Hepatitis Breverse seroconversion andreactivation presenting as a flare in a patient with Multiple Myeloma on Lenalidomide maintenance after loss of previously reactive core antibody

Fatima I. Adhi

Fellow, Infectious Diseases, New York University School of Medicine

Case presentation: A 57 year old female with Multiple Myeloma (MM) presented with 10 days offatigue and dark urine. Two years prior to presentation, she underwent Bortezomib-containing chemotherapy followed by autologous stem cell transplantation (aSCT) and had since been on maintenance with Lenalidomide (10 mg). Physical examination was remarkable for scleral icterus without right upper quadrant tenderness or hepatomegaly. Labs showedmarked elevation in liver enzymes (table). Liver appeared normal on ultrasound and computed tomography.Hepatitis B (HBV) serology panel was significant for: total cAb+,IgMcAb+,sAg+, sAb-, eAg+, eAb-; HBV DNA viral load was 510,000 IU/mL. Hepatitis delta antibody and viral load were undetectable. Extensive history and diagnostic work up for other etiologies of acute liver injury was unrevealing. On review of prior serologies, although she had total cAb+ in 2012, repeat testing prior to a SCT in 2015 had shown total cAb- and sAg-. A diagnosis of HBV flare in the setting of reactivation with reverse seroconversion was made. Lenalidomide was discontinued and she was started on Tenofovir with dramatic improvement in liver enzymes. Lenalidomide maintenance was reintroduced 6 weeks later after normalization of liver enzymes. **Discussion:** In patients with MM receiving a SCT and/or novel therapeutic agents the rate of HBV reactivation is reported to be 8 and 14% at 2 and 5 years respectively; aSCT may be associated with higher risk.[1] Lenalidomide, an immunomodulatory agent with anti-tumor properties,[2] may have a lowerrisk ofHBV reactivation with a small series reporting incidence of 4.2%.[3] A nationwide retrospective study in Japan reported a possible protective effect of Lenalidomide in multivariate analysis, hypothesizing that Lenalidomide-induced decrease in levels of cereblon binding protein argonaute2 may in turn lower HBsAg and HBV DNA levels.[4,5] Ours is the first case of HBV reactivation presenting as flare in a patient on Lenalidomide maintenance. The loss of previously cAb+ was likely due to chemotherapy or MM-induced B-cell dysfunction and hypogammaglobulinemia. Vaccination prior to aSCT may have prevented HBV reactivation.

Hepatic function panel	At presentation	1 month prior
Aspartate Aminotransferase U/L	2479	51
Alanine Aminotransferase U/L	3353	96
Alkaline Phosphatase U/L	196	71
Total Bilirubin mg/dL	8.6	0.8
Conjugated Bilirubin mg/dL	3.7	Not checked

References: 1- Tsukune Y et al. Incidence and clinical background of hepatitis B virus reactivation in multiple myeloma in novel agents' era. *Ann Hematol.* 2016 Sep;95(9):1465-72.

2- Kotla V et al. Mechanism of action of lenalidomide in hematological malignancies. *J HematolOncol.* 2009 Aug 12;2:36.

3- Ataca, P et al. Hepatitis B (HBV) reactivation rate and fate among multiple myeloma patients receiving lenalidomide containing regimens: a single center experience. *Blood* 126, 5377 (2015).

4- Tsukune Yet al. Incidence and risk factors of hepatitis B virus reactivation in patients with multiple myeloma in an era with novel agents: a nationwide retrospective study in Japan. *Blood Cancer J.* 2017 Nov 23;7(12):631.

5- Hayes CN et al. Hepatitis B virus-specific miRNAs and Argonaute2 play a role in the viral life cycle. *PLoS One.* 2012;7(10):e47490.

Concomitant Herpes Simplex and Cytomegalovirus Reactivations in a Mycosis Fungoides Patient under Romidepsin Treatment: A Case Report

Ahmet Cagkan Inkaya[1], Sibel Dogan[2], Sehnaz Alp1, Murat Akova[1]

Hacettepe University School of Medicine, Ankara, Turkey.

[1]Department of Infectious Diseases, [2]Department of Dermatology

Introduction & goal: Histone deacetylase inhibitor (HDACi) sare relatively new class of antineoplastic agents used in various neoplastic and neurological diseases and in HIV treatment. However, treatment related side effects of these agents have not been clearly described. Here, we present a case in whom severe Herpes simplex and CMV infections developed during romidepsin treatment for mycosis fungoides (MF).

Case: The female patient has been followed-up for MF at Dermatology outpatient clinic for 17 years. In 2013, she developed invasive ductal carcinoma of the breast, which successfully treated with surgery and adjuvant hormon-therapy. After the cancer diagnosis her MF lesions started to progress. Methotrexate, intravenous immunoglobulin, bexaroten, interferon alpha were used for progressing MF. As she did not respond to previous interventions extracorporeal photopheresis was implemented with which lesions improved. Later the patient developed recurrent catheter related *S.aureus* bacteremia that ledceasing extracorporeal photopheresis and patient was put on cyclosporine and azathioprine under which the lesions again progressed. In 2016, dermatologists decided to initiate vorinostat, another HDACi. However, because of the medication supply problem, the treatment was switched to romidepsin. Intially, MF lesions started to improve. In April 2017, patient developed disseminated erythematous, ulcerated skin lesions compatible with herpetic ulcers. Intravenous acyclovir was initiated as the histological examination and Herpes NAAT from lesionswere positive for HSV. Lesions healed after 10 days of treatment and acyclovir was discontinued. In June 2017, patient developed tender, red, and discharging mass at her pretibial zone. Cultures yielded *S.aureu*s and she was admitted to the hospital for antibiotic therapy. During admission, shortness of breath and fever developed. Radiological imaging indicated pneumonic consolidation and broad-spectrum antibiotics were given. Patient respiratory parameters worsened and she was put on non-invasive mechanical ventilation. BAL was performed which revealed positive CMV PCR (24633 copies/ml). A possible CMV pneumonia was diagnosed and ganciclovir was given. The patient's respiratory parameters improved after ganciclovir treatment. Two months later the patient developed multi-organ failure and died.

Conclusion: Latent virus reactivation is detrimental for immunocompromised patients. Romidepsin may have contributed to Herpes virus and CMV reactivations in this clinical setting. Clinicians should be aware about the side effects of the emerging new chemotherapies.

Evaluation of Two Commercial Assays for the Rapid confirmation of OXA-48 Carbapenemases from Klebsiella pneumoniae Isolated from Cancer Patients

Pinar Zarakolu[1], Abdullah Tarik Aslan[2], John Perry[3], Murat Akova[1]
Hacettepe University School of Medicine, Ankara, Turkey
[1]Department of Infectious Diseases and Clinical Microbiology; [2]Department of Internal Medicine; [3]Freeman Hospital, Microbiology Department, Newcastle Upon Tyne, UK

Introduction: Rapid and accurate confirmation of carbapenemase production is essential to guide antimicrobial therapy and to ensure prompt implementation of infection control measures to prevent spread of carbapenemase producing enterobacteriaceae (CPE).

Goals: Two commercially available multiplex RT-PCR assays [BDMAX CRE assay (Becton Dickinson, Canada) and immunochromatographic assay, Resist-3 O.K.N K-SeT (Gembloux, Belgium)] for the rapid detection of CPE with OXA-48 were compared.

Materials and Methods: In a previous CPE surveillance program at the Hacettepe University Adult and Oncology Hospitals, 279 isolates of *K. pneumoniae* were recovered from rectal screening swabs from single patients. Two hundred and seventy consecutive isolates produced OXA-48 and one produced IMP, as confirmed by in-house PCR methods. One hundred and ninety nine of these isolates were selected for inclusion in this study including 192 isolates with OXA-48 and seven isolates without carbapenemase. Prior to testing for carbapenemase activity, each isolate was retrieved from storage at -80°C. Each isolate was tested with the two commercial assays in exact accordance with manufacturer's instructions. The BD MAX CRE assay is an automated RT-PCR assay allowing detection and distinction of the 3 most commony encountered carbapenemase genes: KPC, OXA-48 and NDM. The RESIST-3 O.K.N. K-SeT is an immunochromatographic cartridge that allows the detection and distinction of KPC, OXA-48 and NDM carbapenemase from a single colony of Enterobacteriaceae. The result is visible within 15 minutes in the form of red lines on the strip. For both assays, the pre-analytical handling time was 5-7 minutes.

Results: In blind testing, both the BD MAX CRE and the RESIST-3 O.K.N. K-SeT successfully detected OXA-48 in 192 isolates and gave negative results for the 7 negative controls. No other carbapenemases were detected and no repeat tests were necessary. For the RESIST-3 O.K.N. K-SeT, no instrumentation is required and a result can be generated in around 20 minutes, compared with at least 95 minutes for the BD MAX CRE assay (including handling time). The cost of the BD MAX assay is approximately 28.7 Euro per sample compared with 10.5 Euro for the RESIST-3 O.K.N. K-SeT.

Conclusion: The sensitivity and specificity of the two assays were 100%. It was concluded that both assays are convenient, accurate and rapid 'first line' tests for confirmation of OXA-48 carbapenemase producers.

Turkish Experience for Galactomannan Antigen Detection as a Screening Tool for the Early Diagnosis of Invasive Aspergillosis

Gökhan Metan[1], Hamdi Akan[2], Murat Akova[1]
[1]Department of Infectious Diseases and Clinical Microbiology, Faculty of Medicine, Hacettepe University, Ankara, Turkey; [2]Department of Hematology, Faculty of Medicine, Ankara University, Ankara, Turkey

Goal: We aimed to to review the recently published national literature and evaluate the role of GM screening for the early diagnosis of invasive aspergillosis (IA) in adult patients at Turkish centers.
Materials and methods: Pubmed was searched with keywords "galactomannan" and "Turkey". Only studies that investigated the performance of the GM antigen as a screening test were included in the literature analysis. **Results:** A total of 301 adult patients with 459 neutropenic episodes and with hematological malignancies and 13 patients who underwent allogeneic HSCT were included in four studies where twice weekly sampling was performed. Screening were started at the day of neutropenia (<500/m^3) until recovery except in one center where screening sinitiated at day 1 of hospitalization. The EORTC/MSG criteria were used to define the probability of IA. GM antigen testing was performed in 2662 serum samples. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) were as follows; 23.07-100%, 5.7-90.36%, 6.7-73.07%, and 55.5-100% (Table 1). **Conclusion:** The benefit of GM screening in serum was limited in adult patients with hematological malignancies at Turkish centers. However, the test should retain in the laboratory inventory as a diagnostic test.

Table 1. Characteristics of the studies and diagnostic performance of galactomannan antigen

Study center Time period	Number of the patients	Number of the patients with IA Diagnostic criteria	Number of the serum samples	Antifungal prophylaxis	Cut-off	Sen (%)	Spe (%)	PPV (%)	NPV (%)
Hacettepe University 2001-2003	58 neutropenia episodes in 45 patients	1 proven 4 probable 20 possible EORTC/MSG 2002	545	None	Single positive results ODI ≥ 0.5 Two consecutive positive results ODI ≥ 0.5	100 60	5.7 20.8	9.1 6.7	100 84.6
Uludag University 2003-2004	165 neutropenia episodes in 106 patients	4 proven 11 probable 65 possible EORTC/MSG 2008	1385	Antifungal administration in 111 episodes, types of antifungal drugs were not stated	Single positive results ODI ≥ 0.5 Two consecutive positive results ODI ≥ 0.5	100 86.7	27.1 71.8	19.5 35.1	100 96.8
Osmangazi University 2008-2011	161 neutropenia episodes in 99 patients	1 proven 17 probable 60 possible EORTC/MSG 2008	358 from high risk patients and 20 from non-neutropenic patients without fever	Antifungal administration in 106 episodes, mold active drugs but exact types were not stated	Single positive results ODI ≥ 0.5	23.07	90.36	73.07	55.55
Erciyes University 2012-2013	75 neutropenia episodes in 64 patients	12 probable 1 possible EORTC/MSG 2008	354	Posaconazole in 31 episodes Fluconazole in 42 episodes Voriconazole in 2 episodes	Single positive results ODI ≥ 0.7	35.7	99.6	3.1	96.8

Compliance to the Guideline of Diagnostic Tests in Febrile Neutropenic Patients at a Turkish University Hospital

Gökhan Metan[1], Pınar Zarakolu[1], Zeynep Baştuğ[2], Mine Tanrıöver Durusu[3], Ömer Dizdar[4], Yahya Büyükaşık[6], Murat Akova[1]

Hacettepe University School of Medicine, Ankara, Turkey.

[1]Department of Infectious Diseases and Clinical Microbiology; [2]Infection Control Committee; [4]Department of Medicine; [5]Department of Oncology; [6]Department of Hematology

Introduction: Unnecessary use of diagnostic testscan cause a significant financial load and overtreatment. We have implemented a written febrile neutropenia (FN) diagnostic tests guideline in our hospital at 2016. **Goal:** We aimed to identify the compliance to diagnostic test guideline in the management of febrile neutropenia. **Material and methods:** The guideline was prepared by ID physicians and hemato-oncology faculty members. The final text (Table 1) was released electronically onhospital server and sent as an e-mail to all internal medicine residents, hemato-oncology specialists. Hard copies were hanged to boards located at the computers where doctors fill in the diagnostic test request forms. An infection control nurse followed the patients with their first FN episode and filled in follow-up forms to discuss the compliance with ID specialist. **Results:** A total of 125 patients with 138 FN episodes were followed between June 2016 and August 2017. Seventy-six of the patients were male. The median age was 51 (17-81). The median duration of neutropenia was 9 (2-102) days. The compliance rates for proper requesting of laboratory tests were as; C-reactive protein (CRP) 100%, procalcitonin 0%, galactomannan antigen (GM) 93.6%, CMV PCR 56.6%, *Clostridium difficile* PCR 100%, and rectal swab for carbapenem resistant *Enterobacteriaceae* (CRE) 39.1%. **Conclusion:** While the compliance for CRP, GM, and C: difficile PCR was high, there was an overuse of CMV PCR and procalcitonin tests. Also, compliance to CRE screening was very low despite the results were available in 24-hours after request.

Table 1. The indications for diagnostic tests

Test	Indication
C-reactive protein	Twice weekly after neutropenic fever developed until recovery of neutropenia (>500 mm^3)
Procalcitonin	Suspicion of Gram negative sepsis and for monitorizing response to antimicrobial therapy for bacteremia
Galactomannan antigen in serum	Twice weekly from patients with expected duration of neutropenia >7 dayswithoout mold active prophylaxis, starts with detection of neutropenia and ends with recovery from neutropenia or initiation of a mold active antifungal therapy. Diagnostic test in all patients with suspicion of invasive aspergillosis
CMV PCR	Allogeneic and otologous transplant patients, starts with transplantation until day 100 of the transplantation (longer for patients with GVHD). ALL, starts with induction chemotherapy and until recovery from neutropenia
C. difficile PCR	Patients who had unformed stools >3/day after chemotherapy or antibacterial therapy
Rectal swab for Carbapenem resistant Enterobacteriaceae screening	In 48-hours after detection of FN

Impact of Effective Antibiotic Therapy on Mortality in Patients with XDR Acinetobacter baumannii Bloodstream Infections (BSIs)

Murat Özdede[1], Pınar Zarakolu Kösker[2], Gökhan Metan[2], Cemile Selimova[1], Özgen Köseoglu Eser[3], Murat Akova[2]

Hacettepe University School of Medicine, Ankara, Turkey

[1]Departmant of Internal Medicine; [2]Department of Infectious Diseases and Clinical Microbiology; [3]Department of Clinical Microbiology

Background: Acinetobacter infections have become recently a major problem in our cancer patient population. We aimed to identify the factors associated with 7- and 30-day mortality in patients with XDR A *baumannii* BSIs.

Materials and Methods: A retrospective, observational study with all cases of XDR A. *baumanni* BSIs in adults (≥18 years) from January 2010 to December 2015 was performed. Patients with polymicrobial bacteraemia and inadequate medical records were excluded. Data were obtained from electronic databases to analyse patient demographics, clinical characteristics and outcomes. Two logistic regression models were used for determining risk factors for 7- and 30- day mortality.

Results:A total of 106 patients met inclusion criteria. Mortality rates were 45.2% and 65.1% for 7- and 30-days, respectively. Age, gender, days at risk, ratio of ICU-acquired BSI were not statistically significant different in survivors and non-survivors stratified by 7-day and 30-days. Ratio of appropriate empirical treatment did not differ, either. Patients who survived in 7 days were more likely to be treated by appropriate definitive treatment, but this difference was not statistically significant (p= 0.1). The group of patients who didn't survive within 7 days after the onset of BSI were significantly more likely to have kidney diseases, malignancies, history of immunosuppressive therapy and neutropenia and those who didn't survive within 30 days were significantly more likely to mechanically ventilated (p=.007). In multivariate logistic regression analysis, factors independently associated with 7-day mortality included shock (OR: 10.46, CI: [1.7-102.5], p=.04), inappropriate definitive therapy (OR: 7.61, CI: [1.16-49.67], p=0.04) and previous immunosuppressive therapy (OR: 12.44 CI [1.91-81.13] p= 0.008). Independent predictors of 30-day mortality was mechanical ventilation (OR: 5.5 CI [0.7-40.31] p=0.08), shock (OR: 8.01 CI [1.6-38.06] p=.001), malignancy (OR: 8.9 CI [2.2-36.61] p=<.001).

Conclusion: In this study, we demonstrated that 7-day and 30 day in-hospital mortality rate of patients with significant XDR A. *baumannii* BSI could be affected by different factors including severe underlying disease; such as malignancy, or previousimmunosupprssive therapy rather than appropriateness of antibiotic therapy. Inappropriate definitive antibiotherapy was associated with 7-day mortality, but this association could not be demonstrated with 30-day mortality. There is no debate about the importance of severity of sepsis. Status of shock is significantly associated with 7-day and 30-day mortality.

Early Cessation of Empirical Antibacterial Therapy in High-risk Febrile Neutropenic Patients with Fever of Unknown Origin (FUO)

Korucu B[1], Inkaya C[2], Erbil A[1], Okay M[1], Etgul S[1], Ascioglu S[2], Altunay HT[2], Akova M[2]
Hacettepe University School of Medicine
[1]Department of Medicine; [2]Department of Infcetious Diseases

Goals: Cancer patients with neutropenic fever are usually treated with empirical antibacterials until recovery from neutropenia. Recent ECIL guidelines proposed that therapy can be discontinued after 72 hours of empirical therapy if defervescence occured for >48 hours in neutropenic patients with FUO. But, the supporting evidence for this recommendation is still weak. Our aim was to compare the outcomes of patients whose antibiotics were discontinued when they were still neutropenic (SNp) with the patients who had recovered from neutropenia (RNp).

Methods: This is a retrospective cohort of all the neutropenic episodes of high-risk patients including acute leukemia, lymphoma, multiple myeloma, chronic myeloid leukemia, myelodisplastic syndrome with or without hematopoietic stem cell transplantation (HSCT) in our University Hospital between January 2010 and August 2015. The general treatment strategy at our centre is to stop antibacterials in neutropenic patients with no apparent source of infection after 5 days of defervescence, irrespective of their neutropenia. There was no significant policy changes in treatment of these patients during the study period. We extracted detailed data from electronic medical records regarding the baseline characteristics, treatment and outcome details. Univariate tests and multivariable logistic regression were used for comparisons.

Results: Study included 400 neutropenic episodes of 287 patients. Median follow-up was 34,5 weeks. In 272 of these episodes no source of fever was identified and patients were treated empirically as neutropenic FUO. In 31,2% of these episodes, empirical antibiotics were stopped after patients became afebrile but still neuotropenic (SNp). Recurrent fever in 7 days after the cessation of empirical antibiotics occured significantly more in SNp compared to RNp group (23,1% vs 5,2%, p=*0,001*). Mortality was not higher in the SNp group within 1 month and 1 year (p >*0,05*). Results of multivariate logistic regression showed that SNp patients when the antibiotics stopped were 4,4 times more likely for recurrence of fever in 7 days, however early cessation was not a significant predictor of mortality.

Conclusion: Early cessation of empirical antibiotic treatment for neutropenic FUO is a significant risk factor for fever recurrance in 7 days. However, our anlysis did not show a significant change in mortaliy due to early cessation of empirical treatment.

Deep learning for recognition of invasive mold disease from chest computed tomography imaging in haematology-oncology patients with data acquisition augmented by natural language processing of chest CT reports

Michelle R Ananda-Rajah[1,2], Titus Tang[4], Horace Josh[4], Samantha Ellis[5], Anthony Kam[5], Dinesh Varma[5,6], Gholamreza Haffari[7], Ming Liu[7], Jarrel Seah[5], ChristophBergmeir[7], Anton Y Peleg[2,8], Danny Liew[9], Francois Petitjean[7], Geoffrey I Webb[7], Christopher Bain[7], Tom Drummond[4]
[1]General Medical Unit, Alfred Health, Melbourne, Victoria, Australia; [2]Dept of Infectious Diseases, The Alfred Hospital and Central Clinical School, Monash University, Melbourne, Victoria, Australia; [4]Faculty of Engineering, MonashUniversity, Clayton, Victoria, Australia; [5]Dept of Radiology, Alfred Health, Melbourne, Victoria, Australia; [6]Dept of Surgery, Monash University, Clayton, Victoria, Australia; [7]Faculty of Information Technology, MonashUniversity, Clayton, Victoria, Australia; [8]Biomedicine Discovery Institute, Department of Microbiology, Monash University, Clayton Victoria, Australia; [9]Dept of Epidemiology and Preventative Medicine, Monash University, Clayton, Victoria, Australia

Introduction: Chest computed tomography (CT) dominates the initial diagnostic workup in patients with suspected invasive mold diseases (IMD). Improving the efficiency and rigor of radiologic IMD diagnosis is important for a range of activities, including bedside practice, clinical trials and radiologist workflow. **Goal:** The aim of this study was to develop image analysis software based on artificial intelligence for detection of IMD from chest CT.
Materials and Methods: Haematology-oncology patients with IMD were identified in 2 steps: in step 1, using previous studies from 2004 to 2011, and in step 2, by natural language processing (NLP) of chest CT reports from our data warehouse (2008-2016)followed bymanual chart review and expert medical adjudication. A fully convolutional neural network (CNN) was trained with CT images hand labelled by 3 senior radiologists using pre-specified criteria. Training the CNN in step 1 was augmented by machine-assisted radiologist annotation that accelerated the labelling and training process in step 2.
Results: The final cohort in step 2 comprised 158 patients with 174 episodes of IMD, of which 29% were probable/proven according to international definitions. Number of patients with corresponding axial CT slices, increased between steps 1 and 2 from 72/307 to 158/11,532, with NLP increasing acquisition of training databy over 3600%. Area under the receiver operating curve in steps 1 and 2 increased from 93.0% to 99.3%, indicating system learning. For a range of thresholds, sensitivity (Sn)/specificity (Sp) pairs were (%): (Sn 94.6, Sp 97.6), (Sn 96.4, Sp 96.7), (Sn 98.3, Sp 94.1), (Sn 99.0, Sp 92.2) and (Sn 99.9, Sp 79.2). Deep learning using a CNN achieved state-of-the-art performance for a challenging and diverse condition demonstrating an ability to learn with increasing data. A platform technology integrating NLP, image recognition and adjunctive clinical data could enable multiple activities including radiology decision support and electronic IMD surveillance, addressing important unmet needs of a rare disease.

Evidence from Clinical Trials: Might the Global Burden of Immunocompromise Increase in the Future?

Robin Avery[1] MD, **Philip Hashkes**[2] MD MSc, **Rafael Harpaz**[3] MD, MPH
[1]Johns Hopkins, USA; [2]Shaare Zedek Medical Center, Israel; [3]Centers for Disease Control and Prevention, USA

Introduction: With growing interest in inflammatory and immune-mediated mechanisms in common chronic diseases, increasing numbers of clinical trials are being performed to evaluate the effects of immunosuppressive and/or anti-inflammatory drugs outside of traditional uses (e.g. Ridker et al, NEJM 2017; 377:1119-31, on canakinumab and cardiovascular disease.) While 2.7% of US adults currently self-identify as being immunosuppressed,[1] newer uses of immunosuppressive agents could significantly increase the global burden of immunocompromise in the general population.

Goals: To survey current clinical trials in order to estimate the increase in the prevalence of immunocompromise in the future based on projected newer uses of immunosuppressive and anti-inflammatory drugs.

Materials and Methods: A search of www.clinicaltrials.gov in 12/2016 identified ongoing trials involving systemic use of any of 38 immunosuppressive drugs, for indications other than transplantation, oncology, or classic immune-mediated conditions. Also, trials were identified that used immunosuppressive or anti-inflammatory agents (other than aspirin and nonsteroidals) for treatment of common conditions including aging, Alzheimer's, cardiovascular or cerebrovascular disease, heart failure, depression, diabetes, and obesity. Results: 176 clinical trials met the case definition. Agents used in 3 or more trials included anakinra, canakinumab, etanercept, infliximab, methotrexate, mycophenolate, sirolimus, steroids, tacrolimus, and tocilizumab, with 28 agents used in 1 – 2 trials each. Over 20 trials involved coronary artery disease, cardiac inflammation and heart failure, with 3 on Alzheimer's disease and 2 on aging.

Conclusions: If even a few of these trials affect clinical management of very common conditions, prevalence of immunosuppression in the general population could increase, particularly in the elderly. Although the immunosuppressive potency of these agents varies and depends on dose and duration, the cumulative effect could be significant, especially if combinations of immunosuppressants are administered for multiple new indications. More quantitative research is needed regarding the consequences of using immunosuppressive and anti-inflammatory agents in newer indications for common chronic diseases.

1. Harpaz R, Dahl RM, Dooling KL. Prevalence of immunosuppression among US adults, 2013. *JAMA.* Published online October 28, 2016. doi:10.1001/jama.2016.16477

Assessment of Virologic Responses to Interventions for BKV DNAemia in Kidney Transplant Recipients Deemed Refractory to Reduction of Immunosuppression

Khalid Alfares MD*, **Nouf Turki** MD* *(co-first authors)*, **Robin Avery** MD *(Johns Hopkins, USA)*

Introduction: Reduction of immunosuppression (IS) is the mainstay of management of BK virus infection for the prevention of allograft loss in kidney transplant recipients with BKV infection and BKV allograft nephropathy. Most patients respond to reduction of IS, but a few continue with rising BKV viral loads and ultimately, graft loss. Optimal management of these patients is unclear, and off-label therapies have been used, with uncertain benefit.

Goals: To devise methods to assess virologic responses to candidate BKV therapies in patients deemed to have failed reduction of immunosuppression.

Materials and Methods: After a positive BKV qPCR on screening, patients were monitored with blood BKV qPCR every 1 – 4 wk for a median of 30 months (range 18-48). The median log of the BKV qPCR blood viral load was calculated for each 3 month period (median log BKV3m), and the "delta median log BKV3m" for any one time period was defined as the value from the preceding 3 month period minus that of the following 3 month period. Off-label therapies were administered per transplant clinician choice. Time periods were categorized as: quinolone alone (Q), leflunomide alone (LEF), quinolone plus leflunomide (Q+LEF), IVIg +/- other therapies (IVIg) or no added therapy (None).

Results: 8 renal transplant recipients received quinolones, leflunomide, IVIg or combinations for treatment of refractory BKV. All patients had declines in viral load over time; one developed graft loss. The median peak viral load was 6.15 log (5.1 – 7) and last median viral load in ongoing followup was 3.3 log (2.9 - 4.4). 7 patients received quinolones, 6 LEF and 6 IVIg. A total of 73 time periods were evaluable. Delta median log BKV3m values for Q (0.4), L (0.05), and QL time periods (0.8) were not significantly different from no therapy (0.5); but the delta median log BKV3m for IVIg time periods (1.0) was significantly higher than for Q, L, and QL periods combined (p=0.05).

Conclusions: It has been difficult to assess the efficacy of off-label therapies in patients receiving multiple interventions plus reduction of immunosuppression for refractory BKV DNAemia. The "delta median log BKV3m", expressing change of the median viral load in 3 month periods over longer periods of followup, may be useful as a parameter to assess responses. In this preliminary study, IVIg appeared to have a more significant effect than other off-label therapies, but this finding should be confirmed in larger studies.

Improving local surveillance for invasive mold disease (IMD) using natural language processing of computed tomography (CT) chest reports and implications for antifungal stewardship (AFS)

Baggio D[1,2], Avery S[2], Wei A[2], Haffari G[3], Peleg A[1,4], Morrissey CO[1], Ananda-Rajah MR1[5]
[1]Department of Infectious Diseases, Alfred Health, Monash University, Melbourne, Victoria, Australia; [2]Malignant Haematology and Stem Cell Transplantation Service, Alfred Health, Melbourne, Victoria, Australia; [3]Faculty of Information Technology, Monash University, Melbourne, Victoria, Australia; [4]Biomedicine Discovery Institute, Department of Microbiology, Monash University,Melbourne, Victoria, Australia; [5]General Medicine Unit, Alfred Health, Melbourne, Victoria, Australia

Introduction: Barriers to strengthening antifungal stewardship include the lack of hospital-level incidence data for IMD. This study aimed to describe theepidemiology of IMD and to explore metrics of relevance to antifungal stewardship.

Methods: We identified haematologypatients with IMD at Alfred Health from January 2010 to August 2016, by screening chest CT reports with natural language processing (NLP) followed by expert review. Host, microbiological and antifungal drug characteristics were manually extracted.

Results: 156 IMD-episodes were identified in 144 patients. 37% of cases were probable/proven, with *Aspergillus* species accounting for 68% of isolates. Underlying disease was acute myeloid leukaemia (56%), acute lymphoblastic leukaemia (ALL, 15%), lymphoma (8.3%), multiple myeloma (8.3%), myelodysplastic syndrome (3.8%), and chronic lymphocytic leukaemia (3.2%). Haemopoietic stem cell transplant (HSCT) recipients represented 33% of cases, andpoor prognosis disease (refractory/progressive, relapse) underpinned 42% of IMD-episodes. Breakthrough IMD despite antifungal prophylaxis (AFP) occurred in 89 (58%) episodes. Among 67 IMD-episodes lacking AFP, 37% occurred post-HSCT with 64% occurring >100 days post-allogeneic HSCT (median 364 days). Of these, 5 patients had graft vs host disease. In 15 IMD-episodes among pre-transplant ALL patients, one patient did not receive prophylaxis and 14 represented breakthrough IMD, associated with intermittent liposomal amphotericin prophylaxis in 10 episodes (71%).

Conclusion: Technology such as NLPoffers an inclusive approach to IMD surveillance, yielding detailed patient-level data across all haematology patients, identifying gaps in practice and defining new risk groups who may benefit from preventative strategies.

Disclosure of Interest Statement: *The authors have no conflicts of interest to disclose relevant to the contents of this study.*

Chronic granulomatous disease (CGD) – 50 years report of Minnesota experience

[1]**Kiran K. Belani** MD, [2]**Tamara Pozos** MD PhD, [3]**Paul G Quie**, MD,
[4]**Kumar G. Belani**, MBBS, MS, FAAP
[1]Consultant, Pediatric Infectious Disease, Children's Hospital of Minnesota; [2]Consultant, Pediatric Infectious Disease & Clinical Immunology, Children's Hospital of Minnesota; [3]Regent's Emeritus Professor, Department of Pediatrics, University of Minnesota; [4]Professor, Departments of Anesthesiology, Medicine & Pediatrics, University of Minnesota

Table 1

Number of patients	Male	Female
53	47	6
X-linked	42	3 (lyonised)
Autosomal recessive	2	3

CGD in male children was first described by Minnesota Physicians **Robert Good (1957) and *Paul Quie discovered the neutrophil phagocytic defect in microbial killing (1967). This report is a cohort review of 53 patients with CGD who received care between 1968-2018 at above institutions in Minnesota. Table 1 provides demographic and available inheritance data. Family history allowed the diagnosed to be made at birth in 25%. The majority (45%) were diagnosed at age < 2 years with the remainder being diagnosed between >2-20 years (20%) and > 20 years (10%). The diagnosis was by evaluation of bacteria killing by neutrophils, superoxide/hydrogen peroxide production and nitro blue tetrazolium (NBT) test prior to 1980. Chemiluminescence was added after 1980, the dihydro rhodamine test (DHR) after 1995. Mode of inheritance was established by genetic testing after 2000. Associated anecdotal gene defects noted were presence of the Mcleod Phenotype and cardiomyopathy. They all had the classic manifestations of CGD namely, pneumonias, inflammatory colitis (35%), poor wound healing, granulomas of the skin, GI and GU tracts ,adenitis, choreoretinitis and, hypersensitivity pneumonitis, bronchocentric granulomatosis, mycotic aneurysms. Some patients also had diabetes mellitus, celiac disease, IGA deficiency, WPW arrhythmia, myocardial infarction, aortic dissection and Idiopathic thrombocytopenia with Intracranial hemorrhage. All patients had the usual spectrum of organisms seen in CGD. Prophylactic antibacterial therapy was started in all after 1970, followed by antifungal prophylaxis after 1988 and γ-interferon in 30%-50% since 1991. Steroids were used as adjunctive treatment in inflammatory conditions. Multiple surgical procedures were required but now minimally invasive procedures by radiologists in the last 2 decades have played a role in decreasing morbidity. Hematopoietic stem-cell transplantation (HSCT) has been recently done in 7 patients. Of these 5 were done < 5 years of age with engraftment in 4 (all are alive); the other 2 transplanted in adulthood have expired. Table 2 list the long-term outcome of our patients. **Conclusions:** This is the longest reported experience of patients with CGD. Earlier genetic diagnosis can allow for earlier HSCT and improved outcomes and potential gene therapy in the future.

Table 2

Number	Alive	Died
*53 (*9 lost to follow up)	26 (3-42 yrs.)	18 (4-53 yrs.)

**Berendes, H, Bridges, RA, and Good, RA. *Minn Med.* 1957; 40: p3092.*Quie, PG, White, JG, Holmes, B et al. *J Clin Invest.* 1967; 46: 668–679

Changing Epidemiology of Blood Stream Infections (BSI) in Cancer Patients

Anne Marie Chaftari, MD; **Ray Hachem**, MD; **Ying Jiang**, MS; **Issam Raad**, MD
UT MD Anderson Cancer Center, Houston, TX. USA.

Introduction/Goals: Gram-positive microorganisms have been the predominant pathogens in bloodstream infections (BSIs). We compared the distribution of etiologic organisms in cancer patients at our hospital between two cohorts separated by more than a decade to examine if there is a change in the epidemiology and if the empiric guidelines need to be reassessed in this patient population.

Materials Methods: We evaluated all cancer patients who had simultaneous quantitative blood cultures drawn from the central line and peripheral site that were positive for the same organism at MD Anderson Cancer Center. Cohort 1: between September 1999 and November 2000; and Cohort 2: January 2013 and March 2014. We restricted our analysis to patients with CVC, excluding patients who had bacteremia without a CVC.

Results: We compared 169 patients from Cohort 1 to 283 patients from Cohort 2. We observed a significant decrease in the frequency of BSI episodes considered as Catheter-Related Bloodstream Infection (CRBSI) (44% in Cohort 1 vs. 25% in Cohort 2; p<0.0001). When comparing the two cohorts we saw that the frequency of Gram negative organisms as etiologic agents of CRBSI has significantly increased form 17% in cohort 1 to 41% in cohort 2 (p=0.0005), while the Gram positive decreased from 76% in cohort 1 to 56% in cohort 2 (p=0.006). Furthermore, we examined the duration form insertion of central venous catheter to development of bacteremia in cohort 2. We found that CRBSI occurred after a median of 58 days from CVC insertion date for all organisms. While gram positive CRBSI occurred after a median duration of 30 days, gram negative CRBSIs occurred later after a median duration of 74 days. Candida CRBSI occurred after a median duration of 30 days. We have observed new findings that in cancer patients, gram negative organisms have become the predominant etiologic organisms of BSIs (52%) and contribute now to 41% of CRBSI. CRBSI occur after a median of 58 days from the time of CVC insertion but occur sooner for gram positive organisms and candida (median of 30 days).

SCY-078: A first-in-class, orally-bioavailable, glucan synthase inhibitor has activity alone and is synergistic with azole antifungal agents against *Aspergillus* spp.

S. Barat, K. Borroto-Esoda, D. Angulo
SCYNEXIS, Inc.

Introduction: SCY-078 is a novel, oral and intravenous (IV), triterpenoid-class glucan synthase inhibitor with broad-spectrum activity against *Candida, Aspergillus* and *Pneumocystis* spp. currently in clinical development for use in the treatment of various fungal infections. Invasive aspergillosis (IA) continues to be a disease of high morbidity and mortality, especially in immunocompromised patients. Triazoles have become the drug of choice for the treatment of IA, but with a growing concern of azole-resistant *Aspergillus*, there is a need for new agents and strategies for treatment of this disease.

Goals: To understand the in vitro and in vivo activity of SCY-078 alone and in combination with other antifungal agents against *Aspergillus*, SCY-078 was tested against both susceptible and resistant isolates of *Aspergillus* spp. as a single agent and in combination with azoles.

Results: SCY-078 utility against *Aspergillus* spp., including azole-resistant strains, has been demonstrated in vitro in nearly 500 isolates and *in vivo* in murine and rabbit models of aspergillosis. SCY-078 exhibits fungistatic activity *in vitro* against *Aspergillus* spp., with microbiological outcome presenting as a stumpy phenotype attributed to the blocking of hyphal growth in the filamentous organisms. Activity of SCY-078 against azole-resistant strains of *Aspergillus* has been shown in murine models. Evaluations *in vitro* with SCY-078 in combination with an azole antifungal (voriconazole or isavuconazole) have shown synergistic interactions against all tested wild-type *Aspergillus* spp. (*A. fumigatus, A. flavus, A. nidulans, A. terreus*, and *A. niger*), with FICI reported for SCY-078/voriconazole combination of 0.15 – 0.5 and for SCY-078/isavuconazole of 0.03 – 0.5. Studies in rabbits with SCY-078 (2.5 and 7.5 mg/kg) in combination with isavuconazole (40 mg/kg) have shown synergistic activity against *Aspergillus* spp., which was evidenced in all study endpoints measured (cumulative survival, galactomannan index, lung infarction score and residual fungal burden) when compared to either SCY-078 or isavuconazole alone. The microbiological profile of activity of SCY-078 against *Aspergillus* spp. is complemented by a favorable PK/PD profile, as the systemic exposures necessary for activity across the murine and rabbitmodels of aspergillosis, and the respective MECs reported, are achievable in humans. Additional animal models have shown that SCY-078 has high tissue permeability, readily distributing into tissues - including the lung - and achieving tissue-to-blood ratios ranging from 15-fold to more than 50-fold, thereby demonstrating an ability to distribute into various sites of potential infection at therapeutically meaningful concentrations. Collectively, the existing preclinical data indicates the potential utility of SCY-078 as an emerging treatment for invasive aspergillosis.

Outcomes of Invasive Aspergillosis after Hematopoietic Stem Cell Transplantation: A 7-Year Cohort Study

Sung-Yeon Cho[1,2,3], Hyeon-Jeong Lee[1], Su-Mi Choi[1,2], Dong-Gun Lee[1,2,3]
[1]Division of Infectious Diseases, Department of Internal Medicine, [2]Vaccine Bio Research Institute, [3]The Catholic Blood and Marrow Transplantation Center, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Seoul, Korea

Introduction: Although the outcomes of invasive fungal infection (IFI) have been improved based on the effective preventive strategies and newer azole agents, invasive aspergillosis (IA) is still a leading cause of morbidity and mortality after allogeneic hematopoietic stem cell transplantation (allo-HSCT).

Goals: The aim of this study was to investigate the outcomes and risk factors for death in IA patients after allo-HSCT.

Materials & Methods: Patients diagnosed as IA after allo-HSCT were identified from the IFI cohort of the Catholic Blood and Marrow Transplantation Center, Seoul St. Mary's Hospital. Data were analyzed according to the following phases: pre-engraftment (from conditioning to days 30), post-engraftment (days 31–100), late phase (days 101–365), and very late phase (after one year fromallo-HSCT). Cox-regression models were applied to evaluate risk factors for death.

Results: From January 2011 to April 2017, 553 of IA cases were identified and 160 cases were IA developed after allo-HSCT. The frequency of IA diagnosis was in the order of late phase (n=66), post-engraftment phase (n=45), very late phase (n=26), and pre-engraftment phase (n=23). The 6-week mortality was significantly different according to the phase after transplantation; highest mortality of 42.4% during the late phase, followed by 38.5% in very late phase, 26.7% in post-engraftment phase, and 17.4% in pre-engraftment phase (p=0.037). Only 28.1% of patients were survived after 2-year from the diagnosis of IA. Coinfection with common respiratory virus infection (hazard ratio [HR] 2.197, 95% CI 1.354–3.567, p=0.001) and concomitant bloodstream infection (HR 2.854, 95% CI 1.283–6.348, p=0.010) was significant factors related to death.

Conclusion: IA still remains as a major infectious complication presenting high mortalityrate in allo-HSCT recipients. Prognosis differs according to the time of IA development after allo-HSCT. Coinfection is significantly related to poor outcome.

Epidemiology and clinical characteristics of infectious complications in patients with solid tumours that receive biologic therapies. Experience from an Oncology Hospital from Argentina

Costantini Patricia, Luck Martin, Vallejos Mara, Garcia Patricia, Sorge Adriana
Instituto de Oncología Angel H. Roffo, Universidad de Buenos Aires, Argentina.

Introduction: Biological therapies have been incorporated to the armamentarium for cancer treatment. Due to their low frequency, little is known about the incidence, clinical and microbiologic characteristics of their infectious complications.
Goals: To describe the epidemiology and clinical characteristics of infectious complications in patients with solid tumours that receive target therapies.
Material and Methods: Prospective observational descriptive study of infection complications in adult patients with solid tumours that received EGFR, VEGF, HER2, TK, MTOR, BRAF or cicline inhibitors in the last six months.
Results: One-hundred and six episodes identified in patients from November 2016 until November 2017 were included. Fifty men and 56 women, mean age 57 (range 26 to 90) years old, the underlying diseases were cancer of colon (29), breast (26), kidney (14), melanoma (11), head and neck (11) and others (15). Biologic therapies were vascular endothelial growth factor –VEGF-(31), epidermal growth factor –EGFR- (21), HER 2 (15), BRAF (11), MTOR (10), TK (10) and cycline (8) inhibitors.
Fifty-two patients had received chemotherapy in the last six months and 24 of them in the last month. Twenty were currently receiving corticosteroids. Forty patients had ≤ 1000 lymphocytes and 10 patients were neutropenic.
There were 49 microbiologically documented infections and 57 clinically documented infections. In 104 cases, one or more sources of infection were identified. Fifty-three patients required admission, 13 of them to the ICU and 9 patients (8.5%) died.
Microorganisms isolated were: 34 Gram negative, 21 Gram positive cocci, 5 fungal, 3 viral and 2 nocardial infections.
Sources of infection were: pulmonary (32), skin and soft tissue-SSTI- (39), abdominal (23), urinary tract (8), catheter (4) and others (9). Twenty-two patients had abscess, 15 fistulae and 9 bowel perforations. The most frequent focus of infection in patients receiving VEGF were abdominal (42%) and SSTI (26%) and in those under EGFR, HER2, cycline, BRAF and TK inhibitors were SSTI (39%) and pulmonary (28%). In anti MTOR treated patient's pneumonia (70%) was the most frequent infection.
In conclusion, a wide range of sources and pathogens were identified. Morbidity and mortality were high. An association was made between specific therapies and focus of infection. More studies are needed to better characterize infection complications in patients receiving target therapies.

Bartonellahenselae infections in renal transplant recipients: differences in severity and course

A.A.E de Joode[1], C. van Leer[2]
[1]Department of Internal Medicine; [2]Dept. of Medical Microbiology, University Medical Center Groningen, the Netherlands

Background/Introduction: Infectious complications related to immunosuppression remain major cause of morbidity and mortality in renal transplant recipients. For all types of infection, disease severity in the immunocompromised tends to be worse compared to healthy individuals. *Bartonellahenselae* is cause of cat-scratch disease, an infection transmitted by cats, which usually causes self-limiting regional lymphadenopathy. Immunocompromised individuals are more prone to developing disseminated disease; here, we describe three renal transplantation patients with disseminated *Bartonellahenselae* infection.
Goals: Underscore the need for vigilance in immunocompromised patients who may present with a variety of signs and symptoms which may be mistaken for something else.
Materials and Methods: Three renal transplant recipients were diagnosed with *Bartonellahenselae* infections; course and severity were different and varied between seemingly harmless to severe.
Results: Patient A, a 52 year old female, almost 1 year after combined pancreas-kidney transplant, was admitted for prolonged fever, mild gastro-intestinal problems and diarrhoea. Otherwise she had no clear symptoms. Routine microbiological tests were negative, except for EBV, which was detected in blood at 50,000 copies per ml. A PET-scan showed diffuse high activity of lymph nodes. The liver which also showed high activity, was biopsied. Histological examination of the material revealed granulomatous tissue changes, which prompted testing for *B. henselae*.
Patient B, a 51 year old female, 1 year after second renal transplant and 3 months after high dose methylprednisolone for rejection, was admitted for fever and diarrhoea. While admitted, she developed a pustulous facial skin rash and she claimed to have been scratched by her cat. PCR testing on blood was positive for *B. henselae*.
Patient C, a 19 year old male, 15 years after renal transplant and recently treated for rejection, had a new painful swelling in his left groin without fever or other systemic signs. Interestingly, two years earlier, he had been treated with doxycycline during four weeks for *B. henselae* eye infection. Biopsy of the groin swelling and PCR testing for *B. henselae* revealed the diagnosis.
All patients were treated with an azithromycin-containing regimen of a minimum of three month duration. In patient A, after diagnosing hepatosplenicbartonellosis, rifampicin was added. Patient B was treated with azitromycine only. Patient C was initially treated solely with azitromycine, but doxyclin was added after the patient was readmitted with sepsis, for which no explaination was found other than Bartonella.
Conclusions: B. henselae infections in transplantation patients may present in different ways, potentially leading to wrong diagnoses. Treatment of these infections is long and could lead to interactions with immunosuppressants. A dedicated team of specialists is required to diagnose and treat such uncommon and difficult infections.

Efficacy and tolerability of the treatment with elvitegravir, cobicistat, emtricitabine and tenofovir alafenamide (EVG / COBI / FTC / TAF) in patients with HIV infection. Analysis to 24 weeks

A. Bautista, D. Martín, M.F. Ampuero, J.J. Curbelo, A.M. Antequera, I. de los Santos
Department of Internal Medicine. Hospital de la Princesa. Madrid. Spain.

Introduction: the combination EVG/COBI/FTC/TAF is a preferred treatment in HIV infection. The prodrug TAF included in the new co-formulation has a similar pharmacological action and tolerance profile than TDF with a lower rate of adverse effects. As it is a recently introduced drug and that we currently accumulate little evidence in real clinical practice, we have done this work in our center with the aim of evaluating its efficacy and tolerability in HIV-infected patients.

Goals: to evaluate the efficacy of treatment with EVG/COBI/FTC/TAF in näive and pretreated patients. Virological efficacy was defined as HIV-RNA<50 copies/ml in the different phases of the study and not to have modified or abandoned the ART. Secondary objectives: immunological recovery, changes in the renal function and lipid level, appearance of adverse effects during the treatment.

Patients and methods: observational, descriptive, retrospective study. We included patients evaluated in the outpatient clinic of Infectious Diseases of our Hospital who started EVG/COBI/FTC/TAF between 06/30/2016 and 12/31/2016, with control in the following 12-24 weeks. Baseline data were collected to analyze its evolution (viral load, CD4 number, renal function by eGFR and lipid profile). We included patients in 3 groups: 1) initial therapy in naïve patients, 2) switch from another treatment while viral replication was suppressed, 3) salvage regimen for virological failure. Statistical analysis with SPSS.

Results: we included 153 patients. Virological efficacy was 98.4% (adherence 98.5%). Adverse effects: 4%. Median increase in CD4 cells: 47.07/ml [*IC 12.36-81.77, p 0.008*]. We found a decrease in the eGFR of 3.62 ml/min/m2 [CI 0.009-0.05, p 0.005], an increase in total cholesterol of 17.19 mg/dl [IC 11.51-22.87, p 0.000] and in LDL of 9.32mg/dl [CI 2.06 - 16.59, p 0.012].

Conclusion: EVG/COBI/FTC/TAF is safe and effective, presenting a high efficacy in terms of immunoviral success, superior to that described in the published clinical trials. It should be considered a first line drug in the treatment of naïve patients, although we do not see the potential benefits of renal safety in our population.

Longitudinal Risk Modeling to Characterize Outcomes Associated with Cytomegalovirus Infection in Haploidentical HCT recipients

M. Veronica Dioverti, Chiung-Yu Huang, Megan Morales, Na Lu, Willa Cochran, Douglas Gladstone, Darin Ostrander, Robin Avery, and **Kieren A. Marr**

Introduction: CMV reactivation is associated with both direct morbidity (end-organ disease) and indirect morbidities in hematopoietic stem cell transplant (HSCT) recipients, ultimately leading to high risks for nonrelapse related death. Understanding cumulative morbidity is difficult as estimates are biased in time-to-first-event analyses that do not control for death.

Goals: To investigate nonrelapse – related morbidities in a large cohort of haploidentical HSCT recipients at Johns Hopkins Hospital using novel analytic methods to detail recurrent events and estimate cumulative risks.

Material and Methods: Data collected included demographics, transplant variables, CMV reactivation and disease, and other outcomes (infections, GVHD and hospitalization 6 months post-HSCT). Recurrent events were longitudinally depicted and risks were analyzed using cumulative rate functions and by log-rank tests.

Results: 683 people who received haploidenticalHSCT at JHH were included in the study. The majority were Caucasian (76.5%) and male (61.2%), with mean age of 53.9 (range 17.5 – 78.2). Most frequent underlying conditions included acute myeloid leukemia (29.5%) and non-Hodgkin's lymphoma (28.8%). Conditioning regimens were non-myeloablative in 91.6% with post-HSCT cyclophosphamide, mycophenolate and tacrolimus for GVHD prophylaxis. Donor/recipientserostatus were D-/R+ 22.6%, D+/R+ 31.5%, D+/R- 13.9%, and D-/D- 31.8%. 340 patients (49.8%) died at a mean 16.3 months after transplant (range 0.7 – 107). CMV viremia occurred in 252 (36.9%), with documented disease in 18 (2.6%). Recurrent episodes of CMV viremia were recorded in 27% of cases; with 14 (19.4%) having 3 viremias recorded. Risks of death in people who had CMV infection trended higher in log-rank analyses ($p = 0.1$); associations between CMV reactivation and other recurrent event were appreciated in longitudinal analyses.

Conclusion: In a large cohort of haploidentical HSCT recipients, CMV viremia remains common although tissue-invasive disease is uncommon. Trends to high risks for death are witnessed in log-rank analyses but better appreciated using longitudinal monitoring for recurrent events.

Characterization of Viral Infections in Brazilian Center of Bone Marrow Transplantation in a 2 year period

Diogo Boldim Ferreira, Roselene Passos, Janaina Midori Goto, Renata Nunes, Mauro Jorge Jr, Leila Perobelli, Paula Tuma
Institution:Hospital Euryclides de Jesus Zerbini (HTEJZ), Brazil

Introduction: Infections are an important cause of morbidity and mortality among patients undergoing hematopoietic cell transplantation (HCT). The use of alternative donors, new immunosuppressive agents and other measures directly influence the type and intensity of immunosuppression and modify the risk of developing infection.
Viral infections are still an important challenge for both diagnosis and management due to nonspecific clinical manifestations, lack of diagnostic resources, and few therapeutic options. With the extensive use of acyclovir, the main diagnoses became cytomegalovirus (CMV) and hemorrhagic cystitis (HC). Respiratory viral (RV) infections are another recurring reality among patients.
Goals: Characterization of viral infections in Center of Bone Marrow Transplantation in a 2 year period
Metodologia: In this retrospective study, all patients were included who underwent HCT at Hospital Euryclides de Jesus Zerbiniin the period 2016-2017. The clinical characteristics, prevalence of viral infections, agents, main risk factors, treatment and 30-day mortality rate in were analyzed.
Resuldatos: During the study period, 110 patients underwent HCT, with 24% allogeneic. Among the allogeneic HCT (allo-HCT), 81% were compatible and 19% haploidentical, with RIC being the most frequent type of conditioning (58%). The main indication for autologous (auto-HCT) was myeloma (63%) and allo-HCT was acute leukemia (62%). Sixteen (76%) patients had at least one episode of viral infection among allogeneic HCT and one (1%) among auto-HCT.
Among the 26 allo-HCT, 73% were malesand mean age was 42.5 years. There were 24 episodes of viral infections in 16 patients. CMV reactivation was the most frequent (54%), followed by HC (33%) and RV infection (13%). The mean time after HCT was 141 days. Among the major risk factors, in 77% of CMV reactivation, patient was on GVHD treatment and lymphopenia was observed in 15%. In the cases of HC, 88% was on GVHD treatment, lymphopenia was observed in 38% and CMV reactivation occurred previously in 63. Among HC, adenovirus was the most frequent agent (55%).
Influenza A and B was isolated in 2 cases (1 alloand 1 auto-HCT), respiratory syncytial virus (RSV) in 1 case (allo-HCT) and *Rhinovirus* in 1 case (allo-HCT). One case (RSV) had progression to the lower respiratory tract.
Among the patients with CH, the 30-day mortality was 57%. None of the patients with RV died. Among patients with only CMV reactivation, 1 died within 30 days due to relapse of the underlying disease.
As expected, the prevalence of viral infection was higher in allo-HCT, with CMV reactivation and HC being the most frequent. Treatment for GVHD was the most recurrent risk factor. HC presented higher mortality.

Impact of colonization by multidrug-resistant organisms on bloodstream infection, empirical therapy and mortality in hematopoietic cell transplantation

Diogo Boldim Ferreira, Ingvar Ludwig Augusto de Souza, Maria Daniela Bergamasco, Ana Paula Freitas da Silva Tanaka, Carlos Alberto Pires Pereira, Paola Cappellano
Hospital São Paulo, Universidade Federal de São Paulo (UNIFESP), Brazil

Introduction: Patients undergoing hematopoietic cell transplantation (HCT) are at relevant risk for developing severe bacterial infections. The growing emergence of multidrug-resistant organisms (MDRO) such as vancomycin-resistant enterococci (VRE) and multidrug-resistant enterobacteriaceae is a challenge particularly in immunocompromised patients. Colonization with MDRO often precedes the development of severe infections. In our BMT center, all patients were screened for multidrug-resistant Gram-negative bacteria (MRGN) and VRE with swab from anus weekly.

Goals: To evaluate the impact of colonization by MDRO on bloodstream infection (BSI), empirical therapy and mortality in hematopoietic cell transplantation

Materials & Methods: A retrospective study which included patients undergoing HCT who developedBSI from 2012 to 2014, at the Hospital São Paulo, from Universida de Federal de São Paulo, Brazil. The clinical characteristics of the patients, correlation between colonization and BSI, empirical therapy and mortality were evaluated.

Results: In the study period, there were 38 episodes of BSI in 31 patients. Median age at time of BSI was 44 years and the males were the most frequent (61%). Acute leukemias(32%) were the most frequent underlying disease and allogeneic HCT was the most common modality (65%).The surveillance swab for MRGN was previously collected in 82% of the episodes and for VRE in 76%. The positivity rate for MRGN was 19% and VRE was 14%. All MRGN identified wascarbapenem-resistant *K. pneumoniae* (CRKP). In six episodes with CRKP colonization,BSIby CRKP occurred in 83%. In the absence of previous confirmed colonization, the rate of CRKP BSI was 8%. Empirical therapy with polymyxin B was initiated in 67% of colonized patients, compared to 12% in non-colonized. The adequacy in the first group was 67% and mortality 33%. Two patients had a polymyxin B resistant strain of *K. pneumoniae*. One of them died within 4 days. The other patient who died had relapse of the underlying disease after HCT. In the episodes without previous colonization, empirical therapy with polymyxin B occurred in 12% and the mortality rate was 16%.

In cases with VRE colonization, no episodes of VRE bacteremia occurred. Empirical therapy with linezolid was initiated in 2 (50%) cases. One of the patients died, but she was also colonized by CRKP and showed bacteremia by CRKP. In episodes without prior VRE colonization, there were 3 episodes of bacteremia by the agent. No empirical therapy with linezolid was initiated.

We observed a higher rate of CRKP BSI in patients with previous colonization. Empirical therapy with polymyxin B was more often used in this group. However, we did not observe a lower mortality rate.

Stoolscreening for CRE colonization in Oncology patients – An Indian Perspective

Abdul Ghafur[1], Vidyalakshmi P R[1], Shruti Rayappa[2], Shyam Sunder[2], Anjana Anantharaman[2], Anil Tarigopula[3]
[1]Consultant Infectious Diseases, [2]Research Fellow, Infectious Diseases, [3]Consultant, Molecular diagnostics, Apollo Cancer Institute, Chennai, India

Introduction: Increasing prevalence of Carbapenem Resistant *Enterobacteriacea* (CRE) is a global and regional challenge. Stool screening to identify carriers of CRE will help augmentinfection control measures and in selecting empirical antibiotic regimen when these patients develop sepsis.

Goals: Screen stool samples of oncology patients undergoing HSCT or chemotherapy to identify CRE colonizers and to analyse whether stool screening results correlate with carbapenem resistance status of the subsequentgram-negative bacteremic isolates.

Materials and methods: We did retrospective analysis of oncology patients who had stool screening for CRE over the last 2 years (Jan 2016-Dec 2017). Xpert® Carba-R test was used to screen stool swabs for the rapid detection and differentiation of the *bla*KPC, *bla*NDM, *bla*VIM, *bla*OXA-48, and *bla*IMP. Case records of these patients were analysed to identify *Enterobacteriaceae* blood stream isolates, subsequent to the stool screening.

Results: Stool screening was done in 220 patients and the test was positive in 86 (NDM 41, VIM3, NDM+OXA 20, KPC -1, NDM+VIM-6, IMP+NDM-1, NDM+OXA+KPC-1, NDM+KPC-2, OXA48-10, VIM+NDM+OXA-1]. Out of the 220, blood culture was done in 196 patients. Of these (196), 79 had stool screening positivity and 117 negativity. Five out of the 79 stool screening positivity patients (6.3%) and 3 out of the 117 (2.5%) stool screening negative patients had CRE bacteremia, though not statistically significant (p= 0.272). Four patients in each grouphad carbapenem sensitive *Enterobacteriaceae* in blood.

Conclusion: Oncology patients with stool screening positivity for CRE had a numerically higher chance for the subsequent bacteremia to be carbapenem resistant. Larger studies are required to delineate the full significance of this investigation from an antibiotic stewardship perspective (in addition to its utility to strengthen infection control measures) in high CRE prevalence countries such as India.

Respiratory viral infections in Korean children and adolescents with hematological malignancies

SeungBeom Han[1,2], Kil-Seong Bae[1,2], Seongkoo Kim[1,3], Jae Wook Lee[1,3], Dong-Gun Lee[2,3,4], Nack-Gyun Chung[1,3], Bin Cho[1,3], DaeChul Jeong[1,2], Jin Han Kang[1,2]

[1]Department of Pediatrics; [2]The Vaccine Bio Research Institute; [3]The Catholic Blood and Marrow Transplantation Center; [4]Division of Infectious Diseases, Department of Internal Medicine, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

Introduction: Acute infections of respiratory viruses (RVs) may cause grave outcomes in hematopoietic cell transplant recipients, and therefore, antiviral therapy is recommended for some viral infections. However, it is not conclusive whether antiviral therapy for acute RV infections in pediatric patients with hematological malignancies is useful because the clinical impact of acute RV infections in those patients has not been sufficiently reported.
Goals: This study was performed to evaluate the clinical characteristics and outcomes of acute RV infections in Korean children and adolescents with hematological malignancies.
Materials and methods: Among the children and adolescents (<20 years of age) with underlying hematological malignancies and respiratory symptoms with or without fever, those in whom a multiplex polymerase chain reaction test for RVs was performed were included in this study. Patients in whom RV infections were identified and not identified were categorized into the Group I and II, respectively. Medical records of the enrolled patients were retrospectively reviewed, and clinical characteristics were compared between the Groups I and II and between patients with upper respiratory tract infections (URIs) and lower respiratory tract infections (LRIs).
Results: Between December 2016 and November 2017, a total of 106 respiratory episodes were identified in 82 patients. Group I included 48 (45.3%) RV infections, including 33 (68.8%) URIs and 15 (31.2%) LRIs.Among RVs, rhinovirus (n=18, 37.5%) was most frequent, and parainfluenza virus (n=14, 29.2%) and respiratory syncytial virus (n=11, 22.9%) followed. Patients in the Group Iwere more likely to receive maintenance chemotherapy (*P*=0.037) and complain of rhinorrhea (*P*<0.001) than those in the Group II. However, patients in the Group II were more likely to have hospital-onset respiratory symptoms (*P*=0.004) and receive oxygen (*P*=0.016) and intensive care (*P*<0.001) than those in the Group I.In the Group I, patients with LRIs were more likely to have uncontrolled underlying malignancies (*P*=0.043) and receive re-induction or palliation chemotherapy (*P*=0.009) than those with URIs. Although patients with LRIs were more likely to receive oxygen therapy (*P*=0.001) than those with URIs, mortality was not significantly different between the two patient groups (13.3% vs. 0.0%, *P*=0.093).All of the fatalities were caused by uncontrolled underlying malignancies.
Conclusions: RV infections were identified in 45.3% of patients with hematologic malignancies and respiratory symptoms. Although RV infections did not cause significantly grave outcomesin patients with hematologic malignancies, they increased severity of respiratory illnesses in patients with uncontrolled malignancies.

Inflammatory Cytokine Profile in Subjects with Inherited Chromosomally Integrated Human Herpesvirus 6

Joshua A. Hill,[1,2] Wendy M. Leisenring,[3]Richard L. Lawler,[3]Terry Stevens-Ayers,[2] Danielle M. Zerr,[3]John A. Hansen,[1,4]Michael Boeckh[1,2]

[1]Department of Medicine, University of Washington, Seattle, WA, USA; [2]Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA; [3]Seattle Children's Research Institute, University of Washington, Seattle, WA, USA; [4]Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA, USA

Introduction: Inherited chromosomally integrated human herpesvirus 6 (iciHHV-6) was associated with graft-versus-host disease (GVHD) in a study of hematopoietic cell transplant (HCT) recipients and angina pectoris in a population-based study. Specific pro-inflammatory cytokines are associated withboth the development of GVHD and angina pectoris. **Goals:** We sought to determine whether HCT recipients and healthy donors with iciHHV-6 have higher plasma levels of pro-inflammatory cytokines than matched controls without iciHHV-6. **Materials & Methods:** We identified 75 HCT recipient cases in which either the recipient or donor harbored iciHHV-6 and 75 controls without iciHHV-6 matched for transplant year, conditioning regimen, HLA-matching, and donor relation (*Cohort 1*). We identified 28 healthy donor cases with iciHHV-6 and 56 controls without iciHHV-6 matched for sex, age, and race (*Cohort 2*). We tested plasma samples collected before GVHD onset at days 7, 14, and 21 (+/- 3 days) post-HCT from Cohort 1 and one plasma sample per patient from Cohort 2 for TIM3, TNFRp55, ST2, IL-6, TNFα, and CRP using the Luminexmicrobead-method (Luminex, Austin, TX). Values below the limit of detection (LOD) were assigned a value ofLOD/2. We comparedmedian biomarker concentrations between cases and controls using two-sample Wilcoxon rank-sum tests. **Results & Conclusions:** We tested atotal of 466 samples. Every subject had ≥1 sample tested. The number of subjects in Cohort 1 with a sample at each time point is shown in **Table 1.** MostTNFα results were <LOD, so this cytokine was excluded. Cases in Cohort 1 had a higher median ST2 at day 14 and CRP at days 7 and 14 (**Table 1**). Other cytokines examined did not have significantly different values. There were no significant differences in Cohort 2 (data not shown). HHV-6 gene expression early after HCT using donors or recipients with iciHHV-6warrants study as a potential mechanism leading to higher pro-inflammatory cytokines and GVHD.

Table 1. Plasma cytokine levels in HCT recipients with and without iciHHV-6 (Cohort 1)

Day post-HCT	Cytokine	D/R iciHHV-6neg	D or R iciHHV-6 pos	*P*
7		N = 75	N = 44	
	TNFRp55	3.6 (3.4-3.7)	3.6 (3.5-3.8)	0.10
	CRP	7.4 (6.5-7.8)	7.7 (7.2-8.1)	0.008
14		N = 72	N = 59	
	ST2	1.9 (1.9-2.4)	2.2 (1.9-2.7)	0.03
	TNFRp55	3.6 (3.4-3.8)	3.7 (3.6-3.9)	0.07
	CRP	7.5 (6.9-7.9)	7.8 (7.3-8.1)	0.05
21		N = 74	N = 58	
	TIM3	3.9 (3.7-4.1)	4.0 (3.7-4.2)	0.08

Comparisons with $P \leq 0.1$ are shown. Data are shown as median $\log_{10}$pg/mL (interquartile range). N indicates number tested; D, donor; R, recipient; neg, negative; pos, positive.

Molecular and Clinical Epidemiology and Outcomes of Methicillin-Resistant *Staphylococcus aureus* Bloodstream Infections in Cancerand Non-cancer Patients

Noman Hussain MD, **Khulood Rizvi** MD, **Ana Cecilia Bardossy** MD, **Mary Perri** MT (ASCP), **Marcus Zervos** MD, **George Alangaden** MD
Division of Infectious Diseases, Henry Ford Health System, Detroit, MI, USA

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSI) are common in patients (pts) with cancer. In the general population MRSA strain USA300 has been associated with worse outcomes compared to strain USA100. However, there is limited data on the distribution of these MRSA strains and associated outcomes in cancer pts. We characterized MRSA strains isolated from pts with MRSA BSI and compared the molecular and clinical epidemiology and outcomes of MRSA BSI in pts with and without cancer. **Methods:** This retrospective study was performed at a tertiary-care health system in Michigan from 2005 to 2014. Pts with history of active cancer<30days prior to onset of MRSA BSI were included. Pt demographics, risk factors and outcomes were collected. The following outcomes were compared: 30-day all-cause mortality from index blood culture, infection- related readmission and MRSA BSI recurrence <30 days from end of therapy. Pulse-field gel electrophoresis to identify USA100 and USA300 strain types was performed on all MRSA isolates. **Results:** Of 1,126 consecutive pts with MRSA BSI,97 (8%) had cancer. Pt characteristics and outcomes are shown(Table 1). Advanced age, Charlson score, prior hospitalization and centralline-associated BSI were significantly higher in the cancer group.The distribution of MRSA strains USA100 and USA 300 were comparable in both groups. Mortality was significantly higher (35% vs 18% p<0.001) in cancer pts. Adjusted multivariate analysis showed cancer [OR1.97(95%CI 1.24-3.13)p.004] and age [OR 1.04 (95% CI 1.03-1.05) p <.00] were independent risk factors for mortality. **Conclusion:** Our study shows higher mortality associated with MRSA BSI in pts with cancer compared to non-cancer pts. The worse outcomes in cancer pts could be related to advanced age and greater underlying comorbidities, including cancer. MRSA strain type did not affect outcomes.

Table 1: Comparison of characteristics and outcomes of MRSA BSI in patients with and without cancer

Characteristics	Non-Cancer N=1,029	Cancer N=97	P-value
Age	59.4 ± 17.7	66.3 ± 15	< 0.001
Gender - Male	613 (60%)	50 (52%)	0.125
Centralline BSI	204 (20%)	32 (33%)	0.002
CharlsonScore median(IQR)	3 (1, 4)	6 (4, 7)	< 0.001
Prior Hospitalization	498 (48%)	68 (70%)	< 0.001
Prior ICU	149 (14%)	23 (24%)	0.016
MRSA USA100	437 (43%)	49(51%)	0.130
MRSA USA300	451(44%)	29(30%)	
MRSA other CDC groups	141 (13%)	19 (19%)	
Infection-related readmission	149 (15%)	13 (14%)	0.827
Recurrence of MRSA BSI	76 (7%)	5 (5%)	0.444
30-day all-cause mortality	184 (18%)	34 (35%)	< 0.001

Novel T2Candida Panel Assay Compared to Blood Cultures for Detection of Candidemia in Transplant and Non-Transplant Patients

Noman Hussain M.D., **Zachary Osborn** MPH., **Mayur Ramesh** M.D., **Odaliz Abreu-Lanfranco** M.D., **Ramon DelBusto** M.D., **George Alangaden** M.D.
Division of Infectious Diseases, Henry Ford Hospital, Detroit, MI, USA

Background: Blood culture (BC) the current "gold" standard for detection of Candida bloodstream infectionhas overall sensitivity of ~50% in invasive candidiasis and a turn-around-time (TAT) of 2-5 days. T2Candida Panel (T2) (T2 Biosystems, Lexington, MA, USA) is a magnetic resonance nano-diagnostic test done directly on blood samples, that detects: *C.albicans/C.tropicalis, C.krusei/C.glabrata, C.parapsilosis*. Clinical trial of T2 showed good sensitivity, specificity, NPV 99% and TAT of 3-5 hours. T2 was implemented at our institution for the detection of Candida in patients with suspected candidemia, defined as patients with sepsis syndrome unresponsive to empiric broad-spectrum antibiotics. We compared the performance characteristics of T2 and BC (Trek Diagnostic Systems, Oakwood, OH, USA) in our transplantand non-transplant patient populations. **Methods:** An observational, retrospective, cross-sectional evaluation of patients with suspected candidemia that had T2 done from 10/2015 - 10/2017 at Henry Ford Health System, a multihospital tertiary-care healthcare system in Detroit, MI. Samples received from all hospitals were tested at the core laboratory between 7am-10pm, 7 days a week. The performance characteristics of the T2 and BC in transplant andnon-transplant patients were compared. BC obtained within 7 days before or after the T2 test were included in the analysis. The TAT,sensitivity, specificity, PPV and NPV were calculated using positive BC as the standard. Differences between groups were assessed using two sample proportions testing at alpha = 0.05. **Results:** A total of 1272 patients with suspected candidemia had T2 done:1162 (91%) non-transplant and 110 (9%) transplant patients.The average TAT for T2 was 13 hours (5-41) vs. 34 hours (21-109) to initial positive BC result and 4 days (3-13) to final positive BC result. In 4 non-transplant patients with negative T2, *C. lusitaniae, C. dubliniensis* and *C. kefyr* were isolated in BC. The performance characteristics of T2 and BC in the two groups is shown in Table 1. Of the 19 transplant patients with T2 positive / BC negative results, the organ transplanted were small bowel 6 (32%), liver 6 (32%), kidney 3 (16%), HSCT 3 (16%). In this group 2 (11%) had retinitis; 3 (16 %) candida colonization, 2 (11%) liver abscesses, 2 (11%) bowel leak and 2 (11%) enterocutaneous fistulas. **Conclusion:** The rapid TAT and high NPV of the T2 assay especially in transplant patients has clinical implications and can help support antifungal stewardship efforts in this population. The clinical significance of T2 positivity in the presence of negative BC needs further investigation.

Table1: Performance characteristics of T2 as compared to blood cultures (N=1272)

	Transplant N=110	Non-transplant N=1162	P-value
T2 positive and blood culture positive	5 (4.5%)	35 (3.01%)	0.3917
T2 positive and blood culture negative	19 (17.3%)	86 (7.4%)	0.0003
T2 negative and blood culture positive	1 (0.9%)	41 (3.5%)	0.1431
Sensitivity	83.3 %	46.1 %	
Specificity	81.9 %	92.4 %	
PPV	20.8 %	28.9 %	
NPV	98.8 %	96.2 %	

Distribution of Gram Negative Bacteria Isolated from Blood Cultures of Febrile Neutropenic Patients and Their Antimicrobial Susceptibilities: Seven Years of Experience

Caglayan Merve AYAZ[1], Banu SANCAK[2], Serdar CEYLAN[3], Murat AKOVA[1]
Hacettepe University School of Medicine: [1]Department of Infectious Diseases and Clinical Microbiology, Ankara, Turkey; [2]Department of Medical Microbiology; [3]Department of Medicine

Introduction: Bacterial infections particularly bacteremia are the leading infectious complications of hematologic cancers and hematopoietic stem cell transplantation (HSCT). Despite the appropriate antimicrobial prophylaxis used during the neutropenic period, bacteremia due to gram negative bacteria remains one of the most common causes of mortality.

Goals: In this study, we aimed to present the seven-year distribution and the antimicrobial susceptibility of gram negative microorganisms isolated from febrile neutropenic patients with hematologic malignancies and/or HSCT in adult age group.

Materials & Methods: Between January 1, 2010 and January 31, 2017, gram-negative bacteria isolated from patients with febrile neutropenia (defined as, absolute neutrophil count < 500/mm^3 and the timpanic fever measured once above 38.3°C or for at least during one hour >38°C, with multiple measurements) were analysed. The Bactec ® semi-automated blood culture system for patients' blood cultures, the automated system of VITEK® 2 (BioMérieux, France) for bacterial identification and for in vitro susceptibility testing were used. When required, conventional microbiological methods were also applied.

Results: Gram negative bacteria were identified in 254 blood cultures taken during febrile neutropenic episodes in153 patients. *Escherichia coli* was the most common gram-negative bacteria with % 46 percent (117 out of 254 isolates), followed by *Klebsiella pneumonia* (24%, 61/254 isolates) and *Acinetobacter baumannii* (15.3%, 39/254 isolates). Overall carbapenem resistance among all isolates was 33%. *Acinetobacter baumannii* complex were all resistant to carbapenems, while in two additional isolates resistance to colistin was detected. Carbapenem resistance was found in 44.2% (27/61 isolates) of *K. pneumonia* and in 5.1% in *E. coli* (6/117). The rate of extended spectrum beta-lactamase (ESBL) production was 38.6% in all Enterobacteriaceae. ESBL positivity was 42.6% percent (26/61) in *K. pneumoniae* and 41.9% (49/117) in *E. coli*.

Conclusions: These results represent a very high-rate of antimicrobial resistance among gram-negative bacteremia isolates from febrile neutropenic cancer patients in our center and they may be a harbinger of treatment difficulties and high morbidity and mortality due to bacteremia in this patient population.

Chronic Granulomatous Disease: An updated large, US single-center experience

Zacharoula Oikonomopoulou, MD, **Ben Z. Katz,** MD
Northwestern University Feinberg School of Medicine, Ann and Robert H. Lurie Children's Hospital of Chicago, Department of Pediatric Infectious Diseases

Introduction: Chronic granulomatous disease (CGD) is a rare, hereditary primary immunodefi-ciency that results from the inability of phagocytes to mount respiratory burst and kill catalase-positive bacteria and fungi.

Goals: Update infectious and non-infectious complications in a large, single-center cohort of pa-tients with CGD.

Materials & Methods: We performed a retrospective update of all patients with CGD at Ann and Robert H. Lurie Children's Hospital of Chicago from November 2013 to November 2017. Pa-tients that were referred to our hospital from March1985 to November 2013 have been reviewed previously. The diagnosis of CGD was suspected based on clinical features and was subse-quently confirmed by functional and/or genetic studies. Serious infections were defined as those requiring inpatient hospitalization or intravenous antibiotic therapy.

Results: There are currently 26 patients (80% males) in our cohort with a median age of 13 years. The most frequent clinical presentation at diagnosis was pneumonia (n=6) and lymphadenitis (n=6) and the most frequent infectious agents on presentation were Aspergillus fumigatus (n=4) and Serratia marascenes (n=3). Ten patients (38.4%) developed CGD-related colitis, half within the last 4 years. Two patients developed eosinophilic cystitis and four developed ophthalmologic complications including choriorerinitis and retinitis pigmentosa. There were 21 serious infections in the last 4 years. Three patients were evaluated for stem cell transplant (SCT; none of them has received a SCT to date). One patient developed a filamentous basidiomycetes lung infection and another developed kidney stones,both rarely reported compli-cations of CGD. Two additional patients have been identified. One has ornithine transcarbala-mase deficiency (OTCD) who because of two slow-to-heal infections and the contiguity between the genes for OTCD and CGD was screened for CGD and found to be an X-linked carrier of CGD with extreme Lyonization. A second, new patient was diagnosed elsewhere following a bout of Pneumocystis pneumonia, an unusual complication of CGD. One patient was lost to follow up and another (who recently married) was transitioned to adult care in the last 4 years.

Conclusions: We have had no deaths in the last 4 years. Almost all of the patients are maintained on thrice-weekly administration of subcutaneous interferon-γand daily oral prophylaxis with Bactrim and an azole.

The role of peptide antigen, antigen-presenting cells and CD4+T cells in modulating BK polyomavirus (BKPyV)-specific CD8+T cell responses *in vitro*

Amandeep Kaur[1], Sabrina Wilk[1], Maud Wilhelm[1], Klaudia Naegele[1], Marion Wernli[1], Fabian H. Weissbach, Hans H. Hirsch[1,2]

[1]Transplantation and Clinical Virology, Department of Biomedicine (Haus Petersplatz), University of Basel, Switzerland; [2]Infectious Diseases & Hospital Epidemiology, University Hospital Basel, Basel, Switzerland

BKPyV is one of at least 13 HPyV and infects more than 90% of the general adult population and then asymptomatically persists in the kidney. Despite the presence of functional BKPyV-specific T-cell responses and neutralising antibodies, BKPyV is shed in low levels into the urine of at least 10% of *bona fide* healthy blood donors. In immunocompromised patients, BKPyV replication is readily reactivated and very high urine viral loads of more than 9 log10 GEq/mL are detectable, which may lead to manifest diseases such as allograft nephropathy in 1% - 15% of kidney transplant patients[1] and hemorrhagic cystitis in 5% - 20% of allogeneic hematopoietic stem cell transplant recipients.[2] These specific patient groups share impaired immune control and allogeneic constellations between infected host cell and immune effectors.[3] We have reported that BKPyV-specific T-cell responses expand in kidney transplant patients clearing BKPyV viremia,[4] a response that involves CD8+Tcells targeting immunodominant 9mer epitopes.[5,6] Here, we characterized the role different antigen-presenting cells (APCs) and CD4+T cells in modulating BKPyV-specific CD8+T cell responses. Healthy blood donors (HD, n=12) were tested for BKPyV-Vp1-VLP by ELISA,[7] and 7 seropositive HD were HLA-typed using NGS sequencing. Using cryopreserved PBMC of the selected HD, we found that plastic-activated monocytes (act-Mono) pulsed with overlapping 15mer peptide pool covering the entire BKPyV-LTag sequence (15mP) were efficient in inducing BKPyV-specific CD8+T cell responses. Monocyte-derived dendritic cells (Mo-DCs) were better than act-Monoin eliciting CD8+Tcell responses. Thirdly, the responses were reduced following selective CD4+T cells removal indicating CD4+Tcells were required for Mo-DCs generated BKPyV-specific CD8+T cells. Further experiments are under way to characterize the effect of immunosuppressive drugs in these constellations, and to develop new strategiesof boosting of BKPyV-specific cellular immunity in patients at risk or suffering from BKPyV disease post-transplant.

1. Hirsch HH, Babel N, Comoli P, et al. European perspective on human polyomavirus infection, replication and disease in solid organ transplantation. *Clin Microbiol Infect.* 2014;20 Suppl 7:74-88.

2. Cesaro S, Dalianis T, Hanssen Rinaldo C, et al. ECIL guidelines for the prevention, diagnosis and treatment of BK polyomavirus-associated haemorrhagic cystitis in haematopoietic stem cell transplant recipients. *J Antimicrob Chemother.* 2018;73(1):12-21.

3. Hirsch HH. Virus infections post transplant: risk and immunity. *Transpl Infect Dis.* 2005;7(3-4):97-98.

4. Binggeli S, Egli A, Schaub S, et al. Polyomavirus BK-Specific Cellular Immune Response to VP1 and Large T-Antigen in Kidney Transplant Recipients. *Am J Transplant.* 2007;7(5):1131-1139.

5. Cioni M, Leboeuf C, Comoli P, Ginevri F, Hirsch HH. Characterization of Immunodominant BK Polyomavirus 9mer Epitope T Cell Responses. *Am J Transplant.* 2016;16(4):1193-1206.

6. Leboeuf C, Wilk S, Achermann R, et al. BK Polyomavirus-Specific 9mer CD8 T Cell Responses Correlate With Clearance of BK Viremia in Kidney Transplant Recipients: First Report From the Swiss Transplant Cohort Study. *Am J Transplant.* 2017;17(10):2591-2600.

7. Kardas P, Leboeuf C, Hirsch HH. Optimizing JC and BK polyomavirus IgG testing for seroepidemiology and patient counseling. *J Clin Virol.* 2015;71:28-33.

Predicting mortality in Candida blood-stream infection

Keighley, C.[1], Chen, S.[1,2], Marriott, D.[4], Chapman, B.[3], Pope, A.[5], Van Hal, S.[6], Kennedy, K.[7], Bak, N.[8], Underwood, N.[8], Wilson, H.[7], McDonald, K.[4], Halliday, C.[1], Kidd, S.[10], Sorrell, T.[2,3], Hajkowicz, K.[11], Darvall, J.[12], Slavin, M.[13]

[1]Centre for Infectious Diseases and Microbiology Laboratory Services, ICPMR, Westmead Hospital, Westmead, Sydney, NSW; [2]Centre for Infectious Diseases and Microbiology, Westmead Hospital and the Marie Bashir Institute for Infectious Diseases and Biosecurity, University of Sydney, Sydney, NSW; [3]Westmead Institute for Medical Research, The University of Sydney, Sydney, NSW; [4]Department of Microbiology and Infectious Diseases, St. Vincent's Hospital, Sydney, NSW; [5]Department of statistics, The University of Sydney, Sydney, NSW; [6]Department of Infectious Diseases and Microbiology, Royal Prince Alfred Hospital, Sydney, NSW; [7]Department of Infectious Diseases and Microbiology, Canberra Hospital, Australian National University Medical School, Canberra, ACT; [8]Department of Infectious Diseases, Royal Adelaide Hospital, Adelaide, SA; [9]Infection Management Services, Princess Alexandra Hospital, Brisbane, QLD; [10]National Mycology Reference Centre, SA Pathology, Adelaide, SA; [11]Department of Infectious Diseases, Royal Brisbane and Women's Hospital, School of Medicine, University of Queensland, Brisbane, QLD; [12]Department of intensive care, Royal Melbourne Hospital, Melbourne, VIC; [13]Department of Infectious Diseases, Peter MacCallum Cancer Centre, Victorian Infectious Diseases Service at the Doherty Institute for Infection and Immunity, Melbourne, VIC.

Introduction: *Candida* blood-stream infections (BSIs or candidemia) are increasing with associated high mortality (~ 40%). **Goals:** We sought to assess clinical and treatment factors impacting on candidemia outcomes, describe complications and establish a mortality prediction score. **Materials & Methods:** A multi-centre prospective cohort study was performed in eight Australian tertiary hospitals. Consecutive cases of candidemia were identified by laboratory-based surveillance commencing in March 2014; at each site, the study duration was 1 year. Adults ≥18years of age with at least one blood culture positive for *Candida* species were included. Endocarditis, endophthalmitis and hepatosplenic candidiasis were recorded as complications of candidemia. Data were analysed using R. **Results:** We studied 140 episodes of candidemia in 146 patients, yielding 148 isolates; two episodes were classed as "recurrent". Predisposing factors included surgery within the preceding 30 days (50%), malignancy (18%), indwelling vascular catheters (72%), urinary catheters (59%) and antimicrobial use (88%). The likely/proven source of BSI was intravascular in 33%, gastrointestinal in 29% and genitourinary in 25%. Candidemia from a likely gastrointestinal source was more often associated with *Candida glabrata* complex than thosefrom an alternate source (20/43, 47% vs 27/105, 26%; p = 0.014); similarly,candidemia with a likely intravascular source had *C. parapsilosis* complex isolated more commonly than those with an alternate source (15/51, 29% vs 4/97, 4%; p < 0.001). Non-*Candida albicans* species comprised 58% of isolates and outnumbered *C.albicans,* independent of setting or patient factors. Fifty percent of patients received an echinocandin as empiric therapy, whilst 44% received fluconazole. There was no association between choice of empiric therapy and 30-day mortality. The average total duration of antifungal therapy for uncomplicated *Candida* BSI was 17.5 days. All-cause mortality at 30-days was 31%. Multiple logistic regression analysis identifiedage, source of *Candida* BSI, prolonged use of antibiotic therapy, intensive care setting, absence of recent surgery, a haematology comorbidity and organ failure as associated with mortality and a risk prediction score was developed. **Conclusions:** Demographic and predisposing factors are no longer useful in predicting cases of *Candida* BSI caused by non-*C. albicans* spp. Seven factors were incorporated into a simple mortality prediction score.Further prospective studies evaluating the accuracy of the mortality predictive model are indicated.

Cefepime versus cefepime plus amikacin as an initial antibiotic choice for pediatric patients with febrile neutropenia

Na HeeLee[1], Ji-Man Kang[2], Ji Won Lee[3], KeonHee Yoo[3], Ki Woong Sung[3], Hong Hoe Koo[3], Yae-Jean Kim[3]

[1]Department of Pediatrics, Cha Bundang Medical Center, Cha University, Seongnam, Korea; [2]Department of Pediatrics, Center for Pediatric Cancer, National Cancer Center, Goyang, Korea; [3]Department of Pediatrics, Sungkyunkwan University School of Medicine, Samsung medical center, Seoul, Korea

Background: Bacteremia in pediatric cancer patients with neutropenia is an important and urgent issue which needs prompt antimicrobial treatment. We investigated the treatment outcome of patients with bacteremia before and after the addition of amikacin to cefepime monotherapy as an initial empirical antimicrobial treatment in pediatric cancer patients with febrile neutropenia. **Methods:** From January 2011 to December 2016, pediatric cancer patients who visited emergency room (ER) at Samsung Medical Center (SMC), Seoul, Korea due to chemotherapy induced febrile neutropenia were included. All bacteremia episodes occurred at ER were investigated by retrospective chart review. At SMC, the regimen of empiric antimicrobial treatment for febrile neutropenia at ER has been changed from cefepime to cefepime plus amikacin since September 2014 because increasing cefepime resistance rate was suspected. **Results:** For six years, a total of 230 episodes of positive blood cultures were identified in 168 patients. Five episodes were excluded due to contamination. Finally, 225 bacteremia episodes in 164 patients were included. Approximately 54% of episodes (122/225) were treated with cefepime monotherapy and 37% of episodes (83/225) were treated with cefepime plus amikacin combination therapy. Remained 20 episodes were treated with other antimicrobial regimens. Gram-negative organisms accounted for 59% (132/225) and gram-positive organisms for 41% (93/225). There was no fungemia episode in this study. The bacteremia caused by cefepime-resistant gram-negative organisms occurred in 16% (11/69) before September 2014, and 21% (12/57) since September 2014 (p =0.331). The percentage of appropriate empiric antimicrobial treatment increased from62% to 83% since the additional administration of amikacin at ER (p = 0.004). The duration of fever was shorter in the cefepime plus amikacin group than in the cefepime group (34 hours vs. 22 hours, p = 0.014); however, the rate of septic shock and pediatric intensive care unit (PICU) hospitalization were not significantly different between two groups (septic shock 7% vs 7%, p = 0.968; PICU 3% vs 1%, p = 1.00). There was no infection related mortality in both groups. There was no significant difference in creatinine levels between cefepime and cefepim plus amikacin group during follow-up within one week (p=0.760)

Conclusion: For gram-negative organisms, antimicrobial resistance rate to cefepimewas around 18.5%. Although the percentage of appropriate empiric antimicrobial treatment increased by adding amikacin, no difference in progression to septic shock or PICU hospitalization were observed.

Evaluation of cardiovascular risk in HIV positive patients under HAART

Sara Lardo, Katleen de Gaetano Donati, Valentina Mazzotta, Valentina Mazzocato, Marco Olivieri, Simona Costanzo, Amalia De Curtis, Licia Iacoviello, Enrica Tamburrini, Roberto Cauda

1)Infectious Diseases Department, Catholic University, Roma; 2)Environmental and Genetic Epidemiology, Cellular Biology Laboratory and Statistical Methods in Epidemiology Unit, IRCCS Neuromed, Pozzilli, Isernia

Background: Since the beginning of HAART use, numerous reports of heart attacks and premature atherosclerosis in young HIV-positive patients were published. Initially the attention was focused on protease inhibitors (PI) and their metabolic effects. More recently it was proposed a direct role of HIV virus in endothelium proinflammatory activation. **Material and methods:** Only HIV-positive patients were included. A questionnaire on personal data was administered to each patient: history of HIV infection; diet; cardiovascular risk factors; medical examination. Blood, urine and instrumental tests were performed: electrocardiogram, echocardiogram and carotid ultrasound as well as endothelial markers. All recruited patients have entered the phase of follow-up. Data management and statistical analysis were perfomed by SAS statistical software. **Results:** At the end of the study (36 months), among 315 HIV+ patients consecutively arrived at the Infectious Diseases Department of Gemelli Hospital, 298 (94,6%) decided to participate, among which 16 questionnaires were not included because incomplete. Transversal phase: 36% of the population was in advanced disease stage, while HIV viremia was undetectable in 90% of the cohort. Mean time of antiretroviral therapy was 10 years. Ecocardiography alterations were more present in male group, while ECG and carotid doppler alterations were distributed in equal manner among males and females, as well as metabolic syndrome. Half percent of the population smoke, 75% drink alcohol, only 25% practice sport. Among the different therapeutic classes, symptomatic patients presenting AMI (9) and ischaemic cardiopathy (16), were homogenously distributed. Mean HDL level was lower while mean triglyceride and fibrinogen levels were higher in protease inhibitor group respect to non-nucleoside analogues. IMT>1 mm prevalence is higher in protease inhibitor group. Longitudinal phase: the 12 months follow-up was performed on 75% of patients. Nineteen patients were lost at follow-up. Regarding fibrinogen, platelet and less glycemia, there was a statistical significant difference between baseline and follow-up. Regarding endothelial molecule levels vWF and 8-isoprostane were reduced between baseline and follow-up. Among different antiretroviral classes, only vWF presents level reduction at follow-up in particular for NRTI+NNRTI class. Cardiovascular risk chart was applied to a subgroup of 197 patients between 40 and 65 years without comorbidities. The majority presents a cardiovascular risk of =3%. A statistically significant association between metabolic syndrome and high IMT prevalence was observed. **Conclusions:** There is a reduction of adhesion molecules and markers of inflammatory damage, especially in the group of patients taking protease inhibitors.Applying the cardiovascular risk chart, most of our patients had a cardiovascular risk predicted 10-year level low.

Actual antiretroviral classes										
	NRTI +NNRTI, N 44		NRTI +IP, N 32		NRTI/NNRTI + In.Integ, N 21		salvataggio + (maraviroc + IP/NRTI), N 10		*pvalue ANOVA*	pvalue* MANOVA
	media	DS	media	DS	media	DS	media	DS		
vWF										
T0	1389,34	351,76	1427,06	453,93	1408,2	395,02	1251,3	377,79	0,67	0,63
T1	1254,43	417,81	1424,53	365,32	1404,2	531,14	1010,2	388,79	0,033	0,013
Delta T1-T0	-134,91	344,35	-2,53	333,34	-4	465,69	-241,1	283,98	0,16	0,11
Creatinuria										
T0	148	79,59	151,66	79,66	137,79	68,82	169,83	59,76	0,74	0,65
T1	122,67	62,65	102,99	52,59	119,84	77,64	132,06	57,05	0,46	0,46
Delta T1-T0	-25,33	80,43	-48,68	76,19	-17,94	81,22	-37,77	66,73	0,48	0,66
8_isoprost										
T0	1868,47	1221,21	1856,25	1298,77	1616,38	730,07	1439,26	558,61	0,62	0,75
T1	1543,71	753,97	1694,16	963,97	1350,76	847,11	1514,9	655,51	0,54	0,77
Delta T1-T0	-324,76	1128,93	-162,08	778,97	-265,62	690,91	75,64	661,44	0,62	0,61

Invasive Mold Infection of the Central Nervous System In Children With Cancer or Undergoing Hematopoietic Stem Cell Transplantation – Analysis of 25 Cases

T. Lehrnbecher[1], A. Attarbaschi[2], G. Cario[3], M. Döring[4], O. Moser[5], U. Mücke[6], F. Poyer[2], S. Rieken[7], C. Temme[8], S. Voigt[9], M. Lauten[7] and A.H. Groll[10]

Pediatric Hematology /Oncology [1]University of Frankfurt, [3]Kiel, [4]Tübingen, [5]Aachen, [6]Freiburg, [7]Lübeck, [8]Essen, [9]Berlin, and [10]Münster, Germany, and [2]St. Anna Kinderspital, Vienna, Austria

Introduction and Goals: Invasive mold disease (IMD) of the central nervous system (CNS) is a particular severe form of invasive fungal infection. Since pediatric data of CNS-IMD are scarce, we retrospectively analyzed presentation, characteristics, and outcome of CNS-IMD in children.

Patients & Methods: Pediatric cancer patients or allogeneic hemaotopoietic stem cell transplant (HSCT) recipients (<18 years) in whom CNS-IMD was diagnosed between 2007 and 2016 were collected in a multi-center, retrospective survey. Compatible CNS imaging or macroscopic autopsy findings in combination with positive microbiological results of brain biopsy or cerebrospinal fluid, respectively, was classified as proven, and compatible CNS imaging in combination with proven/probable IMD at another site as probable CNS-IMD.

Results: A total of 25 patients [17 m/8 f, median age (range) 14.6 (0.6-17.6) years] were identified. Underlying diseases were acute lymphoblastic leukemia (ALL, n=15), relapsed ALL (4), myelodysplastic syndrome (2), chronic myeloid leukemia, lymphoma and Ewing sarcoma (1 each). Ten patients had received allogeneic HSCT. Proven and probable CNS-IMD was diagnosed in 12 and 13 patients, respectively, with pulmonary involvement in 24 out of 25. Pathogens included *Aspergillus* spp (n=20), *Fusarium, Rhizopusand Rhizomucor* spp (1 each), and unidentified molds (3). Sixteen patients presented with CNS symptoms, whereas 9 patients were asymptomatic and CNS imaging was performed due to IMD at another site (n=6) or due to other reasons (3). A total of 11 patients had received prior mold-active antifungal prophylaxis/treatment, and initial antifungal therapy after diagnosis of CNS-IMD included voriconazole in 11/25 patients. After a median time (range) of follow-up 455 (1-1868) days, 15 patients were alive. Seven of the 15 survivors carry long-term neurological disabilities.

Discussion: Our analysis of CNS-IMD demonstrates a predominance of teenagers and patients with ALL or allogeneic HSCT. Since CNS-IMD is asymptomatic in a considerable number of patients with primary lung involvement of IMD, routine imaging of the CNS has to be discussed for all patients with pulmonary mold infection.

Invasive fungal disease in children undergoing therapy for hematological malignancy of receiving allogeneic hematopoietic stem cell transplantation: analysis of the prospective multicenter trial IFI-PED

T. Lehrnbecher[1], A .Attarbaschi[2], F. Poyer[2], J. Georg[1], A. Becker[1], S. Schöning[1], K. Gordon[3], A.H. Groll[3]

Pediatric Hematology /Oncology [1]University of Frankfurt and [2]Münster, Germany, and [3]St.Anna Kinderspital, Vienna, Austria

Background: Data on the incidence and outcome of invasive fungal disease (IFD) in children with hematological malignancies (HM) or after allogeneic hematopoietic stem cell transplantation (HSCT) are mostly based on monocenter, retrospective studies and/or studies performed prior to the availability of newer triazoles or echinocandins.

Methods: In a prospective multicenter study(DRKS00006341), we collected data on the incidence and prognosis of IFD in children treated for HM or undergoing allogeneic HSCT.The 2-year study started April 2014. All patients were followed for at least one year after finishing intensive chemotherapy or after HSCT.

Results: The analysis included301childrenwho underwent a total of 359 therapies (210 chemotherapies, 138 allogeneic HSCTs and/or 11 experimental therapies, which were not included in the analysis). HSCT was mostly performed for hematological malignancies (84%). Chemotherapy was given for acutelymphoblastic leukemia [de novo ALL, (n=136), relapsed ALL (15)], acute myeloid leukemia [de novo AML (23) relapsed AML(5)], and Non-Hodgkin lymphoma (NHL, 31 patients). Possible IFD were diagnosed in 23 patients(6.6%; 12 patients receiving chemotherapyand 11 HSCT recipients). Proven/probable IFDs occurred in 8 and 7 patients, respectively [4.3%; 7 patients with chemotherapy, and 8 HSCT recipients), and 10 of them had received mold-active prophylaxis. Proven/probable IFDs were due to *Aspergillus* spp (n=9), *Candida* spp (n=3), *Fusarium* spp (n=1), *Rhizopus* spp (n=1) and co-infection with *Aspergillus* spp and *Rhizopus* spp (n=1), respectively. Complete and partial response were seen in 9 and 3 patients, respectively, and 3 patients died due to IFD. One year after end of chemotherapy/HSCT, 10 of the patients with proven/probable IFD were alive.

Conclusion: This prospective multicenter study demonstrates that *Aspergillus* spp is still the most importantfungal pathogen in children treated forALL, AML or undergoing HSCT. Since one third of the patients with proven/probable IFD did not receive antifungal prophylaxis, further analysis might help to better identify patients which will benefit from antifungal prophylaxis.

The study was supported by an unrestricted grant by Gilead Sciences

Real world evidence on the burden of illness experienced by patients with systemic mycoses

Anna Forsythe, PharmD;[1] **Jaclyn Hearnden**;[1] **Gareth Lewis**, PhD;[2]
Rhonda Schreiber BSCN, MSSL[2]
[1]Purple Squirrel Economics, New York NY, USA; [2]Mayne Pharma, Raleigh NC, USA

Introduction: Systemic mycoses, or fungal infections of the internal organs, may result from infection with several different fungal organisms. Systemic mycoses are commonly opportunistic infections where immunocompromised patients, including those with a history of serious illness, are disproportionately affected. **Goals:** Our goal was to understand the burden of illness experienced by patients with systemic mycoses across different populations of interest. **Materials& Methods:** Electronic medical records from over 34 million patients in 30 US hospital institutions were queried and patients with mycoses including aspergillosis, histoplasmosis, and blastomycosis were identified via ICD-10 codes.Mycoses patients were divided into mutually exclusive cohorts consisting of (1) otherwise healthy patients andthosewith a history of (2) immunosuppressant treatment, (3) cancer, (4) transplants, or (5) HIV. Cohorts 2-5 werecompared to control cohorts, consisting of similarly categorized patients (i.e., with cancer) but without mycoses. **Results:** Thesearch identified 11,619 patients with mycoses who were treated with antifungals over five years. The mean age of patients was similar across cohorts (52-57). A similar proportion of patients were male and white across the cohorts (50-62%, 65-78%), except for the HIV cohort (79% males, 44% white). Most mycoses patients were subject to a form of immunosuppression (cohorts 2-5, 82%). Symptomatic burden was much greater in all mycoses patients versus controls without mycoses (Table). Additionally, the rates of constitutional symptoms experienced by patients with cancer, transplants, or HIV were far greater than those experienced by healthy (>60%) and immunosuppressant-treated patients (>30%, p<0.05 for all comparisons). The severity of the primary illness may dictate the symptomatic burden of systemic mycoses.

COHORTS	Healthy	Immunosuppressant Treatment		Cancer		Transplant		HIV	
Symptoms			vs control		vs control		vs control		vs control
Malaise, fatigue	11%	13%	246%	57%	759%	35%	68%	47%	756%
Depression, mood disorders	10%	14%	137%	36%	452%	22%	42%	44%	188%
Headache	5%	7%	88%	37%	1050%	19%	95%	36%	610%
Vision disturbances	3%	3%	100%	21%	1230%	7%	114%	26%	703%
Sleep disorders	8%	13%	149%	41%	642%	21%	19%	28%	500%
Fever	9%	10%	233%	65%	1415%	47%	72%	52%	1035%
Pain	6%	9%	141%	37%	650%	15%	19%*	30%	783%
Dizziness	3%	3%	94%	22%	1024%	10%	69%	22%	1028%
Edema	6%	10%	425%	39%	1220%	22%	18%	24%	1189%
Rash	4%	5%	17%*	39%	1388%	22%	74%	33%	680%
Abnormal weight loss	4%	5%	550%	22%	1161%	7%	45%	28%	890%

**p-value >0.01, all other comparisons p<0.01*

In Vitro Pharmacodynamics of Isavuconazole, Voriconazole and Posaconazole Against Agents of Aspergillosis, Mucormycosis, Phaeohyphomycosis, Fusariosis and Scedosporiosis

Russell E. Lewis,[1] Nicholas D. Beyda,[2] Nathan D. Albert,[3] Dimitrios P. Kontoyiannis[3]
[1]Infectious Diseases Hospital- Policlinico S. Orsola-Malpighi, [2]The University of Texas M.D. Anderson Cancer Center, [3]University of Houston College of Pharmacy

Background: Little is known about the pharmacodynamics of isavuconazole (ISA) versus voriconazole (VOR) or posaconazole (POS) against less common and potentially-resistant moulds. **Materials/Methods:** We characterized the in vitro pharmacodynamics of ISA, VOR and POS against a collection of clinical mould isolates representing common agents of aspergillosis, mucormycosis, phaeohyphomycosis, fusariosis and scedosporiosis. Fungal hyphae viabilityfollowing 24-hour drug exposure (0-16 mcg/mL) was measured using the XTT reduction assay. A three-parameter logistic regression model was fit to raw hyphal viability data to estimate the effective concentration 50% (EC50) and 90% (EC90) for each triazole. **Results:**

Pathogen (number of isolates)	Isavuconazole mcg/mL		Voriconazole mcg/mL		Posaconazole mcg/mL	
	EC50 (95% CI)	EC90 (95% CI)	EC50 (95% CI)	EC90 (95% CI)	EC50 (95% CI)	EC90 (95% CI)
Aspergillus fumigatus (n=10)	0.44 (0.34-0.54)	1.26 (0.93-1.58)	0.72 (0.56-0.88)	1.64 (0.99-2.30)	0.17 (0.12-0.21)	0.53 (0.27-0.79)
Aspergillus flavus (n=10)	0.38 (0.31-0.45)	0.67 (0.45-0.86)	0.82 (0.54-1.09)	2.67 (1.00-4.32)	0.62 (0.41-0.82)	1.98 (0.76-3.20)
Aspergillus terreus (n=10)	0.31 (0.21-0.41)	0.81 (0.53-1.10)	0.53 (0.33-0.73)	1.63 (0.55-2.70)	0.80 (0.31-1.30)	3.10 (1.65-4.52)
Rhizopus oryzae (n=10)	1.08 (0.84-1.32)	2.08 (1.24-2.92)	3.47 (2.73-4.21)	6.07 (3.78-8.37)	0.87 (0.72-1.01)	1.23 (0.95-1.51)
Rhizomucor spp. (n=10)	1.15 (0.71-1.59)	3.39 (1.81-4.97)	4.28 (3.51-5.05)	6.34 (4.47-8.21)	0.87 (0.69-1.04)	1.23 (0.88-1.58)
Mucor spp. (n=10)	1.87 (1.10-2.63)	2.36 (0.34-4.44)	6.34 (4.99-7.79)	12.43 (7.28-17.60)	0.22 (0.13-0.31)	0.59 (0.24-0.94)
Cunninghamellabertholletia (n=5)	1.28 (1.28-1.28)	1.78 (1.18-1.99)	9.75 (5.76-13.75)	15.42 (4.45-26.40)	0.61 (0.35-0.87)	1.11 (0.28-1.93)
Alternaria spp. (n=5)	0.44 (0.01-0.82)	0.51 (0.22-0.79)	0.13 (0.07-0.20)	0.42 (0.17-0.67)	4.74 (3.46-6.01)	6.70 (2.81-10.58)
Curvularia spp. (n=5)	0.79 (0.12-0.55)	1.67 (0.82-2.50)	0.32 (0.21-0.42)	0.62 (0.36-0.88)	0.32 (0.21-0.43)	0.58 (0.37-0.80)
Fusarium solani (n=7)	1.16 (0.81-1.51)	2.49 (1.35-3.62)	4.11 (3.11-5.12)	8.22 (4.67-11.79)	1.55 (0.89-2.21)	6.76 (2.94-10.58)
Lomentospora prolificans (Scedosporium prolificans) (n=5)	7.97 (4.39-11.57)	18.40 (1.58-15.63)	2.53 (1.10-3.96)	8.60 (1.58-15.6)	41.21 (22-79.9)	64.0 (55.2-128.2)
Scedosporium apiospermum (n=5)	0.33 (0.21-0.46)	0.85 (0.35-1.35)	0.15 (0.09-0.20)	0.32 (0.15-0.50)	0.28 (0.12-0.44)	0.79 (0.31-1.26)

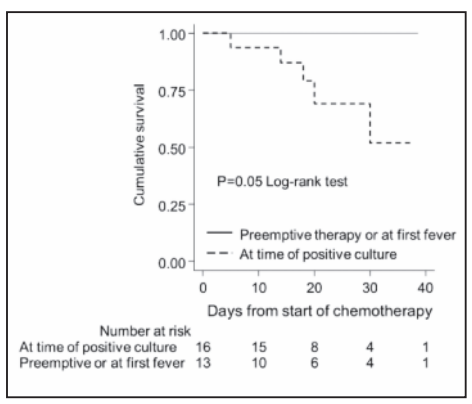
ISA, VOR and POS displayed different pharmacodynamic patterns against the test isolates. ISA EC50 and EC90 values were lowest (< 1 mcg/mL) for *Aspergillus* and *Alternaria* species, between 1-3 mcg/ml for agents of mucormycosis and *F. solani,* and 7 mcg/mL for *L. prolificans*. Voriconazole EC50 and EC90 values were generally higher than ISA for all tested species, and above 6 mcg/mL for agents of mucormycosis, *F. solani,* and *L. prolificans.* POS EC50 and EC90 values were similar to ISA for most *Aspergillus* and Mucorales,but higher EC90 values were observed for *A. terreus* (3.1 mcg/mL), *Alternaria* (6.70 mcg/mL), and *F. solani* (6.76 mcg/mL). **Conclusions:** PD patterns of triazoles varying considerably when tested against agents of mucormycosis, fusariosis, phaeohyphomycosis, and scedosporiosis. While some of these differences were expected (e.g., decreased activity of VOR for Mucorales), new findings suggest ISA may be an effective alternative to VOR and POS for black moulds, *Fusarium* spp. and *S. apiospermum* at clinically-achieved drug concentrations. These findings should be confirmed in relevant animal models.

The Impact of KPC-Carbapenemase Producing *Klebsiella* pneumoniae Colonization on Infection Risk and Mortality During Chemotherapy for Hematological Malignancies

Giovanni Marco,[1] Marta Stanzani,[1] Nicola Vianelli,[1] Simone Ambretti,[2] Michele Cavo,[1] Russell Lewis[3]

[1]Seràgnoli Institute of Hematology, [2]Microbiology and [3]Infectious Diseases, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

Background: Approximately one out of every four patients with hematological malignancies who are colonized with KPC-carbapenemase producing *Klebsiella pneumoniae* (KPC-Kp) will develop a bloodstream infection (BSI) during chemotherapy. We explored how patient risk factors and KPC-Kp colonization (detected by routine rectal swab on admission to the unit) affected the risk and timing of serious KPC-KP infections including BSI. **Methods:** We prospectively studied 21 adult patients over multiple hospitalizations (n=40) where KPC-KP colonization or prior infection was present prior to scheduled chemotherapy. **Results:** Patients were receiving treatment for acute myeloid leukemia (45%); acute lymphoblastic leukemia (25%); lymphoma (17.5%) , aplastic anemia (5%), chronic lymphocytic leukemia (5%), and multiple myeloma (5%). More than one-half (52.5%) of admissions were associated with an underlying malignancy in complete or partial remission (52.5%); 25% were newly diagnosed, and 25% of patients had relapsed malignancies The most common indications for chemotherapy were consolidation treatment (32.5%); induction treatment (20%); rescue treatment (15%); allogeneic HSCT (7.5%); targeted therapy (2.5%); or other chemotherapy (2.5%). Most admissions (80%) were associated with severe neutropenia (ANC < 100 cells/mm3) during colonization; 57.5% of chemotherapy regimens were associated with high mucositis risk. Fifteen admissions in seven patients were associated with a previous history of KPC-Kp BSI. Rectal swabs for KPC-Kp were positive in 40% of admitted patients on the first day of admission, with the remaining patients becoming positive on average of 15-20 days after hospitalization. Fourteen (35%) admission episodes with KPC-Kp colonization developed an episode of breakthrough fever of which 57.5% (8 cases; 20%) were KPC-Kp BSI, and 22.5% as KPC-Kp pneumonia. Infections developed on average 11 days (± 5 days) after the first positive rectal swab and 6 days (± 4 days) after the start of chemotherapy. The overall mortality rate was 35.7%. Pre-emptive administration of KPC-active combination antibiotic regimens after the start of chemotherapy but prior to the onset of fever, or at the first onset fever, was associated with significantly lower cumulative mortality. **Conclusions:** Patients colonized with KPC-KP are at high risk for serious infections during chemotherapy. The mortality of KPC-Kp infections may be substantially reduced with either preemptive (before fever) or early empiric KPC-active combination regimens.

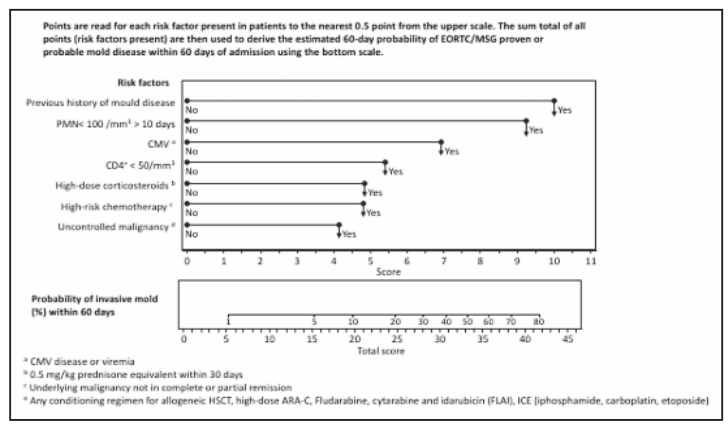


Development and Validation of a Simple Nomogram for Estimating the 60-day Probability of Developing Invasive Mould Disease During the Treatment of Hematological Malignancies

Marta Stanzani,[1] Nicola Vianelli,[1] Riccardo Ragioneri,[1] Michele Cavo,[1] Russell E. Lewis

[1]Seràgnoli Institute of Hematology, [2]Infectious Diseases, S. Orsola-Malpighi Hospital, University of Bologna, Bologna, Italy

Background: Many decisions surrounding the management of invasive mold disease (IMD) are based on the patient's estimated probability for developing the infection in the future. The multivariate and dynamic nature of risk factors for IMD make this risk estimation difficult, especially in patient populations who are often considered to be at low-risk overall (e.g., lymphoma). **Methods:** We re-calibrated a previously described risk score (BOSCORE) using data from 4,694 consecutive admissions of 2,187 patients with hematological malignancies from 2007-2017. The overall 60-day incidence of EORTC/MSG proven or probable IMD in the patient cohort was 2.8%. Seventeen candidate risk factors plus variables related to antifungal prophylaxis were analyzed stepwise by multivariate regression. The performance of the final model was internally validated using 100 bootstrapped resampling runs to evaluate model performance and bias. The final risk model was then rendered as a simple visual nomogram to facilitate bedside calculation. **Results:** Seven risk factors for invasive mold disease were retained in the final risk model: (i) underlying malignancy not in remission; (OR 1.96,1.34-2.90, P=0.001); (ii) Receipt of high-risk chemotherapy-e.g., conditioning regimen for allogeneic HSCT, high-dose ARA-C, FLAI, ICE (OR 2.20, 1.40-3.46, P=0.001); (iii) receipt of greater than 0.5 mg/kg prednisone equivalent in previous 30 days (OR 2.21, 1.37-3.57, P=0.001); (iv) CD4+ < 50 cells/mm3 (OR 2.43, 1.60-3.69, P<0.0001); (v) CMV infection (OR 3.12, 1.63-5.96, P=0.001), (vi) PMN < 100 cells/mm3 > 10 days (OR 4.56, 2.69-7.73, P<0.0001); and (vii) prior history of IMD (OR 5.17, 2.89-9.25, P<0.0001). The model was discriminative (aROC 0.85, 0.84-0.86, P<0.0001) and well calibrated with minimal bias at predicted versus observed rates of IMD ranging from 0-40%. At a 5% risk probability cut-off, the nomogram exhibited high negative predictive values (0.96-1.00) across a wide range of IMD prevalence and effectively identified high-risk subgoups of non-transplanted patients with CML, CLL, and lymphoma. **Conclusion:** Using this simple nomogram, we were able to accurately estimate the probability of developing IMD within 60 days in our institution. Individualized risk assessment may improve targeted use of diagnostics and or antifungal prophylaxis, thus improving the overall management of IMD.



Infections Following Umbilical Cord Blood Transplant: A Single Center Experience

Kathleen A. Linder, MD; **Carol A. Kauffman**, MD; **Marisa H. Miceli**, MD
University of Michigan Health System&VA Ann Arbor Healthcare System

Introduction: Umbilical cord blood (UCB)is a source of stem cells for patients who need a hematopoietic cell transplant (HCT), but who do not have a matched donor. UCB cells take longer to engraft than standard allografts, & patients (pt) may be at increased risk of infection.

Goals: To review infectious complications following UCB transplant (UCBT) at the University of Michigan Health System between 2006-2015.

Materials and methods: Charts of pt who received UCBT were reviewed to detail specifics on conditioning regimens, engraftment, infectious episodes, & mortality.

Results: 40 pt received UCBT; 21 were women, mean age was 43+13 years. Most common indications for UCBT were acute leukemia/myelodysplastic syndrome(28 pt) & lymphoma (9 pt). Pre-UCBT conditioning wasbusulfan/fludarabine in 20 pt, cytarabine/fludarabine in 17, & cytarabinealone in 3. Mean number of nucleated cells infused was 4.6 x10^7 cells/mL; 34 pt had >1 HLA mismatch. 38 pt had neutrophil engraftment at a median of 19 days (d), & 32 had platelet engraftment. Graft-versus-host disease was present in 34 pt.
A total of 132 infectious episodes occurred; 18 pt had>3 episodes. Of these 132 episodes, confirmed viral infections were present in 52%, bacteria (predominantly Gram positive organisms) 42%, & fungi only 4%. 41% of episodes occurred in the first 30d after UCBT, 29% between d 31-100, & 30% after d 100. In the first 30 d, HHV6 infection was most common (28% of episodes) & *C. difficile* infection was second most common (17%). Viral infections predominated after d 30; between d 31-100, CMV infection caused 37% & HHV6, 21% of episodes. After d 100, CMV infection & respiratory viral infections occurred in 17% & 15% of pt, respectively.
Overall mortality 2 years after UCBT was 62.5%; median time to death was 113 d (21-468 d). 12 pt died from relapsed malignancy, most often >100 d after UCBT, & 6 from GVHD. Only 6 deaths were due to infection (2 bacterial, 2 viral, 1 concurrent bacterial/viral infection, and 1 with undetermined cause). Mortality was associated with failure to engraft platelets (p=.014), having >3 infectious episodes (p=.03), & *C. difficile* infection in the first 30 days after UCBT (p=.007).

Conclusions: Infections, particularly those due to herpes viruses & *C. difficile*, were common after UCBT. Although frequent, herpes virus infections were rarely fatal. Gram-positive infections were more common than Gram-negative infections & fungal infections were uncommon.

Infection related complications during maintainance phase treatment for children with acute lymphoblastic leukemia in developing countries, single center experience, Egypt

Youssef Madney*[1], Wlaa Ahmed[1], Hader Almahalway[2], Emad Ebeid[1]
[1]Pediatric Oncology, National Cancer Institute, Cairo University, Egypt; [2]Clinical Microbiology,National Cancer Institute, Cairo University, Egypt.

Introduction: The improvement in overall survival in children with acute lymphoblastic leukemia (ALL) over the last 5 decades has been considerable, with around 90% now surviving long term. Despite the recent advances in supportive care, infection related morbidity and mortality comprise a major challenge for successful treatment. Limited number of studies were done to analyze the type and the incidence of infections encountered during different phases of treatment. Type and frequency of infection vary according to the phase of treatment.

Goal: To evaluate epidemiology and outcome of infectious complications during maintenance phase of chemotherapy.

Materials & Methods: Retrospective study for ALL pediatric patients who treated onmaintenance phase (30 month) St. Jude total XV protocol at National cancer institute, Egypt, during the period from 2011 to 2014. According to treatment phases of maintenance chemotherapy and degree of neutropenia, each febrile and infectious episodes recorded, analyzed then categorized as a bacteremia, viral, fungal, clinically documented infection or FUO. Finally, the outcomes of the infectious complications and infections related mortality-were analyzed.

Results: A total of 1052 infectious episode recorded in 146 ALL pediatric patients during maintenance chemotherapy; (42.1%) in low risk, (50.3%) in standard risk and (7.6%) in high risk group. Most of infectious episodes (39.16%) occurred during early phase of maintenance chemotherapy. FUO was the most common infectious episodes (36.8%) followed by clinically documented infections (26%), viral (17%), bacterial (16.8%) and fungal infections (3.6%). The majority of the infection episodes (53%) reported during neutropenia. Statistically significant relation between relapse and number of patients who had infections during course of maintenance therapy (P=0.046). Mortality was 15/152 (8%) during the whole course of maintenance chemotherapy. Most of deaths were infection related 12 /15 (80%).

Conclusions: The incidence of infection-related death was high. Infectious complications still a major morbidity and mortality challenge for children with Acute lymphoblastic leukemia in developing countries.

Keywords: *Acute lymphoblastic leukemia. Infectious complications. Maintenance. Total XV protocol. Childhood. Neutropenia.*

Emergence of Candida resistance among pediatric cancer patients, single center experience

Youssef Madney[1], Reham Khedr[1], Hanfy Hafiz[1], Lobna Shalby[1], Mervat Gaber[2], Khaled ELsheshtawy[4], Naglaa Adel[3], Alaa Alhaddad[1]
Children cancer hospital Egypt (CCHE) [1]Pediatric oncology; [2]Clinical microbiology; [3]Clinical pharmacology; [4]Research department

Introduction: Cancer patients are at risk for candidemia, and increasing *Candida* spp. resistance represent an emerging threat.
Aim: To identify candida resistant strains and breakthrough candida among our pediatric cancer patients.
Methods: Between 2014 and 2017, we retrospectively reviewed the medical records of patients with candidaemia in Children Cancer Hospital Egypt CCHE. Resistant candida species pattern and outcome are analyzed.Breakthrough candidaemia was defined as candidaemia if it developed during the administration of anti-fungal agents. Candida spp. were identified using the Vitek and Vitek2 systems.
Results: 175 candida isolates form 2014 till 2017 in pediatric cancer patients out of which 52 % are hematological malignancies.Non-albicans accounts for 70% of cases (C. tropicalis 30%, C parapsilosis 16 % and C. krusei 5%).
Resistance to various antifungals was seen in 37 isolates (20%). Distribution of resistance is shown in Table 1.C. parapsilosis 28/175 (16%) was the most common resistant strain. Breakthrough candidemia seen in 28 cases/ 175 (16%). 17 /28 was on micafungin, 10/17 candida parapsilosis , 6 C. tropical , 4 C. albicans and 4 C. kresui. 4/28 are resistant candida strains.
Theoverall 30 -day mortality rate was 28 % (47/165 patients). Candida attributable cause of mortality 12 cases (7%). Resistant candida wasa direct cause of mortality in 3 cases (3/175 = 2% from total & 16% (3/12) from overall 30 day mortality).

Table 1

Candida susceptibility	Fluconazole	Voriconazole	Echinocandin	Liposomal Ampho
Sensitive	148 (84%)	169 (96.5%)	172 (98%)	161 (92%)
Intermediate	5(3%)	1 (0.6%)	0	7 (4%)
Resistance	22 (13%)	5 (3%)	3 (2%)	7 (4%)

Conclusion: Resistant Candida is a major threat in high risk hematological pediatric cancer patient with high mortality rate. Therefore, clinicians should pay attention to resistance and Breakthrough Candida even patient under antifungal prophylaxis. Antifungal stewardship may be helpful.

Clinical characteristics and mortality-related factors of bloodstream infections in patients with acute leukemia: a single center experience with 152 patients

Gustavo A. Méndez*[1], Carla Niveyro*[1], Karina A. Salvatierra*[3], José L. Fernández*[1], Silvina Villamandos*[1], Pedro A Villalba Apestegui*[1], Haydee I. Bernard*[2]
*Hospital Escuela de Agudos Dr. Ramón Madariaga. Country: Argentina - Posadas, Misiones. *[1]Department of Infectious Diseases and Infection Control *[2]Department of Hematology and Stem Cell Transplantation *[3]Microbiology Division UNaM Faculty of Exact Chemical and Natural Sciences.*

Introduction: Bloodstream infection (BSI) is an important cause of morbidity and mortality in patients with acute leukemia (AL) undergoing chemotherapy or stem cell transplantation. BSI was documented in 11-30% of the febrile neutropenia (FN) episodes. The epidemiology of BSI in FN constitutes the basis for selection of empiric antibiotic therapy for febrile neutropenia.

Objectives: To establish the incidence, microbial etiology, risk factors and prognosis of BSI in patients with AL.

Materials and methods: Retrospective observational study. All patients with AL and FN (absolute neutrophil count of <500/mm^3) consecutively hospitalized between june 2010 and december 2017 were included. The package program was used for statistical analysis.

Results: In total, 365 episodes of FN (in 152 patients) were evaluated, 126 BSI were documented (34.5%), including 13 (10.3%) episodes polymicrobial bacteremia. The mean age of the patients was 34.1 17.2 years and 58% were male. Low-risk group (according MASCC Risk Index) 294 episodes (80.5%). Twenty-five (6.8%) patients died. Gram-negative bacteria (GNB) were found in 62.5%, Gram-positive bacteria (GPB) 36.6% and one patient had funguemia (*C. parapsilosis*) of the isolates. Clinically documented infections could be observed in 162 of 365 febrile episodes (44.3%). The majority of them localized in the abdomen 44 cases (enterocolitis, 12%), catheter-associated infections 39 cases (10.6%) and lung infections 36 cases (9.8%). Risk factors associated with BSI were relapse of hematological disease (*p* 0.009), hospitalization in the last 30 days (p 0.003), antibiotics in the last 30 days (*p* 0.03). In the group of BSI patients mortality was higher than in non-bacteremic patients (*p* 0.0003)

Conclusions: Bacterial epidemiology and antimicrobial resistance in these patients should be regulary monitored, which will provide guidance for local policies for the use of antimicrobial agents for empirical antibiotic therapy in FN. Mortality in BSI and FN is worse than in non-bacteriemic patients. Reducing the fatality rate of bacteremia remains a major challenge.

Role of caspofungin therapy in Candida haemulonii/auris Candidemia in immunocompromised neonates

Dr Dip Narayan Mukherjee, MD[1] **, Dr S Seal** MD[2]
Woodlands Multispecialty Hospital, Kolkata, India[1,2]

Introduction: The incidence of hematogenous infections due to Candida specially non-albicans species among immunocompromised neonates has increased significantly in recent decade. The emerging fungal pathogens comprising the Candida haemulonii complex are notable for their antifungal resistance with higher mortality and morbidity. Caspofungin is effective, safe and well-tolerated as an alternative therapy for persistent and progressive candidiasis in those neonates who are resistant, unresponsive to or intolerant of conventional antifungals.

Material and methods: We here report our experience of caspofungin therapy in four cases of neonatal fungemia caused by C haemulonii. All these neonates were pre term, low birth weight with multiple invasive devices and had history of bacterial sepsis for which were on broad spectrum antibiotics. All the isolates were recovered in BACTEC Peds plus/F culture vials. Species identification was done in VITEK 2 yeast ID system. Confirmation of the species was done by PCR based molecular methods. All of these isolates of C.haemulonii were resistant to amphotericin B and azoles but sensitive to caspofungin. Caspofungin therapy started with serial blood culture. Caspofungin therapy was continued two weeks after last negative culture. In both the cases clinical and microbiological cure were possible.

Result: Candidemia frequently complicates the clinical course of hospitalized preterm immunocompromised neonates, especially those who have some underlying disease or congenital malformation. The mortality rate due to sepsis by Candida species is high. *Candida haemulonii*, one of the non-albicans *Candida* species, is an emerging yeast pathogen that is known to be resistant to amphotericin B and other antifungal agents such as azoles. Conventional anti-fungal agents have often been associated with clinical treatment failure, so no treatment regimen has been clearly established for invasive *C. haemulonii* infections in those neonates. An echinocandin such as caspofungin may be an appropriate empirical choice of antifungal agent for an invasive *C. haemulonii* infection in neonates.

Goals/ Conclusion: The resistance of C. haemulonii represents a therapeutic challenge in the treatment of invasive candidiasis in immunocompromised neonatal patients. Caspofungin therapy is well tolerated , safe and effective in these resistant fungal infections. These promising results suggest a potential role for caspofungin as an additional first-line treatment of systemic resistant candidiasis in immunocompromised neonates. This drug should be further investigated in this special patient population group.

Intravenous fosfomycin therapy in critically ill cancer patients infected with colistin resistant enterobacteriacae

Dr Dip Narayan Mukherjee, MD[1] **, Dr S Seal** MD[2]
Woodlands Multispecialty Hospital, Kolkata, India[1,2]

Introduction: Carbapenem resistant enterobacteriacae (CRE) emerged in recent years as one of the most challenging group of antibiotic resistant pathogens. Patients with malignancy are more prone to develop nosocomial sepsis by resistant bacteria because of their immunocompromised status. Polymyxins are considered as the last resort for the treatment of infections with carbapenem resistant gram negative bacilli (GNB). Inadequate or extensive use of colistin leads to emergence of colistin resistance, increasing mortality and morbidity and necessitating prudent use of alternative antibiotics. Fosfomycin is a broad spectrum antibiotic showing promising result against multi drug resistant (MDR) /Pan Drug Resistant (PDR) pathogens.

Material and methods: A total of twenty six colistin resistant (MIC>=4) GNB were isolated from ICU patients with nosocomial MDR infections during a period of two years. All of these patients had multiple co-morbidities including malignancy and recent history of colistin exposure. All isolates were *Klebsiella pneumonia.* Among these patients twelve had blood stream infection (BSI) and fourteen had ventilator associated pneumonia (VAP). All the isolates were sensitive to fosfomycin in vitro. Intravenous fosfomycin was given as a combination therapy.

Result: Both clinical and microbiological cure seen in ten VAP patients with fosfomycin therapy with a success rate of 70%. Among twelve BSI patients eight cured completely with a success rate of 66%. Overall clinical response of IV fosfomycin as a combination therapy against MDR/PDR infection is satisfacory. Average duration of antibiotic therapy in all these cases was ten days. Hypernatremia developed in one patient during antibiotic therapy probably as a consequence of sodium content of the antibiotic.

Goals/Conclusion: Based on the evidence of clinical experience and available studies, intravenous fosfomycin therapy may be considered as the last option for the treatment of MDR GNB infection in cancer patients where there is documented colistin resistance and where there is literally no other choice of antibiotic therapy. The success of the therapy is encouraging in selected group of patients. Further research on intravenous fosfomycin use specially against MDR pathogens and on the effectiveness and safety of the drug in the treatment of patients with such infections may be warranted.

Descriptive analysis of blood stream infections (BSI) caused by *Candida spp* in a center of reference in pediatric oncology

Silva, AMPS[1]; Teixeira, BB[1]; Pignati, LT[1]; Marques, LMA[2]; Germano, PPC[2]; Petrilli, AS[1,2]; de Moraes-Pinto, MI[1]; Caslesse, F[1,2]

[1]Federal University of Sao Paulo, Brazil; [2]PediatricOncologyInstitute – Grupo de Apoio ao Adolescente e a Criança com Câncer/Federal University of Sao Paulo, Brazil

Introduction: Invasive Fungal Disease (IFD) is an important cause of morbidity and mortality in hospitalized and immunosuppressed children, with blood stream infection (BSI) by *Candida spp* the most prevalent infection.The recognition of patients at risk for invasive cadidemia is paramount, since this infection does not have specific clinical signs and symptoms and the delay in diagnosis and therapy has an impact on the prognosis. **Goals:** To characterize the BSI caused by *Candida spp* in a reference center in pediatric oncology.
Materials and Methods: A retrospective cohort study was carried out through the evaluation of data from medical records of pediatric patients, aged 0 to 18 years old, followed at the Institute of Pediatric Oncology, São Paulo, Brazil, who presented at least one positive blood culture for *Candida spp* and clinical signs of sepsis from January 2004 to December 2016.
Results: 64 episodes of candidemia were analyzed, with an incidence of 1.6 episodes/1000 patient-year. The median age was 4.1 years (0.1-17.9), with a predominance of males (59.4% - 38/64) and solid tumors (54.7% - 35/64). Among the associated factors to BSI by *Candida spp*, presence of central venous catheter (CVC) (90.6% - 58/64), previous use of antibiotic (84.4% - 54/64) and chemotherapy (75.0% - 48/64) were highlighted. The most common Candida species were *C. albicans* (32.8% - 21/64), *C. parapsilosis* (29.7% - 19/64) and *C. tropicalis* (20.3% - 13/64).BSI by *C. tropicalis* was more associated with neutropenia when compared to the other species ($p = 0.010$). Presence of CVC ($p = 0.045$) and previous use of chemotherapy ($p = 0.009$) were more associated with BSI by C. albicans. Mechanical ventilation was more associated with BSI by Candida non albicans compared to *C. albicans* ($p = 0.050$). Almost all patients had fever (96.9% - 62/64) and patients with *C. tropicalis* had more skin lesions ($p = 0.019$). The majority used polyenes as the first therapeutic option (78.1% - 50/64) and in 23/64 episodes (24.5%) antifungal replacementwas needed. Therapeutic success was achieved in 42/64 episodes (65.6%), with advanced age ($p = 0.015$) and thrombocytopenia ($p = 0.037$) related to therapeutic failure. Death in 30 days was 23.4% (15/64). Predictive factors of death were advanced age ($p = 0.025$), intensive care unit (ICU) admission ($p = 0.002$) and *C. albicans* infection, compared to *C. parapsilosis* ($p = 0.027$).
Conclusion: There was a high incidence of candidemia in the service, with *C. tropicalis* more related to neutropenia and evolution to skin lesions when compared to other species. Death rate was significant, with advanced age, ICU admission and BSI by *C. albicans* associated with a worse prognosis.

Fungal Infection in Patients who died on Renal Replacement Therapy in Australia: A review of the ANZDATA registry

Parry, Louise[1], Jose, Matthew[1,2,3], Cooley, Louise[1,2]

[1]Royal Hobart Hospital, Tasmania, Australia; [2]School of Medicine, University of Tasmania, Australia; [3]Australia and New Zealand Dialysis and Transplant Registry (ANZDATA)

Introduction: Despite infection being a significant complication of renal replacement therapy (RRT), the epidemiology of fungal infections in this population are a poorly defined. The Australia and New Zealand Dialysis and Transplant Registry (ANZDATA) was established in 1977 to prospectively collect information on the practicepatterns and outcomes of dialysis and kidney transplantation.

Goals: This registry was interrogated with the aim of describing the epidemiology of deaths due to fungal infection in the Australian context.

Methods: The ANZDATA registry was searched for all deaths attributable to infection, using the following criteria (age, sex, ethnicity, state of residence, date of death, mode of RRT at death, organism identified, site of infection and comorbid diabetes, cancer and lung disease) between 1st of January 2000 and the 31st of December 2015. Death due to fungal infection was defined death when a fungus was the primary organism. Data was analysed using Stata 15. Ethics approval was obtained from THREC (H0016339)

Results: During the 16-year study period 2833 patients were recorded as dying from infection, and 238 were attributed to fungal infection. Twenty-six patients were excluded,due to incorrect organism coding, no organism entered or return of native renal function, leaving 212 (8.4% of deaths from infection). Comparing the fungal and non-fungal infective deaths, renal transplantation was a significant risk factor ($p<0.001$), and peritoneal and central nervous system site of infection were more common in the fungal infection cohort ($p<0.001$). Death due to fungal infection was most frequently attributed to *Candida, Aspergillus* and *Pneumocystis*. There were significant differences in risk of fungal infections with respect to type of RRT, including age, the presence of diabetes mellitus or malignancy, site of infection and specific pathogen(all $p<0.01$). Aboriginal or Torres Strait Islander status was over represented in deaths due to filamentous fungi and Cryptococcus.

Conclusion: Deaths due to fungal infection are more common in transplant patients when compared to deaths due to other forms of infection, and more work to identify risk factors and targets of preventative strategies is required to decrease mortality in this group.

Breakthrough invasive fungal infections (bIFI) in adult patients with leukemia receiving isavuconazole (ISA): analysis of 100 consecutive patient courses

Caitlin R. Rausch, PharmD[1]**; Adam J. DiPippo,** PharmD[1]**; Dimitrios P.Kontoyiannis*,** MD[2]
[1]Division of Pharmacy [2]Department of Infectious Diseases, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Introduction: ISA is a new broad spectrum triazole antifungal for the treatment of IFIs. As the drug has both oral and intravenous formulations, the ability to be administered once-daily, a favorable pharmacokinetic profile, and good tolerability, it is being increasingly used. ISA may be considered as prophylaxis, combination, or salvage therapy for treatment for a variety of IFIs. Limited data exists on the incidence and pattern of bIFI in leukemia patients receiving ISA. **Goal:** To identify the frequency and type of bIFI in leukemia patients receiving ISA for either prophylaxis or treatment. **Materials & Methods:** We retrospectively reviewed the records of all adult patients with leukemia who received >7 days of 200 mg ofISA (intravenous or oral) or > 5 days of 200 mg of ISA following a loading dose (200 mg every 8 hours for 48 hours) while hospitalized between March 2015 and March 2017. bIFI was defined according to EORTC/MSG criteria. Patients receiving combination antifungal therapy with ISA were excluded. **Results:** One-hundred consecutive patients received ISAfor treatment of suspected IFI (57%) or as primary (27%) or secondary prophylaxis (16%).70% of patients had acute myeloid leukemia, 10% had acute lymphoblastic leukemia, and the remaining 20% had either chronic leukemia or another high-risk bone marrow disorder. Within 90 days of starting ISA, all but 1 patient was actively receiving chemotherapy. Chemotherapy was treating relapsed/refractory disease in 72% of patients. At the time of ISA initiation, 70% of patients had been neutropenic (ANC < 500 cells/mm^3) for at least 7 days.

Thirteen (13%) patients had bIFI (11 definite, 2 probable). The most common proven bIFI was fungemia due to *C. glabrata* (n=2), and 1 each of *C. parapsillosis, C. guilliermondii,* and *Trichosporonasahii*. The remaining proven bIFI included1 *C. albicans* esophagitis, 2 disseminated infections, (1 each due to *Rhizopus spp*. and *C. krusei*) and 2 pneumonias (1 each due to *Mucorales spp.,* 1 *Penicillium spp.*). Lastly, 1 patient had both *Rhizopus spp.* pneumonia and *C. glabrata* fungemia.

Probable bIFIs included 1 pneumonia due to 1 *Rhizomucor spp.* and 1 disseminated infection due to unidentified *Aspergillus spp.* An additional 7 patients had presumed breakthrough fungal pneumonia while receiving ISA.

All but 1 patient with bIFIhad relapsed/refractory disease, and 70% of patients were neutropenic at the time of bIFI.

Conclusion: 13% of leukemia patients developed documented bIFI while receiving ISA, typically fungemia due to *Candida spp.*, in addition to pneumonia and disseminated infections, mainly due to Mucorales. These bIFIs were observed in the setting of profound neutropenia and active leukemia.

Probable donor-derived BK polyomavirus-associated nephropathy in two recipients with kidneys from the same donor

Lorentzen EM[1,2], Kro GBK[3,4], Henriksen S[1,2], Hammarström CL[5], Midtvedt K[6], Rinaldo CH[1,2]
[1]University Hospital of North Norway, Department of Microbiology and Infection Control, Tromsø, Norway; [2]UiT The Arctic University of Norway, Department of Clinical Medicine, Tromsø, Norway; [3]Oslo University Hospital, Rikshospitalet, Department of Microbiology, Oslo, Norway; [4]University of Oslo, Institute of Clinical Medicine, Oslo Norway; [5]Oslo University Hospital, Rikshospitalet, Department of Pathology, Oslo, Norway; [6]Oslo University Hospital, Rikshospitalet, Department of Transplantation, Medicine, Section of Nephrology, Oslo, Norway.

Introduction: BKPolyomavirus (BKPyV) re-activation andinfection causes polyomavirus-associated nephropathy (PyVAN) in 2-7% of kidney transplant recipients. There is limited data on donor-derivedinfection leading to PYVAN. We present a case where two kidney transplant recipients (KTx) receiving organs from the same deceased donor (DD) simultaneously developed PyVAN earlypost-engraftment. **Goals:** To investigate if PyVAN was caused by donor-derived infection. **Material & methods:** Two KTx received kidneys from the same DD. Both received standard immunosuppressive protocol;i.v. basiliximab induction, low dose steroids and tacrolimus (trough levels3-7 ng/ml from engraftment), MMF 750 mg bid. Recipient #1: 62 years, APKD, HLA-mismatch 3-1, CMV D+/R+, protocol biopsy at 8 weeks post-tx i0t0v0 C4d neg. Recipient #2: 68 years, Wegener, HLA-mismatch 2-1, CMV D+/R+. Immunohistochemistry, BKPyV quantitative PCR, BKPyV PCR, Sanger DNA sequencing and hemagglutination inhibition test (HAI). **Results:** When plasma was first time analyzed for BKPyV DNA at 8 or 5 weeks post-tx, 8x10^4 and 8x10^3 Geq/ml was found in recipient #1 and 2, respectively. At 10 weeks post-tx,increased s-creatinineand increased levels of BKPyV DNA in plasma was detected inboth recipients, leading to a graft biopsy. Immunostaining of the biopsies revealed LT-ag positive epithelial cells, giving the diagnosis PyVAN (recipient # 1: s-creat 80-134, biopsy: i2t3v0, C4d neg.; recipient #2: s-creatinine 100-148, biopsy: i0t1v0, C4d neg.). In both recipients, BKPyV in plasma and urine was of archetype strain belonging to the genotype Ib-2. For treatmentMMF was reduced from 750 to 250 bid, tacrolimus trough levels remained low. About 5.5 months post-tx recipient#1 cleared the virus ands-creatininewas stable at 151. Recipient #2 still has viremia (>8 months post-tx) but stable s-creatinine at 117. Retrospectively, no BKPyV DNA could be detected in plasma taken from the donorat tx and LTag immunostaining of the baseline biopsy was negative. HAI revealed that the donor and both recipients were BKPyV seropositive before tx. Increased antibody titers were observed from 8 or 12 weeks post-tx, respectively. **Conclusion:** The finding that the donor was BKPyV IgG seropositive together with the rapid simultaneous onset of PyVAN in the two recipients suggest a donor-derived infection. Detection of BKPyV of the same genotype and strain in both recipients support this. Currently, presence of BKPyV IgG or DNA is not investigated in donors pre-tx.The best strategy is frequenttesting of recipients for BKPyV replication followed by reduction of immunosuppression when PyVAN is diagnosed.

Predictive value and outcomes of positive human Cytomegalovirus PCR on skin and mucous membrane swabs

Carly Hughes[1], Stephanie Spring[1], Ravindi Radalage[3], Maryza Graham[1,2], Claire Dendle[1,2], Benjamin Rogers[1,2]

[1]Monash Infectious Diseases, Monash Medical Centre, Monash Health, Melbourne, Victoria, Australia 3168; [2]Monash University, Centre for Inflammatory Diseases, Melbourne, Victoria, Australia, 3168; [3]Monash University, School of Clinical Sciences at Monash Health, 3168

Introduction: Human cytomegalovirus (CMV) infection is common and presents a particular problem in immunocompromised patients. With the widespread use of multiplex PCR assays for Herpesviruses, the significance of a positive PCR result for CMV on a skin or mucous membrane swab is unclear. **Goals:** Our aim was to perform a retrospective review of patients with a positive PCR results for CMV (CMV-pos) on mucous membrane and external skin swabs to define the potential clinical implications of this test.
Materials and Methods: All CMV-pos PCR results on skin and mucous membrane swabs were extracted from the laboratory information system. A retrospective review of indication for the test, further CMV diagnostic tests performed, diagnosis of CMV disease and antiviral medication use was determined. Release of the CMV-pos result to the requestor was at the discretion of the clinical microbiologist. The implications of the CMV-pos result on the diagnosis and/or management of active CMV disease was categorised into three groups. It was **Clinically Relevant** if the release of the HMPCR swab result led to a diagnosis of CMV disease which was not otherwise suspected, OR if CMV disease was diagnosed after the suppression of an HMPCR result (i.e the release of the result may have expedited the diagnosis of CMV disease). It was **Not Contributory** if the patient had a pre-existing diagnosis of active CMV disease beforePCR was collected OR if other CMV tests, that yielded the diagnosis, were requested before the result was available. It was **Potentially Detrimental** if the result led to excess investigation, length of stay or unrequired treatment (antiviral therapy)on the basis of the swab result where CMV was not otherwise suspected AND a diagnosis of CMV disease was not made.
Results: Of 4626 samples collected for Herpes multiplex PCR, 158 (3.4%) were positive for CMV from 139 patients. 84 patients (60.4%) were immunocompromised hosts. 60 (39%) results were visible to the requestor, and 98 (61%) were suppressed. In total 9/158 (5.7%) CMV-pos results were **clinically relevant,** in 7/139 (5%) patients. Two of these CMV-pos results were missed opportunities, as the initial result was hidden from the requesting clinician and both were later diagnosed with CMV disease. 10/158 (6.3%) CMV-pos were **non-contributory**, in patients in whom CMV disease was already known or suspected. Six CMV-pos results visible to requesting doctor (10%) were **potentially detrimental** as patients had further CMV PCR performed on blood samples without a diagnosis of CMV disease. No patient received inappropriate empiric therapy.

Pharmacodynamic and immunomodulatory effects of micafungin on host responses against biofilms of *Candida parapsilosis* in comparison to those of *Candida albicans*

Maria Simitsopoulou[1], Katerina Chlichlia[2], Daniela Kyrpitzi[1], Thomas J. Walsh[3], Emmanuel Roilides[1]

[1]3rd Department of Pediatrics, Aristotle University School of Medicine, Thessaloniki; [2]Department of Molecular Biology & Genetics, Democritus University of Thrace, Alexandroupolis, Greece; [3]Cornell University, New York, NY

Introduction: *Candida albicans* (CA) and *Candida parapsilosis* (CP)are the most fruquent fungi causingbiofilm-related infections. Little is known about the immunopharmacological benefit micafungin (MFG) may exert on the antibiofilm activity of phagocytic cells following exposure to CA or CP biofilms.
Goals: To investigate if pre-exposure of CA and CP to sub-MIC MFG concentrations could a) augment the efficacy of human neutrophils (PMN) and b) regulate the immune response of human monocytes (THP-1) exposed to CA or CPmature biofilms.
Materials & Methods: 10^6blastoconidia/mL of CA and CP BF strains were grown for 24h with sub-MIC MFG concentrations. MFG-pretreated and untreated isolates were subsequently grown 48h-72h to produce biofilms.PMN were isolated from healthy donors. Biofilms were incubated with PMN at 5:1 effector:target for 24h. In separate experiments, CABF or CPBF were co-incubated with 10^6THP-1/mLand MFG at 0.06, 1 or 4mg/L, at 37ºC/5% CO_2 for 4h. TLR2, TLR4, TLR6,and NLRP3 were detected by RT-PCR and quantified byTotalLabQuant. The released cytokines were detected by multiplex ELISA and analyzed by Q-View. The PMN-induced BF damage was assessed by XTT assay.Statistical analyses were performed by ANOVA (n=3-4; $P<0.05$).
Results: MFG MIC for CABF and CPBF were 0.25mg/L and 4mg/L. PMN added to MFG-pretreated CABF at 0.5xMIC caused more damage than PMN against intact CABF (81%±1.8vs. 60%±3.5;$P<0.01$). In contrast, PMN exerted similar damage to drug-pretreated CPBF and tointactCPBF. Exposure of THP-1 to CPBF caused 2-to 3-fold greater expression of TLR2 and TLR4 than CABF, while the two organisms induced similar up-regulation of NLRP3 inflammasome. Co-incubation of CABF with MFG at 0.06, 1 and 4mg/L increased IL-1β levels compared to untreated controls ($P<0.05$). Although similar levels of TNF-α were released by THP-1 exposed to CABF under all conditions, increased IL-8 and decreased IL-23 levels were induced by 0.06 and 1mg/L of MFG compared to untreated controls ($P<0.05$). Incubation of CPBF with 0.06mg/L of MFG caused higher release of IL-8 from THP-1 than untreated CPBF (7914±511vs. 5664±223pg/mL; $P<0.05$); similar amounts of IL-1β, IL-23 and TNF-α were observed under all conditions.
Conclusions: Sub-MIC MFG concentrations increase antifungal activity of PMN against CA but not CPbiofilms. MFG exerts differential immunomodulatory effects on THP-1 exposed to the twospecies.CPBF increasesIL-8-induced immune cell recruitment, but it displays an immunosuppressive potential by limiting the production of TNF-α; this response may constitute an immune-evasion mechanism permitting prolongation of BF with serious clinical complications.

Cryptococcal infection in lung transplant recipients: a five-year retrospective review at an Australian transplant centre

Asma Sohail[1], Olivia Smibert[2], Greg Snell[4], Miranda Paraskeva[4], Adam Jenney[1,3]
[1]Department of Infectious Diseases, The Alfred Hospital, Melbourne, Australia; [2]Department of Infectious Diseases, Peter MacCallum Cancer Centre, Melbourne, Australia; [3]Department of Microbiology, The Alfred Hospital, Melbourne, Australia; [4]Department of Allergy, Immunology and Respiratory Medicine, The Alfred Hospital, Melbourne, Australia

Introduction: Cryptococcosis is a common invasive fungal infection in solid organ transplant (SOT) recipients and is associated with a significant risk of dissemination and mortality. Infection is limited to the lungs in 6-33% of SOT recipients, whereas central nervous system (CNS) disease and fungaemia occurs in 52-61% and 20-25%, respectively. Infection typically occurs later in the post-transplant period, although early post-transplant infection has been described (< 30 days post-transplant). Lung transplant recipients have one of the highest risks of cryptococcosis due to exposure of the allograft to the external environment and high levels of immunosuppression. However, limited data exists regarding the spectrum of disease, treatment and outcomes in this group of patients.
Goals: We aimed to describe the epidemiologic and clinical characteristics, time to diagnosis, risk factor profiles, treatment, and outcomes of cryptococcosis in a cohort of lung transplant recipients at a single tertiary center.
Materials and Methods: We undertook a retrospective, observational study of *Cryptococcus* infection in lung transplant recipients at The Alfred Hospital in Melbourne, Australia, from April 1 2012 to March 31 2017. All potential cases of *Cryptococcus* infection were identified from the Alfred Health Cerner Clinical System. Demographic data, comorbidities, clinical findings, investigation results, treatment and outcome data were collected from electronic medical records.
Results: Eleven patients were identified during the study period; of these 7 (64%) were male and 4 (36%) female. The median overall age was 54.7 years (range 34 – 69 years). Nine patients (82%) were diagnosed with isolated pulmonary *Cryptococcus* disease and two patients (18%) with disseminated disease; 1 with pulmonary and CNS disease, and 1 with CNS disease only. Diagnosis of *Cryptococcus* infection occurred at a median of 233 days (range 1-3650 days). 64% of patients did not have any symptoms and their infection was detected by incidental positive *Cryptococcus* culture of post-transplant surveillance respiratory specimens.Risk factors included soil exposure such as gardening and/or lawn mowing (45%); presence of eucalypt/gum trees at home or work (27%), chopping or pruning tree branches or burning wood (45%), and hiking and camping in bushland (9%). No patients reported any close contact with pigeons. Only 2 patients (22%) with pulmonary disease had a positive serum cryptococcal antigen test, compared to all patients with disseminated disease. Fluconazole therapy was the mainstay of treatment in those with pulmonary cryptococcosis (8 patients; 89%). At the time of writing, six patients (67%) had completed treatment, having received a mean duration of 6.5 months of therapy (range 5.5-11 months).

Sirolimus induced alveolar proteinosis in a heart transplant recipient: Case report

Monireh Kamali, Majid Marjani, Afshin Moniri, Mihan Pourabdollah, Behrooz Farzanegan, Payam Tabarsi
Clinical TB and epidemiology Research Center,NRITLD,ShahidBeheshti university of medical Sciences,Tehran,Iran

Introduction: Sirolimus has known pulmonary manifestation such as interstitial pneumonia, diffuse alveolar hemorrhage and organizing pneumonia. Here we report rare case of alveolar proteinosis in a heart transplant recipients.
Case presentation: A 25 years old man, known case of heart transplant due to dilated cardiomyopathy since 2 years ago was admitted with dyspnea.1 year after transplantation he was admitted due to anemia and was diagnosed as Parvovirus B19 viremia and was treated by IVIG.
Parvovirus B19 viremia was repeated and second course of IVIG was transfused. Immunosuppressive treatment of patient was changed to sirolimus.
One month before admission, patient had dyspnea which gradually deteriorated. He had also fever and productive cough. On physical examination he was tachypnic and O2 saturation without oxygen was 80%.on CT-ScanMixed pattern of alveolo interstitial infiltrations was seen. Blood cultures were negative. Nasopharyngeal swab for Influenza A and B was negative.PCR of blood for CMV, EBV, HHV6, HHV8, and HSV was negative but PCR was positive for Parvovirus B19. Broad spectrum antibiotics and oseltamivir was started without significant improvement.
Bronchoscopy was performed. White mucoid secretion was seen bilaterally. Smear and culture of BAL was negative for bacteria, Mycobacterium and fungi.PCR of BAL was negative for Influenza,CMV,EBV AND HSV.On cytology casts of pink granular material suggestive of pulmonary Alveolar Proteinosis (PAP) was seen.
Sirolimus was discontinued and Tacrolimus was started. Whole lung lavage was performed and white milky material was extracted. Patient gradually improved and discharged without oxygen supplement.
Conclusion: Sirolimus induced PAP has been reported rarely. It must be considered as differential diagnosis of patients with pulmonary manifestation.

Screening for diabetes mellitus in HIV patients in a referral center in Iran

Parvaneh Baghaei, Majid Marjani, Afshin Moniri, Payam Tabarsi MD[1]
[1]*Clinical Tuberculosis and Epidemiology Research Center, National Research Institute of Tuberculosis and Lung Diseases (NRITLD), ShahidBeheshti University of Medical Sciences, Tehran, Iran.*

Background: The prevalence of diabetes mellitus (DM) along tuberculosis (TB) has increased in HIV people. There is limited information about screening for DM in HIV patients. The aims of this study were to screen HIV people with and without TB for DM, and the number needed screen (NNS)to diagnose new cases of DM.

Method: A prospective cohort descriptive study was conductedin Iranian adults HIV admitted to the National Research Institute of Tuberculosis and Lung Disease from 2015 to 2016 with and without TB. Sputum smear was utilized for TB diagnosing, as well as glycatedhemoglobin (HbA1c) and fasting blood glucose (FBG) were measured for these patients.

Result: Of the 101 patients included, 61 (60.4%) had TB and 28 (27.7%) had DM. DM was newly diagnosed in 12 (57%) and 9 (43%) in patients with and without TB respectively.The number needed to screen was 4 to identify one new DM case. After adjustment for TB, age≥40, and gender, only age≥40 was statistically associated with DM (adjusted OR 2.44, 95% CI 1-6.01).Sensitivity of HbA1c and FBG were 71% and 29% respectively.

Conclusion: In HIV people, screening for DM should be performed with an HbA1c test without considering toexist TB or not.

Key words: Glycatedhemoglobin (HbA1c), fasting blood glucose (FBG), screening, tuberculosis (TB), diabetes mellitus (DM), human immunodeficiency virus (HIV)

Declaration of interest: The authors have no competing interests to declare. I have received a fund for this study. This study has been supported by NIMAD.

Safety and efficacy of penicillin allergy skin testing in immunocompromised hosts at a comprehensive cancer center

Mahnaz Taremi[1], MD, MPH, **Annette Artau**[1], MD, **Farnaz Foolad**[1] PharmD, **Sheila Berlin**[1], ACNS-BC, **Candice White**[1], PA-C, **Hanine El Haddad**[1], MD, **Victor Mulanovich**[1], MD, **Issam Raad**[1], MD, **Javier Adachi**[1], MD
[1]*The UT MD Anderson Cancer Center, Houston, Texas, USA*

Background: Patients with reported penicillin (PCN) allergies often receive alternative antibiotic therapy, associated with significant health and economic disadvantages. The use of penicillin skin testing (PST) to rule out PCN allergies is safe and effective in immunocompetent patients, however there is limited data in immunocompromised patients.

Materials/methods: A quality improvement process using PST to clarify PCN allergies and guide antibiotic therapy was implemented at a comprehensive cancer center (April - October 2017). Patients admitted to Leukemia and Genitourinary Medical Oncology (GUMO) services with a history of Type 1 reactions to PCN were eligible.

Results: A total of 218 consecutive patients with reported PCN allergies were screened; 100 patients met inclusion criteria, were consented, and underwent PST (67 Leukemia, 33 GUMO). 61% tested patients reported cutaneous reactions, and 79% reported reactions > 20 years ago. The most common reported allergy was to penicillin V/G (64%). Notably, 48% were on steroids and 49% were on immunosuppresive therapy at the time of PST. For leukemia patients, the median absolute neutrophil count was 0.78 (0 - 64.88 k/µL) and absolute lymphocyte count was 0.81 (0 -116.71 K/ µL). 95% patients tested negative for PST and only 4% tested positive (3 Leukemia and 1 GUMO patients).
One test was indeterminate (negative histamine control). After PST, 24 of 47 (51%) patients receiving antibiotic therapy were changed to PCN-based antibiotics (PBA). During the follow-up period (up to 6 months), 47 patients who tested negative were readmitted at least once (total 101 readmissions) and PBAs were prescribed in 32 of those readmissions (22 patients). The most common indications for PBAs included neutropenic fever, pneumonia, and bacteremia. No patients given PBAs after PST experienced allergic reactions during therapy.

Conclusions: PST is safe and effective to rule out PCN allergies in immunocompromised patients, with 95% of patients testing negative for PCN allergy, suggesting that patient-reported allergy is unreliable. The rate of negative tests is comparable to data in immunocompetent patients. The use of PST in immunocompromised cancer patients allows for optimization of antimicrobial therapy and stewardship, which is vital in this patient population at heightened risk for infections.

Keywords: Penicillin skin testing, Immunocompromised, Penicillin allergy

High Shear Forces Increase *Rhizopus* Virulence

Alexander M. Tatara,[1] Ph.D.; **Nathaniel D. Albert,**[2] M.S.; **Dimitrios P. Kontoyiannis,**[2] M.D., D.Sc.
[1]Rice University, USA; [2]MD Anderson Cancer Center, USA.

Introduction: It has been observed in both civilian and military populations that high energy events, such as tornados and blast injuries, have been associated with mucormycosis in otherwise immunocompetent patients. However, the effects of high shear force directly on fungal biology have not been explored.

Goals: The goal of this work is to elucidate the relationship between fungal mechanobiology and virulence. To accomplish this, *R. oryzae* was exposed to high shear stress. Subsequent changes in virulence were measured in a validated fly model. Lastly, spores were simultaneously exposed to high shear forces and calcineurin inhibitors to determine if this classical stress pathway was involved in changes in virulence in response to shear force.

Materials and Methods: 10^4 or 10^7 spores/mL of R. oryzae in 100 mL saline were either: 1) grown in static culture (CNTRL); 2) subjected to stirring at 1100 RPMs for 30-45 minutes (Tornadic Physical Shear Challenge, TPSC), or 3) subjected to TPSC in the presence of the calcineurin inhibitor tacrolimus (TPSCS + TAC). Wild type flies were subsequently infected via dorsal thorax inoculation and monitored for survival over 7 days (n=26 per group; performed in triplicate).

Results: Flies inoculated with *R. oryzae* exposed to high shear stress experienced significantly greater mortality compared to spores grown under static conditions ($p<0.0001$). Co-culture of spores grown under TPSC with tacrolimus (1 mg/mL) resulted in increased fly survival ($p<0.0001$). In fact, there was no significant difference between flies inoculated with spores subjected to high shear and TAC and spores grown under static conditions ($p=0.934$). Fungal exposure to high shear stress increases virulence. As calcineurin inhibition completely mitigated the effect of shear stress on Mucorales virulence, activation of the calcineurin stress response might be important.

Treatment of Cutaneous Aspergillosis With Voriconazole-loaded Poly (Diol Fumarate) Microparticles

Alexander M. Tatara,[1] Ph.D.; **Nathaniel D. Albert,**[2] M.S.; **Emma Watson,**[1] B.S.; **Antonios G. Mikos,**[1] Ph.D.; **Dimitrios P. Kontoyiannis,**[2] M.D., D.Sc.
[1]Rice University, USA; [2]MD Anderson Cancer Center.

Introduction: Local delivery of antifungals may allow for high concentrations of therapeutic directly to wound beds infected with invasive fungi. In this work, microparticles (MPs) fabricated from a novel biodegradable polymer synthesized from 1,10-decanediol (DD) and fumaric acid for the delivery of voriconazole (VRC) in a murine model of cutaneous aspergillosis. The MPs are capable of delivering VRC while also degrading into byproducts which themselves have activity on fungal viability and host wound healing.

Goals: The goal of this work is to determine the effects of DD-based MPs on treatment of cutaneous aspergillosis.

Materials and Methods: The *in vitro* release kinetics of VRC-loaded MPs were measured over 6 days in PBS at 37°C under mild agitation. Immunocompromised BALB/c mice with 5 mm full thickness cutaneous defects infected with *A. fumigatus* were treated with: Group 1) no infection, no treatment; Group 2) no treatment; Group 3) unloaded blank MPs; and Group 4) VRC-loaded MPs (n=10 per group). Six days after treatment (nine days after initial infection), mice were euthanized. Wound bed size, fungal wound bed CFU, and histological presence of fungi were evaluated to determine the effects of MPs on wound healing and infection.

Results: MPs were capable of releasing VRC at concentrations above *A. fumigatus* MIC for at least six days. Mice treated with VRC-loaded MPs had significantly decreased wound size than mice with no treatment (64.2% vs 19.4% wound reduction, $p=0.002$) and were not significantly different than uninfected controls (64.2% vs 58.1%, $p=0.497$). Although wound healing was increased with VRC-loaded MPs, total fungal burden was not significantly different between infected groups. Diol-based MPs are capable of local delivery of VRC to treat infected wound beds in an immunocompromised murine model of cutaneous aspergillosis. VRC-loaded MPs restored normal wound healing. As fungal burden was unchanged, the exact mechanism of enhanced wound healing needs to be further explored.

Cryptococcal infections in patients with cancer: A multi-centre case series

Olivia C. Smibert[1], Jason A. Trubiano[1,2,3], Karen Urbancic[2,3], Kyra Chua[2], Monica A. Slavin[1,3,4], Sharon C. Chen[3,5], Benjamin W. Teh[1,3,4]

[1]Department of Infectious Diseases, Peter MacCallum Cancer Centre, Parkville, VIC, Australia; [2]Department of Infectious Diseases, Austin Health, Heidelberg, VIC, Australia; [3]National Centre for Infections in Cancer, Parkville, VIC, Australia; [4]Sir Peter MacCallum Department of Oncology, University of Melbourne, Parkville, VIC, Australia; [5]Centre for Infectious Diseases and Microbiology Laboratory Services, ICPMR, Westmead Hospital and the University of Sydney, Sydney, NSW, Australia.

Introduction: Infections due to cryptococci occur globally and in a wide variety of hosts. Historically, patients have been analysed dichotomously as either those with HIV or those without HIV, however there is increasing appreciation for the differences in presentation and outcomes in subgroups including patients with cancer.

Goals: We sought to characterise the epidemiology of cryptococcal disease in cancer patients acrossthree tertiary referral cancer centres inAustralia. **Materials & methods:** All patients with either haematological or solid organ malignancy, diagnosed with a cryptococcal infection at the Peter MacCacllum Cancer Centre, Austin and Westmead Hospitalsbetween January 1st2011-December 31st2017 were reviewed. A standardised data collection tool was used to capture date retrospectively from electronic and hardcopy medical records. Baseline variables including patient demographics, primary tumour type, site and therapy were collected. Cryptococcal disease variables including site of disease, microbiological tests, antifungal therapy and outcomes at day 14, 30 and 60 were collected. Continuous variables were expressed as median (range) and categorical variables as frequency (percentage).

Results: For the study period, 16 patients with cryptococcal infection were identified. The median age of patients was 60 years (range 27-83) and 81.2% were male. Half (8/16) of patients reside in regional areas and all were HIV negative. Nine patients had a haematological malignancy, 4 had a solid malignancy and 3 patients had both a haematological and solid malignancy diagnosis. Six patients (37.5%) had a diagnosis of chronic lymphocytic leukaemia (CLL) and 11 were receiving chemotherapy at the time of infection. Two patients were receiving azole prophylaxis at the time of disease, posaconazole and voriconazole in 1 case each. Eleven patients presented with central nervous system (CNS) involvement while 4 had isolated pulmonary lesions and one had fungaemia with osteomyelitis without CNS involvement. 81.3%(13/16) were culture positive, all *Cryptococcus neoformans*, while the remainder were diagnosed by a positive cryptococcal antigen (serum or CSF). Of the patients with CNS disease, 9 patients were treated with amphotericin based induction therapy and 3 were treated with azole-based regimen. One patient with CNS disease treated with azole therapy required re-induction with amphotericin after remaining culture positive on CSF after 6 weeks of therapy. Four patients with isolated pulmonary disease were treated with oral azoles. Two patients (12.5%) died with death attributed directly to CNScryptococcus. Risks for cryptococcal infection in particular cancer patient groups such as CLL require further study.

Trends in the Epidemiology of Bloodstream Infections in a Pediatric Cancer Center from Northern Greece

Nikoletta Kazakou[1], Myrsini Chatzi[2], Athanasios Tragiannidis[1], Efthymia Protonotariou[2], Emmanuel Hatzipantelis[1], Olia Vasilaki[2], Andreas Giannopoulos[1], Lemonia Skoura[2]

[1]Hematology Oncology Unit, 2nd Dept. of Pediatrics, AHEPA Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; [2]Microbiology Department, AHEPA Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece

Introduction: Bloodstream infections (BSIs) are one of the most dangerous complications in cancer treatments and remain a significant contributor to morbidity and mortality for both adults and children. Fever during neutropenia is a common and critical constellation which requires an effective antibiotic therapy according to the suspected pathogen, the current local epidemiology, the duration and the severity of the immunosuppression and of the underlying disease. Little data exist on the current epidemiology of BSIs in pediatric patients with hematologic malignancies and solid tumors from Pediatric Hematology Oncology Departments in Greece.

Goals: The purpose of our study was to investigate the epidemiology and microbiology of the BSIs in pediatric patients with hematological malignancies in the last 2 years.

Materials and methods: In a single-center retrospective study we analyzed all BSIs in children and adolescents with hematological malignancies and solid tumors over a 2-yearperiod (2016-2017). All patients received prophylaxis thrice weekly with trimethoprime /sulfamethoxazole (TMP/SMX) and underwent MRSA-screening weekly. Blood cultures were obtained for evaluation of fever and/or signs of systemic infection and further processed using standardmethods. Bacterial identification and antimicrobial susceptibility testing were performed using the VITEK2 automated system (bioMerieux,France). Isolates were defined as susceptible, intermediate or resistant according to CLSI guidelines.

Results: 46 positive BSI were obtained during 30 episodes of fever following bacteremia in 21 patients (47.6% male; median age: 7.89 years;84.78% hematological malignancies; 15.21% solid tumors; 95.2% with indwelling permanent catheter). There was a predominance of Gram-positive (60.87%) versus Gram-negative organisms (39.13%). *Staphylococcus epidermidis* was the most common bacteria recovered (30.43%), followed by *Klebsiella pneumoniae* (13.04%), *coagulase-negative staphylococci* (10.86%), *Streptococcus viridan*s and *Serratia ficaria* (6.52 % each), *Pseudomonas aeruginosa, E.coli* and *Acinetobacter baumannii* (4.34% each), *Klebsiella oxytoca*, *Erysipelothrix rhysiopathiae, Streptococcus mitis/oralis, Acinetobacter lwoffii, Proteus mirabilis* and *Enterococcus faecium* (2.17% each). Multidrug resistance was identified in all *A. baumannias* well as in 63% of the *K. pneumoniae* isolates while 83% of coagulase-negative Staphylococci were methicillin-resistant. Only 2% of the catheters were removed and the 30-day overall mortality was 13.04%.

Plasma Exposures following Posaconazole Delayed Release Tablets (DRT) in Children and Adolescents

Athanasios Tragiannidis[1,2], Eleni Vasileiou[2], Heidrun Herbrüggen[1], Martina Ahlmann[1], Silke München[3], Heike Thorer[1], Birgit Fröhlich[1], Carsten Müller[4], and **Andreas H. Groll[1]**
[1]Infectious Disease Research Program, Center for Bone Marrow Transplantation and Dept. of Pediatric Hematology/Oncology, University Children's Hospital Münster; Munster, Germany; [2]Hematology Oncology Unit, 2nd Dept. of Pediatrics, Aristotle University of Thessaloniki, Thessaloniki, Greece; [3]Dept. of Pharmaceutical and Medical Chemistry, Clinical Pharmacy, University of Münster; [4]Dept. of Pharmacology, University of Cologne; Cologne, Germany

Introduction: Posaconazole is a recommended option for antifungal prophylaxis in pediatric patients > 12 years of age and approved for this indication in the United States. The novel delayed release tablet (DRT) formulation has been shown to provide improved oral bioavailability in adults. Little is known, however, about the exposures following administration of the DRT in children and adolescents.

Goals: In a retrospective descriptive fashion, we analyzed trough concentrations at steady state of posaconazole in all pediatric patients who had received the DRT formulation between January 2015 and July 2017 for primary or secondary antifungal prophylaxis.

Material and Methods: Dosing was guided by an early population pharmacokinetic model with the following weight-based dosing regimen: >50 – 30 kg body weight, 300 mg load and maintenance; 30 – 20 kg, 300 mg load, 300/200 mg alternating maintenance; 20 – 10kg, 200 mg load and maintenance. Drug concentrations in plasma were measured by a validated high performance liquid chromatographymethod. Laboratory parameters of hepatic function while on treatment and the rate of drug discontinuations due to adverse effects were also assessed. A total of 26 patients (19 males/7 females) with high-risk leukemia/recurrent leukemia (18), bone marrow failure (3), non-Hodgkin lymphoma (NHL) or relapsed NHL (2) central nervous system histiocytosis (1) chronic granulomatous disease (1) and Wilms' tumor (1) of whom 11 were status post allogeneic HSCT were identified.

Results: The median age was 12.93 years (range: 5.17-17.58; 12 < 13 years), and the median body weight was 44.85 kg (range: 16-85). Posaconazole DRT were administered at the approved dosage in 21 and at a modified dose in 5 patients for a median duration of 120.96 days (range: 20-391). A total of 52 trough levels were obtained; 15 patients had at least 2 levels. The median trough plasma concentration was 2233.12+/-1799.48 ug/L (range: 501-8485); through concentrations were above the dosing target of 700 ug/l in 47/52 occasions. Posaconazole was well-tolerated without adverse event-related discontinuations or signals of grade 3-4 laboratory hepatic toxicity (baseline vs. end of therapy, mean +/-SD; serum bilirubin: 0.96 +/-0.67 vs 1.10 +/-1.01 mg/dL; SGOT: 59 +/-74 vs. 58 +/-54 U/L).

Conclusions: In this small pediatric and adolescent case series, administration of posaconazole DRT guided by a population-pharmacokinetic derived dosing algorithm resulted in predictable and potentially effective exposures and was well-tolerated over prolonged time periods.

Evaluation of a new dosing regimen of intravenous Voriconazole for the treatment of invasive aspergillosis in pediatric immunocompromised patients: therapeutic drug monitoring and safety

M. Barraza[1], J. Morales[1] R. Valenzuela[2], J Palma[3], P. Catalán[3], JP Torres[2], ME. Santolaya[2]
[1]Pharmacy unit, Hospital Dr. Luis Calvo Mackenna, Santiago, Chile; [2]Research Unit, Department of Pediatrics, Faculty of Medicine, Universidad de Chile, Santiago, Chile; [3]Bone Marrow Transplant Unit, Hospital Dr. Luis Calvo Mackenna, Santiago, Chile.

Introduction: There are several recommendations for the dosage of voriconazole (VCZ) for the treatment of invasive aspergillosis fractionated in two daily (BID) doses in pediatrics. In immunocompromised children with suspected invasive aspergillosis, achieve early drug levels (DLs) of VCZ> 1 ug/mL, is associated with lower mortality. In this context we proposed that start conventional doses of VCZ IV fractionated three times a day (TID) would be related to better DL.

Goals: Evaluate and compare DLs and safety of VCZ, fractionated BID or three times a day

Material & Methods: Retrospective study in immunocompromised children with VCZ treatment, between January 2015 and December 2017, in the Oncology and Bone Marrow Transplant Units at Hospital Calvo Mackenna, Santiago, Chile. Were evaluated and compared DLs according to dosage and range of age, considering the optimal DL ≥ 1ug/mL. Kidney function, liver function, and adverse reactions were evaluated.

Results: 136VCZ treatments were analyzed (59 patients), where 63 were BID (46%) and 73 TID (54%). Average age and weight among groups were: a) BID 7 years [0-17]; 23.5kg [6-83]) b)TID 9 [1-16]; 26kg [9.3-60] Patients between 2-12 years used an average dose 15.2 mg /kg /day BID or 16mg / kg /day TID, obtaining in 51% of cases DLs≥ 1 ug/mL in BID v/s 73.2% in TID, with an average level of 1 and 1.6 ug/mL; respectively. Patients older than 12 years, the average dose was 8.5 mg / kg /day for BID and TID, obtaining in 67% DLs ≥ 1ug /mL in dosages BID v/s 47% TID. Patients under 2 years of age, the average dose was 18 mg / kg /day for BID and 15.8 mg/kg/day for TID, obtaining in 12.5 % DLs ≥ 1ug /mL in dosages BID v/s 100% TID. There were no alterations in hepatic or renal function in both group. Alterations visuals were detected in 7/59 patients (11.8%).

The dosages TID in patients between 2-12 years achieved better DLs compared to conventional BID regimens, in equal daily doses. On the contrary, patients older than 12 years achieved better levels in conventional dosages of adults. Both regimes presented good security profiles.

Fondecyt n° 1161662

High Incidence of Ganciclovir –Resistant Cytomegalovirus Infections in Solid Organ Transplantation Patients

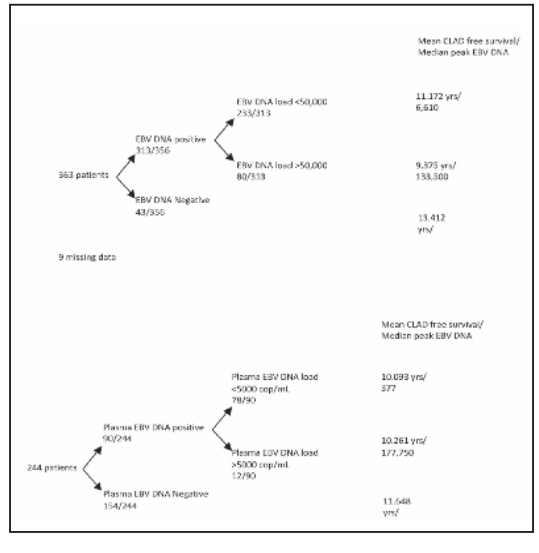
Coretta C. Van Leer-Buter, Anoek de Joode, Danielle de Voogd, Sylvia Smit, Hubert GM Niesters
Division of Clinical Virology, Department of Medical Microbiology, University Medical Center Groningen, University of Groningen, The Netherlands

Introduction: Human cytomegalovirus (CMV) is a pathogen in immunocompromized individual such as recipients of solid organ transplants. CMV-seronegative recipients of organs from CMV-seropositive donors have a very high risk of developing CMV infections. CMV-seropositive recipients may develop reactivations, or possibly reinfections.
First line treatment of CMV infections is intravenousgancicolvir or oralvalgancicolvir. Studies have shown that antiviral resistance may develop in up to 10% of treated individuals(Chou et al. 1999). Resistance testing should be performed when there is doubt about treatment response. This is usually done by sequencing the targets for ganciclovir, the protein kinase which activates Ganciclovir, coded by UL97and the viral polymerase gene coded by UL54. In this study we determined how frequently CMV resistance occurred in our hospital, which is the largest organ transplantation center in the Netherlands.
Goals: To determine how often CMV resistance occurs during treatment with (val)ganciclovir.
Methods: Stored plasma samples of patients with CMV DNAemia were retrospectively investigated for antiviral resistance by sequencing the UL97 and UL54 genes. All patients who had DNAemia at levels> 10 000 copies/ ml plasmafor more than 2 weeks were included.
Results: 109 patients undergoing treatment for CMV diseasewere included who were all treated with (val)-ganciclovir). In 25(23 %) patients with mutations were detected known to be associated with resistance. In 66 (61 %) patients no mutations were detected. In 18(16%)patients mutations were detected which were not previously described. Thirteen of 25 patients with resistance associated mutation had mutations which only affected UL97, the target for (val)- ganciclovir. Twelve had mutations in UL54, causing resistance against more than one antiviral agent in nine.
Resistance associated mutations occurred more frequently in patients with high levels of CMV DNA (>100 000 copies/ml) (P= 0.005). High levels of CMV-DNA were more frequently observed during primary CMV infections.
Conclusions: Our research shows that in patients with CMV DNA levels of >10 000 copies, the incidence of antiviral resistance is high. Also, while patients only receive (val)-ganciclovir, mutations may occur that lead to resistance to other antiviral agents as well.

The use of Quantitative EBV Measurements following Lung Transplantation may help identify Patients at risk of both CLAD and EBV-related Complications

E. Gore[1], E. Verschuuren[2], Wim vd Bij[2], HGM Niesters[1], C. Van Leer Buter[1]
[1]Dept Medical Microbiology, University Medical Center Groningen, [2]Dept. of Pulmonary Medicine, University Medical Center, the Netherlands

Introduction: There is currently not a good biomarker for adapting the immunosuppression (IS) of lung transplant patients. Currently trough plasma levels of IS drugs are used to alter the dose. However, when patients appear to be prone to rejection, IS levels may be increased. Conversely, IS may be reduced in patients who are prone to infections. In this context, EBV is of particular concern. Many lung transplantation patients have EBV reactivations and up to 9% develop EBV-driven lymphomas. The necessity of reduction of IS in patients with significant EBV problems, may put these patients at risk for development of rejection. We investigated if fine-tuning IS in relation to quantitative EBV measurements can be used to protect patients from infectious complications as well as chronic allograft rejection. **Goals:** To determine the value of EBV measurements for fine-tuning immunosuppression in lung transplantation patients. **Materials & Methods:** Of all lung transplant recipients (N=363) transplanted between June 2001 and May 2016 surviving over 1 month, routine serial EBV DNA loads in whole blood were investigated. Plasma was tested if whole blood was positive. Paediatric patients andre-transplants were excluded. Patient outcome with regards to overall survival (OS), development of chronic lung allograft dysfunction (CLAD). **Results:** Before transplant 95% of our 363 patients were seropositive for EBV. Following transplant 88% had active EBV replication found in whole blood (88%) and plasma (25%). The presence of EBV in whole blood appears protective in terms of OS, with mean OS 10.4 years in EBV negative patients and 11.9 years in patients with EBV <50,000 copies/ml. This trend is not replicated when considering plasma EBV as plasma negative patients have OS of 13 years compared to 11.3 years in patients with >5000copies/ml (p>0.05). EBV is a strong risk for the development of post-transplant lymphoma (PTLD) with 16out of 17 PTLD patients in our cohort being EBV positive in whole blood. CLAD occurs much more quickly in patients with high levels of EBV in both whole blood and plasma. Mean time to CLAD was 7.3 years for patients with plasma EBV load>5,000 copies/mL, and 9.3 years for patients with whole blood EBV load>50,000 copies/mL. This compares to 12.4 years in patients without detectable EBV in whole blood and plasma, and 11.7 years patients with EBV in whole blood but negative plasma. **Conclusion:** Our data shows that EBV identifies patients at a higher risk of developing complications such as CLAD and PTLD.



Intermittent Hepatitis C Viremia after Completion of Direct Acting in HCV/HIV Co-Infected Patients does not correlate with Treatment Failure

Karen J. Vigil, MD; **Mohanad Al Obaidi; Ben Barnett**
Mc Govern Medical School, The University of Texas Health Science Center at Houston

Introduction: AASLD/IDSA guidelines recommend 12 weeks of ledipasvir/sofosbuvir for HCV genotype 1 infection treatment. HCV viral load (VL) is measured at baseline, week 4 of treatment, and at end of treatment (EOT). The aim of this study is to describe HCV/HIV patients who had EOT and/or post EOT viremia that did not correlate with treatment failure.
Methods: We reviewed data of patients with HCV/HIV co-infections treated with ledipasvir/sofosbuvir and post EOT viremia. Viral load was detected using Roche Second-Generation CobasAmpliPrep/CobasTaqMan which has high sensitivity and specificity with no reported cross-reactivity. **Results:** Over the course of two years, we treated a total of 112 HCV/HIV co-infected patients. Six patients had EOT viremia (5%). During post-EOT HCV VL monitoring single episodes of HCV viremia (157-4511 IU/mL) were detected at 0-14 weeks post-EOT. All occurrences were preceded and followed by at least two undetectable HCV VL. All patients reported excellent adherence to HCV therapy (pill count and patient report) except for one patient who missed two weeks of therapy. All patients had absolute CD4+ cell count >250 cells/mm3. **Conclusion:** Post-EOT HCV viremia should not be considered as HCV relapse or treatment failure. Furthermore, we recommend a repeat test in at least 4 weeks of detectable HCV VL to justify any future treatment decisions.

Table 1. Hepatitis C RNA Viral Load Monitoring

	Baseline HCV VL (IU/mL)	Week 4 HCV VL	Week 12 End of Treatment HCV VL	Post Treatment HCV VL (Weeks after EOT)	Retest Post Treatment HCV VL (Weeks after EOT)
Pt #1	4'574,542	<15	Not detected	**157 IU/mL (week 14)**	Not detected (week 16)
Pt #2	5'916,672	<15	Not detected	**978 IU/mL (week 4)**	Not detected (week 12)
Pt #3	930,145	<15	Not detected	**257 IU/mL (week 28)**	Not detected (week 29)
Pt #4	6'415,450	Not detected	Not detected	**4,511 IU/mL (week 12)**	Not detected (week 16)
Pt #5	45,892,448	Not detected	**1795 IU/mL**	Not detected (week 46)	Not detected (week 50)
Pt #6	3'552,214	Not detected	**747 IU/mL**	Not detected (week 24)	Not detected (week 48)

Activity of Amphotericin B Formulations and Voriconazole against Biofilms of *Scedosporium apiospermum* and *Fusarium solani*

A. Vikelouda[1], M. Simitsopoulou[1], C. Antachopoulos[1], I. Stamouli[1], A. Chatzimoschou[1], L. Skoura[2], E. Roilides[1]
[1]Infectious Diseases Laboratory, 3rd Department of Pediatrics, and [2]Microbiology Department, Aristotle University School of Medicine, Thessaloniki, Greece

Introduction: *Scedosporium apiospermum* and *Fusarium solani* are widely spread in nature including potted plants, polluted soil and water. Both fungiare able to cause a broad spectrum of infections in humans that affect virtually every organ in the body, including locally invasive or disseminated infections in immunocompetent as well as immunocompromised patients. *S. apiospermum* frequently colonizes airways of patients with cystic fibrosis chronically impairing respiratory function, while *Fusarium* spp. are related to vision-threatening keratitis among other infections. Both pathogens can grow in biofilms on both polystyrene and tissue culture surfaces; however, the correlation between biofilm formation and antifungal drug susceptibility has not yet been fully elucidated.
Goals: To investigate the antifungal activity of deoxycholate amphotericin B (DAMB), liposomal amphotericin B(LAMB) and voriconazole(VRC) against *S.apiospermum* and *F.solani* biofilms(BF) or planktonic cells (PL).
Materials/methods: Clinical strains of *S. apiospermum* (SA) and *F.solani* (FS) were isolated from human lungs or cornea respectively (3 strains/organism).10^5 cfu/ml were incubated in 96-well plates with RPMI at 37°C for 48h. The plates were then stained with 1% safranin and BF formation was assessed spectrophotometrically at OD 490nm. After 48-h maturation BF as well as 2*10^5 cfu/ml PL were incubated with DAMB, LAMB or VRC at two-fold dilutions of 0.007 to 256 mg/l for 24h (9 experiments/organism). Fungal damage was assessed by XTT reduction assay. MIC50 was determined as ≥50% damagecompared to controls.Ordinary ANOVA with Bonferroni post-test was used to analyze differences in drug susceptibilityagainst BFor PL ($p<0.05$).
Results: PL MIC50's of DAMB, LAMB and VRC against SA (0.25, 0.5 and 0.125mg/l) were comparable to those against FS (0,125, 0.25, 0.06mg/l). All strains of both organisms exhibited strong BF formation. DAMB, LAMB and VRC BF MIC50's for SA were 1, 2 and 32mg/l,whereas MIC50'sfor FS were 0.5, 2 and >256mg/l, respectively. DAMB and LAMB were significantly more effective against BF of SAand FS compared to VRC (0.5-2mg/l vs >32mg/l, respectively; $p<0.05$),exhibiting comparable activities against either organism. DAMB at concentrations ≥2mg/lachieved >85% biofilm damage of the two fungi.
Conclusions: While a comparable antifungal effect is achieved by DAMB and LAMB against BF of *S. apiospermum* and *F. solani,* voriconazole activity is poor against BF of either SA or FS. In contrast, PL show similar susceptibility to all antifungal agents studied.

Human rhinovirus infections in recipients of hematopoietic cell transplantation (HCT): risk score for progression to lower respiratory tract infection (LRTI)

Alpana Waghmare[1,2,3], Hu Xie[3], Jane Kuypers[4], Mohamed L. Sorror[3,5], Keith R Jerome[3,4], Janet Englund[1,2], Michael Boeckh[3,5], Wendy Leisenring[3]

[1]Department of Pediatrics, University of Washington, Seattle, WA; [2]Seattle Children's Hospital, Seattle, WA; [3]Fred Hutchinson Cancer Research Center, Seattle, WA; [4]Department of Lab Medicine, University of Washington, Seattle, WA; [5]Department of Medicine, University of Washington, Seattle, WA

Introduction: Human rhinovirus (HRV) is the most common virus detected from respiratory specimens in HCT recipients. HRV LRTI is associated with significant mortality; however, few data exist regarding specific risk factors affecting progression to LRTI. **Goals:** To develop a risk scorefor progression to LRTI in a cohort of HCT recipients presenting with upper respiratory tract infection (URTI). **Materials and Methods:** HCT recipients with HRV URTI between 1/2009-3/2016 were included. LRTI was defined as proven LRTI (HRV detected in bronchoalveolar lavage with radiographic abnormalities) or possible LRTI (HRV detected in upper respiratory tract only but with radiographic abnormalities). Risk factors for progression to LRTI within 90 days were analyzed in Cox regression. The final multivariable model included factors that had a meaningful effect on the bootstrapped optimism corrected concordance statistic (c-statistic). Scores were weighted based on the hazard ratio for each factor. Receiver operating characteristic curves were utilizedto define optimal score cutoff values. Cumulative incidence curves estimated the probability of progression to LRTI; comparisons usedlog-rank tests. **Results:** Of 595 HRV events with URTI at presentation, 101 (17%) progressed to LRTI within 90 days (32 proven, 69 possible). In final multivariable models for any LRTI event in all subjects, allogeneic transplant, prior HRV URTI, low monocyte count and steroid use ≥2 mg/kg/day were associated with progression to LRTI. Among allogeneic recipients only, low monocyte count and steroid use ≥2 mg/kg/day were significantly associated with progression to LRTI. Theoptimal weighted risk score (Table) cutoff was 34 for all events (sensitivity 58%, specificity 75%) and 22 for allogeneic recipients (sensitivity 56%, specificity 71%). Subjects (all and allogeneic only) with risk scores higher than the optimal cutoff were at higher risk of developing LRTI (log-rank test: both p<0.001).The weighted clinical score for risk of progression to LRTI can help identify and risk stratify patients for clinical management and for future clinical trials of novel therapeutics.Though bootstrapping was used to conservatively evaluate score accuracy, validation in an independent cohort is needed.

		MODEL 1: All subjects		MODEL 2: Allogeneic only	
Covariates	**Categories**	**HR (95% CI)**	**Score Weight**	**HR (95% CI)**	**Score Weight**
Min monocyte count* (10^6 cells/L)	>100	1	–	1	–
	≤100	2.9 (1.9-4.4)	25	2.9(1.9-4.6)	50
Max steroid use* (mg/kg/day)	0 to <1	1	–	1	–
	≥1 to <2	2.0 (0.9-4.2)	17	1.3 (0.5-3.5)	22
	≥2	3.5 (1.6-7.7)	30	2.9 (1.2-7.3)	50
Albumin*	>3	1	–		
	≤3	1.6 (1.0-2.64)	14		
Donor type	Autologous	1	–		
	Allogeneic	1.9(1.1-3.2)	17		
Any previous events	No	1	–		
	Yes	1.7 (1.1-2.6)	14		

**in 2 weeks prior to HRV URTI*

Increased Incidence of Nocardial Infections In An Era of Atovaquone Prophylaxis In Allogeneic Hematopoietic Stem Cell Transplant Recipients

Drew J. Winston, Alfonso Molina, Darren Pan, Gary J. Schiller

UCLA Medical Center, Los Angeles, CA, USA.

Introduction: Nocardial infections have been rare after allogeneic hematopoietic stem cell transplantation (HSCT). We describe a recent increase in nocardial infections in allogeneic HSCT recipients at the UCLA Medical Center.

Methods: A retrospective review of patients' medical records and UCLA Clinical Microbiology culture results was performed to identify allogeneic HSCT recipients with a diagnosis of nocardiosis between January 1, 2000 and August 30, 2017. Patient characteristics, type of *Pneumocystis jiroveci* pneumonia (PJP) prophylaxis, clinical features associated with nocardial infection, and *Nocardia* species antimicrobial susceptibility results were included in this review. Diagnosis of nocardiosis was based on at least one culture of respiratory secretions or blood positive for *Nocardia* from a patient with clinical features of nocardial infection not explainable by other causes.

Results: 10 cases of nocardiosiswere identified between 2000 and 2017. (7 males; 3 females; median age 42 years, range 15 – 63 years). Underlying diseases were leukemia (7 patients), lymphoma (2 patients), and myelofibrosis (1 patient). 8 patients had matched-related donors, and 2 had matched unrelated donors. Source of stem-cells was peripheral blood (6 patients) and bone marrow (4 patients). Conditioning regimen was myeloablative (7 patients) and non-myeloablative (3 patients). 7 patients had acute and/or chronic GVHD. All 10 patients were on immunosuppressive drugs (tacrolimus, corticosteroids) and PJP prophylaxis (atovaquone 7, IV pentamidine 1, low-dose intermittent trimethoprim-sulfamethoxazole or TMP-SMX 2).

Mean time of onset of nocardiosis was 449 days post-HSCT (range, 116-806 days). 9 patients had only pulmonary nocardiosis, and1 patient had both pulmonary infection and brain abscesses. All *Nocardia* isolates were sensitive to TMP-SMX, which was used to treat most infections. No deaths directly from nocardial infection occurred, but over-all mortality was 40%.

After initiation of atovaquone prophylaxis for PJP prophylaxis in 2012 to avoid cytopenia with TMP-SMX, 9 cases of nocardiosis occurred in 411 allogeneic HSCT patients (2.2%) over the next 6 years (2012–2017), compared to only one case in 575 patients (0.17%) during the previous 12 years (2000– 2011).

Conclusion: The use of atovaquone for PJP prophylaxis in place of TMP-SMX may be associated with an increased risk for previous rare nocardial infections after allogeneic HSCT.

Bloodstream infections among solid organ transplant recipients

Yesilkaya A[1], Soy E[2], Akçil Ok M[3], Demirkaya MH[1], Azap ÖK[1], Arslan H[1], Moray G[2], Sezgin A[4], Haberal M[1]

[1]Department of Infectious Diseases and Clinical Microbiology, Başkent University Faculty of Medicine, Ankara, Turkey; [2]Department of General Surgery, Başkent University Faculty of Medicine, Ankara, Turkey; [3]Department of Nutrition and Dietetic, Baskent University Faculty of Health Sciences, Ankara, Turkey; [4]Department of Cardiovascular Surgery, Baskent University Faculty of Medicine, Ankara, Turkey

Introduction: Bloodstream infections (BSI) continue to be the most important cause of morbidity and mortality among solid organ transplantation (SOT) recipients. **Goals:** To evaluate the incidence and spectrum of etiologic agents of BSI according to the time after transplantation among SOT recipients at Baskent University Ankara Hospital. M**aterials & Methods:** Each consecutive SOT recipient transplanted in between April 15th 2014 and April 15th 2016 were evaluated prospectively if they had BSI. We compared the incidence of BSI within the first month (early BSI), between two and twelve months (mid-term BSI) and more than one year (late BSI) following the transplantation. The etiologic agents and antimicrobial resistance profiles of pathogens of bacteremia episodes were evaluated. All statistical analyses were carried out using the SPSS version 11.0. **Results:** Two hundred sixteen patients had 220 SOT (one patient had both liver and kidney transplantation, three patient had liver retransplantations) during the study period. As a total, 127 kidney, 65 liver and 28 heart transplantations were performed. Patients were excluded if they were died within first 24 hour after transplantation (n=4), if they were living outside Turkey (n=3). The study population comprised of 210 patients with 213 SOT. Of these 210 patients, 65 (31%) were younger than 18 years of age and the male gender (140/210, 66.7%) was prominent. Sixty two patients developed 115 BSI episodes [59 (51.3%) in liver, 39 (33.9%) in kidney and 17 (14.8%) in heart transplantation]. Of these 62 patients, 17 were younger than 18 years of age at the time of BSI. The frequency of BSI among 17 paediatric recipients was 24.3% (28/115episodes). The median age of SOT recipients at the time of BSI was 48 years (0-65 years, IQR: 32). The male gender (44/62, 71%) was prominent. The incidences of BSI by type of transplantation were demonstrated in Table 1. Fourty-seven (40.9%) of the total episodes were diagnosed within the first month after transplantation, 54 (47%) within the mid-term and 14 (12.2%) in the late period (Figure 1). Both early and mid-term BSI was seen more often in liver than kidney or heart transplantation (55.3%, p=0.723; 48.1%, p=0.557; respectively). Late BSI was distributed equally in between liver and kidney transplant recipients (p=0.188). Gram negative BSI were the most frequent aetiological agents for all types of SOT (Table 1). The most frequently isolated five pathogens were *E. coli* (24%; 56.3% ESBL production), *Klebsiella* spp. (18.8%; 76% ESBL production; 24% carbapenem resistant), enterococci (18%; 8.3%VRE), staphylococci (11.3%; 60% methicillin resistant) and *A. baumannii* (6.8%, 88.9% XDR, % 11.1 PDR).

Table 1. Characteristics of the recipients of a SOT with BSI in the study group according to the type of transplantation

	Kidney	Liver	Heart	Total
Transplants performed	124	62	27	213
Living donor	90	45	0	135
Number of BSI episodes	39	59	17	115
Number of BSI episodes >1	8	14	3	25
Number of patients with BSI	25(20%) (CI_{95} 13-27)	29 (46%) (CI_{95} 33.6-58.4)	9 (33%) (CI_{95} 15.3-50.7)	63 (29%) (CI_{95} 23-35)
Ratio BSI episodes/patients	1.56	2.03	1.88	1.82
Incidence by episodes	31.4%	95.1%	62.9%	53.9%
Incidence by patients	20.1%	46.7%	33.3%	29.5%
Microbiology of BSI				
Gram negative	33	33	13	79
Gram positive	5	35	1	41
Ratio of gram negative to gram positive BSI	6.6	0.94	13	1.92
Candidemia	4	5	3	12
Polymicrobial	3	14	0	17

Cytomegalovirus Viral load plasma levels prior to CMV gastrointestinal disease in allogeneic stem cell transplant recipients: discordance between CMV plasma and tissue activity

Michelle K. Yong[1,2], David Ritchie[3,4], Jeff Szer[3], Andrew Roberts[3], Ashish Bajel[3], Paul U. Cameron[2], Allen C. Cheng[5], Sharon R Lewin[2,5], Monica Slavin[1,6]

[1]Department of Infectious Diseases, National Centre for Infections in Cancer,Peter MacCallum Cancer Centre, Melbourne, Australia; [2]The Peter Doherty Institute for Infection and Immunity, The University of Melbourne, Melbourne, Australia; [3]Department of Clinical Haematology and Bone Marrow Transplant Service, The Royal Melbourne Hospital, Melbourne, Australia; [4]Department of Medicine, University of Melbourne, Australia; [5]Department of Infectious Diseases, Monash University and Alfred Hospital, Melbourne, Australia; [6]Victorian Infectious Diseases Service, Royal Melbourne Hospital at The Peter Doherty Institute for Infection and Immunity, Melbourne, Australia

Introduction: Gastrointestinal cytomegalovirus (CMV) disease is the most frequent site of CMV disease in recipients receivingan allogeneic haematopoietic stem cell transplantation (HSCT). Pre-emptive monitoring using frequent CMV viral loads is used to trigger commencement of anti-CMV drugs in order to prevent CMV disease. We evaluated the kinetics of CMV viral load in recipients who developed post-HSCT tissue invasive CMV disease.
Methods: A retrospective cohort study was conducted of all consecutive patients undergoing allogeneic stem cell transplantation from January 2006 to December 2010 from the Royal Melbourne Hospital, Melbourne Australia. Data was collected on basic demographics, conditioning regimen, graft source, the occurrence of acute graft versus host disease (AGVHD) and mortality. All patients undergo CMV pre-emptive monitoring. CMV disease was defined as histologically proven viral inclusion bodies or CMV immunohistochemistry positive evidence of tissue invasive disease. Univariate analyses were performed where $p<0.05$ was considered to be significant.
Results: A total of 256 allogeneic haematopoietic stem cell transplants were performed during the study period of which 13 (5.1%) recipients developed CMV disease.The median age of all HSCT recipients was 43 years [IQR 33-53]. All 13 participants (100%) with CMV disease had the gastrointestinal system as the site of disease. The median time to diagnosis of CMV disease was 95 days [IQR 46-156] following HSCT. Participants with CMV disease were more likely to have received reduced intensity conditioning compared to those without CMV disease (61.5% vs 32.1%, p=0.037 Fishers exact). Severe acute graft versus host disease (AGVHD Grade III-IV) was also more frequently observed in recipients with CMV disease (30.8% vs 8.6%, p=0.03, Fishers exact). In 77% of CMV diseases cases (10 of 13 cases), the peak CMV viral load preceding the diagnosis was <1000 copies/ml with 6 of the 13 (46%) having no detectable viral load prior to diagnosis. The 12 monthoverall mortality in those with and without CMV disease was 61.5% vs 35.8% (p=0.08 Fishers exact). **Conclusions:** In this study, allogeneic haematopoietic stem cell transplant recipients with gastrointestinal CMV disease frequently experienced low or absent plasma levels of CMV viremia in the period preceding tissue invasive disease. The current pre-emptive monitoring strategy which relies upon detection of an increasing CMV plasma viral load to indicate risk of CMV disease is imperfect in tissue invasive gastrointestinal CMV disease.

Central Nervous System (CNS)Toxoplasmosis in AdultNon-HIV Patients

Shiwei Zhou, David Seward, Sandra Camelo-Piragua, Carol Kauffman, Tejal Gandhi, Marisa Miceli
University of Michigan Health System & VA Ann Arbor Healthcare System

Introduction: CNS disease due to *Toxoplasma gondii* is a rarelife-threatening opportunistic infection. CNS toxoplasmosis is an AIDS-defining illness & typically affects patients with advanced HIV infection. Patients with defects in cell-mediated immunity, such as those receiving TNF inhibitors & cytotoxic drugs, patients with hematologic malignancies, solid organ transplants (SOT) & those receiving immunosuppressive medications including corticosteroids & methotrexate, would appear to be at increased risk for CNS toxoplasmosis, but it is rarely reported.

Goals: To identify & describe cases of CNS toxoplasmosis in adult non-HIV patients diagnosed at our institution over a 15-year period.

Materials& Methods: We conducted a retrospective chart review of adult non-HIV patients with CNS toxoplasmosis at the University of Michigan Hospitals between 2000 & 2015. Patients were included if they had a brain biopsy showing *T. gondii* tachyzoites, a positive immunohistochemical stain on brain tissue for *T. gondii,* or a positive *Toxoplasma*-specific PCR on cerebrospinal fluid(CSF).

Results: Seven non-HIV patients had CNS toxoplasmosis; all were immunosuppressed. Three patients were SOT recipients, 1 was ahematopoietic cell transplant recipient, &1 each hadchronic lymphocytic leukemia, systemic lupus erythematosus,& rheumatoid arthritis. All patients were receiving at least 2 immunosuppressive agents at diagnosis; none were taking prophylaxis directed against *T. gondii*. Main presenting symptoms were confusion, headache, & gait abnormalities; only 2 patients were febrile. None had infection outside the CNS. Six patients hadsingle or multiple rim-enhancing lesions with vasogenic edema on brain MRI. Definitive diagnosiswas made by brain biopsy in 5 patients & by positive CSF *T. gondii* PCR in 2. Four patients received initialtherapy with sulfadiazine, pyrimethamine& leukovorin. Due to intolerance, 1 patient received atovaquone, pyrimethamine & leukovorin, & 1 received clindamycin, pyrimethamine & leukovorin. One patient was diagnosed postmortem & did not receive treatment; 3 patients were treated but died within a year of diagnosis. Two of 3 patients who survived had persistent ring-enhancing lesions on CNS imaging & all 3 continued suppressive anti-*Toxoplasma* agents for 2-5 years.

Conclusion: CNS toxoplasmosis should be included in the differential diagnosis for transplant recipients & those taking immunosuppressive agents that alter the cellular immune response when they present with new neurological symptoms & compatible CNS imaging.

Determination of lysozyme amount in serum in patients with bacterial infection

Ziamko V.Y.,Okulich V.K.
Vitebsk State Medical University, Vitebsk, Belarus

Introduction: In modern concepts of pathogenesis of inflammatory diseases, much attention is paid to nonspecific humoral factors of immune system, including lysozyme.

The aim of the study was to evaluate level of lysozyme activity in serum in patients with bacterial infection.

Materials and methods: A complex examination of 43 patients with bacterial infection and 43 practically healthy people was performed. On the day of treatment (sample 1) before the treatment and after the end of treatment (sample 2), blood was taken from the ulnar veinbefore meals into sterile test tubes.

Results: We created a simpler and a cheaper way of evaluating lysozyme activity in biological fluids, which demands little time and has clear evaluation criteria. The invention relates to medicine, namely to laboratory diagnosis. From cell walls of *Micrococcus lysodeikticus* culture ATCC 4698 peptidoglycansubstratewas prepared, and the activity of lysozyme was calculated by the formula obtained after constructing calibration curve for lysozyme, which showed the dependence of the concentration of lysozyme and the optical density of the solution of Congo red. The positive effect of the proposed method is that the substrate for the production of reaction is prepared once and can be used for a long time. The way is easy and simple in play. The sensitivity of this method to the human lysozyme produced by Sigma (Lysozyme human recombinant expressed in rice ≥100,000 Unit / mg) was 0.06 mg /ml. This is enough to determine immunodeficiency states, because the content of lysozyme in biological fluids varies according to various data in a wide range from 0.2 to 28 mg / ml in normal.
It was found that the lysozyme activity in the serum was lower in patients with bacterial infection (246.7; 141.2-298.7 μl/ml) than that in donors(445.5; 350.1-816.1 μl/ml). After inactivation of the complement both in patients with bacterial infection(116.0; 56.5-160.1мкг/ μl) and in donors (246,0; 183,6-305,7 μl/ml) a statistically significant decrease in lysozyme activity occured.