (RT) and high viral replication rates. The host deaminase APOBEC3G (A3G) may also contribute to in vivo viral diversification via sublethal GG-to-GA mutagenesis, yet this remains debated. Although the viral protein Vif effectively counteracts A3G, Vif alleles with suboptimal A3G-neutralizing activities have been isolated from patients and these are associated with ART-failure and viral diversification. Thus, using humanized mice (hu-mice), we explored the contribution of A3G to viral diversification and adaptation to antiviral monotherapy (3TC).

Methods
We generated an isogenic HIV clone (HIV-45G) that differed in its ability to counteract A3G due to a point mutation in Vif (wild-type HIV (HIV-WT): 95%; HIV-45G: 20%). Hu-mice were infected with HIV-WT or HIV-45G and one month post-infection some mice were treated with the RT inhibitor, 3TC. Viremia was quantified longitudinally by RT-qPCR to phenotypically assess viral fitness. Plasma and splenic quasispecies were profiled using unique molecular barcodes and deep sequencing to analyze viral diversity over time in different viral compartments.

Results
Both HIV-WT and HIV-45G resulted in robust infection of hu-mice, but over time HIV-45G fitness was significantly reduced compared to HIV-WT ($p < 0.005$). In contrast, in the presence of 3TC, HIV-45G escaped 3TC-inhibition faster and displayed superior replication compared to HIV-WT ($p < 0.005$). Sequencing revealed that the HIV-45G proviral splenic compartment was significantly more diversified, owing to GG-to-GA mutations, than that of HIV-WT in natural infections. In the context of 3TC, diversity and mutation rates were similar between HIV-WT and HIV-45G groups across all quasispecies compartments. However, the 3TC drug-resistance mutation RT-M184I, which results from a GG-to-GA mutation, appeared at a 10-fold faster rate than RT-M184V only in HIV-45G infected mice ($p < 0.001$).

Conclusion
Using humanized mice infected with wild-type HIV or a partially defective Vif variant and deep sequencing, we show that A3G accelerates emergence of 3TC drug resistance in vivo.

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In vivo control of HIV infection by broadly neutralizing antibodies in humanized mice

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Introduction
Combined anti-retroviral therapy (cART) is the cornerstone of HIV treatment leading to undetectable viremia in most patients, reduced morbidity and mortality. However, daily drug intake, side effects and the risk of emergence of resistance make the development of new strategies necessary. One promising approach is based on broadly neutralizing antibodies (bNAbs) targeting the HIV-envelope.
We investigated the anti-HIV effects of bNAbs in HIV infected humanized NOD-scid □c-/- (NSG) mice. The tested bNAbs VRC07, PG9 and 10-1074 target either the CD4 binding site, V1/V2 region or the glycan V3 region and the bNAb LN01, targets the membrane proximal external region of gp41.

Methods
Pharmacokinetics: The half-life of the bNAb was determined in NSG mice. A single dose of bNAbs was injected s.c.. Blood samples were collected prior to the injection and on days 1,3,5 and 7. HuIgG plasma concentration was analyzed by ELISA.
bNAb treatment: HIV infected humanized mice were treated every 2-4 days with a single bNAb or a mixture of 2-3 Abs. Throughout the experiment blood samples were collected to determine viral loads by PCR, plasma concentrations of huIgGs by ELISA and to characterize human immune compartments by flow cytometry.
Characterization of escape mutants: Viruses were isolated by co-culturing mice splenocytes and human peripheral blood mononuclear cells and neutralization capacity of treatment Ab was analyzed by TZM-bl neutralization assay.
Sequencing of escape mutants: cDNA was generated from isolated viral RNA and PCR amplified. PCR products were cloned using the TOPO-TA cloning kit.

Results
The half-life and serum concentration of the bNAbs ranged from 0.4-9.6 d and 19-141 µg/ml. A single bNAb resulted in a significant but transient reduction of viremia after 7 days. The observed rebound was due to escape as confirmed by sequencing and neutralization assays. Delayed rebound occurred with two bNAbs, whereas three bNAbs resulted in long-term suppression of viremia within 1-7 weeks and in reduced expression of activation markers on T cells. The LN01 antibody was as efficient as the gp120 specific antibodies in the mixture of 3 Abs.

Conclusion
We conclude that bNAbs are a very promising alternative to cART, since small molecule drugs lack the ability to induce Fcγ receptor mediated killing of HIV infected cells and bNAbs may be modified for increasing half-life and effector functions, permitting an extended dosing schedule and improved efficacy.

Prior presentation
slighlty differerent version at the clinical day of research at the University Hospital of Zurich this year

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Implementing a One Health community-based surveillance system for zoonotic disease

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Aims

(1) To design a syndromic surveillance system for a low-resource, isolated area in Guatemala targeting key zoonoses, following a One Health Approach. (2) To reduce time to detection and response for patients affected with Brucellosis and Leptospirosis.

Methods

Through a Transdisciplinary process, we integrated a working table comprising stakeholders from the Public Health sector (Ministries in charge of human health and animal health), Academia, Indigenous Maya Councils, community leaders and the private sector, facilitating a process to co-design and validate a surveillance system to be used in three indigenous communities in remote areas. We designed a passive surveillance system using mobile technology at no-cost to households enrolled in the project. Via a series of menus, users notify whether they wish to report a sick human or animal patient and define which Syndrome (febrile, respiratory or diarrhea) they suffer from. This Information is sent to a server in the partner university in Guatemala and reported back to a team of nurses and veterinarians in the field. Personnel is immediately deployed to collect fresh samples from the affected patient to be later sent to the laboratory for analysis. An education campaign to use the system was developed in Maya languages and using pictoric materials, for addressing cultural pertinence in a low-literacy setting. To support passive surveillance, one health unit per site opens half a day to tend to patients seeking care personally. An active surveillance system was also created, where a veterinary doctor and a nurse visit 50% of enrolled housholds once a month to detect sick human or animal patients. The system has been fully operational for six months and is scheduled to run for a year.

Results

A total of 421 households were enrolled, comprising 1886 people and 22,815 animals. The cell-phone based surveillance system is mostly used in one of the three sites, with the other two having too low connectivity to be useful. By April 2018, a total 301 human samples and 73 animal samples of suspected cases have been processed through the three surveillance modes, being able to detect positive cases of Brucellosis and Leptospirosis in human and animal patients.

Conclusion

Preliminary analysis shows the surveillance system has increased detection of cases by 1,200% in relation to prior data. We aim to reduce time to response (Treatment) by creating Treatment protocols not readily available before.

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A treatment as prevention trial to eliminate hepatitis C virus in HIV-positive MSM: the Swiss HCVree Trial

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Aim
Incidence of sexually transmitted hepatitis C virus (HCV) infections among HIV+ men who have sex with men (MSM) is rising worldwide. The Swiss HCVree Trial (NCT02785666) aimed to test the feasibility of a HCV elimination approach among HIV+ MSM participating in the Swiss HIV Cohort Study (SHCS).

Methods
During phase A (10/1/2015-5/31/2016) we systematically tested all MSM in the SHCS by HCV-RNA PCR. During phase B (6/1/2016-2/28/2017) HCV treatment with the DAA grazoprevir/elbasvir ± ribavirin was offered to all MSM with GT 1 or 4 with the goal to reduce the pool of potential transmitters. Individuals with GT 2 or 3 and individuals not eligible for phase B were treated externally with standard of care DAAs. MSM reporting unprotected sex with occasional partners were asked for participation in a behavioral intervention program during phase B to reduce sexual risk behavior to prevent re-infection. During phase C (3/1/-11/30/2017), we re-tested all MSM in the SHCS by HCV-RNA PCR.

Results
During phase A we screened 3'722 out of 4'257 active MSM from the SHCS database (87%) and identified 177 (4.8%) with a replicating HCV infection. Of these 177 infections 31 (18%) were incident. During phase B we treated 122 out of these 177 replicating infections (70%) within the Swiss HCVree Trial and achieved a SVR12 of 99%. 39 infections (22%) were treated externally using standard of care DAAs (SVR 12 100%). Re-screening of 3'723 MSM during period C identified 28 infections (0.8%), of them 16 were incident. The remaining 12 infections were chronic infections not treated during phase A. Of the 28 infections identified during phase C, 22 patients (76%) started DAA before end of period C. Overall, we identified and treated 183 out of 206 replicating infections (89%) during phase A and C within and outside the Swiss HCVree Trial. Of 68 MSM eligible for the behavioral intervention program, 51 (75%) agreed to participate and 46 (68%) completed the program.

Conclusion
A systematic, population based HCV RNA screening approach among HIV+ MSM from the SHCS identified a high number of potential HCV spreaders. Treatment initiation in 89% of individuals with replicating HCV reduced incident HCV infections by 50% during the study. A systematic population based screening followed by prompt treatment of identified infections combined with a strong behavioral intervention can serve as a model to reach WHO elimination targets by 2030 in HIV/HCV co-infected MSM

Conflict of interest
DLB received research and travel grants from Merck, Sharpe & Dohme

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P55

CRISPR/Cas9-mediated insertion of HIV-1-based vector into BACH2 does not lead to viral latency in Jurkat T cells

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The latent reservoir is a major obstacle to cure HIV-1 infection. HIV-1 integrates into the human genome and can persist for life. Hotspots of HIV-1 integration have been described and some might be associated with clonal expansion of latently HIV-1 infected cells. One such hotspot is the gene BTB domain and CNC homology 2 (BACH2), whose product BACH2 functions as a transcription factor in T cells, B cells, and macrophages. To investigate whether HIV-1 integration into BACH2 leads to an active or latent viral state, we inserted our dual-fluorescence HIV-1 based vector LTatC[M] (Kok et al., manuscript in revision) into BACH2 in Jurkat T cells via CRISPR/Cas9 technology to examine the impact of different loci (introns 2 and 5) and transcriptional orientations on the HIV-1 promoter activity. In LTatC[M], the fluorophore Cerulean reports the activity of the HIV-1 promoter in an HIV-1 Tat-dependent manner whereas the expression of mCherry is kept constitutive upon integration by virtue of an independent constitutive promoter and a pair of flanking genetic insulators. LTatC[M] was also inserted into the safe harbour gene AAVS1. Flow cytometric analysis of sorted cell clones showed that a Cerulean and mCherry double positive phenotype was predominant in all loci examined and independent of the transcriptional orientation, and that this phenotype remained unchanged in culture for up to 101 days. Additionally, Western blot analyses confirmed that BACH2 expression levels were not impaired by monoallelic integration of the vector into BACH2. Our results indicate that integration into BACH2 does not intrinsically lead to viral latency in the majority of targeted Jurkat T cells up to 3 months of follow up.

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Susceptibility to Mycobacterium ulcerans disease (Buruli ulcer) is associated with IFNG and iNOS gene polymorphisms

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Background and Aims
Buruli ulcer (BU) is a chronic necrotizing disease of the skin and subcutaneous fat tissue due to Mycobacterium ulcerans. The bacterium has the unique ability to secrete mycolactone that can prevent the action of immune cells and lead to the destruction of infected tissues. In endemic areas such as Sub-Saharan Africa, only a small proportion of individuals exposed to M. ulcerans develop clinical disease, as surrounding macrophages may control the infection by bacterial killing at an early stage, while mycolactone concentration is still low. Such differences among individuals may result from differences in the genetic background of exposed individuals. We hypothesized that some polymorphisms associated to susceptibility to other mycobacteria can also influence the course of infection due to M. ulcerans.

Methods
Single nucleotide polymorphisms (SNPs) from systematically selected genes were genotyped among 96 Ghanaian BU patients and 384 endemic controls without BU. Association between SNPs and BU was performed by logistic regression assuming an additive model of inheritance and was confirmed by functional evidences.

Results
Three SNPs were or tended to be more frequent among BU cases than controls. Carriage of the A allele at iNOS rs9282799 (OR=1.99, 95% CI 1.22-3.26, p=0.006) and of the G allele at IFNG rs2069705 (OR=1.56, 95% CI 1.14-1.99, p=0.007) was associated with BU. Both polymorphisms influence promoter activity in vitro. In addition, carriage of the A allele at SLC11A1 (NRAMP1) rs17235409 tended to be associated with BU (OR=1.63, 95% CI 0.99-2.70, p=0.06).

Conclusion
Altogether, these data reflect the importance of IFNG signaling in early defense against M. ulcerans infection.

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A high C-reactive protein/procalcitonin ratio predicts Mycoplasma pneumoniae infection

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Background
Differentiating Mycoplasma pneumoniae (MP) from Streptococcus pneumoniae (SP) and viral infections in patients hospitalized for community-acquired pneumonia (CAP) is challenging, yet has important implications regarding empiric antibiotic therapy. We patient parameters upon hospital admission to predict MP infection.

Aim
Discrimination of MP from other aetiologies of CAP

Methods
We retrospectively analyzed all patients hospitalized in a tertiary care hospital between 2013 and 2017 for CAP with a confirmed etiology based on blood cultures, multiplex PCR of nasopharyngeal swabs, serology or urine antigen testing. Univariate and multivariate logistic regression analyses as well as the area under the receiver operator characteristics curves (ROC AUC) were used to assess associations between demographic, clinical and laboratory values and the causative pathogen.

Results
We analyzed 568 patients with CAP, including 47 (8%) with MP; 152 (27%) with SP and 369 (65%) with influenza or other viruses in the abence of bacterial superinfection. Comparing MP and SP by multivariate logistic regression analysis, younger age (OR 0.56 per 10 years, 95% CI 0.42 - 0.73), a lower neutrophil/lymphocyte ratio (OR 0.9, 0.82 - 0.99) and an elevated CRP/PCT ratio (OR 15.04 (5.23 - 43.26) for a 400mg/ug cut-off) independently predicted MP. With a ROC AUC of 0.91 (0.80 for the > 400mg/ug cutoff), the CRP/PCT ratio was the strongest predictor of MP versus SP. The discriminatory value resulted from significantly lower PCT values (median 0.19 ug/L vs 3.47 ug/L, $p < 0.001$) , while CRP was high in both groups (median 160 mg/L for MP and 190mg/L for SP, $p = 0.057$). Comparing MP and viral infections by multivariate analysis, significant predictors for MP were younger age (OR: 0.54 per 10 years, 0.43-0.67), longer duration of symptoms (OR: 1.08 per day, 1.02 - 1.15), a pulmonary infiltrate on X-ray (OR: 5.14, 2.09 - 12.62), higher platelet counts (OR: 1.06 per increase of 10G/l, 1.01-1.11) and a CRP/PCT ratio > 400mg/ug (OR 5.55, 2.26 – 13.64).
The ROC AUC for the CRP/PCT ratio to predict MP was 0.83 (0.74 for the > 400 cutoff) versus viral etiology. The higher CRP/PCT ratio in MP was caused by higher CRP values in MP, while PCT was low in both MP and viral pneumonias.

Conclusion
In patients hospitalized with CAP, a high CRP/PCT ratio on admission predicts Mycoplasma pneumoniae infection and thereby can improve the empiric management.

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Nasopharyngeal and middle-ear microbiota in children with acute otitis media

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Aims and Background
Acute bacterial otitis media is usually caused by otopathogens ascending to the middle ear from the nasopharynx (NP). However, it is unknown if the nasopharyngeal microbiota of children with acute otitis media (AOM) can serve as an age-dependent or independent proxy for the microbial communities of the middle ear fluid (MEF) as there is a lack of 16S rRNA amplicon sequencing studies simultaneously analyzing the microbial communities of the two sites.

Methods
Within this study, we performed 16S rRNA next generation sequencing on a total of 286 nasopharyngeal swabs (NPS) collected between 2004 and 2015 from Swiss children (0-6 years) with AOM. In addition, 42/286 children had spontaneous tympanic membrane perforation and, therefore, additional MEF could also be analyzed.

Results
Alpha (Richness, SDI and Evenness) and beta diversity measurements of the nasopharyngeal bacterial microbiota showed a clear dependency of the increasing age of the children. Bacterial richness and personalized profiles (measured by beta dispersion) were higher and more frequent in older children, respectively. Dissimilarity values based on the binary distance matrix of the microbiota patterns of NP and MEF also correlated with increasing age. In general, positive (PPV) and negative predictive values (NPV) of the most abundant operational taxonomic units (OTUs) in the NP were moderately and well predictive for their presence in the MEF, respectively.

Conclusions
As compared to culturing, sequencing-based microbiota studies are more complete and may detect less known bacteria related to AOM. This is crucial to better understand polymicrobial infections and therefore AOM pathogenesis.

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Risk Factors for Central Line-Associated Bloodstream Infections in Children with Tunneled Central Venous Catheters – A Prospective Observational Study over 7 Years

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Aims
Central venous catheters (CVCs) have become an integral part of medical practice in pediatrics. Central line-associated bloodstream infections (CLABSIs) belong to the most common complications of CVCs accounting for significant morbidity and mortality. This prospective single center study on the use of tunneled CVCs in children aims to identify risk factors for CLABSIs.

Methods
Children having a tunneled CVC inserted at the University Children's Hospital between January 2009 and December 2015 were enrolled. Data regarding underlying disease, age, CVC dwell time and CLABSI was collected. Hazard ratios (HR) for CLABSIs were calculated using Cox regression models for age and diagnosis. Life tables were generated to examine the influence of CVC dwell time on CLABSI incidence rates.

Results
55 CLABSIs were observed in 193 patients with 284 tunneled CVCs over seven years. The overall CLABSI incidence rate was 2.20 per 1000 catheter days. Patients with gastrointestinal disorders and patients aged 2 - 5 years showed the highest incidence rates of 3.23 and 4.56 CLABSIs per 1000 catheter days respectively. The combination of underlying gastrointestinal disease and age 2 - 5 years was identified as significant risk factor for CLABSIs (HR 9.44, 95% CI 2.84 - 31.40, $p < 0.001$). Life tables showed an increasing risk for CLABSI in patients without gastrointestinal disease after 90 days of CVC dwell time.

Conclusions
In this pediatric setting every fifth tunneled CVC was removed due to CLABSI. Regular reevaluation should prompt to remove CVCs if no longer needed possibly before day 90 after insertion. In young children with underlying gastrointestinal disorders the need for tunneled CVCs urges for further preventive measures such as antimicrobial lock therapy or antimicrobial coated CVCs. Prospective studies are needed for benchmark and identification of CLABSI prevention measures in children requiring tunneled CVCs.

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P60

Retreatment of patients who failed glecaprevir/pibrentasvir treatment for hepatitis C virus infection

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Background and Aims

Glecaprevir/pibrentasvir (G/P; glecaprevir identified by AbbVie and Enanta) has demonstrated high rates of sustained virologic response at posttreatment week 12 (SVR12) across all six major hepatitis C virus (HCV) genotypes (GT). Roughly 1% of patients treated with G/P in Phase II or III clinical trials, across all genotypes, had virologic failure. These patients were offered enrollment into a retreatment study, MAGELLAN-3.

Method

MAGELLAN-3 is an ongoing open-label, phase 3b trial to determine the efficacy and safety of G/P (300/120 mg once daily) + sofosbuvir (SOF; 400 mg once daily) + ribavirin (RBV; 1,000-1,200 mg daily, divided into two doses) in patients who had virologic failure on G/P treatment in an AbbVie-sponsored clinical trial. Patients who had non-GT 3 infection, without cirrhosis, and were naïve to NS3/4A protease and NS5A inhibitors prior to failure with G/P, received 12 weeks of treatment; all others received 16 weeks. Efficacy (percentage of patients with SVR12), safety, and baseline resistance were assessed. Patients with at least end-of-treatment (EOT) data are reported here.

Results

Of 23 patients enrolled, 19 reached EOT; 2 patients were treated for 12 weeks (both reached EOT) and 21 were treated for 16 weeks (17 reached EOT). Overall, 30% (7/23), 9% (2/23), and 61% (14/23) of patients had HCV GT 1, 2, and 3 infection, respectively, and 30% (7/23) of patients had compensated cirrhosis. Twenty six percent (6/23) of patients had NS3/4A protease and/or NS5A inhibitor experience prior to their original G/P treatment; 39% (9/23) of patients had prior experience to other HCV treatment regimens. Twenty two percent (5/23) of patients had baseline resistance-associated substitutions (RAS) in NS3; the most common were at position D/Q168 (n=4). All 23 patients had baseline RAS in NS5A (14 had multiple NS5A RAS); the most common were at position Q30 (n=6) in GT1, and Y93 (n=11) and A30 (n=9) in GT3. One patient had virologic failure. The retreatment regimen was well tolerated. One patient had a serious adverse event of cholelithiasis at treatment week 10. Complete efficacy and safety data will be presented at the conference.

Conclusion

Preliminary data show that retreatment with G/P + SOF + RBV for 12 or 16 weeks was well tolerated and has demonstrated a high rate of SVR12, regardless of HCV genotype or baseline resistance-associated substitutions.

Acknowledgement

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Laboratory diagnosis of the first human case of larval Versteria sp. infection in a renal transplant recipient

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Aims
Infection with larval stages of cestodes are emerging as opportunistic pathogens in immunocompromised patients. Most prominantly, alveolar echinococcosis, caused by the larval stage of Echinococcus multilocularis, is known to cause a life-threatening liver disorder, especially in patients with immunosuppression-associated conditions. We now describe the first case of human infection with the recently proposed genus Versteria (Cestoda: Taeniidea) causing invasive tumor-like hepatic infection mimicking AE.

Methods
A 53-year-old woman Canadian woman presented with acute onset of fever and malaise. She had a kidney transplant in 1992 and was on minimal immunosuppression. MRI of the liver revealed a large central lesion abutting the middle hepatic and left portal veins, with multiple satellite nodules. Histopathology of liver biopsies showed the presence of a protoscolex-like structure including surrounding hooklets, consistent with a metacestode infection. Morphology of protoscolex and hooklets excluded Echinococcus as infecting organism. Screening E. granulosus HF-ELISA was positive, while species-specific E. multilocularis Em2- and Em18-ELISAs as well as AE- and CE-immunoblots were clearly negative. E. multilocularis- and E. granulosus-PCR were negative as well, but yielded an amplification product requiring sequencing for further specification (see below). Combination chemotherapy with albendazole and praziquantel was initiated empirically, and after 7 months a 50% decrease in the size of the liver lesion and resolution of many satellites lesions was observed. The patient was considered for liver transplantation, depending on her further evolution.

Results
Sequencing of 12S ribosomal RNA-PCR products suggested a match with the genus Versteria (98% identity the so far unique published fatal case reported in a captive orangutan (Goldberg et al., Em Inf Dis 2014, 20:109-113). As wild mustelids are the definitive hosts, we hypothesized that this immunocompromised patient acted as an accidental host by ingesting blueberries contaminated with mustelids feces with Versteria sp. eggs.

Conclusions
The first human case of Versteria sp. infection in a kidney transplant recipient is reported. Versteria sp. may represent a previously unrecognized risk and an emergent opportunistic infection in immuno-compromised individuals. Combination chemotherapy showed promising results.

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RESISTANCE ANALYSES OF BICTEGRAVIR/EMTRICITABINE/TENOFOVIR ALAFENAMIDE SWITCH STUDIES

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Aims
The novel, unboosted integrase strand transfer inhibitor (INSTI) bictegravir (B) has been coformulated with the nucleos(t)ide reverse transcriptase inhibitor (NRTI) backbone emtricitabine (F)/tenofovir alafenamide (TAF). Integrated resistance analyses are described for 2 phase 3 studies of stably suppressed HIV-1 infected adults who switched to bictegravir/emtricitabine/tenofovir alafenamide (B/F/TAF) from a boosted protease inhibitor (PI) + 2 nucleoside reverse transcriptase inhibitors (NRTIs) (N=290; Study 1878) or dolutegravir (DTG) + abacavir (ABC)/lamivudine (3TC) (N=282; Study 1844).

Methods
Historical plasma HIV-1 RNA genotypes and retrospective proviral DNA genotyping of baseline viral isolates were analysed. Viral isolates from patients with HIV-1 RNA ≥ 200 copies/mL at confirmed VF, discontinuation, or W48 were analysed for protease (PR), reverse transcriptase (RT), and integrase (IN) genotype and phenotype.

Results
Of the 572 patients who switched to B/F/TAF, pre-treatment historical genotypes and/or retrospective proviral DNA genotypes of baseline viral isolates were obtained from 394 patients for PR/RT and from 158 patients for IN. Pre-existing primary integrase strand transfer inhibitor (INSTI) resistance (-R), NRTI-R, nonnucleoside RT inhibitor (NNRTI)-R, and PI-R substitutions were observed in 0.6% (1/158), 14.0% (55/394), 18.3% (72/394), and 6.3% (25/394), respectively. Pre-switch resistance to F and/or TAF was retrospectively detected at baseline in 8.9% (35/394) of patients and consisted of K65N/R (n=5), M184V/I (n=30), and/or ≥ 3 thymidine analog mutations (TAMs) that include M41L or L210W (n=4) in RT. Overall, 1.4% (8/572) of B/F/TAF treated patients experienced VF through W48. Of the 35 patients with pre-existing F/TAF resistance, 1 (2.9%) experienced VF due to nonadherence. Post-baseline resistance analyses were conducted on viral isolates from 5 patients in the B/F/TAF group and 7 patients in the comparator groups. No patients on B/F/TAF developed de novo resistance to study drugs. One patient on boosted darunavir+ABC/3TC developed a treatment-emergent L74V substitution in RT.

Conclusion
Low rates of virologic failure occurred among the 572 patients who switched to B/F/TAF, including the 35 with pre-existing F/TAF resistance. Through W48 there was zero treatment-emergent resistance in B/F/TAF-treated patients demonstrating the utility of B/F/TAF in HIV-1-suppressed patients.

Conflict of interest
All authors are employees of Gilead Sciences

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Complementary and alternative medical (CAM) providers' patient-centered, individualized approaches to vaccination in Switzerland

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Aims
Vaccine hesitancy is a multifaceted phenomenon with no universal explanation. Important contributing factors are social networks, the providers consulted, time spent on vaccination discussions and providers' communication strategies. Most literature focuses on biomedical providers, whereas research also suggests a link between complementary and alternative medicine (CAM) use and vaccine hesitancy. Little research has explored this relationship, particularly on a qualitative level, even though studies show 25-50% of the Swiss population use CAM. The aims of our study were 1) to better understand CAM provider perspectives on childhood vaccination, and 2) to gain insights into how CAM providers discuss childhood vaccinations with their patients.

Methods
We conducted in-depth qualitative interviews with 15 CAM providers (13 of whom have a University medical degree) in Switzerland (8 in German-speaking, 7 in French-speaking regions) and observed 13 vaccination consultations (4 and 9, respectively). Interviews were audio-recorded and transcribed verbatim. We took structured notes during the observations and wrote them into a narrative format. Audio transcriptions and observation notes were coded into categories with MAXQDA data analysis software and analyzed using the Framework Method.

Results
CAM providers largely framed vaccination discussions in terms of individual parental choice and parents' personal contexts. Contrary to recurring stereotypes, CAM providers were not all categorically opposed to vaccination. Rather, they expressed skepticism towards the necessity of mass vaccination campaigns and policies as a uniform approach towards disease prevention and focused on individualized patient care. They incorporated patient knowledge, wishes, and context into vaccine discussions. CAM providers did not see their role as prescriptive towards their patients but as informative to guide patients in their vaccine decision.

Conclusion
CAM provider approaches to vaccination align with larger social trends reported in the literature to be associated with vaccine hesitancy, such as patients taking an active role in healthcare decisions, skepticism towards health authorities and institutions, and desire for individualized healthcare. CAM approaches to vaccination consultations may provide valuable suggestions for improved personalized vaccination consultation practices.

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MUCOVIB project : Concordance between upper and lower airway microbiota in children with Cystic Fibrosis

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Background
Inconsistent intra-individual microbiota between upper and lower respiratory niches has been reported among infants with Cystic Fibrosis (CF). We aimed to investigate the concordance between the bacterial community composition of 20 oropharyngeal (OP) samples and 20 corresponding sputa, collected from children with CF above one year of age.

Methods
As part of the ‘’Cystic Fibrosis, respiratory viruses, intracellular bacteria and fastidious organisms’’ (MUCOVIB) project, all children under 18 years of age with diagnosed CF were recruited into a swiss multicentric study. Respiratory samples included OP swabs collected from all children in addition to sputa collected from those able to expectorate. Sequencing and data analysis of amplicons of the V3-V4 variable region of the 16S rRNA-encoding gene were performed. Paired-read were assembled with PANDAseq and clustered into operational taxonomic units (OTUs) using vsearch and assigned to taxonomical ranks using Qiime and the EzBioCloud database. Non-metric multidimensional scaling, ANOVA and PERMANOVA were used to analyze the bacterial diversity in upper and lower respiratory niches.

Preliminary results
Fifty-eight children, of whom 29 (50%) provided 51 sputa samples. From these 29, 10 patients (40 samples) provided concomitant OP and sputa samples collected during the same visit. Equivalent species diversity (alpha-diversity; Shannon index) was documented from both upper and lower samples (P-value=0.26). In most cases, hierarchical clustering based on OTU presence/absence clustered upper and lower samples from the same patient and during the same visit, thus suggesting a signature microbiota in most patients. A similar variance of bacterial microbiota was observed in upper and lower respiratory niches (P-value=0.9422), with some differences in species composition.

Conclusions
Our preliminary findings conducted on a small subset of patients, suggested a good intra-individual concordance of the microbiota in upper and lower respiratory niches, thus suggesting that OP swabs could be used as proxy to measure bacterial biodiversity among children with CF unable to expectorate.

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Phase 3 study of fostemsavir in heavily treatment experienced HIV-1 infected subjects: Day 8 and week 24 primary efficacy and safety results (Study 205888, formerly AI438-047)

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Background
Fostemsavir (FTR) is an investigational attachment inhibitor being evaluated as a new class of antiretroviral (ARV) in heavily treatment-experienced (HTE) patients; those with ≤2 ARV classes remaining and unable to form a viable regimen.

Methods
Randomized subjects, with 1-2 remaining classes and failing their ARV regimen at screening, were randomized (3:1) to blinded FTR 600mg or placebo twice daily (BID) plus current failing regimen for 8 days, followed by open-label FTR 600mg BID plus optimized background therapy (OBT). Non-Randomized (NR) subjects, with no remaining fully active ARVs, started open-label FTR 600mg BID plus OBT on Day 1. The primary efficacy endpoint (mean change in log10 HIV-1 RNA at Day 8), Week 24 efficacy, and cumulative safety results are presented.

Results
272 and 99 subjects were assigned to the Randomized and NR cohorts, respectively. At screening, 72% of subjects had a CD4+ T-cell count < 200 cells/μL; 41% had CD4+ < 50. Eighty percent and 96% had prior exposure to INIs and PIs, respectively. For the Randomized Cohort, the mean decline in HIV-1 RNA at Day 8 was 0.79 log10 c/mL for FTR vs 0.17 log10 c/mL for placebo ($p< 0.0001$); 54% achieved virologic suppression at Week 24. Overall, 91% had an adverse event (AE); most were Grade 1-2. Thirty percent experienced a serious adverse event; pneumonia was most common (13 subjects). Seventeen subjects died; 12/17 deaths were due to AIDS/IRIS-related events and acute infections.

Conclusion
Fostemsavir demonstrated superior efficacy relative to placebo in HTE subjects treated for 8 days with functional monotherapy. 54% of Randomized subjects receiving FTR+OBT achieved virologic suppression at Week 24, along with 36% of NR subjects (81% with FTR as the only active ARV). Fostemsavir-containing regimens were generally well tolerated. These results support further development of FTR as an important option for HTE patients.

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A new method for interpretation of drug utilization indicators in hospitals

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Introduction

Drug utilization research is part of the antibiotic stewardship program (ASP) at our institution. By supporting the optimal use of antibiotics, ASPs reduce inadequate prescriptions and improve patient-related outcomes (Ref. 1-3).

Aims

We aimed at improving the interpretation of data on drug utilization. We defined a mathematical function and developed a new visual interpretation method to describe how the evolution of antibiotic consumption parameters and of hospital activity parameters influences changes in drug utilization indicators over time. Secondly, we assessed agreement between aggregated consumption (Defined Daily Dose, DDD) and patient-level prescription measures (Days of therapy, DOT).

Methods

We measured drug utilization by using the indicators DDD/100 bed days and DDD/100 admissions. Drug utilization was assessed as a function of the evolution of DDDs and bed days and admissions, respectively.

Results

We defined the evolution of the DDD/100 bed days (Δ DDD/bed day) as the (x, y) function Δ DDD/bed day=(x/y)-1, x being the DDDs of the period of interest divided by the DDDs of the previous period (DDD ratio), and y the bed days divided by the previous bed days (bed day ratio). Similarly, evolution of DDD/100 admissions was defined as Δ DDD/admission=(x/w)-1, w being the admission ratio. As example, in one intensive care unit at our institution from 2016 to 2017, because the absolute DDDs decreased (-8%) and bed days remained stable (+1%), DDD/bed days decreased by 9%. However DDD/admissions increased by 4%, because the number of admissions decreased more than the number of DDDs (-11%).
Analysis of DDD and DOT agreement showed DOT being approximately 25-30% lower than DDD. As an example, in general wards of our institution in 2017, patient-level antibiotic use was 48.2 DOT compared to an aggregated consumption of 69.5 DDD, both per 100 bed days.

Conclusion

Reporting and visualizing variations of the DDDs, bed days and admissions, together with variations of the DDD/100 bed days and DDD/100 admissions, allows an elaborated interpretation of these two consumption indicators. Although aggregated and patient-level data may differ, they are both of value as they represent various aspects of antibiotic consumption. The differences between them may be explained by DDD definitions differing from dosing reference guides or by patient-related factors (e.g. impaired kidney function).

Conflict of interest

The authors declare not having potential conflicts of interest

Additional information

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Synovial C-reactive protein for diagnosis of periprosthetic joint infection (PJI)

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Background
An early and correct diagnosis of periprosthetic joint infections (PJIs) is crucial for a tailored surgical and antibiotic treatment. Synovial C-reactive protein (CRP) has been recently described as a new biomarker in the preoperative diagnostic to identify PJIs. The aim of this study was to evaluate synovial CRP in a large cohort of patients with suspected PJIs and calculate the optimal cut-off to diagnose PJIs.

Methods
Between September 2015 and June 2017, we included patients with a suspected PJI and with CRP as an additional preoperative diagnostic in joint aspiration. We analyzed sensitivity and specificity of synovial CRP using receiver operating characteristic (ROC) curves based on standard diagnostic criteria for PJI, published by the Consensus Meeting Guidelines in 2013. The optimal cut-off was subsequently determined using the Youden index.

Results
We included 26 PJI (14.0%) and 166 no PJI cases (mean age 67 years; range 41 – 91) with a preoperative diagnostic joint aspiration of hip (n=80), knee (n=91), or shoulder (n=21). The following pathogens were cultured: Coagulase-negative staphylococci (n=10), Staphylococcus aureus (n=6), polymicrobial infections (n=4), Streptococcus agalactiae (n=1), Propionibacterium avidum (n=1), and Candida tropicalis (n=1). Three PJI were culture-negative. The synovial fluid CRP values combined for all joints were significantly higher in the PJI group compared to the no PJI group (mean: 17.6 vs. 2.1; $p < 0.001$). The optimal synovial fluid CRP cut-off (Youden-Index: 0.71) for the PJI diagnosis combined for all joints was 2.9 mg/l with a sensitivity of 88% and specificity of 82% (AUC: 0.93, 95%CI: 0.88 - 0.97).

Conclusion
The biomarker synovial CRP has a high negative predictive value, allowing to reliably exclude a PJI. However, sensitivity and specificity were lower than previously published. We propose to use synovial CRP only as an additional biomarker together with the already established serum (CRP, erythrocyte sedimentation rate) and synovial biomarkers (leucocytes, neutrophils, microbiological culture) for a reliable diagnosis of PJI.

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Parainfluenza Virus Type 3 Outbreak in a Vulnerable Patient Population, a Retrospective Case-Control Observation

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Aims
In 2017, an outbreak of parainfluenza virus type 3 (PIV-3) occurred in our tertiary care hospital, mostly affecting patients with chronic lung disease and after stem cell transplantation. The present work investigated the transmission routes and the clinical characteristics and impact of PIV-3 infection.

Methods
In this single-center, retrospective case-control study we reviewed all respiratory multiplex PCR results (Pathofinder® Respifinder® 22) during an 8-month period (November 2016 to June 2017) including the outbreak. To identify distinct clinical features and outcome of PIV-3 infection, patients in the PIV-3 cohort were matched for age, gender, immunosuppressive treatment and transplantation with (i), a cohort of patients with rhinovirus or enterovirus infection detected in the respiratory PCR and (ii), a cohort with no virus detected.

Results
Of 492 patients tested, 39 were positive for PIV-3 infection. After propensity score matching, 36 patients with detection of rhinovirus/enterovirus and 39 with a negative PCR were included (n=114 in total, 53% inpatient). Inpatients with PIV-3 infection were isolated within a mean time of 1.0 day (standard deviation 1.5) after virus detection. An epidemic of PIV-3 infections (23/39) emerged during March and April 2017. Baseline characteristics were similarly distributed in all groups with the exception of a more frequent use of steroids in the PIV-3 group (39 vs.17 (rhinovirus/enterovirus) vs. 10% (negative PCR), $p < 0.01$). Solid or stem cell transplantation (54%) and chronic lung diseases (18%) were the most common underlying diseases. Lower respiratory tract infection was diagnosed in 25 (64%), 17 (47%) and 16 (41%) patients, respectively ($p = 0.1$). A total lack of symptoms or signs of respiratory tract involvement was documented in 6 (15%) vs. 8 (22%) vs. 17 (44%) of patients ($p = 0.01$). Mean duration of hospitalization was similar (14 vs. 12 vs. 12 days, $p = 0.9$), and in-hospital mortality was 5.1% vs. 2.8% vs. 2.6%.

Conclusion
We documented the nosocomial transmission of PIV-3 in a vulnerable patient population with underlying lung disease or immunosuppression despite rapid isolation of index patients. PIV-3 transmission may have occurred via health-care personnel or visitors. Further studies investigating preventive measures are needed in order to protect vulnerable patients from viral respiratory infections (e.g. mandatory masking policy also for visitors during the “viral season”).

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To test or not to test? Gonorrhoea in asymptomatic heterosexuals in Switzerland

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Background

The incidence of Gonorrhoea in Switzerland rose from 12.06/100'000 (2008) to 28.61/100'000 (2017). As STI testing is expensive (tests for Gonorrhoea, Chlamydia, Syphilis and HIV cost €350 in Switzerland, paid for by clients) and asymptomatic infection in heterosexuals seems rare, some experts recommend testing only high-risk groups such as MSM and FSW. However, our data calls for a more differentiated approach.

Methods

Since 2016, our anonymous testing clinic offers pooled swabs (pharyngeal, genital and rectal) for Gonorrhoea/Chlamydia (NG/CT) using cobas®4800 multiplex-assay in addition to the previously available HIV/Syphilis tests. In January 2017 we lowered the price for tests to €100 and introduced an online booking-system. Demographic and behavioural data and test results were collected using an anonymous online tool (berdatool.ch). We analysed all STI results from one calendar year focusing on Gonorrhoea cases in our asymptomatic clients.

Results

From January to December 2017, we tested 2323 clients for HIV. Of these, 1347 added additional screening for syphilis and 1106 for NG/CT. The proportion of clients who added NG/CT diagnostics to HIV and Syphilis increased from 19.5% to 66.7% from January to December 2017. Overall, three were positive for HIV, 7 for Syphilis, 47 for Chlamydia and 16 for Gonorrhoea. Most patients with Gonorrhoea were heterosexual (7 men, 2 women), 7 were MSM. Heterosexual men were more likely to have paid for sex in the last year (OR 5.6, p=0.01). Both the number of male and female partners were associated with increased odds for Gonorrhoea infection.

Conclusion

This study demonstrates that the majority of asymptomatic Gonorrhoea infections as a source of onward transmission remain undiagnosed if routine STI testing is based on demographic risk-groups only. We are convinced that easy-access and low-cost STI testing for all people at risk will be crucial to reduce the spread of Gonorrhoea in Switzerland.

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Antiretroviral Drugs Associated with Subclinical Coronary Artery Disease

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Background
Hard coronary artery disease (CAD) events have been associated with certain antiretroviral therapy (ART) agents. In contrast, the influence of ART drugs on early, subclinical atherosclerosis as determined by coronary artery calcium (CAC) scoring and coronary CT angiography (CCTA) is yet to be elucidated. The aim of the study was to assess the association between individual ART agents and the prevalence, extent and characteristics of coronary artery plaque in ≥45 year old HIV-positive persons.

Methods
In this prospective study of ≥45 year old Swiss HIV Cohort Study participants CAC scoring and CCTA were performed. The following subclinical CAD endpoints were analysed separately: CAC score >0, any plaque, calcified plaque, and non-calcified/mixed plaque on CCTA. Minimally adjusted (sex, age, center) and fully adjusted logistic regression models calculated by inverse probability of treatment weights (IPTW) were used to explore any association between the different CAD endpoints and cumulative exposure to the ten most often used individual drugs. The IPTW models were built based on demographics, HIV parameters, presence and/or treatment of CAD risk factors and the availability of the individual drugs.

Results
A total of 403 of 428 CCTA participants were eligible for the analysis (mean age 52 years, 85% men, 91% Caucasian, 36% current smokers, 60% homosexual, median CD4 cell count at cardiac imaging 601 cells/µL, 93% on ART, 88% with undetectable HIV-1 RNA). CAC score >0 was recorded in 188 (47%) patients, any plaque in 214 (53%), calcified plaque in 151 (38%), and non-calcified/mixed plaque in 150 (37%) participants, respectively. Associations between cumulative exposure to individual ART drugs and different CAD outcomes are shown in the figure. CAC score >0, any plaque, and calcified plaque were not positively associated with any individual ART drugs. Non-calcified/mixed plaque was associated with exposure to abacavir (1.46, [1.08-1.98]).

Conclusion
Evidence for an increased risk of coronary artery non-calcified/mixed plaques was only found in patients exposed to regimens containing abacavir.

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Outpatient parenteral antimicrobial therapy in Basel, evaluation of two years of practice

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Aims
Outpatient parenteral antimicrobial therapy (OPAT) programs are established in the minority of Swiss hospitals. We describe our experience and analyse the evolution of the OPAT program at the University Hospital Basel during a three-year period in order to evaluate the need, effectiveness and safety of the program.

Methods
306 patients, which were treated in the OPAT program in 2015 and 2017, were included in the study. Demographic, clinical and OPAT outcome data were extracted from the hospital information system and differences between the treatment periods analysed.

Results
The number of patients enrolled in the OPAT program increased from 114 in 2015 to 192 patients in 2017 (+ 68%). Mean age was 53.5 and 54.3 years ($p = 0.07$), and comorbidities were present in 38% and 50% of patients ($p = 0.04$), respectively.
The most common indication for parenteral treatment was urinary tract infection (36%), followed by bone and joint (22%) and intravascular infection (13%).
Escherichia coli was the most frequently identified pathogen (67 episodes, 32%) followed by Staphylococcus aureus (43 episodes, 20%). Of the identified Gram-negative bacteria, 27% produced extended spectrum beta-lactamases.
Ceftriaxone was the most commonly prescribed drug (41%), though a significant decrease in its use was observed (53 vs. 34%, $p < 0.01$) attributable to the introduction of elastomeric devices and the use of narrow-spectrum penicillins (7 vs. 18%, $p < 0.01$).
Adverse events were rare (10.6%), including predominately drug-related events. Of note, only one serious catheter-related event and no Clostridium difficile infections (3-month follow-up) were encountered. Therapy was completed as planned and significant improvement noted in 284 (96%) and 287 (94%) patients, respectively. 36 (11.8%) patients were readmitted and 2 (1%) patients died during or within a 30-days period after OPAT discharge. Independent predictors of readmission were study period, intravascular infections, diabetes mellitus and age.

Conclusion
This study highlights the need of a formal OPAT program in a Swiss tertiary care hospital, as reflected by the increasing number of patients over a three-year period. Our data demonstrate the safety and effectiveness of this treatment option, even in patients with significant comorbidities and serious infections. Moreover, OPAT represents a valid alternative to hospitalisation for patients with multi-drug resistant infections requiring intravenous treatment.

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Ceftobiprole in orthopaedic infections - pilot experience

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Objective
Ceftobiprole is an advanced generation cephalosporin marketed in Switzerland for the treatment of pneumonia. However, due to its broad-spectrum coverage including Gram-negative rods, comprising Pseudomonas aeruginosa, and methicillin-resistant staphylococci, it may be an ideal agent for polymicrobial / resistant infections, including the orthopaedic domain.

Methods
Single-center experience with ceftobiprole among selected adult patients with polymicrobial and antibiotic-resistant orthopaedic infections. Assessment of clinical responses and potential adverse events in patients benefitting ≥ 10 days of intravenous ceftobiprole for any clinically severe orthopaedic infection, and a minimal follow-up of roughly two years.

Results
We administered ceftobiprole 2-3 x 500 mg daily intravenously in four male patients (median age 70 years; 2 diabetic patients) for a median duration of 17 days (range, 10-21 days). There was only one treatment episode per patient. The actual infections were: total knee arthroplasty infection (n=2) and diabetic foot osteomyelitis (n=2). The infections were severe (sepsis) or chronic. All episodes were polymicrobial with an average of 3 pathogens per episode (Table) and a total of 14 different pathogens. Among them, six (43%) were considered as resistant to usual antibiotics used for their respective infections (4 methicillin-resistances, Gram-negative rods, Enterococcus faecalis). Total antibiotic treatment was continued for all patients on an outpatient basis with various other oral antibiotics for a median of another 45 days. All patients underwent removal of infected hardware and a median of 6 surgical debridements (range, 3-7 debridements) with remission in all cases. We witnessed no clinical or laboratory adverse events during hospitalization and up to a median follow-up period of 22 months (range, 20-26 months).

Conclusions
According to our limited experience, the broad-spectrum antibiotic ceftobiprole, combined with surgical debridement, might contribute to cure adult orthopaedic patients with polymicrobial and antibiotic-resistant infections. Prospective studies for orthopaedic infections are warranted.

Conflict of interest
Prof. Daniel Lew is a member of the Board of Directors of Basilea, the former owner and manufacturer of ceftrobiprole.

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INFLUENCE OF OLDER AGE AND OTHER RISK FACTORS ON HOSPITALISATION FOR PNEUMOCOCCAL PNEUMONIA AND DETRIMENTAL OUTCOME IN ADULTS IN SWITZERLAND IN THE PNEUMOCOCCAL VACCINE ERA

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Background and aims
Whether older age itself should be an indication for pneumococcal vaccination in adults is controversial. We aimed to quantify the effect of age as a risk factor for hospitalisation for pneumococcal pneumonia and increased length of stay (LOS) and mortality.

Methods
We used a database of all hospitalisations in Switzerland which includes ICD-10 diagnoses to obtain the number of hospitalisations for pneumococcal pneumonia among adults from 2002 to 2015. We calculated the effects of age and of those comorbidities, which are national 13-valent pneumococcal conjugate vaccine (PCV13) indications, on pneumococcal pneumonia hospitalisation, associated LOS and all-cause in-hospital mortality.

Results
Pneumococcal pneumonia was diagnosed in 0.1% (21'610/17'619'016) of all hospitalisations and 5.1% of pneumonia hospitalisations (421'760). The diagnosis of pneumococcal pneumonia among hospitalisations was more frequent in patients ≥ 50y (0.2%) than in patients < 50 years (0.06%; $p < 0.001$). The effect was similar for age ≥ 65y (0.2% vs. 0.1%; $p < 0.001$). In 2 separate multivariable logistic regression models, each vaccine indication (except for asplenia; and for sickle cell disease for ≥ 65y) and age categories ≥ 50y (aOR: 2.1, $p < 0.001$) and ≥ 65y (aOR: 1.8, $p < 0.001$) were independent predictors for pneumococcal pneumonia hospitalisation. There was a negative interaction between risk factor and age. Both age categories (≥ 50y and ≥ 65y) were independent risk factors for LOS ($p < 0.001$ for both) and mortality ($p < 0.001$ for both) in patients with pneumococcal pneumonia.

Conclusions
Older age is a risk factor for hospitalisation with pneumococcal pneumonia and for longer LOS and higher mortality similarly to and independent of PCV13 indications.

Conflict of interest
WCA's institution has received money for my participation at advisory boards: GSK, Pfizer. MH received an educational grant from Pfizer AG. However, Pfizer AG had no role in the data analysis and content of this study. FR, FB no COI. This study was funded

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Synergistic interaction of voriconazole and terbinafine against intrinsically azole resistant Aspergillus calidoustus

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Background
Invasive aspergillosis (IA) is an important cause of morbidity and mortality for immunocompromised hosts, especially hematopoietic stem cell and solid organ transplant recipients. While Aspergillus fumigatus remains the main cause of IA, the systematic use of triazole prophylaxis in the post-engraftment period or during neutropenia has shifted the epidemiology of IA towards other Aspergillus spp. Aspergillus calidoustus (section Usti) is an emergent pathogen causing breakthrough infections with high mortality rate because of its intrinsic resistance to triazoles. The aim of this study was to assess the in vitro and in vivo effect of antifungal drug combinations against Aspergillus calidoustus.

Methods
Two clinical isolates of Aspergillus calidoustus, for which species identification was confirmed by multilocus sequencing, were used. Antifungal susceptibility testing was performed using broth microdilution method according to CLSI recommendations. Antifungal drug combinations were tested in vitro by chequerboard dilutions and interactions were characterized by calculation of the fractional inhibitory concentration index (FICI). A survival study of Galleria mellonnella larvae infected by a larvicidal inoculum of Aspergillus calidoustus was performed to assess the in vivo efficacy of antifungal drugs used alone and in combinations.

Results
Both isolates showed high MICs to commonly used azoles. A synergistic effect was observed between terbinafine and triazoles (voriconazole and posaconazole, FICI = 0.5). However, combining amphotericin B with terbinafine or voriconazole resulted in an antagonistic effect. Our preliminary data with the in vivo Galleria model showed a trend towards an improved survival in the group treated by the voriconazole-terbinafine combination compared to the individual drugs and untreated groups.

Conclusion
Our in vitro data coupled with an in vivo Galleria model suggest that the adjunction of terbinafine could potentiate the effect of triazoles in the treatment of Aspergillus calidoustus infection.

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STREPTOCOCCUS PNEUMONIAE RESPONDS TO PEPTIDES FOUND IN RIBOSOMAL PROTEINS OF OTHER BACTERIAL SPECIES

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Background and aims
Pneumococcus colonizes the nasopharynx alongside other bacteria species. We predict that AmiA, AliA and AliB, substrate-binding proteins of a pneumococcal ABC transporter, play a role in interspecies communication. Previously we have shown that nonencapsulated S. pneumoniae recognizes peptides matching other bacterial species by homologues of AliB (AliB-like ORF1 and ORF2). AmiA, AliA and AliB, unlike AliB-like ORFs, are universally present in virulent, encapsulated pneumococci. We aimed to determine: (i) whether AmiA, AliA and AliB also bind foreign peptides of other bacterial species and (ii) the effect of binding on phenotype of the pneumococcus.

Methods
We expressed recombinant AmiA, AliA and AliB proteins and incubated them with human nasopharyngeal swabs to capture specifically bound ligands. De novo peptide sequencing was performed to confirm the sequences of the peptides from their MS/MS spectra. Tryptophan fluorescence assay confirmed binding of the proteins to their ligands. Growth assays were performed in defined peptide-free medium (CDM).

Results
We found a total of 11 possible ligands. Among these, we confirmed binding for one peptide for each protein: AmiA, AliA and AliB bind three different peptides matching ribosomal proteins of Gammaproteobacteria, including common colonizers of the nostrils and nasopharynx. Phenotypic assay showed binding of the peptides results in altered pneumococcal growth.

Conclusions
We propose a novel route of interspecies bacterial communication in the nasopharyngeal microbiota via ribosomal protein-derived peptides which bind AmiA, AliA and AliB proteins, resulting in changes to pneumococcal phenotype. Such interspecies communication is a potential target for intervention.

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Influence of resin-based blood culture media on the time to clearance of Staphylococcus aureus bacteremia – a retrospective cohort study

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Aim
Resin-based (RB) blood culture (BC) media are superior to traditional charcoal-based (CB) BC media concerning the time to pathogen detection and the frequency of pathogen isolation. However, their impact on the duration of Staphylococcus aureus bacteremia has not yet been studied. We aimed to estimate the effect of RB BCs on the time to clearance and intravenous treatment duration in patients with S. aureus bloodstream infection (BSI).

Methods
We conducted a retrospective, single center, cohort study in a tertiary care hospital in Switzerland comparing adult patients with S. aureus BSI between 2011-2013 (CB BC media) and 2015-2016 (RB BC media). Primary endpoint was the time to clearance of bacteremia. Secondary endpoints included duration of bacteremia and intravenous antibiotic treatment and length of hospital stay.

Results
Overall, we enrolled 294 patients, 195 in the CB group and 99 patients in the RB group. Baseline characteristics were similarly distributed with the exception of nosocomial infection (CB 18% vs. RB 30%) and endocarditis (25% vs. 14%). Time to clearance was significantly longer in the RB cohort (Median days 2.9 vs. 1.7, $p < 0.001$) compared to the CB cohort. Similarly, the interval between first and last positive blood culture was significant longer (Median days 2.7 vs 1.3, $p < 0.001$) and ratio of blood culture bottles drawn per day was significantly higher in the CB group (Median bottles 3.3 vs 4, $p = 0.003$). Time-to-positivity (TTP) was similar in aerobic bottles (Median days 14.5 vs 14.6, $p = 0.9$), but significant different in anaerobic bottles (Median days 13.8 vs 16.5, $p < 0.001$). After adjusting for confounding factors, the average duration of bacteremia was 0.8 ($p = 0.03$) days longer in the RB cohort compared to the CB cohort.
Length of hospital tended to be shorter (Median days 22 vs 26, $p = 0.1$) and duration of intravenous therapy tended to be longer in the RB group (Median days 29 vs 27, $p = 0.2$).

Conclusion
In this cohort study, duration of S. aureus bacteremia was significantly longer when using resin-based BC media compared to traditional charcoal-based BC media with a difference of 1.4 days. The impact of this finding on duration of intravenous treatment is unclear and remains to be determined in larger cohort studies.

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SWITCH TO BICTEGRAVIR/F/TAF FROM DTG AND ABC/3TC

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Aims
Bictegravir, a novel, unboosted INSTI with a high barrier to resistance and low potential for drug interactions, has been co-formulated with the recommended NRTI backbone of emtricitabine and tenofovir alafenamide (B/F/TAF) as a fixed-dose combination (FDC). We report the primary Week (W) 48 efficacy and safety Phase 3 results of switching to (B/F/TAF) from dolutegravir plus abacavir/lamivudine (DTG+ABC/3TC) or DTG/ABC/3TC.

Methods
HIV-infected adults virologically suppressed on DTG/ABC/3TC or DTG plus ABC/3TC (DTG/ABC/3TC group) with estimated glomerular filtration rate (eGFR) ≥ 50 mL/min were randomised 1:1 to switch to B/F/TAF (50/200/25 mg) once daily or continue their current regimen as DTG/ABC/3TC through week 48 in a double-blinded fashion. Primary endpoint was proportion with HIV-1 RNA ≥ 50 copies/mL at W48 (FDA snapshot). Non-inferiority was assessed through 95.002% confidence intervals (CI) using a margin of 4%. Secondary endpoints were proportion with HIV-1 RNA < 50 copies/mL and safety (adverse events [AEs], laboratory results, bone mineral density [BMD], and renal biomarkers).

Results
563 participants were randomised and treated (B/F/TAF n=282, DTG/ABC/3TC n=281): 11% women, 22% Black, median age 46 yrs (range 20-71). At W48, 1.1% switching to B/F/TAF and 0.4% continuing DTG/ABC/3TC had HIV-1 RNA ≥ 50 copies/mL (difference 0.7%; 95% CI -1.0% to 2.8%, p=0.62), demonstrating non-inferiority. At W48, proportion with HIV-1 RNA < 50 copies/mL was 93.6% on B/F/TAF and 95.0% on DTG/ABC/3TC. No participant developed resistance to any study drug. The most common adverse events (AEs) were upper respiratory tract infection (10% B/F/TAF, 10% DTG/ABC/3TC), diarrhea (9%, 5%), nasopharyngitis (7%, 8%) and headache (7%, 7%). Few participants (6 [2%], 2 [1%]) had AEs leading to premature study drug discontinuation. Mean BMD increased similarly in both groups. Percentage changes from baseline in renal biomarkers were similar between treatment groups. Lipid parameters were similar between groups with the exception of a small decrease in triglycerides (-5 mg/dL) seen in the B/F/TAF group vs. +3 mg/dL in the DTG/ABC/3TC group (p=0.028).

Conclusion
Switching to B/F/TAF was non-inferior to continuing DTG/ABC/3TC with low rates of W48 virologic failure, high rates of maintained virologic suppression, and no resistance. B/F/TAF was well tolerated, with a similar bone and urine protein safety profile to DTG/ABC/3TC.

Conflict of interest
The presenting author and four of his co-authors are employees of Gilead Sciences.
This study was sponsored by Gilead Sciences.

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NEVIRAPINE PLUS LAMIVUDINE MAINTAIN HIV-1 SUPPRESSION THROUGH WEEK 24

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Aims
Simplification of HIV maintenance therapy may reduce adverse events and cost. The effect of boosted protease-inhibitor monotherapy is limited as shown by increased rates of viral blips and HIV-RNA detection in cerebrospinal fluids, most likely due to insufficient compartment penetration. For 80% of the patients with no hypersensitivity reaction at treatment initiation, Nevirapine (NVP) is characterized by an excellent long-term tolerance. For this single center pilot study we hypothesized, that a combination of NVP and Lamivudine (3TC), two active compounds with excellent compartment activity may provide an optimal HIV maintenance therapy. The aim of this pilot study is testing feasibility and efficacy of this strategy before evaluation in a larger trial.

Methods
Patients with fully suppressed HIV plasma viral load (pVL) > 24 months whereof > 6 months on a NVP containing regimen and without previous failure of any non-nucleoside reverse transcriptase inhibitor regimen were switched to NVP and 3TC. HIV pVL was monitored monthly until week 24. The primary outcome was confirmed viral failure (RNA > 100" copies/ml). The frequency of low level detection of HIV- RNA in plasma (< 20, 20-50, > 50 cp/ml) was compared in each patient with pre-study viral load measurements.

Results
Twenty patients (15 male) were included and reached week 24. After a total of 480 observation weeks, none of the 20 patients experienced HIV pVL > 50 copies/ml. The frequency of low level HIV-RNA detection < 20 copies/ml (10/120) and 20-50 copies/ml (5/120) was not different from the period before randomization.

Conclusion
Our findings do not falsify the study hypothesis. This indicates that dual-treatment with NVP and 3TC warrants further evaluation as a potentially interesting maintenance strategy. A properly sized study to investigate non-inferiority of NVP/3TC bi-therapy to standard triple therapy is planned. If successful, this would result in a maintenance strategy with significant benefits in cost and reduced long-term side effects.

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Degradation of Amoxicillin/Amoxicillin-clavulanate as a function of ambient temperature

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Aims
Amoxicillin and amoxicillin-clavulanate (co-amoxicillin) are among the most frequently used antibiotics for treatment of paediatric infections globally, and expectedly are available as child-appropriate formulations, mostly as dry powder suspensions. For reconstituted co-amoxicillin suspensions, refrigerated storage is recommended by the manufacturer. However, access to fridge technology is a problem in many low and middle income countries (LMIC) with a high infection burden. This study evaluated the stability of amoxicillin and co-amoxicillin suspension in relation to ambient temperature, together with an evaluation of access to fridge technology in LMICs.

Methods
We tested degradation over time under different temperature conditions of six commercially available suspension products using high-pressure liquid chromatography-mass spectrometry (HPLC-MS). Two amoxicillin products and four co-amoxicillin products (two suspensions each with 7:1 or 4:1 ratio of amoxicillin to clavulanate) were tested. For every product, three bottles were tested and average degradation was calculated. Degradation was tested during 8 days with constant ambient temperatures of 8°C versus 28°C. The Demographic and Health Surveys (DHS) Program provides nationally representative data on household characteristics for a number of LMICs, including access to a refrigerator.

Results
Mono-preparations of amoxicillin were stable at 8°C temperature (max. 2% degradation over time), while a maximum of 10% amoxicillin was degraded after 8 days at 28°C. In co-formulated products, amoxicillin showed degradation up to 23% at 8°C and up to 18% at 28°C. Clavulanate showed degradation of up to 33% at 8°C in 8 days and around 70% at 28°C ambient temperature. In 38 African and Asian LMICs, only 25% of households possess a refrigerator (range 1.6-96.5%).

Conclusion
In reconstituted liquid co-amoxicillin formulations neither component is satisfactorily stable at elevated room temperature. Since storage conditions for co-amoxicillin are likely inadequate in many LMICs, robust data for forming recommendations for appropriate use of co-amoxicillin in these countries are urgently required. Furthermore, careful thought needs to be given to alternative solid child-appropriate formulations with better stability profiles in settings with low access to refrigeration.

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P80

Very low hepatitis C viral loads in treatment-naïve persons: do they compromise hepatitis C virus antigen testing?

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Background
Hepatitis C virus (HCV) antigen testing is less expensive than PCR but has lower sensitivity for very low viral loads (VLVL, i.e. HCV RNA ≤ 3,000 IU/ml). Currently the benefits of antigen testing are discussed for HCV screening in resource-limited settings. Data on the prevalence and outcomes of HCV-positive persons with VLVL are scarce.

Methods
We assessed prevalence and predictors of VLVL by logistic regression in treatment-naïve participants in the Swiss Hepatitis C Cohort Study. We analyzed if the last viral load after VLVL was low, and compared cirrhosis and mortality in persons with and without VLVL.

Results
We included 2,533 treatment-naïve persons (46.8% of 5,409 persons enrolled) with available HCV viral loads. Overall, 5.3% had a VLVL. Age 18-40 years, female gender and HIV coinfection were associated with VLVL. Out of 72 persons with a viral load available after VLVL, 14% had a VLVL as last viral load and 17% had spontaneous viral clearance. The prevalence and incidence of cirrhosis and mortality were comparable in persons with and without VLVL; all 24 persons with VLVL and cirrhosis had excessive alcohol consumption or immunosuppression.

Conclusions
The proportion of treatment-naïve persons with a VLVL ≤ 3,000 IU/ml was 5,3% and will likely be lower for single screening tests. Among the persons who would be missed, some had a favorable disease course, but some had immunosuppression and liver cirrhosis. The applicability of HCV antigen testing for screening may be limited by the risk of missing patients with severe liver disease.

Conflict of interest
This work was supported by Swiss National Science Foundation grants 3347C0-108782/1 and 33CS30-148417/1 to the Swiss Hepatitis C Cohort Study and unrestricted grants to the Swiss Hepatitis C Cohort Study Foundation by AbbVie, Bristol Myers Squibb, Gilead.

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Influence of geographical origin on access to therapy and therapy outcomes in hepatitis C virus-infected persons: the Swiss Hepatitis C Cohort Study

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Background
In hepatitis C (HCV) infection, late diagnosis and treatment may increase morbidity and mortality. We explored whether geographical origin is associated with differences in liver disease stage and treatment factors in HCV-infected persons in the Swiss Hepatitis C Cohort Study (SCCS).

Method
We included all persons enrolled in the SCCS. We analyzed the association between their origin and the following outcomes by univariable/multivariable logistic and Cox regressions: antiviral treatment status, sustained virological response, cirrhosis at enrolment, incident cirrhosis, loss to follow-up (LTFU), mortality. Analyses were adjusted for the following baseline characteristics: gender, age, education, source of income, alcohol consumption, injection drug use (IDU), HCV genotype, HIV or HBV coinfection, duration of HCV infection, cirrhosis, (type of) HCV treatment and centre at enrolment.

Results
Among 5,356 persons of known origin, 1,752 (32.7%) were foreign-borns. IDU was more frequent among Swiss-borns (65.5%) compared to foreign-borns (37.7%). There was no association between origin and outcome for treatment status, sustained virologic response and incident cirrhosis. Cirrhosis at enrolment was particularly frequent in Italian-borns. Mortality was similar across groups, with persons from Asia/Oceania showing a reduced mortality. LTFU was more frequent in persons from Germany, Eastern- and Southern Europe and the Americas.

Conclusion
Outcomes among foreign-borns persons were often similar compared to persons of Swiss origin. The high frequency of cirrhosis among Italian-borns probably reflects the high risk of healthcare-associated infection in Italy in the years 1950-70, while LTFU may mirror migration patterns.

Conflict of interest
This work was supported by Swiss National Science Foundation grants 3347C0-108782/1 and 33CS30-148417/1 to the Swiss Hepatitis C Cohort Study and unrestricted grants to the Swiss Hepatitis C Cohort Study Foundation by AbbVie, Bristol Myers Squibb, Gilead.

Additional information
We are in deep sadness that our dear colleague and friend Matteo Brezzi died. We miss you.

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Pediatric population pharmacokinetic modeling for gentamicin – is the current dose recommendation justified?

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Aims

The aminoglycoside antibiotic gentamicin is widely used in children. Monitoring of gentamicin serum trough level (Cmin) is standard practice to prevent toxicity by drug accumulation(1). Cmin < 2 mg/L are recommended. Peak serum concentration (Cmax) is not routinely measured although Cmax between 10 and 12 mg/L have been recommended balancing efficacy and toxicity(2,3). We aimed to develop a population pharmacokinetic (PK) model for gentamicin in children to optimize current dosing regimens accordingly.

Methods

All patients receiving intravenous gentamicin at the University Children's Hospital Zurich between October 2017 and March 2018 were eligible for this study. Children with cystic fibrosis and renal replacement procedures were excluded. Gentamicin was administered once daily at 5 mg/kg in children under 7 days of age and 7.5 mg/kg in older children. Routine Cmin were measured in all patients before administration of the third dose. Additional gentamicin serum levels were measured 30 min (C30) and 4 h after the second dose in patients giving written informed consent. Data were analyzed by non-linear mixed-effects modeling.

Results

86 patients (median age 40.5 days; IQR 22 to 249 days) were included in the study. C30 was available for 32 and Cmin for 65 patients, respectively. C30 (mean 21.2 mg/L, SD +/- 8.2 mg/L) was > 12 mg/L in 29/32 (91 %) and Cmin > 2 mg/mL in 7/65 (11 %) patients. Modeling with a 2-compartment model revealed r = 0.925 for the correlation between observed and predicted serum concentrations when including body weight, height, and a maturation function for age as covariates. Modeling correctly identified 28/29 C30 > 12 mg/L (96%). However, Cmin > 2 mg/L were not predictable. Based on our results, we suggest to calculate the dose (2 min infusion) from the covariate for central volume of distribution according to dose (mg) = target Cmax (mg/L) × exp(-5.43 + 1.44 × ln(height, cm)).

Conclusions

Our current gentamicin dosing regimen rarely leads to accumulation but most Cmax are above optimal range. The latter was successfully modelled. Although no evidence for a Cmax upper limit exists, toxicity has been associated with high drug exposure(3). This calls for an adjustment of our dosing regimen using our PK model based on body height or body weight in order to lower exposure. Further studies investigating the relationship between Cmax levels and clinical outcome and additional data for PK model testing are needed for validation.

Additional information

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"Airborne" Tularemia – a One Health Case Report

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A female jogger was attacked by a common buzzard (Buteo buteo) and was scratched slightly at the back of her head. One week later she was taken ill with fever (40°C), headache and a painful lymphadenopathy of the lymph nodes draining the site of the scratch at the back of her head. After 4 weeks of symptomatic treatment she was seen for the first time in our hospital with continuous fever, very painful lymph nodes, a small ulcer at the site of the initial scratch, malaise and myalgia. A diagnosis of ulcero-glandular tularemia caused by Francisella tularensis could be confirmed by serology. Blood cultures remained negative - initially cultures form the ulcer and lymph nodes could not be taken. Antibiotic treatment with with Gentamicin 1x 5 mg/kg /day iv plus Ciprofloxacin 2x500 mg po/day was initiated. The patient improved soon and temperatures dropped to normal. Unfortunately the painful lymphadenopathy did not improve, abscesses developed and had to be incised (cultures negative). Recovery was finally achieved after prolonged antibiotic treatment (Gentamycin 2 weeks, Ciprofloxacin 6 weeks). This long treatment duration seems to be frequently necessary with late treatment of tularemia .
Tularemia is a well known zoonotic disease, mainly affecting rabbits and hares, but also small rodents. Human infection occurs often following tick bites or bloodsucking insects, or in hunters or slaughterers handling infected animals. Bites by mice have also been reported as a cause of tularemia. For the first time we report this case of tularemia as a result of an attack by a bird of prey. We assume that the bird acted as a vector just carrying the F. tularensis on its claws or beak, but we cannot exclude an infection of the bird itself.
Several other joggers had also been attacked by a common buzzard in the same area shortly after the above described event and one of them also became infected with F. tularensis.

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Performance of Accelerate Pheno System on clinical blood cultures in diagnosis of bacteraemia in bloodstream infections

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Background
Rapid bacterial species and antibiotic susceptibility testing are essential in reducing morbidity and mortality due to bloodstream infections (BSI) and appropriate antibiotic use.
The Accelerate Pheno system (AXDX) is a fully automated test system able to performing bacterial identification (ID) and antimicrobial susceptibility testing (AST) directly from positive blood cultures (BC) within an average of 7 hours. We have performed a pilot study on patients with bacteriemia or sepsis, in order to evaluate the performance of AXDX in comparison to routine diagnostic techniques.

Methods
During a 3-months period, 47 prospective positive BCs collected at the Clinica Luganese Moncucco corresponding to unique episodes of BSI were analyzed both by AXDX and standard laboratory testing (MALDI-TOF for ID, Phoenix BD and Kirby-Bauer for AST). Comparisons between methods were expressed as essential or categorical agreement (EA-CA), very major error (VME -false susceptibility), major error (ME-false resistance), or minor error (Mie-intermediate versus susceptible or resistant). Time from BC reception into the lab to ID/AST result was further analysed.

Results
A total of 41 BCs were evaluated in the study: 22 Gram negative, 14 Gram positive and 3 off-panel microorganisms (Salmonella napoli, Enterococcus gallinarum, Stenotrophomonas maltophilia). 6 samples were excluded: 3 technical failures, 2 ID negative reports (Asaia bogorensis and Lactobacillus sakei), 1 ID partial report in a polimicrobic BC. The Pheno panel coverage was 87.8%. Concerning AST testing, a total of 270 microorganism-antimicrobial combinations were analysed. EA was 94.1%, CA 92,8%. Discrepancies were linked to VME (5.9%), ME (3.7%) and Mie (3.4%). The average time for AXDX to provide ID/AST for the 41 samples was 6:21h (x±DS = 6:27 ± 0,7).

Conclusions
Accelerate Pheno System provides highly reliable results in a timely manner, detecting resistance phenotype of microorganisms responsible of BSI. The technique could have a major impact on clinical management. Cost analysis and potential positive impact on antibiotic stewardship, prescription correctness and clinical outcomes is currently under evaluation.

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Chronic granulomatous ileo-colitis: Not always Crohn's disease

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Case presentation
In February 2017, a previously healthy 31-year old female was referred to an extern gastroenterologist with a 3-year history of intermittent hemorrhagic diarrhea and abdominal cramping. In the last months the frequency of diarrhea had increased, she developed night sweats but neither fever nor weight loss. Physical examination and laboratory findings were normal. Stool examination was negative for pathologic microorganisms, however calprotectin was elevated with 106 mcg/g (< 50mcg/g). The MRI of the intestine showed inflammatory changes of ileum, caecum and colon ascendens. Colonoscopy revealed hypertrophic lesions with aphthous ulcers in the caecum and colon ascendens. Histology showed active inflammation with granulomas, surrounded by epitheloid cells without central necrosis. All findings were highly compatible with Crohn's disease. However, polymerase chain reaction (PCR) for Mycobacterium tuberculosis was performed from formalin fixed colon biopsies with a positive result. To confirm the unexpected finding and allow resistance testing a second colonoscopy with biopsy was performed and cultures were positive for fully susceptible M. tuberculosis leading to the diagnosis of tuberculous enterocolitis. Extraintestinal TB manifestations were excluded clinically and radiologically. The patient was treated with a standard antituberculous regimen for 6 months. Already after one month of treatment, diarrhea ceased and after 6 months the patient had recovered completely.
Most likely, TB was acquired during early childhood since the patient is Filipina and had lived in the Philippines until she was 2 years old. Her mother and siblings had pulmonary TB in the past.

Discussion:
- The ileocaecal region is the most common site of TB enteritis but also of Crohn's disease
- Symptoms, endoscopic appearance and histologic findings of intestinal TB may be very similar to Crohn's disease whereas ascites and lymphadenopathy are more suggestive for TB
- In migrants and people having lived in TB endemic areas intestinal TB should be actively excluded by mycobacterial culture of biopsies before immune modulating treatment for Crohn's disease is initiated
- The differential diagnosis of chronic granulomatous enterocolitis is broad and includes sarcoidosis, yersiniosis, intestinal TB and Crohn's disease
- TB enteritis is treated by a standard 6 months course of antituberculous drugs

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Appropriateness of antimicrobial prescribing in a Swiss tertiary care hospital

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Aims
Inappropriate use of antimicrobials is associated with the emergence of antimicrobial resistance and adverse events. Antimicrobial stewardship programs may both optimize treatment of infections and reduce antimicrobial resistance, but are implemented in only a minority of Swiss hospitals. In addition, data on Swiss prescribing patterns are limited. We conducted a two-point prevalence survey to evaluate antimicrobial usage in a single tertiary care center.

Methods
Two audits of antimicrobial use were conducted (summer 2017 and winter 2018) among all patients admitted to the University Hospital Basel. Data were collected from the electronic health record. Appropriateness of antimicrobial use was evaluated by two infectious diseases physicians according to local and international guidelines.

Results
We evaluated 1112 patients of whom 378 (34%) were receiving 547 prescriptions in total (30% for prophylaxis). Penicillins with β-lactamase inhibitors were most commonly used (30%) followed by cotrimoxazole (12%) and cephalosporins (11%). Intravenous administration was chosen in 56% of patients. Prior to antimicrobial therapy, blood cultures were collected in 62% of patients. Overall, 154 (28%) prescriptions were not appropriate including lack of indication (12%, mostly prolonged administration of surgical prophylaxis), incorrect dosing (7%), lack of intravenous to oral switch (9%) or non-adherence to local guidelines (14%). A minority of patients received antimicrobials despite documented allergies (2%). Almost 50% of empiric prescriptions were inappropriate compared to only 20% of prophylactic and targeted prescriptions. In line, penicillins with β-lactamase inhibitors and cephalosporins were most commonly involved in inappropriate prescribing (>50%) compared to narrow-spectrum penicillins (11%), cotrimoxazole (13%) or carbapenems (27%), and oral administration was involved less frequently compared to intravenous (20 vs. 43%). Infectious diseases consultation and presence of immunosuppression were associated with a reduced odds (both 0.3, p=0.01) of inappropriate prescription in the per-patient multivariable analysis.

Conclusion
Almost one third of prescriptions were inappropriate in our tertiary care center despite local guidelines and a busy infectious diseases consultation service. Our results underscore the need for expanding current antimicrobial stewardship efforts and identify areas for improvement including timely intravenous to oral switch.

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Postsurgical complications after graft implantation are important risk factors for subsequent vascular graft infections – prospective results from the VASGRA Cohort Study

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Aims
Reconstructive vascular surgery has become increasingly common. Vascular graft infections (VGI) are serious complications with a cumulative incidence rate of 1 - 6%, leading to increased morbidity and mortality. Previously described risk factors for VGI include groin incision, wound infections, and comorbidities. We aimed to identify modifiable predictors for VGI as targets for infection prevention strategies.

Methods
Participants of the prospective Vascular Graft Infection Cohort (VASGRA) with surgery between 2013 and 2017 were included. Observation time was calculated from surgery until confirmed VGI or last follow-up. Variables were assessed by infection status using non-parametric tests. Uni- and multivariable Cox proportional hazard regression models, adjusted for demographic factors, were applied to assess risk factors for a VGI.

Results
A total of 438, predominantly male (83.1%) patients with a median age of 71 years contributed to 554 person-years (PY) of follow-up. Thereof, 39 (8.9%) developed a VGI, amounting to an incidence rate of 7.0/100 PY. We found postsurgical wound complications (adjusted Hazard Ratio (aHR) 10.32 [95% CI 2.95 - 36.09]), hemorrhage (aHR 4.94 [1.29 - 19.01]), and renal insufficiency (aHR 4.71 [1.16 - 19.09]) to be risk factors for VGI, while perioperative prophylaxis showed protective effects (aHR 0.37 [0.15 - 0.93]). Even though, both open surgical access during the initial graft implantation and consequently extended procedure time showed an increased risk for VGI (aHR 2.12 [0.89 - 5.06] and aHR 1.23 [1.08 - 1.39], respectively), their association might even be stronger in reality since we assume some effect mitigation in our model due to collinearity.

Conclusion
We identified application of perioperative prophylaxis and several postsurgical infectious and non-infectious complications (including postsurgical wound and bleedings complications) as potentially modifiable predictive factors for VGI and key to improved surveillance programs, closer postsurgical follow-up, and prevention strategies for VGI. Open surgical access and consequently longer procedure times are also among the risk factors for a subsequent VGI development, however, oftentimes the indication for an open surgical access is not a modifiable factor, but given by the circumstances.

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Ceftobiprole as an ultimate successful therapy for MRSE prosthetic endovascular infection judged to be medically untreatable in a profound immunocompromised patient: a case report.

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Aims

We report the case of a severely immunocompromised patient with prosthetic endocarditis and aortitis involving different strains of methicillin-resistant Staphylococcus epidermidis (MRSE) for whom conventional antibiotic therapy has failed with multiple relapses.
At present, the available options to treat methicillin-resistant Staphylococcus aureus (MRSA) and MRSE endocarditis, especially prosthetic endocarditis, remain limited.
Ceftobiprole is a novel 5-th generation cephalosporin with anti-MRSA and MRSE in vitro activity, approved in EU for the treatment of hospital-acquired and community-acquired Pneumonia.

Case description

A 56-year-old man with prolonged and severe pancytopenia after autologous hematopoietic stem cells transplantation (HSCT) for Burkitt lymphoma in remission presented several relapses of MRSE bacteremia despite active prolonged antibiotic therapy (daptomycin, vancomycin, and doxycycline). The infectious source was identified in the aortic valve and the ascending aorta (status post-Bentall 10 years before). The patient was eligible for allogeneic HSCT in order to restore the bone marrow function, however, the active infection prevented the transplant. Based on the microbiological property of ceftobiprole and the failure of the previous therapies, we decided to treat the patient with ceftobiprole and to proceed to the transplantation as soon as the blood cultures were negative. The allogenic HSCT could successfully be undertaken without relapses of bacteremia on ceftobiprole therapy, which was stopped 3 months post-HSCT. At one year, there is no clinical, biological or radiological (PET-CT) sign of infection.

Conclusion

Ceftobiprole was, in this case, a salvage therapy, which permitted not only to control but also to cure an infection considered untreatable without surgery. Ceftobiprole might be considered, next to the current validated use in pneumonia, as a legitimate option for MRSA/MRSE endovascular infections including native and prosthetic endocarditis. Furthermore, a phase III trial is currently evaluating the efficacy and safety of ceftobiprole compared to daptomycin in the treatment of Staphylococcus aureus endovascular infections (NCT03138733).

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Host biomarkers to predict bacterial pneumonia and tuberculosis among patients with lower respiratory tract infections in emergency departments in Tanzania

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Aims
Low respiratory tract infections (LRTIs) are one of the main driver of antibiotic overprescription in outpatients. It is a challenge to identify patients who need antibiotics. We investigated the predictive validity of host biomarkers for bacterial pneumonia and tuberculosis (tb) in emergency departments of Dar es Salaam, Tanzania.

Methods
Consecutive adults with >38° were included in the presence of a clinical LRTI. HIV screening, blood culture, multiplex real-time PCR for respiratory pathogens (7 bacteria and 9 viruses) in nasal swabs and chest x-rays were performed in all patients. Tb screening (Xpert in sputum and TBlam when appropriate) was done in patients coughing for ≥2 weeks and in every HIV infected patient with cough of any duration. Bacterial pneumonia was defined as the presence of a lung infiltrate and a positive nasopharyngeal PCR for a bacteria and viral pneumonia as the presence of a positive viral PCR result in the absence of tuberculosis. Markers of endothelial (Ang-2, sFlt-1, sVCAM-1) and immune (sTREM-1, IL-6, IL-8, CHI3L1, sTNFR1, PCT, CRP) dysfunction were measured, using Luminex® multiplex platform or ELISA. Predictive value of the top biomarkers selected by logistic regression as well as combinatorial models adding top biomarkers to vital signs were measured.

Results
Among 519 febrile patients, 160 (31%) presented with a LRTI. 8 were excluded because of a fungal infection (pneumocystosis or histoplasmosis). Among included patients, 35 presented with pneumonia (21 bacterial and 14 viral), 82 with bronchitis and 35 with tb. PCT and IL-6 exhibited the greatest accuracy to predict bacterial pneumonia among patients with a LRTI (AUCROC 0.81; 95%CI 0.69-0.93 and 0.74; 0.59-0.89). Adding respiratory rate to the biomarker improved the predictive accuracy of the model (to PCT AUCROC 0.88; 95%CI 0.81-0.95 and to IL-6 0.85; 0.77-0.93). The combination of IL-6 and sTREM-1 had the best accuracy to predict pulmonary tb among screened patients (AUCROC 0.79; 95%CI 0.69-0.90).

Conclusion
Among adults with LRTI, PCT and Il-6 were the best predicting biomarkers of bacterial pneumonia. Combining procalcitonin and easy-to-measure vital sign can help identifying patients who will benefit from an antibiotherapy. Using the combination of IL-6 and sTREM-1 could help in identifying patients with pulmonary tb among adults at risk.

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Procalcitonin and lung ultrasonography point-of-care testing to decide on antibiotic prescription in patients with lower respiratory tract infection at primary care level: a pilot implementation

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Aims
Among outpatients with lower respiratory tract infection (LRTI), 60% receive antibiotics while only 5-12% have community-acquired pneumonia (CAP) and require this treatment. Diagnosis of CAP is challenging as it relies on chest X-ray that has limited accuracy.
Procalcitonin (PCT) has been used to decide on antibiotic prescription in patients with LRTIs thanks to its good sensitivity. Lung ultrasound (LUS) is good at detecting lung consolidation in pneumonia, compensating for the insufficient specificity of PCT.
We performed a pilot study to evaluate the feasibility of implementing an algorithm combining procalcitonin and ultrasound (UltraPro) to decide on antibiotic prescription for LRTI at primary care level.

Methods
Observational pilot study conducted in a walk-in centre in Lausanne and in three GP's practices between December 2017 and March 2018. GPs received a full day training on CAP diagnosis, and LUS. All consecutive patients presenting with an LRTI were screened for inclusion. Follow-up was done by phone at day 7 and 28 and by a self-assessment daily diary. LUS were reviewed by an expert radiologist. We performed qualitative and quantitative analyses.

Results
8 GPs were trained for participation. After the half-day LUS training, 50% felt comfortable in using this method. 81 patients were screened and 20 included (65% female, median age 47 years old). PCT measurement was successful in 18/20 patients and LUS performed in all patients (median duration 22 minutes, 88% of exams with good or above quality, 100% with correct interpretation). The level of agreement between antibiotic prescription and the algorithm's recommendation was 90%. Phone follow-up was successful in 95% of the patients at day 7, still ongoing at day 28, and 60% of the patients returned the diary filled in. Patient satisfaction was 100%. Qualitative analysis of the acceptance of the intervention by GPs is ongoing.

Conclusion
GPs successfully used the UltraPro algorithm in most patients. However, half of the GPs did not feel ready to rely on their LUS findings, even after the half-day training. Lessons learned during this pilot phase will lead to an enhanced LUS training, which will be more practical and prolonged by half a day. A cluster randomized controlled trial, testing the impact of the intervention on antibiotic prescription rates will start on June 1st 2018 in Swiss GPs practices.

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Bloodstream Infections: A Single Center Surveillance 2011-2017

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Aims

To characterize the epidemiology of bloodstream infections in a 200 - bed hospital.

Methods

We performed an observational, retrospective, single center laboratory surveillance study. Data on bloodstream infections from 2011 through 2017 were obtained from the laboratory information system. We compared prevalences of pathogen and susceptibility pattern during the study period.

Results

A total of 1363 bloodstream infection episodes were analyzed. The most common isolates were Escherichia coli (n = 465, 34.1%), coagulase negative staphylococcus (n = 316, 23.3%), Staphylococcus aureus (n = 155, 11.4%), and Streptococcus pneumoniae (n = 70, 5.1%). The proportion of E. coli remains stable during the study period. Extended spectrum beta lactamase (ESBL) was found in 24 (5.2%) E. coli. No ESBL producers were found in other Enterobacterales. 70 (15.1%) of E. coli isolates were resistant to ciprofloxacin. 30 (19.4%) of S. aureus isolates were susceptible to penicillin. However, only 2 (1.3%) MRSA were found. All S. pneumoniae isolates were susceptible to penicillin. 164 (51.9%) of coagulase negative staphylococci were resistant to cefoxitin.

Conclusions

E. coli is the predominant pathogen in bloodstream infections in our hospital. The results will influence empirical antibiotic treatment in our hospital.

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Micro-Elimination of Hepatitis C Virus (HCV) in Zurich, Switzerland: A Modelling Study

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Aims
With the development of direct-acting anti-viral agents (DAAs), cure of hepatitis C is now a promising reality. While country wide efforts towards elimination are being implemented in Switzerland, a more decentralized approach of micro-elimination, focusing on breaking down national and international elimination goals into more defined populations or regions, can be considered. In 2014, the Swiss Hepatitis Strategy was developed with the goal to eliminate the hepatitis C virus (HCV) and the associated liver related morbidity and mortality by 2030 [1]. We aimed to identify scenarios to achieve the Swiss Hepatitis Strategy by 2030 in Zurich, the largest canton in Switzerland.

Methods
An Excel-based Markov disease burden model was developed [2]. Population, mortality, hospital, and regional specific data were used to calibrate the model and forecast the current and future prevalence of HCV and associated liver related morbidity and mortality through 2030. Two scenarios were developed: “Base 2017”, representing the current standard of care, and an intervention scenario to achieve the Swiss Hepatitis Strategy goals.

Results
In 2017, the estimated viremic prevalence in Zurich was 0.64% (0.46% - 0.68%) corresponding to 9,500 (6,900 – 10,200) cases. If no efforts to increase diagnosis of new patients will be made; the pool of eligible patients to treat will be depleted by 2025.
In order to achieve the Swiss Hepatitis Strategy goals of a 30% reduction in new infections, total viremic infections, liver transplants, and HCC cases by 2020 and a 90% reduction by 2030, a sustained increase in the annual number of treated and diagnosed patients is required. Treatment must expand from 830 patients in 2017, to 850 patients in 2019 and 2020. This can then be reduced to ~800 patients annually through 2030. The number of patients diagnosed would need to increase to 350 patients annually beginning in 2022. This would result in a 95% reduction in total viremic HCV infections, HCC cases, decompensated cirrhosis cases, and liver related deaths.

Conclusions
Switzerland is on track to achieve elimination of chronic hepatitis C by 2030. Focusing on regional control strategies can help sustain efforts currently in place. In Zurich, a continued increase in both treatment and diagnosis are required in order to eliminate the disease.

Conflict of interest
Dr. Bruggmann has served as advisor and speaker for, and has received project and research grants from Merck, Janssen, AbbVie, Gilead and BMS
Prof. Mullhaupt has served as an advisory board member for Roche, MSD, Janssen Therapeutics, AbbVie, Boehringer

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DISRUPTION OF THE TIGHT JUNCTION COMPLEX WITH RELEASE OF ZO-1, OCCURS DURING TRANSMIGRATION OF PNEUMOCOCCI THROUGH DIFFERENTIATED HUMAN BRONCHIAL EPITHELIAL CELLS

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Aims

We developed a pseudostratified human airway epithelial tissue (HAE) model with air-liquid interface (ALI) to study colonization and epithelial transmigration of pneumococci (SP). The aim was to identify cellular responses to SP including the disruption of tight junction (TJ) proteins.

Methods

Human bronchial epithelial cells (four donors) were cultured for 60 days with an ALI until establishment of a differentiated cell monolayer. TIGR4 SP was inoculated apically at different multiplicity of infection (MOI) and incubated for 30 hours. SP were counted (cfu/ml) at the apical side ("colonizing") and in the basolateral compartment after transmigration. Trans-epithelial resistance (TEER), confocal microscopy (e.g. TJ) and ELISA for ZO-1 levels in supernatant were performed at different time points.

Results

Along the path from SP colonization to transmigration, there was a distinct dynamic of epithelial response. Whereas TEER did not change during colonization, it significantly decreased during transmigration indicating loss of integrity of the epithelial barrier. Accordingly, significantly higher ZO-1 levels were detected in supernatants of HAE cells when there was transmigration ($p = 0.001$). ZO-1 levels distinguished transmigration from non-transmigration with an area under the curve of 0.77. If analysis was restricted to samples with transmigrating pneumococci, neither the inoculated SP concentrations nor the incubation time had a significant effect on the quantitative ZO-1 levels in supernatant.

Conclusion

This differentiated HAE model simulates epithelial response to pneumococci including ZO-1 detection in the supernatant upon transmigration. Further studies are necessary to explain this mechanism i.e. whether this reflects degradation or hyperexpression of ZO-1 induced by SP.

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The effect of alcohol consumption on specific neuropsychological domains among patients enrolled in the Neurocognitive Assessment in the Metabolic and Aging COhort Study (NAMACO)

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Background
HIV-associated neurocognitive impairment (NCI) is diagnosed on the basis of testing specific neuropsychological (NP) domains. The effect of active or previous alcohol consumption on subsequently developing NCI is unknown. We examined the association between alcohol consumption and NP function among well-treated HIV-positive persons.

Methods
The Neurocognitive Assessment in the Metabolic and Aging Cohort (NAMACO) study is an ongoing, prospective, longitudinal, multicentre and multilingual study within the Swiss HIV Cohort Study (SHCS). The results of NP assessments from 981 patients aged > 45 years old enrolled in the NAMACO study were examined in five domains: motor skills, speed of information processing, attention/working memory, executive functions and verbal learning memory. Alcohol consumption was scored using a validated Alcohol Use Disorders Identification Test (AUDIT-C) based on consumption quantity and frequency, and occurrence/absence of binge drinking. For NP outcomes, analysis was conducted per NP domain and after summarising domains. We used logistic and linear regression models, adjusted for socio-demographic data.

Results
Almost all included patients (mean age 54.5 years, 80% men, 92% Caucasian) had undetectable viral loads (96% with < 50 copies/ml; median nadir CD4 180). Binge drinking at least once a week (4.2% of patients) significantly negatively impacted motor skills (OR 2.4, P = 0.01), speed of information processing (OR 2.1, P = 0.02) and overall NP function (OR 1.88, P = 0.06). A significant U-shaped effect of AUDIT-C score was observed for motor skills and overall function. There was also a significant effect of increasing AUDIT-C score and binge drinking on executive and overall functions, while other domains were preserved.

Conclusion
This is the first study to use a validated alcohol consumption score to examine the effect of alcohol consumption on specific NP domains in HIV-positive patients with NCI. We observe that binge drinking at least once a week had a significant impact on motor skills, speed of information processing and overall NP function, and that motor skills and executive function were impaired with increased alcohol consumption. In assessing NCI, it may be possible to examine the contribution of alcohol by restricting analysis to NP domains we observe to be impaired.

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P95

Vertical transmission of Mycoplasma pneumoniae infection

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Background
Mycoplasma pneumoniae is a significant cause of pneumonia in school-aged children and young adults. We report a case of neonatal M. pneumoniae pneumonia in a preterm child manifesting in the first hours of life. Vertical transmission was demonstrated by the detection of M. pneumoniae in inflamed placental tissue indicating chorioamnionitis.

Case presentation
A preterm male neonate was delivered at 29 4/7 weeks of gestation by caesarean section because of recurrent vaginal bleedings and premature contractions. He developed a severe respiratory distress syndrome (RDS) in the first hour of life with an atypical presentation necessitating two-times re-intubation within the first two weeks of life. Empiric antibiotic treatment was discontinued based on negative blood cultures and normal C-reactive protein on day of life (DOL) 2. The unclear situation led to a detailed review of the medical history during pregnancy: The mother recalled a mild respiratory tract infection with intractable cough in 20 gestational weeks, but this was left untreated. The diagnostic work-up in the neonate was extended by PCR for M. pneumoniae, which was found positive in tracheal aspirate on DOL 3 and in a second sample from nasopharyngeal aspirate after extubation on DOL 4. Treatment with erythromycin was initiated on DOL 4 for two weeks and paralleled by clinical and radiographic improvement. M. pneumoniae-specific antibodies were found in the neonate on DOL 22 (IgG) and in the mother two weeks after birth (IgM and IgG, indicating a recent infection). Histologic examination of the placenta showed distinct chorioamnionitis and vasculitis and placental tissues were tested positive for M. pneumoniae DNA by PCR and immunohistochemistry.

Conclusion
This case demonstrates that M. pneumoniae can be considered as possible cause of congenital pneumonia in addition to other 'atypical' organisms. The route of transmission of M. pneumoniae is vertical infection after dissemination of the bacteria following maternal respiratory tract infection.

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P96

Pneumonia with parapneumonic effusion or pleural empyema in children resolves with pleural tap-guided antimicrobial treatment

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Aims
For children with pneumonia and parapneumonic effusion or pleural empyema (PPE/PE) different management approaches and antimicrobial treatment regimens have been described. Six months outcome following empirical treatment with amoxicillin with/without clavulanic acid for a total of two weeks or a pleural tap-guided regimen was evaluated.

Methods
Children ≤16 years of age with radiologically diagnosed PPE and initial diagnostic pleural tap hospitalized at the University Children's Hospital of Zurich were included over a 15-year period (2001-2015). Empirical antibiotic treatment was given for 14 days and rationalized according to microbiological findings and susceptibility testing of culture results from initial pleural tap. Clinical and radiological follow-up was scheduled up to 6 months or until full recovery.

Results
In 113 of 146 children (77%) with PPE/PE and initial pleural tap a pathogen was identified by culture, PCR and/or antigen testing. Streptococcus pneumoniae was detected in 90 (80%), Streptococcus pyogenes in 13 (12%) and Staphylococcus aureus in 7 cases (6%), all but two cultures were sensitive to amoxicillin/clavulanic acid. 70% of all patients received treatment with amoxicillin with/without clavulanic acid for 14 days. Of 138 children with follow-up, 51% and 78% fully recovered after 4 and 6 months respectively, 96% had no sequelae at the end of follow-up.

Conclusions
Overall prognosis in children with PPE/PE was good. Empirical treatment with amoxicillin with/without clavulanic acid was sensitive in most cases and was performed for 14 days in 70% of all children. Tap-guided treatment resulted in full recovery in over 95% of children with PPE/PE.

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P97

A Hospital's Perspective: Use of Hospital Resources by Hospitalized Influenza Patients for the Influenza Season 2017/2018

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Aims

To describe the epidemic of the 2017/2018 influenza epidemic in our 380 bed hospital and it's consequences in terms of use of resources for hospitalized patients

Methods

Influenza PCR (Alere®) was used in the influenza season of 2017/2018 for diagnosis of influenza in hospitalized patients. All hospitalized patients in whom an influenza-PCR had been performed between 27.11.2017 and 8.4.2018 (the time period above the epidemic threshold in Switzerland) were included in this retrospective analysis. We counted hospitalization days, days on ICU or IMC, days on a ventilator and days spent under droplet precautions. We analyzed the diagnosis on discharge.

Results

- Median age was 74y (25-95y), 68 % were > 65y old. 52% were male, 48% female.
- In total 488 Influenza PCR tests were performed on hospitalized patients, of which 100 were positive (20%).
- 30 PCR tests were positive for Influenza A, 70 for Influenza B.
- Median duration of hospitalization was 9 days (range 1-37) for patients with proven influenza
- 29 patients needed intensive treatment:
    - 10 influenza pts. on the ICU (for a median of 8.4 days)
        - Of which 9 patients needed to be ventilated (for a median of 3 days)
    - 19 influenza pts. on intermediate care (for a median of 3.8 days)
- 81 Flu patients spent an average of 6 days on droplet precautions, but:
    - 19 patients with influenza were not under droplet precautions
    - In 11 patients influenza was diagnosed more than 2 days after hospitalization and therefore have to be classified as nosocomial
- Diagnosis at discharge was usually concurrent with influenza (66 cases of influenza including pneumonia or COPD), only rarely other diagnosis were the main reason for hospitalization, the most common cardiac decompensation.

Conclusion

- Patients spent a considerable time in hospital, using high-end resources as ICU and IMC in almost a third of cases. Their median length of stay was longer than average for patients on medical wards.
- Droplet precautions did not completely prevent nosocomial transmission of influenza
- Additional beds and health care workers need to be available during influenza season to cope with this influx of patients for example through internal redistribution of resources.

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P98

Cure of hepatitis C (Genotype 4) after only 3 weeks of Elbasvir/Grazoprevir: a case report

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Case presentation

A 32-year old female with chronic hepatitis C known for 15 years was evaluated for treatment because of persisting fatigue and arthralgias. Physical examination and laboratory findings including liver tests were normal,a search for cryoglobulins was negative. Hepatitis C RNA amounted to 83‘000 IE/ml, Genotype 4a,c,d was confirmed. Abdominal ultrasound showed normal liver parenchyma, elastography was normal (liver stiffness 4.5kPa). Co-infection with HIV or Hepatitis B was excluded.
The extrahepatic manifestations were the reason to start therapy with direct acting antiviral medication. Three days after the patient had reported normal menses, treatment with Elbasvir 50mg/Grazoprevir 100mg daily, planned for 12 weeks, was started. Strict contraception with condoms was advised, a pregnancy test was not performed.
After one week of treatment, new nausea and dizziness prompted an emergency room visit. Physical und laboratory examinations were normal, the symptoms were interpreted as side effect of the medication and therapy was continued. Two weeks later, a pregnancy test was positive and pregnancy at week 6 was confirmed by ultrasound. Our patient wished to carry on with her pregnancy. Because of possible embryotoxicity, antiviral therapy was stopped after 24 days of exposure. At this time hepatitis C viral load in the blood was undetectable, and remained so 7, 10, 15, and 33 weeks after treatment cessation. In February 2018, the patient gave birth to a healthy child after an uncomplicated pregnancy. In this patient, cure of chronic hepatitis C, Genotype 4, after 3 weeks of treatment can be assumed.

Learning points/Discussion

- Always do a pregnancy test before starting a potentially harmful treatment in a woman of childbearing age
- Not all complaints at the beginning of a new therapy are necessarily due to the medication
- We documented cure of a Genotype 4a,c,d hepatitis C with 3 weeks of Elbasvir/Grazoprevir treatment by sustained virologic response up to 33 weeks
- Shorter therapy with Elbasvir/Grazoprevirthan the advised 12 weeks for chronic hepatitis C Genotype 4 might be effective. Our case suggests that this could be even shorter than the recently reported successful 8 weeks duration (Yakoot 2017)
- In our case of very early intrauterine exposure, Elbasvir/Grazoprevir caused no embryotoxicity

Additional information

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P99

Pre-school and school exclusion for communicable disease

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Background
1. The belief is prevalent within our society that excluding an infected individual from the group he regularly attends will stop the interpersonal transmission of this infection within the group.
2. The scientific data supporting the rationale of exclusion is remarkably poor in consideration of the magnitude of the problem and not universally concluding to the usefulness of this practice.
3. Consequently, the decision of excluding is very dependent on the decision-maker's feelings or fears. For that reason, we have developed a website intended for physicians, educators and school managers active on the cantonal territory. This site offers counsel on the need for exclusion as well as information on other preventive measures in the face of a communicable disease.

Method
1. Design of an analytic scheme for weighing pros and cons of excluding a child with a given communicable disease, based on the following items: A) Is this disease predominantly severe, or potentially very severe, or likely to result in chronic sequelae? B) Is this disease still contagious at the time of diagnosis? C) Is the attack rate of this disease expected to be higher in the group of children than in the society at large? D) Is this disease the iceberg tip of a more widespread phenomenon such as carriage or subclinical infection? A negative answer to the first three questions and a positive answer to the fourth one do not favor exclusion of the sick child for the sole purpose of preventing contagiousness.
2. Development of a software listing a large number of infectious diseases and mentioning, for each one, whether or not preventive measures are to be applied to the infected person, or to contact persons or to the premises. The list of diseases purposely contains infections that are not truly communicable because we presume that non healthcare workers consulting the site may be not familiar enough with the topic for distinguishing contagion from infection. Suggested measures may have to be applied to children and/or to adults (caregivers, teachers and other professionals). Preventive measures include exclusion, vaccination (particularly post-exposure immunization), antibiotic-based prophylaxis, disinfection and enforcement of standard hygiene practices.

Conlusion
Although primarily developed for physicians, this site is open to all. Please try it !
evictionscolaire.ch

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P100

Sirtuin 5 deficiency does not compromise innate immune responses to bacterial infections

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Background and aim
Sirtuins (SIRT1-7) belong to the highly conserved family of NAD+-dependent lysine deacetylases. SIRT5, one of the least characterized sirtuins, resides mainly in the mitochondria and catalyses lysine deacetylation, demalonylation, desuccinylation and deglutarylation to regulate metabolic and oxidative stress response pathways. Pharmacologic inhibitors of SIRT5 are under development for oncologic conditions. Nothing is known about the role of SIRT5 in innate immune responses. The aim of the study was to investigate whether SIRT5 deficiency impacts on host defenses against infection.

Methods
Mice were housed in SPF conditions. Thymic and splenic subpopulations were analyzed by flow cytometry. Bone marrow-derived macrophages and splenocytes were stimulated with TLR ligands, bacteria, exotoxins and polyclonal activators and analyzed for metabolic status, cytokine production and proliferation. Mice were challenged i.p. with LPS or E.coli, i.n. with K.pneumoniae or S.pneumoniae and i.v. with L.monocytogenes or S.aureus. Blood was collected to quantify cytokines and bacteria. Weight, severity score and survival were registered.

Results
SIRT5 deficiency did not affect immune cell development. SIRT5 deficiency increased oxidative phosphorylation over glycolysis in macrophages, but did not modulate cytokine production and proliferation by macrophages and splenocytes. SIRT5 deficiency had not impact on cytokine blood levels, bacteremia and survival rates in models of endotoxemia, pneumonia, peritonitis, listeriosis and staphylococcal sepsis.

Conclusions
These data suggest that SIRT5 has no major impact on innate immune responses to bacterial infections and support the safety profile, in terms of susceptibility to infections, of SIRT5-directed therapies under development for oncologic diseases.

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P101

Bacteraemia with Fusobacterium necrophorum: A good reason to look for septic thrombophlebitis

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Case presentation

In September 2017, a 47-year-old previously healthy male originating from Nigeria was admitted to our hospital with fatigue, fever and abdominal pain since four days. His vital signs were as follows: axillary temperature: 39.7°C, heart rate: 100 beats/minute, blood pressure: 149/90 mmHg. Abdominal examination revealed localized tenderness in the lower right quadrant without signs of peritonitis. Routine laboratory analysis was normal besides marked inflammation with neutrophils of 9.32x109/L and a CRP of 246 mg/L. Abdominal CT-scan was compatible with diverticulitis of the colon and empiric antimicrobial therapy with ceftriaxon and metronidazol was initiated. Surprisingly, blood cultures were positive for Fusobacterium necrophorum and Streptococcus constellatus (milleri-group). Subsequently, treatment was adapted toamoxicillin-clavulanic acid (AMC).

Since bacteraemia with F. necrophorumis strongly associated with Lemierre's syndrome, we looked for signs of oropharyngeal infection and septic jugular vein thrombosis without success. However, re-analysis of the initial CT-scan additionally demonstrated acute inferior mesenteric vein thrombosis with several portalemboli of the liver, leadingto the final diagnosis of abdominal Lemierre's syndrome. Despite controversial data in the literature anticoagulation with rivaroxaban was initiated. Clinically, the patient made a rapid and full recovery and was treated for one month with AMC and for 3 months with rivaroxaban. Nevertheless, abdominal ultrasound at the end of treatment showed fibrotic closure of the inferior mesenteric vein with abundant collateralisation.

Discussion

- Classical Lemierre's syndrome is an infrequent complication of bacterialtonsillo-pharyngitis with septic thrombosis of the internal jugular vein.
- Abdominal Lemierre is exquisitely rare and mostly reported after childbirth or caesarian section.
- Fusobacterium necrophorum are anaerobic Gram-negative bacillibelonging to the normal flora of thehuman oropharyngeal, gastro-intestinal and female genital tract. Invasive strains usually express additional virulence factors leading to severe inflammation and activation of platelets and coagulation. They are usually susceptible to AMC and metronidazole.
- Beside appropriate antibiotic therapy surgical drainage and/or transient anticoagulation may be required for successful management of classical or abdominal Lemierre's syndrome

Additional information

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P102

High prevalence of gut colonization with extended-spectrum cephalosporin- and colistin-resistant Enterobacteriaceae in students in Bern

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Aims
Intestinal colonization with extended-spectrum cephalosporin- (ESC-R) and/or colistin-resistant (COL-R) Enterobacteriaceae in the community contributes to the spread of these pathogens. The prevalence of colonized people may vary according to different factors (health status, job, and contact with animals). However, data regarding Swiss students is completely lacking. The aim of this study was to fill up this gap of knowledge.

Methods
Students donated stool samples before and after the spring break (March-April, 2018), along with two corresponding epidemiological questionnaires. Stools were enriched overnight in LB broth supplemented with cefuroxime or COL. Then, 100 µl from each tube were plated on ChromID ESBL/Carba or CHROMagar Orientation plus COL, respectively and incubated overnight. Species identification was achieved using the MALDI-TOF MS. MICs were obtained implementing the Sensititre GNX2F plates and interpreted according to the EUCAST-2018. Microarray CT103XL, rep-PCR, and whole genome sequencing (Illumina/MinION) were used to characterize strains.

Results
Nineteen students (11 to 17-years old) were enrolled. Before holidays, the prevalence of subjects colonized with ESC-R strains was 47.4%, while none of the students carried non-intrinsically COL-R Enterobacteriaceae. All ESC-R Enterobacteriaceae were ESBL-producing (mostly CTX-M-15-, but also CTX-M-1/-9-like) or cAmpC-producing Escherichia coli. Most of these E. coli belonged to heterogeneous clones, but some students shared the same lineages. Notably, some students carried two different CTX-M-producing E. coli. So far, we have only culture screened the post-vacation stools of the 19 subjects. As a result, nine (47.4%) were carries of ESC-R E. coli. However, seven subjects (36.8%) also carried COL-R E. coli strains (all susceptible to ESCs). The presence of plasmid-mediated mcr genes should be investigated.

Conclusion
This is the first study investigating the intestinal prevalence of ESC-/COL-R Enterobacteriaceae in Swiss students. Unexpectedly, our results indicate that students seem more frequently colonized with ESC-R Enterobacteriaceae than healthy adults (who showed in previous studies prevalence around 6-8%). Therefore, a larger epidemiological analysis must be conducted in this specific population to establish the extent of this phenomenon, but also to determine the risk factors that may favor gut colonization and transmission among schoolmates.

Additional information
This work is supported by NRP-72 No. 177378 to AE/AR.

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P103

Does PCR Multiplex Testing of CSF in Suspected Meningitis lead to Changes in Clinical practice?

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Aim

To determine whether clinical treatment of suspected meningitis or encephalitis changes following testing of CSF using a PCR multiplex panel of relevant viral and bacterial pathogens.

Methods

Data from all 101 liquor samples sent to our laboratory from 07/2016 – 03/2017 were retrospectively analysed for cell count, transparency, glucose, protein, gram stain and CSF cultures; as well as the results of PCR panel (Filmarray®, Meningitis/Encephalitis Panel, Biofire).
These patients' records were also retrospectively analysed and clinical treatment decisions based upon PCR results reviewed.

Results

- 20% patients who underwent lumbar puncture for clinical suspicion of (or exclusion of) meningitis were in the end classified as suffering from meningitis and/or encephalitis
- Only 5% patients had the classical clinical trias of headache, fever/hypothermia and changed mental status; this did not predict PCR or bacterial culture results
- CSF protein, cell count or glucose did not correspond to CSF PCR-panels
- Only 2% of cases showed bacterial growth in CSF cultures (Str. pneumoniae)
- 18% of CSF PCR panels showed positive results:
  - 13 of 18 positive PCR panel results demonstrated viral pathogens (72%), mostly Enterovirus
  - 5 of 18 positive PCR panel results demonstrated bacterial pathogens (28%), mostly Str. pneumoniae
- Str. salivarius was found by eubacterial PCR of CSF (brain abscess) in one case
- In 80% of evaluable cases, PCR testing lead to an immediate change of treatment as opposed to no change in management in 20% cases. (Antibiotics were started, stopped, switched to treat another infection or discontinued)

Conclusions

- As there was no control group without PCR panel testing performed, testing for significant difference between use of PCR and no use was not possible.
- PCR panel testing is more sensitive in detecting causative bacterial or viral pathogens in CSF than traditional culture techniques
- Use of PCR testing should therefore be routinely implemented in the diagnostic testing of suspected meningitis/encephalitis.
- PCR panel testing of CSF in suspected meningitis/encephalitis reduced the duration of unnecessary treatment with antibiotics or antivirals as opposed to awaiting culture results.
- Inclusion of TBE into the PCR panel would be helpful in our geographic area

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P104

Case Report: Cerebral Tuberculosis: Differential Diagnosis in a Low Incidence Country

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Kantonsspital Baden

A 69-year-old female presented with mental confusion, headaches, nausea and a 17 kg weight loss. She had been hospitalized in Serbia 4 months ago, where she had tested negative for TB according to her relatives. Laboratory tests showed a slightly elevated CRP with a normal leukocyte count. An antibiotic treatment with ceftriaxon was started to treat an urinary tract infection.

However, the confusion of the patient kept worsening and a cerebral CT/MRI with intravenous contrast revealed brain lesions on day 3.

Initially these lesions were interpreted as metastatic disease of an unkown tumor and treatment with 16mg dexamethasone was started. On the following day a PET-CT was obtained but surprisingly, there was no evidence of any primary tumor.

Lumbar puncture on day 6 and revealed 98 cells/µL, predominately lymphocytes (93%), elevated lactate (7mmol/l) and protein (1.07 g/l), and a low glucose (1.9 mmol/l). A Biofire CNS-PCR-Panel was negative for all tested organisms as were bacterial cultures and a test for cryptococcal antigen. An HIV-screening test was negative. On day 7, the patient had an epileptic seizure. PCR of the CSF came back positive for mycobacteria on the same day.

Standard four drug anti-tuberculosis therapy consisting of isoniazid, pyrazinamid, rifampicin and ethambutol was initiated as DOT and Dexamethason slowly tapered over 6 weeks. The patient showed a clear neurological amelioration and has been seizure-free since. Her treatment was switched in a standard fashion to Rifampicin/isoniazid after 2 months.

Cerebral tuberculosis is a rare, but severe form of TB which has a high mortality and will lead to death if undiagnosed or mistreated. It is more often seen in HIV-infected patients.

Switzerland is a low incidence country for TB. Therefore a number of diagnosis' are more likely than TB in our patient's clinical setting. This includes viral meningoencephalitis, but mostly a neoplastic meningitis or metastatic disease – especially as we found brain lesions in the CT/MRI. Neurosyphilis, Cryptococcosis, Neurocysticercosis, brain abscesses, Neurosarcoidosis or Neurobrucellosis would be other possible illnesses explaining the patients symptoms with differing radiological signs. Multidrug resistance, poor drug compliance, edemas or hydrocephalus are severe complications that should be critically monitored but fortunately did not occur in our patient until now.

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P105

Sticks and stones may break my bones - A case report of conservative treatment of destructive osteomyelitis in disseminated tuberculosis

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Introduction

Despite a worldwide decrease in the infection rate of tuberculosis, almost one third of the world's population is infected (1). Tuberculosis of bone and joints is rare, accounting for only about 2-4% of all cases (2). Incidence of Tuberculosis in Switzerland is low – especially in native Swiss citizens (3). Treatment of bone tuberculosis is controversial and anectodal. There is no clear evidence whether surgical treatment is beneficial (4,5).

Methods

We report the case of a 49year old female who was admitted due to a painful knee and renal failure. MRI showed a destructive mass with osteolysis of the distal femur, advancing to the knee. A CT-guided biopsy showed a purulent mass, and consecutive radiological staging revealed disseminated pulmonary nodules with a miliar pattern and a cavernous lesion in the right upper lobe. Microbiological investigations revealed Mycobacterium tuberculosis and an empirical therapy with ETB, INH, PZA and RIF was established in reduced dosage due to kidney failure. Due to a low-level resistance, INH was replaced with Moxifloxacin after two weeks.
Interdisciplinary discussion of treatment strategy for the osteoarticular lesion around comprised a literature review and international expert opinions. The recommendations ranged from conservative treatment to single or multiple-staged operative procedures with or without drug-impregnated cement spacers.
Several considerations led to the decision of conservative treatment: we expected severe difficulties of obtaining sufficient stability of plates and screws in the osteolytic distal femur, wound healing was considered impaired due to a persistent purulent drainage of the biopsy site and the patient was almost painfree under analgesic treatment.

Results

9 months after establishement of tuberculostatic treatment, the patient was painfree and ambulatory with walking sticks. Sequential CT scans showed complete resolvement of the abscesses and a progressive consolidation of the lytic changes in the distal femur without signs of pending fractures. Drainage of the biopsy site ceased 6 months after the biopsy procedure.

Conclusion

There is a wide range of published treatment strategies without clear evidence – expert opinions are even more comprehensive. In our case, conservative treatment of destructive osteomyelitis in disseminated tuberculosis was successful and the patient regained almost painfree unlimited function of the knee 9 months after establishement of therapy.

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P106

Case report: narcolepsy type 1 in an adolescent with vertical-acquired HIV infection – coincidence or potential trigger?

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Background

The underlying pathogenic mechanism of narcolepsy type 1 (NT1) is thought to be an autoimmune-mediated loss of hypocretin-secreting neurons(1). Epidemiological data reveal a clear association between NT1 and various infections(2,3). However, the association of HIV infection and narcolepsy has not been described so far. We present the case of an adolescent with vertically-acquired HIV infection under effective antiretroviral treatment who was diagnosed with NT1.

Case Report

The 15-year-old boy was diagnosed with HIV-infection at the age of 8 years in Kinshasa. Under effective antiretroviral therapy with abacavir, lamivudine and ritonavir boosted atazanavir the patient showed an uncomplicated course of HIV infection with fully suppressed viral load and no opportunistic infections. Seven years after HIV diagnosis, the patient presented with excessive daytime sleepiness and weight gain. Investigations revealed no signs of anemia, thyroid gland dysfunction or Cushing syndrome; screening for illicit drug intake was negative. A cerebral MRI was normal showing no signs of HIV encephalopathy and no HIV replication in the CSF was detected. Results of polysomnography and multiple sleep latency test (MSLT) were highly suggestive for narcolepsy. Moreover, the patient was tested positive for HLA DQB1*06:02. Eventually the finding of a pathologically low hypocretin CSF level confirmed the diagnosis of NT1.

Discussion

The presented case raises the hypothesis that HIV infection in a host with a distinct genetic susceptibility may trigger autoimmune-mediated destruction of hypocretin-secreting neurons leading to NT1. This association has not been described so far possibly because NT1 is underdiagnosed in children and adolescents due to its less typical presentation in this population. Analysis of large HIV cohorts might answer the question whether there is a significant association of narcolepsy in children and adolescent vertically infected with HIV.

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P107

The sirtuins SIRT2 and SIRT3 act in concert to modulate innate immune responses

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Background and aim
The seven mammalian sirtuins (SIRT) are NAD+ dependent lysine deacetylases. SIRT2 and SIRT3 are the main cytoplasmic and mitochondrial deacetylases, respectively. SIRT2 targets proteins involved in cell cycle, metabolism and signaling pathways. SIRT3 is mainly associated with cell metabolism and homeostasis by targeting reactive oxygen species (ROS) detoxifying enzymes. We have previously shown that neither SIRT2 nor SIRT3 deficiencies affect cytokine production by macrophages exposed to microbial ligands. Here we developed SIRT2/SIRT3 double KO mice and tested whether SIRT2 and SIRT3 act in concert to regulate innate immune responses.

Methods
SIRT2, SIRT3 and SIRT2/3 KO mice were housed in SPF conditions. Bone marrow derived macrophages (BMDMs) were stimulated with microbial products before measuring gene expression and cytokine production. BMDMs were incubated with fluorescent beads and phagocytosis was analyzed by flow cytometry. Mice were injected intraperitoneally with LPS or E.coli. Blood was collected to quantify cytokines and bacteria. Weight, severity scores and survival were registered.

Results
SIRT2/3 KO BMDMs produced higher levels of TNF and IL-6 after stimulation with LPS, Pam3CSK4 and CpG, and had an increased phagocytic activity. SIRT2/3 KO mice were protected from endotoxemia and E.coli peritonitis, which was associated with a trend towards higher circulating cytokine levels and reduced bacterial burden.

Conclusions
Dual deletion of SIRT2 and SIRT3 revealed phenotypic alterations of innate immune responses that were not observed using single knockouts. Our results suggest that SIRT2 and SIRT3 act in concert to control innate immune responses.

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P108
Extrahepatic Manifestations in Patients with Hepatitis C

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Objective
While extrahepatic manifestations of Hepatitis are considered as an important indication for treatment, data about the evolution of these symptoms after successful treatment are spares. We wanted to collect more data about the influence of Hepatitis C treatment on extrahepatic symptoms.

Methods
40 patients with extrahepatic symptoms were prospectively followed. Only symptoms present before treatment start did count (e.g. restrospective amelioration of fatique not mentioned before treatment did not count. Extrahepatic manifestations were subgrouped: Fatique; Pain; Diabetes mellitus; Skin manifestations, renal disease, other. Resolved was defined as no symptoms without the need of specific treatment; Better as possibility to reduce treatment to at least 50% of the dose given before treatment.

Results
Pain: in 2/5 patients, the symptoms resolved, in 3/5 patients, symptoms were better. Fatique: in 7/7 patients, Fatique symptoms completely resolved. Diabetes mellitus: in 4/14 patients, treatment of DM could be stopped, in 5/14 patients DM was better, and in 4/4 patients, DM was not influenced by HCV treatment. Renal problems: in 1/1 patient, GN was cured. Skin manifestations: 2/7 patients were cured, 1/7 patients skin problems were better, and in 4/7 patients, not relieve could be attained. Other manifestation: in 2/4 patient a slight improvement was present, while in 2/4 patients, not improvement occurred.

Conclusion
Most patients with extrahepatic manifestations benefit from treatment. In situations with no improvement, probably no connection between symptom and Hepatitis C was present.

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P109

Physiology and proteomics of nitro drug resistance in Giardia lamblia

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Aims

Metronidazole and other nitro compounds have been used since five decades as a therapy of choice against giardiasis. As a consequence, resistance formation occurs more and more frequently. Model systems allowing studies on biochemical aspects of resistance formation to nitro drugs are, however, scarce since resistant strains are often unstable in culture. In order to fill this gap, we have generated a stable metronidazole- and nitazoxanide-resistant Giardia lamblia WBC6 clone, the strain C4.

Methods

Previous studies have revealed marked differences in the transcriptomes of both strains [1-3]. Here, we present more recent results comparing trophozoites of both strains with respect to their ultrastructure, whole cell activities such as oxygen consumption and resazurin reduction assays, key enzyme activities, several key parameters of oxidative stress such as NAD(P)/NAD(P)H ratios and FAD contents, and proteomics with a special focus on oxidoreductases.

Results

Nitro-compound resistant C4 trophozoites have lower nitroreductase activities, lower oxygen consumption and resazurin reduction rates, lower FAD and NADP(H) contents and a higher NADH/NAD- ratio than wildtype trophozoites. The pool sizes of proteins involved in oxidoreductions of nitro compounds do, however, not differ in both strains, with nitroreductase 1 (NR1; downregulated in C4) as sole exception.

Conclusion

The present results suggest that resistance formation against nitro compounds is correlated with metabolic adaptations resulting in a reduction of the electron transfer rate to FAD-dependent oxidoreductases, especially to NR1, an activator of nitro compounds [4], thereby avoiding nitrosative stress.

Acknowledgements

This work has been supported by the SNF and by COST

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P110

Hepatitis A in Switzerland: still an issue among travellers?

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Aim
Infection with hepatitis A virus (HAV) is notifiable in Switzerland since 1988. We analysed Swiss HAV surveillance data to describe the current epidemiology and to explore how risk groups changed between 1988 and 2016.

Methods
HAV surveillance data were obtained from the National Notification System for Infectious Diseases for the years 1988 to 2016. Notification rates were calculated using population statistics from the Federal Statistical Office. Notifications were grouped into five time intervals (1988-1993, 1994-1999, 2000-2005, 2006-2011 and 2012-2016) for descriptive analysis of trends in case characteristics.

Results
In Switzerland, the HAV notification rate increased from 9.5/100'000 population in 1988 to 14.2/100'000 population in 1990 and decreased thereafter. In 2016, a notification rate of 0.5/100'000 population was observed.
The proportion of cases reported to be exposed abroad increased from 39.3% (1988-1993) to 58.1% (2012-2016). At the same time, the proportion of "unknown or not specified" location of exposure decreased. Recently, African countries were most frequently reported as countries of suspected exposure while previously, European countries were more frequently mentioned.
Median age of notified cases increased from 25 years in the 1988-1993-time interval to 43 years in the 2012-2016-time interval. At the beginning of reporting, about one fifth of cases was hospitalised while recently almost half needed hospitalisation.
In terms of exposure risk, the consumption of contaminated food or beverages is increasingly recorded. In contrast, intravenous drug use was most prominently reported in the 1988-1993-period and decreased substantially afterwards.

Conclusion
The low hepatitis A case numbers in recent years, the limited availability and reliability of information and changes in notification forms have to be considered when interpreting trends. Furthermore, the surveillance system is likely to capture mainly "typical" or severe cases. Therefore, risk groups cannot be reliably identified and the contribution of travellers (including those visiting friends and relatives) and migrants towards HAV transmission in Switzerland cannot be assessed from notification data.
Patients' help seeking, and physicians' approaches towards diagnosing HAV infection and assessing risk exposures can strongly influence surveillance data. Therefore, routine surveillance is in need of complementary research for understanding the epidemiology of HAV in Switzerland.

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P111
The intangible: Legionella spp. in Switzerland

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Since 1976, Legionella spp. is known as the cause of pneumonia outbreaks with a high case fatality rate; however, its epidemiology is not well understood. In recent years, Switzerland and other countries have observed an increase in legionellosis case numbers, heightening awareness in public health specialists and the general population.

The proliferation of Legionella in stagnant, warm, and often man-made waters poses a substantial problem for the construction and maintenance of sanitation and water supply systems. The current recommendation to prevent Legionella contamination is to heat water above a 55 degree Celsius threshold, which comes in stark contrast to energy-saving efforts. It is essential that environmental occurrence, natural propagation and possible human exposure is better understood to allow discussion of such recommendations and to warrant expensive prevention and control measures.

The Swiss government is currently taking a twofold approach to address Legionella: exploring determinants of the disease through both a structural and an epidemiological lens. The Federal Office of Public Health has mandated a comprehensive set of studies to address the trajectory of Legionella from infection, to care-seeking, testing and treatment at different levels of the health system with the aims to provide a foundation of evidence critical to decision-making. For this year's conference, we will present the evidence to policy research portfolio of Switzerland and show the results of the first epidemiological study:
This on-going study explores how legionellosis case notifications fluctuate relative to the number of diagnostic tests performed for the disease using a positivity rate. For this, data of Legionella testing of 14 Swiss diagnostic laboratories between 2007 and 2016 is being evaluated. Apart from the positivity rate, determinants for a positive test result and temporal and spatial trends will be explored.

Preliminary results show that the total number of tests performed increased more strongly than the number of positive test results, thus the positivity rate decreased from 1.5% in 2007 to 1.1% in 2016. Diagnostic methods applied by the 14 laboratories did not change during the study period. Therefore, the cause for the increased testing remains to be clarified in future studies as encompassed in the FOPH mandate.

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P112

Screening open-access libraries for early antischistosomal drug discovery: new leads, old challenges

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Aims
Identify and characterize new antischistosomal drug candidates by screening the two new open-access libraries from the Medicines for Malaria Venture: the “Pathogen Box” and the “Stasis Box”.

Methods
The activity of the 400 compounds from the Pathogen Box and the 400 repurposing drugs from the Stasis Box was first tested in vitro on S. mansoni schistosomula. The hits were then tested on adult worms. The leads were further characterized for their respective IC50 values and structure-activity relationship (SAR) studies were conducted for the most promising hits that had analogues available. The parasites were assessed post drug-exposure based on their phenotype. Selected lead molecules were tested in mice harboring a chronic S. mansoni infection at a dose of 200 mg/kg.

Results
After testing the two libraries on schistosomula, 43 hits for the Pathogen Box and 37 for the Stasis Box were identified. Both screenings identified 11 lead compounds on adult S. mansoni (IC50 < 10 µM) each with satisfying selectivity for the parasite. Moreover, SAR analysis conducted on some Pathogen Box leads identified several active analogues. Altogether, 15 molecules were tested in infected mice but the good efficacy in vitro did not translate in vivo. Indeed, none of the worm burden reduction (WBR) values recorded were statistically significant compared to the controls (Kruskal-Wallis $p > 0.05$). Whereas this lack of efficacy in vivo might be imputable to a strong albumin-binding effect for the Stasis Box drugs, this was not the case for the Pathogen Box compounds. I will highlight some of the challenges encountered in these screenings and suggest improvements in the hit to lead selection process .

Conclusion
Although no prominent in vivo activity was observed, this work resulted in the identification of novel antischistosomal in vitro hits, which expands the repertoire of potent scaffolds to develop suitable alternatives to praziquantel. This confirms that phenotypic screening of open-access libraries are reliable, resource limited and yet essential tools in antischistosomal drug discovery.

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P113

Do Retreatment Tuberculosis Patients Need Special Treatment Response Follow-up beyond the Standard Regimen? Finding of Five-Year Retrospective Study in Pastoralist Setting

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Aims
Treatment outcomes serve as proxy measures of the quality of tuberculosis treatment provided by the healthcare system, and it is essential to evaluate the effectiveness of Directly Observed Therapy-Short course program in controlling the disease, and reducing treatment failure, default and death. Hence, we evaluated tuberculosis treatment success rate, its trends and predictors of unsuccessful treatment outcome in Ethiopian Somali Pastoralist region.

Methods
A retrospective review of five years data (September 2009 to August 2014) was conducted to evaluate the treatment outcome of 1378 randomly selected tuberculosis patients treated in Kharamara, Dege-habour and Gode hospitals. We extracted data on socio-demographics, HIV Sero-status, tuberculosis type, treatment outcome and year using clinical chart abstraction sheet. Tuberculosis treatment outcomes were categorized into successful (cured and/or completed) and unsuccessful (died/faileddefault) according to the national tuberculosis guideline. Data was entered using EpiData 3.1 and analyzed using SPSS 20. Chi-square ($\chi 2$) test and logistic regression model were used to reveal the predictors of unsuccessful treatment outcome at $P \leq 0.05$ significance level.

Result
The majority of participants was male (59.1%), pulmonary smear negative (49.2%) and new cases (90.6%). The median age was 26 years [IQR: 18 – 40] and HIV co-infection rate was 4.6%. The overall treatment success rate was 86.8% [95% CI: 84.9% - 88.5%]; however, 4.8%, 7.6% and 0.7% of patients died, defaulted and failed to cure respectively. It fluctuated across the years and ranged from 76.9% to 94% [$p < 0.001$]. The odds of death/failure [AOR=2.4; 95% CI=1.4–3.9] and pulmonary smear positivity [AOR = 2.3; 95% CI=1.6-3.5] were considerably higher among retreatment patients compared to new counterparts. Unsuccessful treatment outcome was significantly higher in less urbanized hospitals [$p < 0.001$]. Treatment success rate had insignificant difference between age groups, genders, tuberculosis types and HIV status ($P > 0.05$).

Conclusion
The overall tuberculosis treatment success rate in this study has realized the global target for 2011-2015. However, it does not guarantee its continuity as adverse treatment outcomes might unpredictably occur anytime and anywhere. Therefore, continual effort to effectively execute DOTS should be strengthened and special follow-up mechanism should be in place to monitor treatment response of retreatment cases.

Additional information
We are very grateful to Jigjiga University for financing, offering transport service during data collection and providing ethical approval. We are very thankful and want to acknowledge Ethiopian Somali Regional Health Bureau and the study hospitals for their support during data collection including recognition, permission to use the hospital data and recruit nurses who extracted the data. The data collector nurses and the hospitals' management are also strongly acknowledged.

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P114

Delay in Diagnosis of Pulmonary Tuberculosis in Low-and Middle-Income Settings: Systematic Review and Meta-Analysis

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(3) Haramaya University

Aims
Assessment of delays in seeking care and diagnosis of tuberculosis is essential to evaluate effectiveness of tuberculosis control programs, and identify programmatic impediments. Thus, this review of studies aimed to examine the extent of patient, health system, and total delays in diagnosis of pulmonary tuberculosis in low- and middle- income countries.

Methods
It was done following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses. Electronic databases were searched to retrieve studies published from 2007 to 2015 including Pubmed/medline, Springer link, Hinari and Google scholar. Searching terms were pulmonary tuberculosis, health care seeking, health care seeking behavior, patient delay, diagnostic delay, health system delay, provider delay, and doctor delay. Retrieved studies were systematically reviewed and quantitatively summarized using Comprehensive Meta-analysis software.

Results
Forty studies involving 18,975 patients qualified for systematic review, and 14 of them qualified for meta-analysis. The median diagnostic delay ranged from 30 to 366.5 days [IQR = 44 - 77.8], with a 4-199 days [IQR =15 - 50] and 2-128.5 days [IQR = 12 – 34] due to patient and health system delays, respectively. The key determinants of patient delay were poor literacy, long distance to the nearest health facilities, misconceptions about the cause, poor knowledge of the disease, first care seeking from informal providers, self-medication, pulmonary co-morbidity and mild severity of illness among others. Likewise, good functional status, unusual symptoms, first care seeking at private and low level facilities, normal chest X-ray and smear negative results were key determinants of health system delay. The meta-analysis showed 42% of pulmonary tuberculosis patients delayed seeking care by a month or more. Uneducated patients [pooled OR=1.5, 95% CI = 1.1 - 1.9] and those who sought initial care from informal providers [pooled OR = 3, 95% CI = 2.3 - 3.9] had higher odds of patient delay.

Conclusion
Delay in diagnosis is still a major challenge of tuberculosis control and prevention programs in low- and middle- income settings. Efforts to develop new strategies for better case-finding using the existing systems and improving patients' care seeking behavior need to be intensified.

Additional information
We are very grateful to the authors of the articles included in this review.

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P115

Ribosomal protein based MALDI-TOF MS subspecies typing of Streptococcus agalactiae and its potential in GBS epidemiology and vaccine impact monitoring

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(3) Mabritec AG
(4) Aga Khan University

Aims
Streptococcus agalactiae or group B streptococcus (GBS) colonizes between 10-40% of women of reproductive age and is a major cause of early life invasive bacterial disease. In this study, we aimed to develop a MALDI-TOF MS based subspecies typing method to distinguish between major phylogenetic clusters of GBS.

Methods
Publicly available whole genome sequences of 780 GBS isolates, mirroring the global GBS population, were used to (i) perform comparative core-genome analysis and average nucleotide identity (ANI) analysis, (ii) predict variants of major virulence factors and (iii) in silico identify molecular mass variability of 28 distinct ribosomal proteins. Subsequent MALDI-TOF MS analysis of 228 in-house GBS isolates was then applied to validate the in silico predicted mass variability of the 28 ribosomal proteins.

Results
We identified a total of 62 unique mass combinations (mass lineages) based on predefined 28 ribosomal proteins. There are seven dominant mass lineages that appear at high frequencies (> 90%) in the global GBS population. Taking into account the phylogenetic clustering of 780 GBS isolates as defined by core-genome analysis and ANI, the 62 mass lineages can be grouped into 10 clusters, each representing a specific set of GBS genotypes with specific host origin, capsular serotypes and virulence factor variants. MALDI-TOF MS analysis of 228 in-house GBS isolates showed that the 28 ribosomal proteins were detected reproducibly in the generated mass spectra, allowing assignment of clinical isolates to the in silico established mass lineages and clusters. Validation demonstrated a high sensitivity (92%) and specificity (99%) of our typing approach.

Conclusion
We show here that unique 28-ribosomal protein mass patterns measured by MALDI-TOF MS can distinguish between major GBS phylogenetic clusters, thereby providing information on associated host origin, serotype and virulence potential. This method could be a cost efficient tool to monitor future GBS vaccination impact on circulating GBS populations.

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P116

Evaluation of a Strongyloides IgG ELISA with S.papillosus antigen

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Background

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

Methods

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

Results

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

Conclusion

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

Acknowledgements:
We thank Dr. Christoph Schäfer from EUROIMMUN Schweiz AG a PerkinElmer Company for provision of ELISA-kits.

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Evaluation of the Specificity of the POC-CCA Test for Diagnosis of Schistosomiasis in Urine

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Background
The diagnostic possibilities for schistosomiasis have recently been improved by the introduction of a commercial point-of-care (POC) test detecting circulating cathodic antigen (CCA) of the parasite in urine. The POC-CCA test (rapidmedical diagnostics) exhibits the highest sensitivity for S.mansoni infections, but also detects infections caused by other Schistosoma spp.
A recent study has shown the test in combination with serology to be very sensitive for screening [1]. However, there were problems with the specificity of the test, which were further evaluated in this study.

Methods
The specificity of the POC-CCA test was assessed in the following groups:

- Healthy Europeans
- Infants < 3 years
- Patients with urogenital infections
- Patients with haematuria
- Patients with cancer of the urogenital tract or the kidney
- Pregnant Women

Patients with a history of travel to regions endemic for schistosomiasis were not included.

Results
The specificity of the test turned out to be much lower than 80% in certain patient groups like urogenital infections or pregnant women. Furthermore, it turned out that the interpretation of the result was sometimes challenging, especially in cases of very faint bands.

Conclusion
Our findings support the ones reported in reference [1]. A screening for schistosomiasis should never be based on the POC-CCA alone, but be combined with serology and/or a microscopic examination of stool or urine.

Reference:
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Hygiene and water practice compliance in a trial for a home-based environmental intervention in rural, Andean, Peru

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Aims
Compliance mitigates the effectiveness of water, hygiene, and sanitation (WASH) interventions. Without compliance or uptake, infrastructural support can fail to yield health benefits. We investigated if delivery of a kitchen sink in a community randomized controlled trial improved caretaker compliance for a subset of WASH practices called hygiene and water practices (H&W). We compared H&W compliance rates across intervention arms and time-points, and investigated their association with drinking water quality and child diarrhea.

Methods
We assessed compliance using longitudinal data and cross-sectional assessments for 317 homes in rural, Andean Peru. For 40 sentinel homes, we administered a hygiene questionnaire and carried out two rounds of structured observations. We then calculated and compared compliance rates from each data source. From the sentinel homes, we collected drinking water samples from the tap, from stored and reportedly boiled water, and from the child's drinking glass at four time points. Each sample was tested for thermo-tolerant fecal coliforms. We used a mixed effects logistic regression to test for an association between selected H&W indicators, microbiological contamination, and diarrheal prevalence.

Results
The longitudinal data showed stable H&W compliance rates over the course of the one-year study and reflected consistent access to soap and water. The cross-sectional data indicated statistically non-significant increases in compliance rates from the baseline to the end-the-study assessment. Reported data from sentinel surveillance suggested that hands are washed at key times. However, structured observations did not confirm these findings. Contamination was found in all sample types, including boiled water. In the regression, coliform contamination significantly increased the odds of a diarrheal episode and reported boiling significantly decreased the odds of a diarrheal episode. The parameters 'intervention arm' and 'soap near the kitchen sink' showed no effects in the model.

Conclusion
Effective H&W compliance has the potential to reduce diarrheal disease. Participants had access to reliable H&W infrastructure and showed improvement in compliance over time. Consistent reported compliance also indicated an awareness of the links between H&W and health. However low observed compliance and persistent drinking water contamination calls for innovative household behavioral and pathogen transmission studies.

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P119

Factors associated with metabolic syndrome prevalence among adults using traditional cooking and improved cooking devices in the Peruvian Andes: a cross-sectional study

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Aim
To assess the difference in the metabolic syndrome prevalence among Andean adults comparing clean biomass cookstove-use and traditional open fire cooking in rural communities of the Provinces of San Marcos and Cajabamba, Peru.

Methods
The project was embedded within a randomised control trial among children of 320 households and index children in 102 rural Andean communities. This trial focussed on the evaluation of a clean cookstove, food and household hygiene intervention against a control group. The current work focusing on the children's parents assessed CVD risk measuring metabolic indicators - waist circumference, blood pressure, and lipids (triglycerides and HDL cholesterol) and glucose capillary blood levels - and data on 24-hour food recall and socioeconomic information. We define Metabolic Syndrome following the Joint Interim statement of the International Diabetes Federation Task Force.

Results
In total 392 adults (237 women and155 men) participated, 192 in the group with an improved home-environment (since 11 months) and 200 in the control group. Metabolic Syndrome (MS) was prevalent in 23% and statistically significantly more frequent in women (27% versus 15% in men, p = 0.004). No difference was found between improved and traditional cookstove users. The risk for MS more than doubled for the age groups over 30 years in both gender (PR = 2.42, p = 0.002). Living over 2500 MASL we found to be protective for MS (PR = 0.54, p = 0.003)

Discussion
Exposure to smoke-free home environments appears not to influence metabolic syndrome in this high altitude Andean adult population. Rather, prevalence of MS is explained by age, gender and altitude. Older people and women were at higher risk of developing MS. Conversely; the geographic altitude played an important protective role against Metabolic Syndrome in these populations. We speculate that populations at higher altitudes have low levels of urbanisation, which may delay the impact of changes in diet, physical activity and socioeconomic status on the health of the population.

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P120

A quantitative assessment of socio-economic vulnerability to illness in rural Andean Peru

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Despite many efforts to improve the social determinants of health for the Peruvian population, the poor are still lagging behind in many aspects. Out-of-pocket spending and costs of illness render poor populations vulnerable to impoverishment when facing illness. We hypothesise that health interventions decrease household socio-economic vulnerability to illness. No established methodology exists to assess this effect.

Aims
We explored indicators of socio-economic vulnerability to illness in a high-altitude Andean population. We further investigated whether an international wealth index could identify vulnerable populations. Ultimately, we aim to provide practical insights into the use of vulnerability as a tool to identify populations at risk for impoverishment.

Methods
Vulnerability indicators were assessed cross-sectionally within a rural Peruvian context. Exploratory factor analysis identified dimensions of vulnerability which were used to construct indices for further analysis. Using an ordered logit regression, we investigated whether an international wealth index captures the different dimensions of vulnerability.

Results
Vulnerability was expressed in the following dimensions: the occurrence of illness as ‘Exposure’; the direct and indirect cost of illness as ‘Sensitivity’; and the ability of a household to overcome health shocks as ‘Adaptive capacity’. Adaptive capacity in turn constituted ‘Agricultural resources’, i.e. the ability to reach financial liquidity for treatment, ‘Knowledge & Networking’, the potential to draw on friends’ or relatives’ resources, ‘Institutional support’, the potential to receive institutional or programme financial support for treatment, and ‘Pooling resources’, the ability to ensure stable income. We found a statistically significant association of the wealth index with the components ‘Exposure’ and ‘Knowledge & Networking’. The remaining four dimensions ‘Sensitivity’, ‘Agricultural resources’, ‘Institutional support’, and ‘Pooling resources’ could not be captured by the wealth index.

Conclusions
The wealth index does not fully capture a household’s cost of illness, and the ‘Adaptive capacity’ to overcome costs related to physical inability or treatment seeking. Hence, the wealth index employed does not suffice to identify vulnerable households as often done to target national programmes. To identify households at risk, we should use vulnerability assessment tools insead of using measures of economic status.

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P121

Microfluidic platform as a drug screening tool to identify novel treatments against schistosomiasis

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Aims
To develop a novel microfluidic platform for the assessment of the viability of newly transformed schistosomulae (NTS) of Schistosoma mansoni by using an impedance-based readout.

Methods
A microfluidic device was constructed using a biocompatible PDMS matrix. The device allows evaluating the NTS viability by measuring current fluctuations. The electrical changes are caused by NTS upon moving in a compartment between a pair of palladium coplanar electrodes after exposure to the drug candidate. As an initial validation step NTS were exposed to DMSO and mefloquine. The electrical impedance signals were recorded at different concentrations of the drug and at different time points; the results were then compared to the gold standard, the visual scoring using microscopy

Results
We obtained an IC50 curve for mefloquine that resembles the curve obtained by visual scoring. The combination of a microfluidic structure for containing the NTS and an electrical-readout allows a great reduction in parasites usage, as only 5 NTS of solution are required per measurement, as compared to over 100 NTS for well for the standard evaluation.

Conclusion
An electrical readout of NTS viability will pave the way for automation and for real time evaluation of drug libraries. This will allow increase the drug screening output to fill the empty antischistosomal drug pipeline and will allow to gather further understanding of the drugs mechanism of actions (MOA).

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P122

Nanobodies: A new addition to the biomarker toolbox for Toxoplasma gondii

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Toxoplasma gondii (T. gondii) is an apicomplexan, obligate intracellular parasite that is considered one of the world's most successful pathogens. It is able to infect any warm blooded animal including humans, where the acute stage can cause severe and life-threatening disease in immuno-compromised patients and developing fetuses. Consequences of congenital infections are stillbirth, neurological disease, blindness, and hearing loss. Approximately one third of the human population is infected with the chronic, cyst-forming stages of T. gondii which are currently not treatable. A thorough understanding of the parasite's biology in the intermediate and final host is critical to the design of novel intervention strategies.

Despite the extensive in- vitro research done on T. gondii, only a few fluorescence markers are available that allow characterization of tissue cysts or developmental stages in the definitive host. To generate new markers for cell biological investigation we developed nanobodies against stage specific target proteins. Nanobodies consist of one single monomeric variable domain of the camelid heavy chain only antibodies and are ten times smaller than conventional antibodies, very stable, and harbor full antigen binding capacity.

Here, we generated specific heavy chain only antibodies against Excretory-/Secretory Proteins ESP in alpacas. Nanobody encoding gene fragments of the heavy chain only antibodies were amplified by reverse transcription PCR, ligated in a vector and finally produced as fusion proteins in E. coli. The resulting nanobodies will be used to uncover ESPs by an immunoprecipitation assay, to profile the subcellular localization of ESP, to track the secretion pathways, followed by the investigation of possible roles of ESPs in the formation of the parasite's niche. This expansion of the toolbox will ameliorate the paucity of T. gondii markers and will be used to better characterize the developmental stages that are difficult to access.

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P123

Systematic Review of Tuberculosis Control in Ethiopia with Special Emphasis on Pastoralists: Adaptations of DOTS for Mobile Pastoralists

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Aim and Objectives
The aim of this study was to synthesize evidence-based information from the available literature and to develop an appropriate TB control strategy for mobile pastoralist communities in Ethiopia.

Methods
We reviewed the literature following the PRISMA guidelines. We focused on the access to TB care based on the interplay between the health services, governing bodies and livelihood assets among pastoralists in the country. We searched seven electronic databases: EMBASE, AJOL, MEDLINE/Pubmed, IRIS (WHO database), CABI Direct, Cochrane Library and Web of Science. The final search was run on January 8, 2018.

Results
We screened 686 items and selected 19 of them that met the pre-determined inclusion criteria. We identified six themes from the literature: a) pastoralism in Ethiopia; b) pastoralists' livelihood profile; c) pastoralists' service utilization; d) pastoralists' knowledge and awareness on TB control services; e) challenges of TB control in pastoral settings; and f) equity disparities affecting pastoralists. Our interpretation of triangulating the results across all the studies produced a line of argument synthesis describing the contextual status of TB control services in Ethiopia.

Conclusion and Significance
On the bases of the findings, we described a societal benefit model to empower and engage local communities in the contextual problem solving through participatory processes.

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Evidence for camels (Camelus bactrianus) as intermediate host of Echinococcus canadensis G6-7 in Mongolia

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Background
Cystic echinococcosis (CE), the parasitic disease caused by the larval stage of Echinococcus granulosus sensu lato (s.l.), is a global public health problem. In Mongolia, one million nomadic farmers raise more than 60 million livestock, including sheep, goats, cattle, camels and horses, all of which are potential intermediate hosts, but to date there is not enough information on the molecular characterization of CE infection in livestock As a result, the main transmission cycle contributing to human cases is largely unknown in spite of wide distribution of CE in the country.

Method
We investigated the zoonotic linkages using the data of surgical CE cases and the livestock population of four species, including sheep, goats, cattle, and camels. To support the statistical analysis, samples were collected from CE infected animals in an endemic province. The subspecies identification, genetic diversity, and haplotype network analysis were conducted. The haplotype network analysis was conducted combining our result with previously identified molecular information from CE patients and echinococcus infected wild canids in Mongolia.

Result
In statistical analysis, the incidence of surgical CE cases increased by a factor of 1.71 for one unit increment in camel density. In the 96 camels and 15 goats investigated in an endemic province, CE was found in 19.8%(19) of camels and 6.7%(1) of goats. All animal CE cysts were confirmed to be caused by E.canadensis G6-7. The genetic investigation revealed that four haplotypes were identified within the animal samples. The haplotype analysis identified the common haplotype between humans, camels, goats, and the wolf, all of which were in the same province with the exception of the wolf.

Conclusion
Our study shows evidence that camels play an important role contributing to human CE in Mongolia, which is a critical information for further control and prevention of CE.

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Maternal Health Care Services Use: The Case of a Pastoral Community of South Eastern Ethiopia.

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Aims

Provision of skilled maternal health care during pregnancy and delivery is a key factor in preventing obstetric complications and saving women's life. Understanding factors affecting maternal health care utilization in pastoral community would help to design appropriate and culturally acceptable community based maternal health care service utilization and to reduce maternal mortality. The main aim of this study was to assess maternal health care service utilization and associated factors in Somali pastoral communities of south Eastern Ethiopia.

Methods

A community based cross-sectional mixed-method study was conducted in Adadle district, South Eastern Ethiopia, among 450 women from six lowest from August to September, 2016. A structured questionnaire survey and 3 focus group discussions were carried out to support quantitative data findings. Multiple logistic regressions were used to assess factors associated with antenatal care use and skilled delivery care use, controlling for confounders.

Results

The proportion of antenatal care and skilled delivery service use was 27% (CI 22.8-31.2) and 22.6% (CI 18.7-26.5) respectively. The utilization of antenatal care and skilled delivery varied among pastoral and agro pastoral communities: out of 99 deliveries attended by skilled professionals, 64 took place in agro pastoralist communities. Lifestyle, husband's education, women's attitude toward health care service, support from male partner were significantly associated with antenatal care utilization. Skilled delivery care use was significantly associated with place of residence, women's attitude toward skilled delivery, information of maternal health service fee exemption and antenatal care.

Conclusion

The maternal health care utilization in the study area was much lower than the national goal of 60.7%. Husband education, perceived attitude toward the importance of institutional delivery, male partner support, place of residence were factors associated with antenatal care utilization. A nationwide health care plan that includes pastoral community priority needs could be contribute to make health care accessible to pastoral communities. Improving communities awareness about antenatal care through provision of cultural and belief based guidelines could improve skilled delivery utilization

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Bi-weekly Voice and text messaging to Improve Pregnancy experience in Rural Andean Peru : A Pilot Randomised Controlled Trial using Mixed Methods

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Aims
We evaluate the potential effects voice and text messaging, on the improvement of pregnancy experience of pregnant women and young mothers in rural Andean Peru. Expected outcomes of this system-wide m-Health intervention are: maternal attitudinal change toward a positive/improved view on maternal and child health care provision, improved health literacy, health seeking behaviour and practices. We also explore the technical feasibility and participant's satisfaction of the m-Health intervention in the local population.

Methods
Focus groups were organised to identify format and content of the intervention. 75 participants (37 pregnant women and 38 mothers of a child under 100 days old) were recruited from the San Marcos Province, Cajamarca, Peru and randomly allocated to intervention (n=40) and control groups (n=35). In-depth interviews were carried before the start intervention to: identify the most important determinants of a positive pregnancy and child care experience. A questionnaire enquired about the effects of the intervention on the most important determinants of pregnancy and child-care experiences and collect feedback on the intervention.

Results
Preliminary results show that determinants of a positive pregnancy experience are, among others: Kind treatment by the Health provider, which also impacts trusts, positive perception of medication, supplementation and vaccination given by the Health centre. A majority of intervention recipients (32/40) reported having used the content of the messages. Voice messaging was a main source of information on alarming signs, i.e. symptoms in the mother and the child indicating the need to seek help, for a quarter of them (10/40). Mothers whose husband also received text messages (9/25) reported improved supportive behaviour and attitudinal change towards the new family situation. Text messages are less prone to transmission error than voice messages (0.8% vs 19.9%), mothers preferred voice messaging while pregnant women preferred text messages.

Conclusion
Voice and text messaging is a well-received m-Health intervention that appears feasible to be implemented system-wide in remote high-altitude populations. This current analysis indicates highest value in information transfer to recipients. Analysis of the m-health intervention impact on pre- and postnatal care seeking will be presented.

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Phylogenetics and phylodynamics of rabies virus in West and Central Africa

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(5) Centre Suisse de Recherches Scientifique
(6) Leon Quist Ledlum Central Veterinary Laboratory
(7) Institut Pasteur

Aims

Canine rabies is the main cause of human rabies and is globally responsible for approximately 59 000 human deaths per year, nearly all occurring in low- and middle-income countries (LMICs). It is well known that mass dog vaccination is a cost-effective, sustainable measure to eliminate the disease at its source and prevent humans from exposure (Hampson et al., 2015; Mindekem et al., 2017; Zinsstag et al., 2009, 2017). As domestic dogs are tied to human populations, the role of humans in rabies spread needs to be further investigated. Along with the role of humans, environmental factors like elevation, rivers and landscape have to be considered as well in the planning of appropriate rabies control strategies. It is known that major landscape features, such as oceans, mountains or deserts can act as natural barriers to disease spread. However, very little is known about barrier effects on smaller scales (Bourhy et al., 2016; Brunker et al., 2012; Dellicour et al., 2017). This research projects aims to combine landscape epidemiology with virus genetics to facilitate rabies control programmes in the African partner countries.

Methods

Phylogenetics and phylodynamics are elaborated on animal rabies samples, which were recently collected in urban and rural areas in Chad, Mali, Ivory Coast and Liberia. The full genome is analysed for improved resolution of the molecular analyses. Through a combination of high-resolution epidemiological and genomic data, rabies virus evolution and the spatiotemporal disease dynamic is clarified to understand factors which influence virus spread. Elements such as the environmental factors, urban and rural areas, population density, inaccessibility, major roads, the dog population, the role of geopolitical boundaries and trade and commerce are included in this analysis.

Expected results/Conclusion

Genetic characterization of involved virus strains will improve the resolution of surveillance in the selected African countries and contribute to understanding the geographical distribution and transboundary spread of the disease. Main routes of viral dissemination will be identified and vaccine barriers and surveillance points could then be appropriately placed in the selected partner countries, in line with the overarching aim to eliminate canine-mediated human rabies by 2030.

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Probing the Giardia lamblia ultrastructure with cutting edge volumetric electron microscopy and state-of-the-art machine learning algorithms

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Giardia lamblia (G. lamblia) is a parasitic protozoan responsible for over 300 million cases of diagnosed human gastroenteritis every year. Although prevalent worldwide, giardiasis is of special concern in developing countries with low quality drinking water. Children are affected most due to malabsorption of nutrients and susceptibility to secondary infections. Although nitroimadazoles are effective in the treatment of G. lamblia infections, clearing the pathogen requires multiple doses and the rate of reinfection is high, emphasizing the need for new anti-Giardia drugs. We investigate the major obstacle for this requirement, namely that Giardia shields itself from foreign substances very effectively while constantly sampling the fluid-phase environment via a tubular peripheral vacuole (PV) system just below the plasma membrane. Sampling including secretion of undesired material by the tubular peripheral vacuoles has been proposed to operate in a kiss and flush manner, i.e. sequential opening of PVs to the environment, exchange of fluid phase material, acidification, and reopening. Understanding function and structure of PV organelles is fundamental for the understanding of G. lamblia pathobiology and development of new strategies for its treatment. Since many of these structures are below the light's diffraction limit, Electron Microscopy plays a vital role in deciphering the volumetric ultrastructure of the parasite. We have been using Focused Ion Beam Scanning Electron Microscopy (FIB-SEM), based on the sequential milling and scanning of the surface of a sample using an argon laser and a gallium beam respectively. The SEM technique allows resolving structures at approximately 1 nm, unmatched by any other volume electron microcopy technique. Thus for the first time, a full size trophozoite has been scanned at 5 nm resolution giving us the best look of G. lamblia ultrastructure yet of the PV system. State-of-the-art analysis tools are being used to interpret the dataset. Machine learning algorithms allow semi-autonomous rendering of the scanned volume and 3D virtualization software is used to render the cell in 3D. Deciphering the endocytic pathway of Giardia lamblia is pivotal for devising new strategies and drugs that will help combat this protozoal infection. Having a nanometric view of the parasite structure gets us one step closer to those goals.

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Ticks from lifestock in Sudan and their carriage of Rickettsia

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In the savanna and sahel region ticks are important ectoparasites with relevance for animal of human health. From Sudan only very limited information about the occurrence of ticks and their carriage of pathogens is available.

Ticks were collected from livestock (cattle, sheep, goats and dogs) in the Sudanese states of West Darfur, River Nile and Al-Jazeera in 2017. Ticks were morphologically identified and investigated for carriage of Rickettsia (R) by molecular methods

A total of 1612 ticks were collected, belonging to the genera Amblyomma (A), Hyalomma (H) and Rhipicephalus (R), with a total of 16 species: A lepidum (57), A variegatum (4), H anatolicum (850), H dromedarii (30), H impeltatum (3) H rufipes (128), H truncatum (3), R annulatus (1), R bequaerti (7), R bergeoni (118), R decoloratus (30), R evertsi (328), R guilhoni (2), R muhsamae (1), R praetextatus (35), R senegalensis (13). The infestation per animal varied from 0 to more than 100.

Using a panRickettsial PCR 77/1612 (4.7%) ticks tested positive. This comprised 50/128 (39%) H rufipes, 8/30 (26.6%) H dromedarii, 12/57 (21%) A lepidum, 2/4 (50%) A variegatum, 2/30 (6.6%) R decoloratus, 2/328 (0.6%) R evertsi, and 1/13 (7.6%) R senegalensis. Species identification using a sequencing approach showed that H rufipes and H dromedarii carried R aeschlimannii, while A lepidum carried R africae.

The high rate of tickinfestation shows, that ticks are of great relevance in Sudanese animal breeding. Considering the detection of Rickettsia in ticks it must be assumed that ticks may transmit Rickettsia to humans in Sudan.

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Andes Hantavirus infection imported to Switzerland – one year later: first documentation of prolonged viremia and viral shedding in semen, case report

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Case report
A 55 year old Swiss man, returning from extended travels from Ecuador to Chile in late 2016, presented to the emergency department of Bern University Hospital on December 2, 2016 (=day 1). Respiratory distress requiring non-invasive ventilation occurred on day 3, at which time Hantavirus infection was suspected. The patient was placed on airborne and contact precaution while awaiting virology results. Andes hantavirus-(ANDV) infection was confirmed on day 7. The patient recovered from his respiratory distress within 1 week, after which isolation precautions were stopped. Due to profound physical deconditioning, the patient required 3 weeks of rehabilitation. ANDV may be transmitted interpersonally [1-3], and the virus has previously been detected in urine and saliva [4,5]. Therefore, we started PCR-based monitoring of different compartments. Here, we present follow-up data over 10 months.

Methods
Molecular confirmation of ANDV-infection was obtained by pan-Hantavirus RT-PCR (Bernhard Nocht Institute, Germany) and subsequent sequencing of the amplicon. Phylogenetic analysis showed strongest similarities with the ANDV isolate AH-1. Homology was confirmed by complete genome analysis (Spiez Laboratory, Switzerland). Virus load (VL) was monitored by an in-house quantitative real-time RT-PCR in blood samples (whole blood from EDTA or serum), respiratory specimens (nasopharyngeal swab, tracheobronchial secretions, or bronchoalveolar lavage), urine, and semen until twice negative after a monthly interval (Spiez Laboratory). Monitoring of VL in semen is ongoing.

Results
VL remained detectable in whole blood up to day 150 with a maximum of 807'194 genome equivalents/ml (GE/ml) on day 4. Virus became undetectable in serum early after symptom onset. VL in urine was weakly positive on day 4 and undetectable by day 15. VL monitoring in seminal fluid was started on day 40 and has remained positive for several months: at 2 months 866'876 GE/ml semen, at 4 months 1486 GE/ml, at 6 months 3258 GE/ml and at 10 months 4182 GE/ml. Culture of ANDV is notoriously difficult, and attempts to grow ANDV from blood or semen samples of the patient were unsuccessful.

Conclusion
We report the first case of ANDV-infection imported to Europe and the first case with prolonged viral detection by molecular methods in blood and semen. ANDV may be one of the sexually transmissible zoonotic viruses, although isolation of viable virus is required to establish this pathway.

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Causes of acute undifferentiated fever and the utility of biomarkers in Chiangrai, northern Thailand

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Background
Tropical infectious diseases like dengue, scrub typhus, murine typhus, leptospirosis, and enteric fever continue to contribute substantially to the febrile disease burden throughout Southeast Asia while malaria is declining. Recently, there has been increasing focus on biomarkers (i.e. C-reactive protein [CRP] and procalcitonin) in delineating bacterial from viral infections.

Methods
A prospective observational study was performed to investigate the causes of acute undifferentiated fever (AUF) in adults admitted to Chiangrai Prachanukroh hospital, northern Thailand, which included an evaluation of CRP and procalcitonin as diagnostic tools.

Results
In total, 200 patients with AUF were recruited. Scrub typhus was the leading bacterial cause of AUF (45/200, 22.5%) followed by leptospirosis (15/200, 7.5%) and murine typhus (7/200, 3.5%), while dengue was the leading viral cause (23/200, 11.5%). Bloodstream infections contributed to 7/200 (3.5%) of the study cohort. There were 9 deaths during this study (4.5%): 3 cases of scrub typhus, 2 with septicaemia (Talaromyces marneffei and Haemophilus influenzae), and 4 of unknown aetiologies. Rickettsioses, leptospirosis and culture-attributed bacterial infections received a combination of a 3rd generation cephalosporin plus a rickettsia-active drug in 53%, 73% and 67% of cases, respectively. Low CRP and white blood count were significant predictors of a viral infection (mainly dengue) while the presence of an eschar and elevated aspartate aminotransferase and alkaline phosphatase were important predictors of scrub typhus.

Conclusion
Scrub typhus and dengue are the leading causes of AUF in Chiangrai, Thailand. Eschar, white blood count and CRP were beneficial in differentiating between bacterial and viral infections in this study. CRP outperformed procalcitonin although cut-offs for positivity require further assessment. The study provides evidence that accurate, pathogen-specific rapid diagnostic tests coupled with biomarker point-of-care tests such as CRP can inform the correct use of antibiotics and improve antimicrobial stewardship in this setting.

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Intestinal colonization with multidrug-resistant Enterobacteriaceae in Swiss military deployed to Kosovo

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Aims
Travelers visiting certain areas abroad can frequently remain colonized at intestinal level with extended-spectrum cephalosporin- (ESC-R) and/or colistin-resistant (COL-R) Enterobacteriaceae. This can contribute to the importation and further spread of these pathogens in the community setting of countries with a still low prevalence of multidrug-resistant (MDR) bacteria. Military personnel deployed to high-risk geographic areas may present the same colonization phenomenon as for travelers. However, data regarding this specific population is lacking. The aim of this study was to explore the extent of this aspect.

Methods
Swiss military personnel deployed to Kosovo provided stool samples before and after their 6-month period of service (November - April, 2018) and completed epidemiological questionnaires at the same times. Stools were enriched overnight in LB broth containing cefuroxime or COL. From each tube, properly diluted aliquots were plated on ChromID ESBL/Carba or CHROMagar Orientation plus COL, respectively and incubated overnight. Identification of resistant colonies was achieved using the MALDI-TOF MS. MICs for antibiotics were obtained implementing the Sensititre GNX2F plates and interpreted using the EUCAST-2018. Microarray CT103XL and whole genome sequencing (Illumina/MinION) were used to characterize bacterial strains.

Results
Thirty-five Swiss militaries were enrolled in the study. Before leaving Switzerland, only one subject (#1) was colonized at intestinal level with ESC-R Enterobacteriaceae (two different CTX-M-producing E. coli). Moreover, another person (#25) was colonized with a COL-R E. coli (fully susceptible to ESCs) of ST69 and carrying a mcr-1.2-IncX4 plasmid. At the time of writing the present abstract, we have screened the post-service stools of 14 deployed personnel (not including #1 and #25). None of them returned colonized with ESC- and/or COL-R Enterobacteriaceae.

Conclusion
This is the first study investigating the intestinal prevalence of ESC-/COL-R Enterobacteriaceae in Swiss military deployed in Kosovo. Our preliminary data seems to indicate that the prevalence of repatriated personnel colonized with MDR bacteria is low and does not reflect observations in travelers returning from other regions. This phenomenon will be further explored based on the final microbiological and epidemiological data obtained from the overall cohort.

Additional information
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P133
Dengue diagnostics - as time goes by

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Background
Dengue fever occurs in around 0.5% of travellers returning from Brazil (1). In a study in German travellers, 10.9% of patients met the WHO criteria for dengue with warning signs and 17.8% of patients needed to be hospitalized, none died (2). Diagnosis of dengue fever is based on serology, point-of-care NS1-antigen tests or on direct virus detection using polymerase chain reaction (PCR). To use the adequate test, time since onset of symptoms and previous history of dengue need to be considered. In a study looking at patients with dengue fever, high plasma dengue virus RNA loads were observed during the first week after symptom onset, declining rapidly as dengue-specific IgM became detectable (3).

Case report
A 26-year old female patient presented with fever, retroorbital headache and facial flushing 3 days after returning from Brazil. On initial presentation, the differential diagnosis of denuge fever could be confirmed using a rapid diagnostic test (RDT) assessing NS1 antigen and dengue specific IgM/IgG. Two days later (day 4 after onset of symptoms), the patients presented with warning signs (abdominal pain and persistent vomiting) for severe dengue. At this point, the rapid diagnostic test was negative. A serological test (immunofluoresence) was positive for IgG but not for IgM. PCR done retrospectively was positive at all 3 time points, with a rapid decline from 7.71 log genome equivalents (Geq)/mL on day 1 to 1500 GEq/mL on day 7. Due to the warning signs, the patient was hospitalised for close monitoring. She recovered quickly and was discharged 2 days later.

Conclusion
This case report illustrates the limitations of different serological assays: First, NS1-antigen is detectable only during the first few symptomatic days (1-9 days). The sensitivity of the RDTs is only around 90% (4,5) and is even lower in secondary infection (77.3% vs. 95.4%) (5). Second, serological tests based on antibody detection only become positive after 5 days of symptoms. In a primary infection, IgM increase first, followed by the production of specific IgG. In secondary infection, IgM may remain negative while IgG titres remain high or can further increase.
To conclude, the laboratory diagnosis of dengue has several potential pitfalls including time since onset of symptoms, low sensitivity of antigen based tests or an effect of earlier exposures to other dengue virus strains that need to be considered to avoid that a potentially fatal dengue infection is missed.

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Specificity of point-of-care urine CCA testing for S. mansoni schistosomiasis in Eritrean refugees

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Background

In our recent study screening newly arrived Eritrean refugees in Switzerland, we found a 40.2% prevalence rate of asymptomatic Schistosoma mansoni infection [1]. We identified the combination of serology plus point-of-care circulating cathodic antigen (POC-CCA) urine cassette testing to have a sensitivity of 100% for identifying infected individuals when compared to stool sedimentation microscopy and concluded that the combination of these two tests appears to be the most sensitive screening method in this population [2]. In the current analysis we reassessed the performance of the POC-CCA urine test 12 months after treatment to evaluate its value in follow-up.

Methods

At baseline 107 Eritrean refugees were screened for various infectious diseases, including schistosomiasis [1]. Screening for schistosomiasis was done by serology, POC-CCA and two stool samples for microscopy [2]. Individuals screened positive by either method were treated with two doses of praziquantel (60mg/kg body weight) and invited for a follow-up, repeating the same diagnostic procedures, at 12 months. We were able to trace 48 of the 107 study participants after 12 months and obtain blood, urine and stool samples. Here we report the results of the follow-up testing. The primary objective of the follow-up was to assess the specificity of the POC-CCA urine test in Eritrean refugees. For specificity calculation we assumed that (i) the two administered praziquantel doses are 100% effective and (ii) that reinfection is excluded in a non-endemic region.

Results

Among the 48 Eritrean refugees who were followed-up, the POC-CCA urine test showed a sensitivity of 90%, a specificity of 60-74%, a negative predictive value of 94.7%, and a positive predictive value of 64.3-69%.

Conclusion

The POC-CCA urine cassette test shows high sensitivity and a high negative predictive value, while it appears to have rather low specificity and a low positive predictive value. In line with our previous data, we conclude that the test is valuable for screening [2] but due to its low specificity, we recommend to use the test with caution for the follow-up of treated patients. A positive POC-CCA urine test result in combination with negative serology and negative stool microscopy is more likely to be false positive than to indicate true infection.

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Seroprotection rates of vaccine-preventable diseases among newly arrived Eritrean refugees in Switzerland: a cross-sectional study

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Aims
According to 2016 WHO/UNICEF [1] country estimates Eritrea has overall high vaccination coverage with coverage for 3 doses of diphtheria/tetanus/pertussis and polio vaccine of 95%, for 2 doses measles vaccine of 85%, and for 3 doses Hepatitis B vaccine of 85%. If confirmed, such high coverage would imply that routine basic vaccination of newly arrived Eritreans could be safely omitted.

Methods
We used stored serum samples from two cross-sectional studies that screened newly arrived Eritrean refugees for infectious diseases [2,3]. Consenting refugees aged 16 years and older who registered in one of three selected Swiss cantons (Basel-Stadt, Basel-Land, Solothurn) were enrolled. Antibody titers against the following vaccine-preventable diseases were measured (applied thresholds for seroprotection in brackets): diphtheria (> 0.1 IU/ml), tetanus (> 0.1 IU/ml), measles (> 150 mIU/ml), rubella (only for women,> 11 IU/ml), varicella (> 50 mIU/ml), hepatitis B (antiHBc Index > 0.9 and antiHBs > 10 IE/L). All serologies were conducted at the Institute for Infectious Diseases, University of Bern.

Results
In samples of 128 study participants (18/14% women) with a median age 26 years, IQR 21 – 32), rates of seropositivity were as follows: diphtheria 75.9%, tetanus 45.8%, measles 81.0%, rubella in women 77.8%, varicella 95.2%, anti-HBc 25.6% and anti-HBs 18.4%.

Conclusion
Vaccination coverage for vaccine-preventable infections, except for varicella (for which no WHO/UNICEF data are available) were lower than expected. The high rate of positivity for varicella-zoster virus is surprising as varicella epidemics among adult refugees in refugee centers are frequent, indicating low herd immunity upon arrival in Switzerland. This observed high rate may therefore partly be due to recent exposure en route or within Switzerland, but this cannot be verified. In general, the strategy proposed by the Federal Office of Public Health to offer basic immunization to all newly arrived refugees [4,5], including newly arriving Eritrean refugees, is justified.

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Comparison of Löwenstein-Jensen and BACTEC MGIT 960 culture for Mycobacterium tuberculosis in people living with HIV

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Objective
This study aims to clarify how HIV infection affects tuberculosis liquid and solid culture results in a resource-limited setting.

Methods
We used baseline data from the Study on Outcomes related to Tuberculosis and HIV drug concentrations in Uganda (SOUTH study) which included 268 HIV/tuberculosis (TB) co-infected individuals. Culture results from Lowenstein Jensen (LJ) solid culture, Mycobacteria Growth Indicator Tube (MGIT) liquid culture systems and culture-based correlates for bacillary density from the sputum of HIV/TB co-infected individuals at baseline were analyzed.

Results
Of 268 participants, 243 had a CD4 cell count available and were included in this analysis; 72.2% of cultures showed growth on solid culture and 82.2% in liquid culture systems ($p<0.015$). A higher CD4 cell count was predictive of LJ positivity (adjusted OR: 1.14, 95% CI: 1.03-1.25 per 50 cells/µL increase, $p=0.008$). The same, but insignificant trend was observed for MGIT positivity (adjusted OR: 1.09, 95% CI: 0.99-1.211 per 50 cells/µL increase, $p=0.094$). Individuals with a higher CD4 cell count showed association with higher LJ colony forming unit grades (adjusted OR: 1.14, CI: 1.05-1.25 per 50 cells/µL increase, $p=0.011$) and a shorter time to MGIT positivity (adjusted HR: 1.08, CI: 1.04-1.12 per 50 cells/µL increase, $p<0.001$).

Conclusions
In a resource-limited setting MGIT liquid culture system outperformed LJ solid culture regarding culture yield and dependence on CD4 cell counts in HIV/TB co-infected individuals. We therefore suggest considering an adaptation of diagnostic algorithms: When resources allow only one culture method to be performed we recommend to exclusively use MGIT liquid culture in HIV-positive individuals as a first line culture method, aiming to reduce costs and make TB culture results accessible to more patients in resource limited settings.

Funding
This study was funded by the collaboration between the Infectious Diseases Institute, Makerere University, and the University of Zurich supported by Abbvie, Bristol Myers Squibb, Gilead Sciences, Janssen, Lunge Zürich, Merck, Shimadzu, Swiss HIV Cohort Study and ViiV Healthcare.

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Interactive Access to Current Regional and National Antimicrobial Resistance Data from Switzerland: an Open-Source Project (INFECT)

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Background
Empirical antimicrobial therapy is a vital and widely applied concept in clinical medicine that relies on the availability of local antimicrobial resistance data. To support the availability of such data, we initiated the open-source project INFECT (INterface For Empirical antimicrobial ChemoTherapy), aimed at bringing available up-to-date bacterial resistance data from bench to bedside, while being an easy to use application to inform and assist clinicians with empirical antimicrobial treatment.

Methodology
The INFECT web application was developed using JavaScript, is designed to work with all major internet browsers, and is run on an Ubuntu server. Anonymised antimicrobial resistance data is imported from the Swiss Center for Antibiotic Resistance (anresis.ch) into a datacache after automated processing and mapping with Stata. Each month the data is updated, and includes resistance information for the past year. Susceptibility percentages are given with an Agresti-Coull 95% confidence interval.

Results
Overall, a dataset consists of roughly 2.5 million observations from over 160'000 isolates, from eight representative regions of Switzerland, as defined by anresis.ch. Data can be filtered by users according to microbial (e.g., Gram stain), antimicrobial (e.g., substance class) or population (e.g. geographical region) properties. Susceptibility is displayed as a percentage in a coloured circle, which changes gradually from green (100% susceptible) to red (0% susceptible) while the circle size represents sample size.

Conclusion
With INFECT it is now possible to routinely assist empirical antimicrobial therapy with state-of-the-art information technology using the latest epidemiological data. Due to its flexible modular design, the INFECT application may in the future integrate empirical treatment guidelines or routinely perform automated epidemiological analyses. The platform is now available on infect.info.

Funding
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P138
Hepatitis-free opioid substitution programme

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Background:
In opioid substitution programmes, chronic hepatitis C is highly prevalent and Directly observed therapy guarantees optimal adherence. Pangenotypic Direct-acting antivirals achieve cure rates >95% after 8-12 weeks and make HCV-genotyping dispensable. However, to reach “HCV elimination by 2030”, several gaps in the HCV cascade still have to be closed. Point-of-care tests using capillary blood might be helpful.

Aims
1) All patients with chronic hepatitis C are diagnosed and treated.
2) All patients are immune against hepatitis A and B.

Methodology
Every 4 weeks, an infectious disease specialist and a study nurse will visit the heroin substitution programme, bringing along GeneXpert® IV and mobile Fibroscan® in a passenger car.
The following will be offered:
- HIV and HCV rapid tests using capillary blood (20min)
- HCV-RNA quantification in capillary blood (1h45min)
- Fibroscan® (non-invasive liver fibrosis assessement) (5-10min)
- recommendations regarding further diagnostics, treatment and HAV/HBV-vaccination
- HCV-treatment on site (“Test-and-treat”)
- enrolment into local and national cohort study
- teaching of a dedicated “Hepatitis nurse” on site

To improve acceptance of hepatitis A/B-serology prior to vaccination, point-of-care tests using capillary blood will be evaluated.
Project performance will be assessed by annual cross-sectional chart review.

Results
In April 2018, “HAG” cared for 128 patients. HIV/HCV-serostatus was unknown for 27 and 22, respectively. 50% (53/106) were HCV-antibody-positive and 38.3% of them (18/47) HCV-RNA-positive. 6 had no HCV-RNA-determination. Treatment-uptake was 60% (21/35) (17 cured). 12/14 patients still to be treated would qualify for HCV-treatment on site (i.e. no HIV-co-infection, no cirrhosis). Yearly HIV/HCV-antibody- and HCV-RNA-screening was overdue in 81, 47 and 16 patients, respectively. Overall, <20% were immune against HAV/HBV; >50% needed serology.

Conclusion/Hypothesis
Point-of-care tests using capillary blood and a “test-and-treat/vaccinate” approach on site remove crucial barriers to diagnosis and treatment, making hepatitis elimination in opioid substitution programmes achievable.

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Defect Rates in Touchless Versus Mechanical Hand Hygiene Dispensers

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Background
Mechanical and touchless hand hygiene dispensers (HHD) are frequently being installed across hospitals areas to facilitate hand hygiene. As little is known about the frequency of malfunctioning in touchless HHDs, we aimed to compare malfunctioning rates between touchless and mechanical HHDs.

Materials/methods
Main visitor areas and the hematology reverse isolation unit at the University Hospital Basel have been equipped with one model of touchless HHDs and one model of mechanical HHDs from a single manufacturer, respectively. These HHDs automatically record each hand hygiene event and the device function, which are transmitted by WiFi to a server. We analyzed the daily electronic HHD reports and hand-written HHD repair protocols in order to compare the defect rate between touchless and mechanical HHDs.

Results
A total of 44 touchless and 39 mechanical HHDs were analyzed. The median follow-up in non-defect HHDs was 840 days (interquartile range, 840–840 days), with the overall follow-up accounting for a total of 56,280 dispenser days: The cumulative defect rate was 27% (12/44) with 29,629 dispenser days in touchless and 0% (0/39) with 26,651 dispenser days in mechanical HHDs, respectively (0.4 versus 0.0 defects per 1000 dispenser-days; P = 0.001 for difference in malfunctioning risk over time).

Conclusions
Touchless HHDs had a significantly higher risk of malfunctioning than mechanical HHDs. The ease of use of touchless HHDs for visitors should be balanced with the additional resources required for maintenance, battery replacement and larger size. Mechanical HHDs may be better suitable for healthcare workers due to their high reliability, low requirements for maintenance and battery-free function. Other manufacturers may lead to better results but this type of dispenser has a high acceptance and the WiFi function allows selecting the best location and detecting empty dispensers by e-mail alert.

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The importance of routine viral load monitoring: Higher rates of drug resistance mutations in individuals failing antiretroviral therapy in Uganda and Lesotho compared to Switzerland

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Background
Emerging resistance to antiretroviral drugs may jeopardize the achievements of improved access to antiretroviral therapy (ART), particularly in settings with limited access to viral load (VL) monitoring and genotypic resistance testing (GRT). We compared the prevalence of different resistance mutations in HIV-infected adults with virologic failure in a cohort with regular routine VL monitoring (Switzerland) and cohorts with limited access to VL testing (Uganda and Lesotho).

Methods
We considered individuals who had GRT upon virologic failure (≥1,000 copies/mL) and were on ART consisting of at least one non-nucleoside reverse-transcriptase inhibitor and two nucleoside reverse-transcriptase inhibitors. From Lesotho, individuals with two subsequent VL≥1,000 copies/mL despite enhanced adherence counselling (EAC, N=58) and from Uganda, individuals with a single VL≥1,000 copies/mL were included in the analysis (N=121). From the Swiss HIV Cohort study (SHCS) a population without history of mono or dual therapy with the first GRT upon virologic failure was selected (N=62). We quantified resistance against antiretrovirals used in first-line therapy.

Results
We found that 51.6% of individuals in the SHCS, 72.5% in Uganda and 81.0% in Lesotho harbored HIV with high-level resistance to at least 2 drugs of their first-line regimen, implying they were at most on one “fully active” drug at time of treatment failure. Stanford resistance scores were significantly higher in Lesotho compared to the SHCS for all drugs except Zidovudine ($p<0.01$), significantly higher in Uganda compared to the SHCS for all drugs except Zidovudine and Tenofovir ($p<0.01$), and significantly higher in Lesotho compared to Uganda for all drugs except Zidovudine ($p<0.01$) (Figure).

Conclusion
Frequent VL monitoring and possibly pre-treatment GRT as done in the SHCS pays-off by low levels of resistance even when treatment failure occurs. The high-level resistance patterns in Lesotho compared to Uganda could reflect a selection of strains with multiple resistance during EAC.

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Virological outcome of patients with HIV drug resistance attending an urban out-patient clinic in Uganda: a need for structured adherence counselling and third line treatment options adherence counselling and third line treatment options

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Background
HIV drug resistance and suboptimal adherence are the main reasons for treatment failure among HIV-infected individuals. As genotypic resistance testing for HIV-infected individuals on antiretroviral therapy is not yet routinely available in resource-limited settings such as Uganda, resistance data, especially in patients on second-line treatment, is sparse.

Methods
This study was conducted in the adults out-patient clinic of the Infectious Diseases Institute in Kampala, Uganda, as part of a longitudinal study. Initially (study start), the proportion of patients with virological failure (defined as HIV-RNA ≥1000 copies/mL) among 2511 patients was assessed; now, after 2 years of follow-up, we report the virological outcome of these individuals and repeat HIV drug resistance testing in patients with a viral load of ≥1000 copies/mL.

Results
We included 148 patients, of which 18 (12.2%) were on first-line ART and 130 (87.8%) on second-line antiretroviral therapy (ART). The median age was 39 years (interquartile range (IQR): 32 - 46) and 109 (73.6%) participants were female. A viral load ≥1000 copies/ml was found in 29 (19.6%) patients with a median viral load of 28'387 copies/mL (IQR: 8433-75'364 copies/mL). Twentyfour (82.8%) patients with virological failure were on second-line ART. Relevant drug resistance mutations were found in 25/29 (86.2%) cases, of which 12/29 (41.3%) carried dual and 7/29 (24.1%) triple drug resistance mutations.

Conclusion
The majority of patients followed up by this study had a successful virological outcome two years later. However, we identified a concerning group of patients with virological failure, predominantly on second-line ART, of which a large number had dual or even triple drug resistance.

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Chemsex drugs on the rise – a longitudinal analysis of the Swiss HIV Cohort Study from 2007- 2017

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Background
Chemsex refers to the use of sex-enhancing drugs among men who have sex with men (MSM) in combination with specific sexual and social behavior. Longitudinal data on this development and the associated health-risks is scarce.

Methods
Data on all recreational drugs reported in the Swiss HIV Cohort Study (SHCS) from 2007-2017 was collected. Potential associations between patient characteristics and the consumption of methamphetamine, γ-hydroxybutric acid/γ-butyrolactone (GHB/GBL), 3,4-methylenedioxymethamphetamine (MDMA/XTC), cocaine and amphetamine were analyzed. Furthermore, the information was compared with 109 questionnaires on drug use completed by MSM participating in an HCV elimination trial.

Results
Overall, we observed a stable percentage (9.0%) of recreational drug use (excluding cannabis, amyl nitrite and prescription drugs) among SHCS participants during the study period. For MSM, however, there was an increase in overall drug use of 8.8% in 2007 up to 12.4% in 2017, in particular for methamphetamine (0.2%-2.0%) and GHB/GBL (1.0%-2.9%). The use of each of the drugs methamphetamine, GHB/GBL, cocaine, XTC/MDMA and amphetamine was significantly associated with condomless sex, higher prevalence of depression, syphilis and HCV coinfection. Data comparison showed that participants reported higher drug use when completing the questionnaire themselves (HCV elimination trial) compared to when reporting to a health care professional (SHCS).

Conclusions
The alarming increase in the use of chemsex drugs among MSM living with HIV in Switzerland and the strong association with coinfections and depression calls for action: We need harm reduction programs tailored for MSM as well as training for health care professionals on how to address this topic.