O01

A novel model of spontaneous lethal gut-derived sepsis originating from the native intestinal microbiota

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Background: The gut microbiota are emerging as key members that drive recovery following surgical injury

Hypothesis: We hypothesize that the combination of a high fat diet and antibiotic exposure create a microbiome capable of causing lethal sepsis in mice following surgical injury.

Methods: We developed a novel model in which 7 weeks old C57BL/6 mice are fed a polyunsaturated fatty acid (PUFA) diet typical of a western diet for 6 weeks. Mice were then exposed to 5 days of antibiotics (Abx) consisting of Sub cutaneous cefoxitin and PO clindamycin, as occur during critical illness. Mice were then given water only for 16 hours, similar to NPO after midnight and then subjected to major surgical injury consisting of 30% surgical hepatecotomy. Identically treated chow fed mice served as controls. Mice were followed for the spontaneous development of sepsis and when moribund were sacrified. Blood, liver, spleen, lung, kidney, and cecum were collected for bacterial culture, organ histology and cytokine assays.

Results: 68% of mice treated with PUFA and Abx developed sepsis within 24 hours of surgery and become moribund within 40 hours, whereas only 14% of mice treated with chow and Abx developed lethal sepsis.(N=15/group,$p<0.00001$). The composition of the cecal microbiome in septic moribund mice in the PUFA+Abx group changed significantly with the emergence of Serratia marcescens and Enterobacter cloacae sp, nearly half of which expressed multi-drug resistance(MDR). Dissemination of these strains into systemic compartments (liver, spleen, blood) reached 10^6 CFU per gm of tissue(ml of blood). Recovered MDR S.marcescens strains were highly lethal as judged by their killing effect in mouse and Galleria mellonella intraperitoneal models. Phenotypic microarray analysis using Biolog revealed significant metabolic changes and stress/antibiotic resistance in the cecal microbiota.Organ failure was confirmed histologically in the lung, liver and kidney demonstrating hyline membrane formation, tubular vacuolization, glomerular hyper-cellularity and shock liver. Inflammatory biomarkers were elevated including C reactive protein (increased 7 fold), endotoxin (increased 3 fold) and IL-6 (elevated 30 fold) when compared to non-septic mice,$p<0.005$.

Conclusions: This novel model demostrates that the combination of a western diet and antibiotics exposure can render surgical patients highly vulnerable to lethal sepsis by changing the composition and function of commensal bacterial such that highly virulent phenotypes emerge.

O02

Enterococcus faecalis stimulates collagenolysis by macrophages via

plasminogen activation: a role in anastomotic leak

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Background: We have previously shown that Enterococcus faecalis can cause anastomotic leak (AL) in rodents via its production of collagenase that promotes macrophage matrix metalloprotease 9 (MMP9) activity, resulting in collagen degradation and impaired healing. Despite recent work confirming its role in bacterial virulence, the involvement of the fibrinolytic protease plasminogen (PLG) in the pathogenesis of E. faecalis-mediated AL is unknown. Gut macrophages are known to bind and activate PLG, and its activation is readily inhibited by pharmaceuticals already in use in elective surgery. Therefore, the aim of this study is to define the relative contribution of E. faecalis-induced PLG activation by macrophages on collagen degradation as it applies to AL.

Hypothesis: The interaction of E. faecalis with macrophages leads to overactivation of PLG and contributes to the accelerated collagen degradation seen in AL.

Methods: RAW 264.7 immortalized murine macrophages were incubated with a collagenolytic E. faecalis strain (E44), previously shown to cause AL in rodents. E44 was plated at various multiplicities of infection (MOI). Activation of PLG was assessed kinetically with a PLG-specific fluorogenic substrate. Fluorescein-labeled gelatin was used to assess collagenolytic activity. Given that the activation of PLG by macrophages is through apical surface alpha-enolase (ENO1), and that active PLG can activate MMP9, tranexamic acid (TXA) and anti-mouse enolase antibodies were used to inhibit PLG activation.

Results: When macrophages were plated with live E44, a direct correlation was observed between PLG activity and MOI (no E44 36.9±2.9 AU(PLG activity); MOI2 40.6±3.5; MOI10 80.9±3.6, $p<0.01$). Subsequently, collagenolytic activity was increased in a MOI-dependent fashion, particularly in the presence of pro-MMP9 (no E44 28.8±1.2 AU(collagenase); MOI 10 35.8±1.4 $p<.01$). TXA significantly decreased PLG activation in a concentration-dependent manner and decreased collagen degradation both in the presence and absence of pro-MMP9 (MOI10/no TXA 21.0±1.0 AU(collagenase); MOI10/5mM TXA 16.5±1.0; MOI10/10mM TXA 14.0±1.6, $p<.01$). Anti-mouse enolase antibodies diminished PLG activation in E44-stimulated macrophages (No Ab 22.3±0.3 AU(PLG activity); Control Ab 20.5±0.3; Anti-ENOL 15.6±0.4 $p<.01$).

Conclusions: E. faecalis-mediated PLG activation occurs through a surface-exposed enolase on murine macrophages and significantly contributes to collagen degradation. Titrated use of the FDA approved agent TXA can potentially inhibit excessive collagen degradation at its most proximate point of activation and may play a preventative role in AL.

O03

Global Defects in Neutrophil and Monocyte Function Offer New Targets to Improve Sepsis Survival in Obese, Diabetic Mice

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Background: Sepsis is the leading cause of death in the critically ill population, with an overall mortality rate of 20%. Mortality rates double in the obese, type II diabetic (T2D) population due to infectious complications. Neutrophils (PMNs) and monocytes are essential for bacterial eradication and sepsis survival. The PMN and monocyte functional defects that contribute to the worse sepsis mortality in obesity and T2D are unknown. PMN and monocyte defects are important therapeutic targets to improve sepsis survival, since obesity and T2D is no longer just a disease of high-income countries, but is rapidly becoming a worldwide pandemic.

Hypothesis: We hypothesize that obesity and T2D create a functional immune deficiency by altering PMN and monocyte cellular function, which inhibits bacterial clearance and promotes sepsis mortality.

Methods: 30 week old C57BL/6 (lean) and Diet Induced Obese (DIO) mice underwent cecal ligation and puncture (CLP), (LD20), or sham procedure. At serial time points from 1 to 14 days, n=5 mice/group were euthanized. Peritoneal fluid was analyzed for bacterial counts. Monocytes and PMNs were isolated by MACS separation. Phagocytic ability and reactive oxygen species (ROS) generation were assessed by flow cytometry. Cytokine analysis was done with LuminexTM technology. Genomic analysis of PMN phagocytic pathways was completed with RT2 Profiler Arrays.

Results: Compared to lean mice, DIO mice had significantly less survival after CLP ($p<0.05$). DIO mice failed to eliminate bacteria from the peritoneal cavity when compared to lean mice ($p<0.01$). DIO PMNs are immature and expressed less CD11b and CXCR3 following sepsis compared to lean PMNs ($p<0.01$). PMN and monocyte phagocytic and ROS ability in DIO mice was dramatically reduced ($p<0.01$) up to 14 days after sepsis. Genomic analysis revealed significantly less Mertk and Axl transcripts in DIO PMNs, which regulate phagocytosis of necrotic and apoptotic cells. DIO mice also produced far less plasma MIP1A and MCP-1 cytokine levels ($p<0.05$) and hence recruited significantly less M1, M2A, and M2B monocytes into the peritoneal cavity when compared to lean mice ($p<0.05$).

Conclusions: DIO mice demonstrate global defects in PMN and monocyte phagocytosis and ROS generation, which hinder bacterial eradication and worsen sepsis mortality. Augmentation of Mertk and Axl transcripts, and plasma MIP1A and MCP-1 levels may counteract these defects through improved PMN function and monocyte recruitment respectively.

O04

Current Evaluation of Antibiotic Usage in Complicated Intraabdominal Infection After the STOP IT Trial: Did We STOP IT?

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Background: Our objective was to evaluate antibiotic usage for complicated intraabdominal infections (CIAI) at our institution after the publication of the STOP IT trial, to determine if we were successfully implementing these findings into practice, and to evaluate outcomes.

Hypothesis: We hypothesized that we could demonstrate successful reduction in antibiotic course duration after publication of the STOP IT trial, with similar patient outcomes.

Methods: This was an analysis of patients presenting to the emergency department with CIAI from February 2014 through May 2017. CIAI were defined as patients with a perforated viscus, complicated appendicitis, and ischemic bowel. Exclusion criteria were if the patient did not undergo source control, ie., either operative or radiologic intervention, if no post-operative antibiotic course was given, or if the post-operative antibiotic course was not completed due to withdrawal of care, change in code status, or death. Patient outcomes and antibiotic usage were compared before and after the publication date. For this study, antibiotic courses of 5 days or less were defined as short course (SC).

Results: A total of 132 patients met inclusion criteria. There were 47 patients in the pre-STOP IT group, and 85 in the post-STOP IT group. These groups were well-matched in terms of demographics and other characteristics (Table 1). There was a statistically significant decrease in both total antibiotic days and antibiotic days after source control after the publication of the STOP IT trial. There were no differences in hospital length of stay (LOS), ICU LOS, surgical site infections, intraabdominal abscesses, or death between the two groups. The percentage of patients receiving SC antibiotics significantly increased after publication from 23.4% to 44.7%.

Conclusions: This is the first study to our knowledge that attempts to evaluate the implementation of the STOP IT findings into clinical practice. We successfully demonstrated decreased antibiotic days and increased use of SC antibiotic regimens after the publication of the STOP IT trial. However, there still appears to be significant room for improved antibiotic stewardship with respect to adherence to SC antibiotic regimens.

O05

Sepsis Derived Exosomes Transfer Functional DNA Methyltransfereases with Resultant Immunosuppression and Gene Silencing

Jon Wisler; Kanhaiya SIngh, Ohio State University; Helen Hou, Ohio State University; Chandan Sen, Ohio State University

Background: Each year sepsis affects over 750,000 individuals with a high mortality of 30-40%. Following a septic insult patients exhibit profound immunosuppresion, which is associated with increased short and long-term mortality. Patients that survive the initial insult have high rates of secondary infections with worsened mortality. We have previously demonstrated that multiple components of epigenetic modification are involved in the generation of this immunosuppressed phenotype. Specifically, DNA methylation via DNA Methyltransferases (DNMTs) acts to silence various genes during sepsis. Circulating exosomes are important in the transfer of cellular information and signal amplification. They are known to alter recipient cell function in diseases like sepsis.

Hypothesis: We hypothesize that circulating exosomes contain DNMT protein that is transferred to recipient cells and results in promoter methylation and gene silencing.

Methods: Circulating exosomes were isolated from patients with sepsis. DNMT 1, 3A, and 3B levels were determined using an ELISA based assay. Colormetric assays were used to assess activity levels. In order to assess functional transfer, naive monocytes were treated with sepsis derived exosomes. Methylation was assessed using bisulfate sequencing.

Results: Significant elevations in DNMT 1, 3A, and 3B expression were seen on days 1, 3, and 5 of sepsis. These increases correlated with increased activity. When transferred to naive monocytes, DNMT activity is retained and methylation events occur with significant increases in promoter methylation seen at TNF-alpha. Cultured monocyte derived exosomes were found to contain high levels of DNMT 1, 3A, and 3B when stimulated with endotoxin suggesting these as the source for the high level of activity within exosomes of patients with sepsis. These exosomes are taken up by naive cells with resultant methylation events and gene silencing.

Conclusions: These data demonstrate that sepsis derived circulating exosomes contain high levels of DNMTs and that these DNMTs are transferred to recipient cells with resultant methylation at promoters of genes involved in the inflammatory response. This results in gene silencing and subsequent immunosuppression. This is important in that it identifies circulating exosomes as a key process in the development of sepsis and sepsis related immunosuppression.

O06

Deepwound: Automated Postoperative Wound Assessment and Surgical Site Surveillance through Convolutional Neural Networks

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Background: The incidence of postoperative wound infections after lower extremity bypass can be as high as 10%-20%. An automated method of diagnosing wound complications would serve to limit the expense of time and money from hospitals, doctors, insurers, and patients. The algorithmic classification of wound images, due to variability in the appearance of wound sites, is a challenge. Deep convolutional neural networks (CNNs), a subgroup of artificial neural networks that exhibit great promise in the analysis of of visual imagery, may be leveraged to categorize surgical site wounds. We present Deepwound, a multilabel CNN trained to classify wound images with image pixels and labels as the sole inputs. Mobile devices paired with deep neural networks have the ability to provide real-time clinical insight into the state of post-operative wounds. The ubiquitous nature of smartphones provides an ideal means through which professional-grade wound assessment and triaging may be delivered.

Hypothesis: CNNs can be used to label the state of post-surgical wounds and provide a wound infection risk score.

Methods: Over 1,000 smartphone images of postoperative wounds were collected and individually labeled by three medical experts. The variability and sheer number of images necessitated augmentation through several random rotations and translations. Three CNNs were built. Each utilized transfer learning on the VGG-16 CNN

architecture, pretrained on over 1.2 million images over 1,000 classes from the Imagenet database. Deepwound (our final algorithm) is a majority-voting ensemble composed of these CNNs, with weights frozen at three different layers for optimal generalization. An output layer equipped with a sigmoid activation function replaced the final layer of the CNNs, which were developed using Python. A mobile app, able to track various clinical variables pertinent to postoperative wound progression, was created using Deepwound.

Results: The Receiver Operating Characteristic AUC served as our evaluation metric, achieving scores of 0.85, 0.92, 0.92, 0.87, 0.93, 0.96, 0.93, 0.90, and 0.92 across our 9 labels: the presence of drainage, fibrinous exudate, granulation tissue, a surgical site infection (SSI), an open wound, staples, steri-strips, or sutures.

Conclusions: Through our research we have built a deep learning algorithm, Deepwound, that can accurately identify the presence or absence of common post-operative wound findings.

O07
Patient-Monitored Surgical Site Infections in Karachi, Pakistan

Katherine Albutt; Gustaf Drevin, Program in Global Surgery and Social Change

Background: Background: Surgical site infections (SSI) are the most common hospital-acquired infection in low- and middle-income countries (LMICs), occurring in one in ten surgical patients and taxing already fragile health systems. The majority of SSI occur after discharge rendering prompt and accurate diagnosis and treatment challenging. Such limitations have catalyzed the development of alternate surveillance strategies, including self-monitored SSI surveillance.

Hypothesis: We evaluated the accuracy of patient self-screening and evaluation by trained nurses, referred to as infection control monitors (ICMs), in order to develop a simple, accurate, and reproducible method of SSI detection.

Methods: Between October 2015 and September 2017, a two-year non-inferiority study was conducted at the Indus Hospital in Karachi, Pakistan. A questionnaire designed to elicit signs and symptoms of SSI was provided to surgical patients to self-screen for infections after discharge. Results from this screening questionnaire were compared to surgeon evaluation (the gold standard for SSI diagnosis) and ICM evaluation at follow-up.

Results: A total of 348 patients were enrolled, counseled regarding SSI signs and symptoms, and went on to complete the study. Among these patients, 18 (5.17%) developed a SSI based on surgeon evaluation. Patient self-screening had a sensitivity of 39%, specificity of 95%, positive predictive value (PPV) of 28%, negative predictive value (NPV) of 97%, and Gwet's AC1 of 0.91 (95% CI: 0.77-0.93). The most common patient-identified symptom used to correctly identify a SSI was drainage (86%) followed by increasing surgical site pain, redness, fever, and swelling (57%, respectively). ICM screening had a sensitivity of 82%, specificity of 99%, positive predictive value (PPV) of 82%, negative predictive value (NPV) of 99%, and Gwet's AC1 of 0.98 (95% CI: 0.91-0.99).

Conclusions: Despite the low sensitivity observed, there was high inter-rater reliability between surgeon diagnosis of SSI and patient self-screening. The high specificity and low false positive rate suggest that patients are able to correctly identify an uninfected surgical wound. Supplementing regular post discharge follow-up with patient self-screening in a low-resource settings has the potential to increase the rate of SSI detection with minimal additional burden to the health system. There was near perfect agreement between surgeon diagnosis and ICM assessment at follow-up with high sensitivity and specificity. Trained nurses can correctly identify SSI and may be used as a proxy to surgeons for SSI detection, thereby reducing the burden on the specialized surgical workforce in LMICs.

O08

The Impact of Intraoperative Adverse Events on the Risk of Surgical Site Infection in Abdominal Surgery

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Background: Intraoperative adverse events (iAEs) were recently shown to independently correlate with an increased risk of postoperative mortality, morbidity, readmissions and length of hospital stay. We sought to further understand the impact of iAEs on surgical site infections (SSIs) in abdominal surgery and delineate which patient populations are most affected.

Hypothesis: All patients with iAEs have an increased risk for SSI, especially those with pre-existing risk factors for SSI.

Methods: To identify iAEs, a well-described 3-step methodology was used: (1) the 2007-2012 ACS-NSQIP database was merged with our tertiary academic center's administrative database, (2) the merged database was screened for iAEs in abdominal surgery using the ICD-9-CM-based Patient Safety Indicator "accidental puncture/laceration", and (3) each flagged record was systematically reviewed to confirm iAE occurrence. Univariate and backwards stepwise multivariable analyses (adjusting for demographics, comorbidities, type and complexity of surgery) were performed to study the independent correlation between iAEs and SSIs (superficial, deep incisional, and organ-space). The correlation between iAEs and SSIs was especially investigated in patients deemed a priori at high risk for SSIs, specifically those older than 60 and those with diabetes, obesity, cigarette smoking, steroid use or ASA class ≥3.

Results: A total of 9288 operations were included and iAEs were detected in 183 (1.9%). Most iAEs consisted of bowel (44%) or vessel (29%) injuries and were addressed intraoperatively (92%). SSI occurred in 686 (7.4%) cases and included 331 (3.5%) superficial, 32 (0.34%) deep and 333 (3.6%) organ-space infections. As in our prior studies, iAEs were independently correlated with deep/organ-space SSI [OR=1.94, 95% CI 1.2-3.4, p=0.007]. Most interestingly, the occurrence of an iAE was correlated with increased SSI rate in the low-risk but not the high-risk patient populations.

Specifically, iAEs increased SSI in patients younger than 60 [OR=2.69, 95% CI 1.55-4.68, p<0.001], non-diabetics [OR=1.69, 95% CI 1.08-2.67, p=0.02], non-obese [OR=3.03, 95% CI 1.89-4.85, p<0.001], non-smokers [OR=1.7, 95% CI 1.1-2.64, p=0.018], with no steroid use [OR=1.77, 95% CI 1.18-2.65, p<0.005], and with ASA class <3 [OR=2.26, 95% CI 1.31-3.87, p=0.003].

Conclusions: iAEs are independently associated with increased SSIs, particularly in patients with less pre-existing risk factors for SSI. Preventing iAEs or mitigating their impact, once they occur, may help decrease the rate of SSIs.

O09

Tight Junction Changes in Neonatal Enteroid Model of Necrotizing Enterocolitis

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Background: Necrotizing enterocolitis (NEC) is a severe and often fatal gastrointestinal disorder of the newborn. Improved survival in early premature infants due to advances in neonatal care has led to an increase in the incidence of NEC globally. Despite decades of research, our understanding of the pathogenesis NEC is incomplete. Enteroids are 3-dimensional structures that allow for the study of the intestinal epithelium and the manipulation of such, serving as a human tissue model of NEC. Tight junction (TJ) proteins are pivotal in regulating intestinal permeability.

Hypothesis: We hypothesize that strengthening TJ proteins, such as Claudin 4 (C4), will be underexpressed, and pore-forming proteins, like Claudin 2 (C2), will be increased in an enteroid model of NEC.

Methods: Human intestinal stem cells were harvested from bowel resection samples obtained from neonates with NEC vs other conditions (control). The isolated stem cells were grown in a basement membrane matrix with clean media vs media with lipopolysaccharide (LPS) to induce NEC. Additionally, we compared findings to an established rat model of NEC, where premature rat pups were fed clean formula (control) vs formula containing bacteria to induce NEC. Human tissue, enteroids, and rat bowels were collected and analyzed by RT-PCR, western blot, and mean immunofluorescent intensity (MFI). Differences were compared with student's T-test for significance.

Results: C4 gene expression was downregulated in enteroids with experimental NEC and in humans with NEC (p<0.005). Likewise, C4 protein expression was decreased in enteroids and rats with experimental NEC (p=0.025). Conversely, C2 gene expression and protein were increased in enteroids and rats with experimental NEC vs control (p=0.02). Enteroids, rats, and humans with NEC had increased immunofluorescence of C2 (MFI 714±27 vs 528±29, p<0.0001). Not only was the MFI different in NEC, but there were also congruent changes in the subcellular localization of C2 and C4.

Conclusions: Human NEC is associated with changes in TJ protein structure that may be responsible for the changes in intestinal permeability seen in these infants. Neonatal human enteroids are a novel model in the study of NEC that allow for the manipulation of study parameters in human tissue. Further research into the pathophysiology and

therapeutic targets against NEC using this new model is warranted.

O10

Survival and pulmonary injury after neonatal sepsis: PD-1:PD-L1's contributions to mouse and human immunopathology.

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Background: Morbidity associated with neonatal sepsis remains a healthcare crisis. We recently demonstrated survival advantage of PD-1-/- mice following sepsis(80%) compared to wildtype counterparts(40%). We also demonstrated that 24hrs post-CS induced neutrophil influx, increased IL-6, IL-10 and TNF-α expression, all of which were attenuated among PD-1-/- mice. A clear role for these changes and their temporal significance has yet to be elucidated.

Hypothesis: Indices of indirect acute lung injury and overall mortality will be attenuated across all time points in the setting of PD-1 and/or PD-L1 gene deletion. Further, lung tissue derived from human neonates who succumbed to sepsis will express increased levels of PD-1 and/or PD-L1.

Methods: Polymicrobial infection was induced by intra-peritoneal injection of CS into C57BL/6, PD-1-/-, and PD-L1-/- neonatal mice. Lungs were harvested at 4, 12 and 24hrs. Survival analysis included q6hr checks for the 1st 48hrs followed by daily checks thereafter. Cytokine/chemokine and MPO assays were conducted, and pulmonary edema(PE) was measured by wet:dry ratio. Cultured pulmonary endothelial cells(ECs) were immunofluorescently(IF) stained for adhesion molecules. With IRB approval, human neonatal lung autopsy tissue was obtained and immunostained for PD-1 and PD-L1.

Results: Unlike at 24hrs (where PE, MPO and several cytokines/chemokines were markedly increased), at 4hrs(n=3-10/group) and 12 hrs(n=3-6/group), there was no marked difference between sham and CS mice in terms of PE or MPO expression; and while cytokine/chemokine analysis revealed a trend toward increased IL-6 and KC after CS, this did not reach significance. Like PD-1-/- mice, survival analysis(n=29) of PD-L1-/- neonatal mice after CS resulted in 72% survival. On IF, zona occludens-1(ZO-1) cellular habitation shifted from membranous to peri-nuclear after CS in wildtype murine cultured ECs at 24hrs, but remained membranous among PD-1-/- lungs. Finally, assessment of human neonatal lungs(n=20) showed consistently more PD-1 expression in septic patients; this difference was not noted for PD-L1 expression.

Conclusions: PD-1:PD-L1 ligation affects lung injury, but akin to experimentally septic adult mice, also affects murine survival after polymicrobial insult. This is echoed in part by septic human neonatal histology documenting increased pulmonary PD-1 levels. Together, these data suggest that aberrant signaling through the PD-1:PD-L1 pathway may be a viable therapeutic target in the septic neonate.

O11

Antimicrobial stewardship reduces SSI rate, number and severity of pancreatic fistulae following pancreatoduodenectomy

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Background: Surgical site infections (SSIs) remain a major source of morbidity following pancreatoduodenectomy (PD). We noted a higher than anticpated incidence of SSI in our patients undergoing PD, and after an internal audit and detailed analysis of the microflora of SSIs, as well as a multidisciplinary discussion, the local prophylactic antibiotic policy was changed based on sensitivities to the bacteria isolated from postoperative wounds.

Hypothesis: The hypothesis was that a targeted change in antibiotic prophylaxis would reduce the rate of SSIs. The aim of the current study was to analyse the results of a change in prescribing policy on SSI rates, and in addition, on the occurrence and severity of postoperative pancreatic fistulae (POPF) as this complication is often linked to the presence of an organ space SSI.

Methods: After implementing a change of prophylaxis policy from Cefalexin to Cefrtiaxone and Metronidzole, surgical residents were educated on the importance of compliance. A prospectively maintained departmental database was used to identify 200 consecutive patients undergoing PD, 100 pre- and 100 post institution of policy change. Incidence data relating to SSIs and POPF were obtained from the American College of Surgeons - National Surgical Quality Improveent Program (ACS-NSQIP) data set and the details of culture results and organism sensitivity extracted from the electronic medical record, as were details on the severity of fistulae.

Results: Following change in the antibiotic prophylaxis policy, analysis of the NSQIP data revealed that the overall SSI rate fell from 29% to 16% (p=0.04). After excluding patients with a penicillin allergy (n=11) from the post-implementation cohort, the rates of SSI were compared in cases adherent (53/89) and non-adherent (36/89) to the new antibiotic policy. In this comparison, the SSI rates were 7.5% vs. 27.8% respectively (p=0.02), the later being comparable to the 29% in the pre-implementation cohort. The overall incidence of POPF fell from 37% to 24% (P=0.04), and furthermore, the rate of clinically significant fistula from 24% [21 Grade B and 3 Grade C] to 9% [9 Grade B] (p=0.03).

Conclusions: A change in the prescribing policy for prophylactic antibiotics prior to pancreatectomy, based on the local microflora, resulted in a significant reduction in the SSI rates following resection. In addition, antimicrobial stewardship also resulted in a statistically significant reduction in the overall incidence, as well as the incidence of clinically-significant POPF. The lack of complete compliance to policy has lead to the development of a fixed preoperative order set with only two antibiotic options for standard and penicillin-allergic patients. Following this additional venture, and further education on adherence to the policy a re-audit is in process.

O12

NRF2 and NLRP3 gene activation rescues inflammatory response in TLR-4 deficient animals after FER electroporation

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Background: Introduction: Toll-like receptors are important components of immune responses to microbial products. TLR4 deficiency results in tremendously accelerated mortality after pneumonia challenge. We recently described that airway electroporation of human FER gene could rescue mice upon lethal challenge combining lung contusion and pneumonia. Here we set to study whether acute overexpression of FER in lung tissue could rescue TLR4 deficient mice (24h 100% mortality upon pneumonia) exposed to bacterial pneumonia

Hypothesis: Hypothesis: We recently described that overexpression of FER gene uses a Signal Transduction and Transciption-3 (STAT-3) pathway to improve survival in a pneumonia model. FER will activate downstream STAT-3 signal transduction mechanisms despite TLR-4 deficiency and rescue the lung inflammatory response

Methods: Methods: TLR-4 -/- mice were subject to an initial unilateral lung contusion injury and later a 6 h were inoculated with 500 CFU of Klebsiella sp. In between insults they received a DNA plasmid encoding human FER (PNA/pFER-EP) via pharyngeal drop followed by 8 electroporation pulses (EP) inducing FER expression in the lung. Bronchial alveolar lavage (BAL) and lung samples were processed while cellular subpopulations, bacterial CFUs, histology, gene and protein expression, and cytokines were analyzed.

Results: Results: Acute overexpression of FER gene in lung tissue significantly extended survival of TLR4-/- mice upon bacterial pneumonia challenge (0%/48h vs 40%/96h). In contrast to wild type animals, activated STAT-3 and TNF-α levels were surprisingly depressed despite FER electroporation treatment. However, transcription factor NRF2 and inflammasome component NLRP3 were significantly overexpressed, allowing the maturation and secretion of IFN-γ, KC and CXCL2 and thus enhanced leukocyte recruitment. TLR4-/- were able to survive 48 h longer, time until transient gene expression of FER disappears.

Conclusions: Conclusion: Manipulation of immune response with short-lived FER overexpression in resolution of lung contusion complicated with bacterial pneumonia rescued deficient in TLR4-/- mice monocytes and neutrophils recruitment into an airway. FER overexpression significantly extended survival of TLR4-/- mice upon lethal pneumonia challenge. FER drives prolonged expression of Nrf2 gene in BAL cells of pneumonia challenged mice.

O13

Association of Quarterly Antimicrobial Class Exclusion and Resistance Rates

Christopher Guidry; Addison May, Vanderbilt University Medical Center

Background: Our Surgical Intensive Care Unit (SICU) utilizes an antimicrobial rotation protocol that includes quarterly exclusion of key antimicrobial classes.

Hypothesis: We hypothesized that the exclusion of these classes would be associated with reduction in quarterly resistance rates.

Methods: All isolates from culture-proven pneumonias diagnosed in the SICU from October 2013 through December 2016 were retrospectively evaluated. Resistances to beta-lactam / beta-lactamase inhibitor combinations (BLIC), fluoroquinolones (FQ), carbapenams (CARB), and 3rd- and 4th-generation cephalosporins (3/4 CEPH) were evaluated and recorded for each isolate. Quarterly resistance rates were evaluated based on quarterly exclusion of one of the above antimicrobial classes. BLIC's were excluded in the first quarter, FQ's in the second, CARB's in the third, and 3/4 CEPH's in the fourth quarter. Cumulative quarterly rates of resistance to each of these classes, including multi-drug resistance (MDR), were evaluated.

Results: There were 442 isolates identified during the study period. Overall class-specific resistance rates during the study period were 9.8% for BLIC, 14.5% for FQ, 7.7% for CARB, and 10.6% for 3/4 CEPH. Quarterly resistance rates displayed below. Exclusion of BLIC's in the first quarter was statistically associated with lower resistance rates (BLIC Q1 vs. Q2: 4.5% vs. 17.1%, p-value = 0.04 and 3/4 CEPH Q1 vs. Q2 4.5% vs. 19.5%, p-value = 0.02). The decrease in resistances in Q4 was not statistically significant. There was a statistically lower rate of CARB resistance in the quarter following its exclusion (Q3 vs. Q4: 10.3% vs. 1.4%, p-value = 0.05). There was no clear statistical association between MDR or FQ resistance by quarter.

Conclusions: We identified a temporal relationship between exclusion of antimicrobial classes and quarterly resistance rates. Further evaluation is needed to fully evaluate the impact of excluding antimicrobial classes on overall resistance patterns.

O14

Unmasking unique immune altering aspects of the microbiome as a tool to correct sepsis induced immune dysfunction

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Background: Sepsis mortality is driven by lymphocyte dysfunction and anergy. Although PD-1 induces T-cell anergy, PD-1-high-T-cells prevent immune mediated tissue injury from infections. Bidirectional microorganism– immune cell cross talks exists. Gut Bacteroides fragilis-T-cell cross talk maintains innate immune cell/pathogen homeostasis. Commensal gut Clostridia spp suppress inflammation and induce gut tolerance. However, microbiota therapies for sepsis-induced microbiome disruptions are rarely tailored to induce specific, or required, immune responses.

Hypothesis: Among options commonly employed as probiotic therapy, Bacteroides fragilis (BF) will induce the least anergic and most restorative (IL-33 and PD-1-high) lymphocyte phenotype.

Methods: 1x106 T-lymphocytes [primary T-cell(ATCC-HB-11052)] were cultured with monomicrobial (MMicr) B. fragilis (BF), C. perfringnes (CP) or L. acidophilus [LA] or PBS for control. Polymicrobial environments (PMicr) were dominant in either BF(B50),

CP(C50) or LA(LA50). Cytokines included IL-22 & IL-33 (mediators of gut epithelium–bacteria interactions and epithelial repair). Flow cytometry was used for phenotying. T-cell DNA was extracted for pyrosequencing (CpG islands) for epigenetic changes. For translation, blood was obtained from septic SICU patients with either PMicr or MMicr infections.

Results: In reviewing T-cell cytokine responses, LA & LA50 consistently induced both IL-22 (42.6 vs 24.5 vs 24.2pg/ml;$p<0.05$) and IL-33. MMicrCP only induced IL-22, and BF only induced IL-33 under PMicr(B50) conditions(65 vs 30 vs 24 pg/ml;$p<0.05$). Within SICU patients IL-33 levels were higher in PMicr vs MMicr patients. Phenotype: All exposures uniformly elevated CD69. PD-1+ expression was lowest with either MMicr BF exposure (65.2% vs 85.7% vs 82.3%;$p<0.05$) or PMicr B50(79% vs 86% vs 95.3%;$p<0.05$). Conversely BF exposure induced a distinct PD-1-high subpopulation [BF (20.6%) & B50 (16.3%)]. BTLA expression did not differ following individual MMicr. Among PMicr, B50 and C50, but not LA50 increased BTLA+ expression(23.1% vs 20.6% vs 5.5%;$p<0.05$). Epigenetic changes: No methylation variation for cytokines. Only B50 induced methylation of HLA-DR4. BF & PMicr B50 induced demethylation of CTLA.

Conclusions: L.acidophilus induced the potential for short term resolution (IL-22 & IL-33) whereas B. fragilis induced a T-cell phenotype consistent with potential long term immune recovery. Microbiota therapies tailored to specific sepsis induced immune dysfunctions may obviate the need for prolonged antimicrobial therapy in immune paralyzed septic patients.

O15

Blue light improves survival after pneumonia by augmenting circadian protein expression

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Background: Pneumonia is a major cause of sepsis and acute lung injury, with three million cases reported annually in the US; it is the sixth most common cause of death. The causal mechanisms of acute alveolar damage include an excessive accumulation of neutrophils in the lung and subsequent production of inflammatory mediators and neutrophil-mediated oxidant damage. Light has been shown to influence an organism's response to stress. Circadian proteins, including REV-ERB, are known to attenuate inflammation and regulate mitochondrial biogenesis.

Hypothesis: We hypothesize that blue light enhances regional control of a septic focus and that modulating circadian protein expression will augment lung innate immunity and bacterial clearance.

Methods: Male C57BL/6 mice were intratracheally administered Klebsiella pneumoniae (6000 CFUs) and immediately exposed to 36 hours followed by 12 hours daily of bright (1400 lux) blue (442nm), bright red (617nm); or ambient white (400 lux) light. In parallel experiments, mice were subjected to pneumonia and then administered the REV-ERBα agonist, SR9009. Mice were euthanized at 72 hours, the lungs lavaged, and the

blood/organs harvested. Tissue and blood were analyzed for bacterial CFUs. Tissue expression of REV-ERBα was analyzed by immunofluorescence and immunoblot. Cytokine concentrations were quantified by ELISA. Statistical analysis was performed by Wilcoxon rank-sum, and a $p<0.05$ was considered significant.

Results: Mice exposed to blue light survived longer than red or ambient light (log-rank $p = 0.02$). They exhibited faster bacterial clearance ($p = 0.06$), but did so with reduced neutrophil counts ($p = 0.0001$) and tissue cytokine concentrations. Blue light induced elevated expression of REV-ERB in the lungs, alveolar macrophages, and spleen. Mice administered the REV-ERB agonist SR9009 survived longer than the control group. Similar to blue light, SR9009 enhanced bacterial clearance and reduced bacterial dissemination ($p = 0.14$), while reducing neutrophil influx into the lung ($p = 0.001$). This appeared to be due to an inhibition of pulmonary chemokines, as SR9009 reduced KC, MIP-1α, MIP-2 within the lung, as well as TNFα and IL-6.

Conclusions: Blue light functions through a visual and cholinergic pathway and the spleen to augment lung innate immunity and bacterial clearance, while reducing neutrophilic inflammation. The mechanisms involve an augmentation in REV-ERB expression in alveolar macrophages and lung tissue, whereby the REV-ERB agonist SR9009 yielded similar results to blue light. Further studies are required to determine how altering REV-ERB affects macrophage phagocytic function.

O16

Trauma Causes an Immunosuppressive Response to Secondary Microbial Challenge

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Background: Background: Traumatic injury is associated with a 3-fold increase in the rate of ventilatory associated pneumonia (VAP) resulting in 40% of trauma patients requiring intubation developing VAP. To determine how injure effects the systemic response to infection, we measured the inflammatory response secondary LPS challenge in a clinically relevant murine model of injury induced immune dysfunction.

Hypothesis: We hypothesized that injury would suppress the inflammatory response to secondary microbial challenge.

Methods: C57BL/6 mice were subjected to polytrauma comprised of a 30% blood volume hemorrhage, bilateral lower extremity pseudofracture and a liver crush injury, a modification of our previously described protocol. 2 cohorts of mice were studied 48 hours after injury. In cohort 1, animals were challenged 1 mg/kg LPS and plasma cytokines were measured 6 hours after LPS. In cohort 2, peripheral blood leukocytes (PBL) and peritoneal exudate cells (PEC) were isolated, stimulated with LPS or heat-killed Pseudomonas Aeruginosa (HKPA) and inflammatory cytokine production measured ex-vivo. Cytokines were assayed by cytometric bead array (BD) and compared by t-test.

Results: In injured animals, LPS challenge resulted in elevated levels of IL-10 (79+/-51 pg/ml vs. 30+/-13 pg/ml, $p<0.05$) and a significantly decremented Interferon-gamma response (27+/-14 pg/ml vs. 90+/-24 pg/ml, $p<0.05$). Ex-vivo stimulation of PBL with LPS or HKPA demonstrated that cells from injured mice produced significantly higher levels of TNF-alpha and IL-10 as compared to uninjured controls. PEC from injured mice produced higher levels of TNF-alpha, MCP-1 but produced lower levels of IL-10 as compared to controls.

Conclusions: Traumatic injury significantly altered the systemic response to secondary challenge with microbial products. PBL and PEC demonstrated a heterogenous response, with PEC manifesting a proinflammatory phenotype and PBL an mixed phenotype. In-vivo, the systemic cytokine response to LPS after trauma was immunosuppressive with exaggerated IL-10 production and abrogated production of IFN-gamma.

O17

Does Elevated Initial Creatinine Clearance Predict Infections in Critically Ill Trauma Patients?

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Background: Infections pose a major risk of morbidity and mortality following trauma, despite early use of powerful antibiotics. One possibility is augmented renal clearance (ARC= creatinine clearance (CLCr) > 130 mL/min), which frequently occurs early after trauma and might alter antibiotic pharmacokinetics.

Hypothesis: We test the hypothesis that CLCr significantly differs in those that develop infection.

Methods: In 158 consecutive trauma ICU patients with admission serum creatinine (SCr) ≤1.65 mg/dL, 24 hr CLCr was measured within 5 days of admission to the ICU, and correlated with three traditional clinical estimates of CLCr: Cockroft-Gault (CG), modification of diet in renal disease (MDRD), and chronic kidney disease epidemiology (CKD-EPI). Data are expressed as M±SD if parametric, or median [interquartile range] if not, and compared with univariate analysis and multivariate logistic regression.

Results: The population was 44±20 years, 67% male, 10% burn, 71% blunt, and 20% penetrating mechanism of injury. Admission SCr was 0.97±0.24mg/dL, CLCr was 154±76 ml/min and the ARC incidence was 58.2%. Length-of-stay was 17[10-33] days, infection rate was 43.7% and mortality was 7.6%. The mean CLCr was 140 ml/min patients with positive blood, urine or bronchoalveolar lavage cultures vs 165 ml/min ($p=0.044$) in those without positive cultures. Of 17 potential risk and protective factors, including age, body mass index, admission vital signs, Abbreviated Injury Scale chest/abdomen/head >2, injury mechanism, transfusion and catheter history, mechanical ventilation was the only independent predictor of infection (OR 3.17 [1.187-

8.479], p=0.021), while elevated CLCr was the only factor protective from infection (OR 0.99 [.983-.997], p=0.009.) Additionally, clinical estimates CKD-EPI, MDRD, and CG underestimated CLCr by 29%, 23% and 14%, respectively (all p<0.01).

Conclusions: These data confirm that ARC is present in the majority of severely injured trauma ICU patients and that traditional clinical estimates of CLCr fail to detect this phenomenon. More importantly, this is the first demonstration that, counterintuitively, CLcr is significantly higher in those that resist infection. We speculate that augmented CLcr either provides some protective mechanism for patients at risk of infection, and/or is merely a manifestation of an overall beneficial compensatory survival response after trauma. Thus, CLcr could play a potential role for targeted therapy. Further studies are warranted.

O18

The impact of Sarcopenia on Mortality in Patients with Necrotizing Soft Tissue Infections

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Background: Necrotizing soft-tissue infections (NSTIs) are surgical emergencies associated with high morbidity and mortality. Identifying risk factors for poor outcome is a critical part of preoperative decision-making and counseling. Sarcopenia, the loss of lean muscle mass, has been associated with an increased risk of mortality and can be measured using cross-sectional imaging. Our aim was to determine the impact of sarcopenia on mortality in patients with NSTI.

Hypothesis: We hypothesize that sarcopenia will be associated with an increased risk of mortality in patients with NSTI.

Methods: This is a retrospective cohort study of NSTI patients admitted from 1995 to 2014 to two academic institutions. Average bilateral psoas muscle cross-sectional area at L4, normalized for height (Total Psoas Index [TPI]), was calculated using computed tomography. Sarcopenia was defined as TPI in the lowest sex-specific quartile. Primary outcome was in-hospital mortality. Multivariate logistic regression was performed to assess the association between sarcopenia and in-hospital mortality.

Results: There were 108 patients with preoperative imaging, 62% males and a median age of 58.3 years (IQR 47–68.2). 24 (22%) were immunocompromised. Overall in-hospital mortality was 16%. There was no significant difference in gender, body mass index (BMI), comorbidities and American Society of Anesthesiologists classification (Table 1). Sarcopenic patients were older and had a higher in-hospital mortality rate (p<0.05). After multivariate analysis, sarcopenia was independently associated with increased in-hospital mortality (Odds ratio, 3.5; 95% Confidence Interval [CI], 1.05-11.8).

Conclusions: Sarcopenia is associated with increased risk of in-hospital mortality in patients with Necrotizing soft-tissue infections. Sarcopenia identifies patients with higher likelihood of poor outcomes, which can possibly help surgeons in counseling their patients and families.

O19

Accurate Risk Stratification for Development of Organ/Space Surgical Site Infections after Emergent Trauma Laparotomy

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Background: Organ/space surgical site infection (OS-SSI) develops frequently after trauma laparotomies and is associated with significant morbidity. Currently, no valid model exists to accurately risk stratify the probability of OS-SSI development after emergent laparotomy. Risk stratification for OS-SSI in these patients could guide promising, but unproven, interventions for OS-SSI prevention, such as more frequent dosing of intraoperative antibiotics or direct peritoneal resuscitation.

Hypothesis: We hypothesize that in trauma patients who undergo emergent laparotomy, probability of OS-SSI can be accurately estimated using patient data available during the index operation.

Methods: Retrospective review was performed of a prospectively maintained database of emergent trauma laparotomies from 2011-2016. Patient demographics and risk factors for OS-SSI were collected. We performed Bayesian multilevel logistic regression to develop the model based on a 70% training sample. Evaluation of model fit using area under the curve (AUC) was performed on a 30% test sample. A Bayesian model was chosen in the setting of a low ratio of observed events to predictors, which permits estimation of probabilities when sample size is small.

Results: 1,308 patients underwent laparotomy, of which 165 (13%) developed OS-SSI. Variables included in the model and their contribution to the model are presented in the Table. Three variables that contributed most to OS-SSIs were damage control laparotomy, colon injury, and colon resection. The AUC of the predictive model validated on the test sample was 0.80 (95% CI 0.73-0.86). An example of how the model can be used to calculate the probability of OS-SSI are also presented (Table).

Conclusions: Using a combination of factors available to surgeons prior to the end of an emergent laparotomy, the probability of OS-SSI could be accurately estimated using this retrospective cohort. A web-based calculator is under design to allow the real-time estimation of probability of OS-SSI intraoperatively. The calculator could be used to improve intra- or post-operative management of moderate and high risk patients. Prospective validation of its generalizability to other trauma cohorts and of its utility at the point-of-care is required.

O20

Downregulation of occludin protein in necrotizing enterocolitis is associated with altered expression of microRNA-874

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Background: Necrotizing enterocolitis (NEC) is a devastating intestinal disease of neonates. NEC is associated with increased intestinal permeability due to changes in tight junction proteins in the intestinal epithelium (i.e. occludin). MicroRNAs (miRNAs) are small non-coding RNAs that serve as key regulators of tight junction proteins by inducing translational inhibition or transcript degradation. Aberrant expression of miRNAs is found in the intestinal epithelium of patients with inflammatory bowel disease and other intestinal disorders; however, no studies have examined the role of miRNAs in NEC.

Hypothesis: We hypothesize that decreased occludin is regulated by miRNA expression in the intestinal epithelium during NEC.

Methods: To test our hypothesis, we analyzed patterns of 3 occludin-regulating miRNAs (miR-21, miR-122, and miR-874). We examined human intestinal NEC (N=6) vs control samples (N=6) as well as an in vitro enteroid model. The enteroids (intestinal epithelial organoids) were exposed to lipopolysaccharide (LPS) for 24 hours to create an in vitro model of experimental NEC compared to untreated controls. Changes in miRNA, mRNA and protein were analyzed by RT-PCR, western blot and immunofluorescence. Data was analyzed with Student's t-test or ANOVA.

Results: Significant changes of miR-21 or 122 were not identified. Decreased expression of miR-874 ($p=0.002$) in human intestinal NEC samples was associated with decreased occludin mRNA ($p=0.006$) and protein expression ($p=0.009$). Similarly, enteroids treated with LPS expressed lower levels of miR-874 than the controls ($p=0.008$). This finding was accompanied by a 2.7 fold decrease in occludin mRNA ($p=0.005$).

Conclusions: There is a downregulation of occludin RNA and protein in NEC preceded by decreased miR-874 expression. Thus, miR-874 may be an important regulator and biomarker of NEC.

O21

Are patients with perforated peptic ulcers that are negative for H. pylori at a greater risk?

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Background: The link between Helicobacter pylori (H. pylori) infection and peptic ulceration is well known. However, in recent years studies have shown a decline of H. pylori related peptic ulcers. Emergence of the antibiotic era may be the reason for a decrease in H. Pylori associated peptic ulcers.

Hypothesis: We hypothesize that H. pylori positive perforated peptic ulcer disease (PPUD) patients requiring surgical intervention have worse outcomes than patients who are negative.

Methods: Prospective data were collected on 106 patients having PPUD and tested for H. Pylori serum IgG test. Patients were divided into two groups; H. Pylori positive (HPP) and H. Pylori negative (HPN). Demographics, social history, medication history, esophagogastroduodenoscopy and admission blood reports were collected. Students T test was used for continuous variables and X2 test was used for categorical variables.

Results: We identified 79 patients who had H. Pylori serum IgG testing. 42(53%) tested positive and 37(47%) tested negative. HPN PPUD was more frequent in females (70%), Caucasians (84%) and patients with higher BMI 29±8.8. HPN group had a significantly longer length of stay (LOS) (20.2±13.8 vs 8.5±7.2 p=0.0001), ICU LOS (10.97±11.6 vs 1.9±4.6 p=0.0001), Ventilator days (4.54±6.7 vs 0.98±2.8 p=0.004), 30 day readmission (11; 68.7% vs 5; 31.3% p=0.049), ASA (3.11±0.85 vs 2.6±0.7 p=0.005), Charlson comorbidity index (4.8±2.7 vs 2.9±2.71 p=0.004) and a lower serum Albumin level (2.9±0.96 vs 3.86±0.9 p=0.0001). HPN PUD was associated with statistically significant higher risk of rebleed or ulceration (7, 88% vs 1, 12%, p=0.023) more than 6 months after the operation. No difference in the mortality was found between the groups.

Conclusions: In contrast to what we expected, HPN patients had clinically significantly worse outcomes than HPP patients. These findings may represent a difference in the baseline pathophysiology of the PUD process. Further investigation is warranted.

O22

Role of Nrf2 in the Protective Effect of Remote Ischemic Conditioning in Hemorrhagic Shock/Resuscitation

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Background: Oxidative stress and immune cell activation remain the major contributors to the development of secondary complications in resuscitated trauma patients. Anti-oxidant interventions targeting these inflammatory events have potential to improve outcomes. We have previously demonstrated that remote ischemic conditioning (RIC) exerts hepatoprotection in a murine model of hemorrhagic shock/resuscitation (HS/R) that is mediated by antioxidant response and elaboration of humoral factors. In the current study, we examined the mechanisms of RIC using murine and zebrafish models of injury.

Hypothesis: Humoral factors released by RIC exerts remote organ protection that is

mediated by the anti-oxidant transcription factor Nrf2.

Methods: Wildtype (WT) C57/BL6 or Nrf2 KO mice were subjected to hemorrhagic shock for 2h at 30mmHG MAP and resuscitated with blood taken from donor WT or Nrf2 KO mice that had undergone RIC (4 cycles of 5-min hindlimb ischemia/reperfusion) and two volumes of Ringer's Lactate. Mice were sacrificed at 2h post resuscitation for evaluation of liver injury by serum ALT. In zebrafish studies, zebrafish were subjected to morpholino knockdown of Nrf2a and microinjected with plasma (5%) taken from WT or Nrf2 KO mice after RIC. Neutrophil migration was assessed after tailfin transection and survival studies were conducted under LPS (100ug/ml) or H2O2 (2mM) treatment. Zebrafish Oxidative Stress RT2 Profiler PCR Array was used to investigate the effect of RIC plasma on oxidative gene expression.

Results: WT mice resuscitated with WT RIC blood significantly reduced liver injury. However, the protective effect of WT RIC blood was abolished when resuscitated in Nrf2 KO mice. Furthermore, WT mice resuscitated with Nrf2 KO RIC blood failed to exert hepatoprotection. In parallel, WT zebrafish microinjected with WT RIC plasma had significantly lower neutrophil migration towards the site of injury – an effect that was abrogated in zebrafish with Nrf2a knockdown or when WT zebrafish were microinjected with Nrf2 KO RIC plasma. In addition, zebrafish microinjected with WT RIC plasma significantly improved survival following incubation with LPS or H2O2. The mRNA levels of anti-oxidant genes (myoglobin, hmox1) were up regulated and pro-oxidant gene (duox) was down regulated in zebrafish microinjected with WT RIC plasma.

Conclusions: Nrf2 is a central mediator in the elaboration of humoral factors and organ protection of RIC against HS/R. Up regulation of cytoprotective antioxidant genes and down regulation of oxidative genes may contribute to the downstream mechanisms of RIC. RIC represents a potential therapeutic for trauma patients.

O23

The Need for Accredited Surgery Centers to Perform Non-Elective Cholecystectomy in Elderly Patients

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Background: The American College of Surgeons' accreditation process for surgical centers verifies specific criteria to ensure standards and optimize outcomes. We investigated the relationship between hospital volume for non-elective cholecystectomy and mortality rate in an elderly population to assess the need for verified centers for older patients with surgical emergencies.

Hypothesis: We hypothesized that increased hospital volume for non-elective cholecystectomy in the elderly would lead to decreased post-operative in-hospital mortality for older patients.

Methods: Patients ≥65 years who underwent urgent laparoscopic or open cholecystectomy for cholecystitis were identified in the California State Inpatient Database for the years 2010-2011. Beta regression models for proportions as outcomes

examined the relationship between 2-year operative volume and in-hospital risk-adjusted mortality at the hospital-level.

Results: A total of 17,429 older patients underwent cholecystectomy at 298 hospitals. The average risk-adjusted morality rate was 3.9%. For every increase in hospital cholecystectomy volume in the elderly, mortality consistently decreased ($p<0.001$; figure 1), from >10% at the lowest-volume hospitals to <1.5% at the highest-volume centers. If an institution performed ≥28 cholecystectomies over the 2 years, there was a 95% chance that that institution performed at or above the average risk-adjusted mortality rate; 209 hospitals (70%) achieved this benchmark. Over the study period, for every 100 non-elective cholecystectomies performed at hospitals doing <28 cases, 3 elderly lives may have been saved if the operation had been done at a ≥28-case hospital.

Conclusions: Older patients undergoing non-elective cholecystectomy for cholecystitis might reduce their risk of mortality by having the operation performed at a higher-volume hospital. These results support the concept of verification for accredited surgery centers that provide emergency care to elderly patients.

O24

Prolonged benefit of Reltecimod in treatment of patients with NSTI is independent of brief plasma half-life

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Background: Reltecimod (AB103) is a short CD28 receptor mimetic peptide that improves the host's ability to fight severe infections. In spite of a brief half-life in plasma (mice, pigs, humans), a single dose of Reltecimod suffices to provide sustained survival benefit in animal models of sepsis and long-term clinical benefit in patients with necrotizing soft tissue infections (NSTI). Reltecimod is currently being evaluated in a Phase 3 multicenter clinical trial in NSTI patients.

Hypothesis: Reltecimod's long-term efficacy benefit may be based on distribution to target sites and rapid intervention with signaling pathways, irrespective of its short residence time in plasma.

Methods: Male Balb/c mice (n=36) were administered a single IV dose of radiolabeled Reltecimod ([14C]valine, 5 mg/1000 mCi/kg). Whole blood, plasma and tissues were collected at 2, 4, 6, 8, 10, 20, 30 min and 1, 2, 4, 8, 24 h post-dose. Total radioactivity concentration in all tissues was determined, PK parameters were calculated, modeled and compared between mice and humans. Minimal time to observe efficacy was demonstrated using staphylococcal enterotoxin B-activated human peripheral blood mononuclear cells (hPBMCs), monitoring cytokine responses after different durations of exposure to Reltecimod (5min-9h).

Results: Fast clearance of Reltecimod from plasma was observed, 60.4 mL/min/kg, exceeding hepatic flow and approaching cardiac output, with a half-life of 2.65 min, consistent with parameters obtained after exposure of healthy human subjects and NSTI patients, fitting into a one-compartment elimination model. Reltecimod distributed rapidly across multiple highly perfused tissues/organs, but within 2 min targeted mainly lymphatic organs (lymph nodes and spleen, harboring T cells that express CD28). Peak

accumulation was 20 min and 2 h, respectively, post dose in lymph nodes [26.4±11.3 ugEq/g, mean ± SEM] and spleen [9.61±1.93 ugEq/g, mean ± SEM] (Fig 1). Lymphatic concentrations were 22.1±9.7 fold higher than plasma at 20 min and remain so for several hours. Consistently, blood partitioning indicated that Reltecimod is preferentially and significantly enriched in WBC (6.8% after 2 h). Fast, long-lasting action of Reltecimod was demonstrated in hBPMCs, where a 5-min exposure was sufficient to attenuate IFN-g induction for at least 9h (Fig 2).

Conclusions: Our hypothesis is supported by (i) fast homing into target organs, where redistribution to systemic circulation may occur, leading to availability greatly exceeding plasma half-life; (ii) rapid onset of inhibition of inflammatory cytokine induction, independent of exposure time.

O25

Farnesoid X receptor (FXR) may be necessary for intestinal injury in experimental murine necrotizing enterocolitis

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Background: FXR activation has been reported to decrease gut permeability in chronic injury models protecting against bacterial translocation from the intestinal lumen. However, FXR activation is also known to decrease intestinal cell proliferation, which possibly impedes barrier function following injury.

Hypothesis: Given these inconsistencies, we hypothesize that FXR activation is detrimental to the intestinal barrier in an acute bacterially-induced injury model of necrotizing enterocolitis (NEC).

Methods: Fourteen day-old wild-type (WT) and FXR knock-out (FXR-KO) mice were injected with 75 mg/kg body weight of the zinc chelating agent dithizone or saline via intra-peritoneal route. Dithizone sensitizes the intestine to infectious injury by damaging Paneth cells. After 6 hours, the animals were gavage-fed 1x10^8 CFU Klebsiella pneumoniae per kg body weight. Animals were sacrificed at 16 hours. Terminal ileal sections were quantitatively graded in a blinded fashion on histology using a five-point scale (0-5) based on amount of sub-mucosal separation and edema. Additional small intestinal sections were stained to assess for phosphorylated ERK (pERK) expression with immunofluorescence (IF). Kruskal-Wallis test was performed to compare multiple groups of non-parametric data.

Results: Histological NEC scores in WT mice were significantly increased in dithizone/Klebsiella mice versus saline controls ($p < 0.005$). This effect, however, was attenuated in FXR-KO mice, with histological scores similar to controls, suggesting that FXR is necessary for intestinal injury in this murine bacterial injury model of NEC. Expression of pERK measured by IF was lower in WT control mice compared to dithizone/Klebsiella treated WT mice. Interestingly, FXR-KO mice showed the opposite, with higher pERK levels in untreated versus treated animals, suggesting that FXR-KO mice may be primed to respond to this type of injury.

Conclusions: Dithizone/Klebsiella-induced Intestinal injury was attenuated in FXR-KO

mice compared to WT mice. FXR may be a valuable therapeutic target in NEC and intestinal injury in high-risk infants.

O26

Delayed Mobilization Impacts Length of Stay and Infectious Complications in Elderly Surgical Patients

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Background: Surgical admissions are increasing in older and frailer patients, who are vulnerable to post-operative morbidity and mortality. Early post-operative mobilization may reduce adverse events and length of stay (LOS), but little is actually known about the impact of delayed mobility.

Hypothesis: We hypothesize that delayed mobilization would increase LOS and complications in elderly surgical patients.

Methods: A prospective cohort study was undertaken. Overall, 306 consecutive survivors of emergent abdominal surgery aged ≥65 years who required help with <3 activities of daily living were prospectively enrolled at 2 tertiary-care Canadian hospitals. Time until post-operative mobilization (out of bed) was attained from hospital records and a priori defined as 'delayed' (>35h) or 'early' (≤35h) and analyzed with multivariable negative binomial regression.

Results: Mean age was 76±7.7 years, 45% were women, and 22% were frail according to the Clinical Frailty Scale. Gallstones (23%), intestinal obstructions (21%), and hernia (17%) were the most performed surgeries. Median time to post-operative mobilization was 19h (interquartile range [IQR] 9-35) and median LOS was 9 days (IQR 6-14). One-quarter (n=74) of patients had delayed mobilization, which was associated with much longer median LOS vs early mobilization (14 days [IQR 10-28] vs 7 days [IQR 5-11] p<0.001). After multivariable adjustment, delayed mobilization was still independently associated with longer LOS (adjusted ratio 1.25, 95%CI 1.05-1.44, p=0.03). These patients had increased all-cause complications (47.3% vs 32.3% p=0.02), major infection (9.5% vs 3.5%, p=0.04), and minor infection (14.9% vs 3.0%, p<0.001).

Conclusions: Potentially preventable delays in mobilization following surgery frequently occur in elderly patients and are associated with 25% longer LOS and more complex discharge transitions. Elderly patients with longer than expected periods of immobilization are a group to target for evidence-based interdisciplinary discharge and transition programs. However, since delays in post-operative mobilization are also potentially modifiable and may intersect with other less amendable surgical risk factors (e.g., comorbidity or frailty), elder-specific strategies targeting early mobilization need to be evaluated with the aim of preventing adverse surgical recovery.

O27

Attributable Mortality from Extensively Drug Resistant Gram-Negative Infections using Tracer Antibiotic Algorithms

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Background: The impact of extensive drug-resistance (XDR) on survival from gram-negative infections (GNIs) remains unclear. Tracer antibiotic algorithms may enable the estimation of mortality attributable to XDR among patients with GNIs using large administrative databases.

Hypothesis: In a propensity-matched analysis, patients receiving colistin, marking them as having an extended spectrum gram negative infection will have higher attributable mortality than patients with gram negative infections without significant extended antibiotic resistance.

Methods: Adult inpatient encounters coded for GNIs and associated antibiotic administrations in the Vizient database were analyzed. Colistin cases were defined by >3 consecutive days of intravenous colistin or death while receiving colistin; comparator cases were similarly defined using select non-carbapenem ß-lactams instead. Colistin cases were matched (1:2) to comparator cases by propensity of receiving colistin. XDR attributable mortality was calculated as the difference in in-hospital mortality between propensity-matched groups and 95% confidence intervals (CI) using bootstrapping. Variation in attributable mortality by infection site and onset, sepsis strata, and a propensity-matched carbapenem comparator group was examined. Algorithm accuracy was tested using chart review at 3 hospitals.

Results: Of 232,834 GNI encounters between 2010-2013 at 79 hospitals, 905 of 3,350 (27%) colistin and 9,188 of 105,641 (8.7%) comparator cases died. Mortality among propensity-matched colistin (n=3,099) and comparator cases (n=6,198) was 29.2% and 16.6% respectively [attributable mortality =12.6% (CI 10.8-14.4%)]. This estimate of XDR attributable mortality varied considerably by site and onset of infection, ranging from 1.1% (-7.6-8.2%) for bloodstream to 15.5 (12.6-18.4%) for respiratory ($p<0.0001$), and 4.6% (2.1-7.4%) for community vs. 16.6% (14.3-18.9%) for hospital onset ($p<0.0001$). Mortality attributable to XDR increased 3-fold when coded for sepsis and 9-fold when coded for severe sepsis/septic shock ($p<0.0001$). Using a carbapenem comparator group, attributable mortality decreased to 7.5 (5.6-9.4)%. Chart reviews demonstrated that colistin cases had a positive predictive value of 60.4% and sensitivity of 65.3% for detecting XDR GNIs. The mortality varied significantly within antibiotic groups with the coding for sepsis and severe sepsis/shock.

Conclusions: Using tracer antibiotic algoirthms, mortality attributable to XDR during GNIs was estimated at 12.6%, but varied considerably by site and onset of infection and coding for sepsis or severe sepsis/septic shock.

O28

Stimulation of Systemic Low-Grade Inflammation by Chronic Stress

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Background: Systemic inflammation, a central component of the innate immune system, is composed of the stress response, the acute phase reaction, and the tissue defense response. Appropriately regulated inflammation is beneficial, but excessive or persistent systemic inflammation that frequently characterizes critical illness, often incites further tissue destruction, organ dysfunction, and disease progression. This study sought to determine if the systemic cytokine profile of rodents subjected to chronic restraint stress leads to persistent low-grade inflammation.

Hypothesis: We hypothesize that chronic restraint stress in a rodent model will incite a similar cytokine profile to that of persistent inflammation.

Methods: Male Sprague-Dawley rats were subjected to restraint stress for a total of seven days. The rodents were placed in a nose cone rodent cylinder for 2 hours daily and repositioned every 30 minutes to prevent habituation at which time an alarm was played for two minutes. Control animals underwent daily handling. All rodents were sacrificed on day 8. Urine norepinephrine (NE), epinephrine (EPI), plasma interleukin 6 (IL-6), C-reactive protein (CRP), granulocyte colony-stimulating factor (G-CSF), stromal cell-derived factor 1 (SDF-1) and tumor necrosis factor alpha (TNF-α) were assessed with ELISA. Data presented as mean±SD; *$p < 0.05$ analyzed by t-test.

Results: NE, not EPI, remained significantly elevated on day 8 compared to control rats (Table). Plasma IL-6 expression was also significantly elevated on day 8 compared to control rats. Plasma CRP was double control values on day 8. Both G-CSF and SDF-1, key mediators involved in neutrophil mobilization, remained significantly elevated following chronic restraint stress. Plasma TNF-α was not significantly elevated after 8 days.

Conclusions: Chronic restraint stress led to persistent elevation of urine NE, plasma IL-6, CRP, G-CSF, and SDF-1. Systemic TNF-α levels may not adequately reflect tissue levels following chronic restraint stress. The systemic cytokine milieu associated with chronic stress, as a model of critical illness, is similar to that of persistent low-grade inflammation. Combining this model with trauma and sepsis models will allow evaluation of the contribution of persistent inflammation in disease progression, organ dysfunction, and outcomes.

O29

Resident lead research abstracts from the SIS Annual meeting are frequently published in high impact metrics

Daithi Heffernan; Andrew Stephen, Brown University

Background: Presenting at national scientific meetings is costly and time consuming, commodities in short supply in the 80-hour work week environment. Conversion of abstracts to published manuscripts remains a key goal and critical currency for academic surgeons. Across scientific fields conversion rates of abstracts to manuscripts varies from 8% to 70%. The Surgical Infection Society(SIS) annual meeting and associated Surgical Infections(SI) journal are dedicated to advancing the science and care of surgically related infections, as well as fostering careers of young surgeons.

Hypothesis: Given the SIS commitment to mentorship, the SIS annual meeting is a forum for the presentation of high quality, resident led, basic and clinical research as denoted by high rates of conversion to full manuscripts with high impact metrics including Surgical Infections (SI) journal.

Methods: Abstracts and meeting programs for 2014 and 2015 SIS annual meetings were reviewed. Literature search was conducted for published manuscripts generated from these meetings. Abstracts were categorized Basic(BasSci) or Clinical Science(ClinSci), Plenary(Plen), Oral(OP) or Poster(PP) presentation. Author listings were reviewed for Resident(RA) or New Member(NM) and whether senior authors were SIS members. The senior author was “leadership role” if he/she had served on an SIS committee. If converted, the Impact Factor(IF) of the journal at the time of publication was recorded.

Results: Of the 198 abstracts, 102 Plen or OP. Overall, 119(60%) abstracts converted to manuscripts. 43/119 manuscripts(36%) were published in SI. The other 76 spanned 51 different journals (average IF=5.2 (range 0.5-72.4). 19 of the 21 Plen(90.5%) converted (mean IF=11.8), with 6(31.5%) appearing in SI. Among OP, 70%(51/81) were converted (mean IF= 4.4), and 21 of these 51(41%) were published in SI. The lowest publication rate occurred among PP(46%). The IF of Plen manuscripts was higher than other groups (11.2 vs 3.6;p=0.03). ClinSci were more likely published in SI versus BasSci(63% vs 4%;p<0.01). Resident abstracts(RA) were most likely converted into manuscripts(OR2.1(95%CI=1.1-3.8). Although not statistically different, the IF of manuscripts was highest among RA (4.7 vs 3.8), and was most pronounced among RA ClinSci (IF – 5.1 vs 3.3) manuscripts. 84% of senior authors were members of SIS. Among senior authors rates of conversion were higher if the senior author had held a leadership role in SIS(67% vs 47%;p=0.02). No additive effect was noted for presidents or past presidents of SIS.

Conclusions: The SIS annual meeting is an excellent venue for high impact quality basic and clinical scientific research. In keeping with the core mentorship environment of SIS, residents and leadership roles members most likely converted abstracts to manuscript.

O30

Is There Gender Disparity Within the Surgical Infection Society?

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Background: Women are under-represented in academic surgery and surgical societies despite an increase in the percentage of female surgeons (24.0%) and surgery residents (34.6%). Publications, awards and society leadership positions are used for hiring and promoting surgeons.

Hypothesis: We hypothesized that within the Surgical Infection Society (SIS) females are under-represented.

Methods: The SIS website and databases were evaluated for the number of female members, awardees, and those in leadership positions. The data was divided in four different time periods: 2000-2005, 2006-2010, 2011-2015 and 2016-2017 and compared for changes over time utilizing X2. In addition, council members for five other surgical societies (AAST, ACS, EAST, Shock, Southern) were reviewed and the percentage of female representation in leadership positions compared.

Results: Only 135/587 (23.0%) SIS members are female. There has been an increase in female membership over time ($p<0.001$; Figure). The number of female awardees has risen from 36.5% to over 50% in the last two study periods ($p=0.002$). Female representation in leadership positions decreased from 26.1% in 2000-2005 to less than 15% in the last three study periods ($p=0.234$; Figure). When comparing the SIS with other surgical societies, similar disparities were seen (Table). Although some societies have better representation, most continue to have a disproportionately low number of females in leadership positions.

Conclusions: Female surgeons are under-represented in SIS membership and leadership positions. While the number of female surgeon and resident participation has increased, these trends have not occurred with council membership in the SIS. There is a lack of female representation in leadership positions. This may be related to differences in pathway for membership as opposed to leadership. Membership is largely unrestricted while leadership positions require nominations by past members of the council. There is a need to address this gender disparity.

O31

Examining Healthcare Utilization After use of a Mobile App for Wound-care Follow Up in the Emergency Department (ED).

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Background: mPOWEr (Mobile Post-Operative Wound Evaluator) is a mobile health (mHealth) app developed to communicate patient generated health data to healthcare providers.

Hypothesis: It is feasible to use mHealth in an ED population and to measure follow-up healthcare utilization.

Methods: To study the feasibility of using mPOWEr in two urban EDs, we examined healthcare use after discharge. Patients seen for laceration repair, abscess drainage, or for other wounds were invited to submit images of their wounds after discharge. Clinical care was not changed based on participation. We compared clinic and ED visits and readmissions in a 30-day post-ED window by type of wound (laceration, abscess drainage, other) and by insurance type (commercial [CI], medicare [MC], medicaid [MA], workers compensation [WC], and self-pay [SP]).

Results: Of 237 patients approached, 70 (30%) declined and 67 (28%) were ineligible due to lack of personal cell phone. Of 100 enrolled, 59 (59%) submitted at least one wound photo and 70 (70%) had at least one communication of either photo submission or text message. Within 30 days of ED visit, 29% had >=1 clinic visit, 4% were hospitalized, and 16% had a repeat ED visit. There was no difference in ED or clinic visits across wound types. However, all 4 hospital admissions followed ED visits for "other" wounds (p=0.061; table 1). Of admitted patients, 3 (75%) had CI and 1 had MC. There was no significant difference in utilization by type of insurance (table 2), but trends are toward higher utilization with commercial insurance and less by self-payers.

Conclusions: In demonstrating feasibility of mPOWEr for wound care follow-up, we also observed a variability of post-ED healthcare utilization by wound type and insurance status. There is an opportunity to use mHealth to shift post-ED care utilization in self-pay patients in particular, who are at risk of loss to follow up. Future work will focus on targeting populations to optimize healthcare utilization after an ED visit and validate SSI rates.

O32

Clinical Synergism: Combined Fungal and Bacterial Intra-Abdominal Infections Associated with Increased Mortality

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Background: Multiple synergistic interactions have been identified between fungi and bacteria, including co-aggregation into mixed biofilms, enhanced growth via signaling molecules, and shared metabolic byproducts. However, the clinical implications of these interactions are largely unknown. While fungal and bacterial co-infection is common in complicated intra-abdominal infections (IAI), outcomes from combined infection have not been well studied.

Hypothesis: We hypothesized that synergistic interactions between fungus and bacteria would lead to higher mortality in patients with combined IAI.

Methods: All surgical patients admitted to a single academic institution between 1996 and 2014 were queried for presence of a culture-proven bacterial IAI. Univariate analyses compared characteristics between patients with a combined fungal and bacterial IAI and those with bacterial IAI alone. Multivariable logistic regression evaluated the effect of fungal presence in IAI on in-hospital mortality, while controlling for APACHE II score and select comorbidities. A subgroup analysis evaluated unadjusted mortality rates for common fungal-bacterial combinations.

Results: Of 1887 patients with culture-proven bacterial IAI, 503 (26.7%) were co-infected with fungi. Patients with a fungal component were older (57.0 vs. 55.5 years, p=0.025) with a higher median APACHE II score (15 vs 13, $p < 0.01$) but without differences in trauma or transplant status or comorbidities including diabetes, coronary artery disease, liver disease or kidney disease. The most common bacterial pathogens were Enterococcus spp. (25.6%), E. coli (16.9%) and Streptococcus spp. (12.0%). The

most common fungal pathogens were Candida albicans (40.4%) and Candida glabrata (24.9%.) The presence of fungal species was associated with increased crude in-hospital mortality (16.9% vs. 9.8%, p<0.01), and on multivariable regression, fungal co-infection remained associated with death (Table). The highest mortalities were associated with fungal co-infection with Enterobacter spp. (28.6%), Enterococcus spp. (28.3%), and P. aeruginosa (26.3%).

Conclusions: We identified an association between fungal presence and in-hospital mortality in patients with bacterial IAI. Continued research into cross-kingdom synergistic relationships will identify potential therapeutic targets in the management of IAI.

O33

How latent viruses may contribute to acute lung injury

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Background: Cytomegalovirus (CMV) infects 60-80% of people in this country. Like other herpes family viruses, the virus is controlled in immune competent individuals, but is not eradicated, leading to latent infection. Transient compromise of immunity can lead to viral reactivation which is pathogenic in immune-compromised hosts. Recently it has been recognized that CMV reactivation in immune competent hosts is associated with worse outcomes, with patients manifesting prolonged mechanical ventilation and worsened mortality.

Hypothesis: Using our murine model, we have associated CMV reactivation with a form of acute lung injury (CMV-ALI), but the mechanism of CMV-ALI remains poorly understood. We have recently observed that GR1+ cells accumulate in lungs of latently infected mice. Because GR-1 is highly expressed on neutrophils, we hypothesized that latent CMV infection might influence neutrophil function.

Methods: Neutrophils isolated from CMV-latent mice were compared with age matched CMV-naive mice.

Results: Neutrophil stimulation in-vitro with a TLR agonist cocktail as a surrogate to bacterial infection shows significantly enhanced inflammatory potential by cytokine ELISA with IL-6, MIP-1α, MIP-1γ, and RANTES secretion elevated 2-4 fold in CMV-latent compared to CMV-naive neutrophils. Neutrophils are a major source of reactive oxygen species during inflammation, so we evaluated neutrophil ROS production. PMA stimulation shows significant enhancement of ROS production in CMV latent neutrophils. Stimulation with formyl peptide further confirms that CMV-latent-neutrophils are persistently primed compared to naïve mice, and have exaggerated (5-8 fold) reactive oxygen species production (Figure 1). This exaggerated ROS response persists even 36 weeks after CMV infections, but lessens over time.

Conclusions: These results suggest that CMV-infection induces substantive and long lasting alterations in host innate immunity that persist well after primary infection and during latency. Given the prevalence of CMV and the importance of neutrophils in acute lung injury, our results suggest a possible mechanism explaining why CMV reactivation

is associated with longer durations of mechanical ventilation in immune competent patients.

O34

Retrospective Analysis of Postoperative Antibiotics in Operative Complicated Appendicitis

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Background: There is no consensus regarding the ideal postoperative antibiotic regimen for cases of surgically-managed acute complicated appendicitis. The purpose of this study was to investigate the different antibiotic regimens used for this purpose at our institution and their association with postoperative outcomes.

Hypothesis: We hypothesized that neither route nor duration of antibiotic therapy would be associated with the development of surgical site infection (SSI) in this population.

Methods: 1,102 patients underwent appendectomy from 2012 to 2016. Of these, we performed an extensive chart review on the 146 diagnosed with complicated appendicitis based on standardized definitions. Descriptive and inferential statistics were used to evaluate the demographic and clinical characteristics of these patients, including postoperative antibiotic use and postoperative complications.

Results: Of the 146 cases of complicated appendicitis identified, 120 (82.2%) were classified as perforated by the operative surgeon. These patients were significantly more likely to be started on antibiotics post-appendectomy (88.3% vs 34.6%, $p < 0.001$) and have a longer length of stay (LOS) ($p=0.009$). Patients with and without perforation otherwise did not differ with regards to age, sex, comorbidities, presenting WBC, or ASA classification. The development of a postoperative SSI was significantly associated with the presence of free fluid on preoperative imaging, a decision by the surgeon to leave a drain, and a longer LOS ($p=0.007$, $p=0.006$ and $p<0.001$, respectively). The duration of antibiotic treatment pre-SSI was significantly longer in patients who developed a SSI compared to those who did not ($p=0.042$). On multiple logistic regression, patients receiving 2 days of antibiotics versus 1 day or 3+ days had similar odds of developing a SSI as patients that did not receive postoperative antibiotics. Route of antibiotic administration did not significantly affect the odds of developing an SSI. Both multivariate models were adjusted for free fluid on imaging, decision to leave a drain, and surgeon-defined perforation.

Conclusions: In this cohort, operative surgeons successfully identified patients with complicated appendicitis who did not require postoperative antibiotics as a means to avert development of a SSI. For patients deemed to require antibiotics, 2 days of treatment were associated with reduced odds of SSI compared to shorter or longer antibiotic courses. These findings suggest that a prospective trial could clarify the optimal duration and route of antibiotic therapy in the setting of operative complicated appendicitis.

O35

Risk factors for wound infection in outpatients with lower extremity burns

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Background: Majority of burns are small and treated on an outpatient basis, however, most of the literature on the incidence and risk factors for wound infection has focused on the inpatient population. We sought to evaluate the risk factors for wound infection in patients presenting to the outpatient burn clinic with lower-extremity (LE) burns.

Hypothesis: We would be able to identify independent risk factors for wound infection in patients with LE burns, and specifically identify dressings associated with early wound infection.

Methods: A retrospective study of all adult patients presenting to the outpatient burn clinic following a LE burn from 01/2014-07/2015 was performed. Patients admitted from first clinic visit were excluded. Data regarding demographics, comorbidities, injury characteristics, outpatient course, and outcomes was obtained from review of electronic medical records. Primary outcomes were wound infection at any time and early wound infection (by day 5). Multivariate logistic regression analysis was performed to identify independent risk factors for wound infection.

Results: A total of 317 patients with LE burns were evaluated in our outpatient burn clinic with mean age of 42.9±16.7 yrs and median TBSA of 0.8% (IQR 0.3-1.5%); 22 patients had a component of full-thickness (FT) burn with median TBSA of 0.5% (IQR 0.2-1.0%). Scald burn (59.6%) was the most common mechanism of injury; 212 (66.9%) patients had below-the-knee (BTK) burn with median TBSA of 0.5% (IQR 0.2-1.0%). Median days to presentation after injury was 2 days (IQR 2-5 days). The incidence of wound infection in LE burns was 14.5%, which increased to 18.9% in the BTK burn subgroup. Median time to infection was 5.0 days (IQR 4.0-8.3 days) and majority (60.9%) of patients developed would infection within first 5 days. Patients who developed wound infection at any time were more likely to have a FT burn (21.7% vs. 4.5%, $p<0.001$), and BTK burn (87.0% vs. 63.5%, $p=0.002$), but there was no difference in baseline demographics, comorbidities, etiology or size of burn, or days to presentation between the two groups. Multivariate logistic regression showed age (OR 1.02, CI 1.00-1.04), FT burn (OR 5.33, CI 2.09-13.62), and BTK burn (OR 3.42, CI 1.37-8.52) as independent risk factors for burn wound infection. Use of silver sulfadiazine (vs. other wound care) was associated with early wound infection (30.4% vs. 10.2%, $p=0.005$).

Conclusions: Age, presence of FT burn, and BTK burn are independent risk factors for wound infection in the outpatient burn population with LE burns. Silver sulfadiazine was a factor associated with the development of early wound infection.

O36

Predicting the Risk of Surgical Site Infection Using Interactive and Machine-Learning Optimal Classification Trees

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Background: Most risk assessment tools presume that the impact of risk factors is linear and simply cumulative. Using novel machine-learning techniques, we aimed to design an interactive calculator to predict the risk of surgical site infection (SSI) for Emergency Surgery (ES).

Hypothesis: Not applicable

Methods: All ES patients in the ACS-NSQIP 2007-2013 database were included. Optimal Classification Trees (OCT) were leveraged to train machine-learning algorithms to predict SSI. Unlike classic heuristics (e.g. logistic regression), OCT is adaptive and reboots itself with each variable thus accounting for non-linear interactions among variables. An application was then designed as the algorithms' interactive and user-friendly interface. We tested the ability of our application and models to predict SSI in a separate 2014 NSQIP validation cohort.

Results: Out of 382,960 ES patients, comprehensive decision-making algorithms predicting superficial, deep incisional and organ/space SSIs were derived where the provider's answer to a question interactively dictates the subsequent question [Figure 1]. For any specific patient, the number of questions (thus tree branching/variables) needed to predict SSIs ranged from 4 to 10. The c-statistics of the models predicting superficial, deep incisional and organ/space SSIs in the validation cohort were 0.68, 0.75, and 0.79, respectively.

Conclusions: We thus reveal a novel, evidence-based, adaptive and user-friendly calculator capable of accurately predicting the risk of SSI in ES. Such a tool might prove useful for bedside preoperative counseling of ES patients and families, as well as for quality benchmarking of ES care.

O37

Effects of DAMPs level changes following CVVH therapy on outcomes in AKI patients with sepsis

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Background: Damage-associated molecular patterns (DAMPs) were released by injured cells can alarm of tissue damage and activate cellular receptors leading to downstream inflammation, which plays a role in sepsis. Continuous veno-venous hemofiltration (CVVH) has been suggested to play a part in immunomodulation by cytokine removal.

Hypothesis: To investigate whether the magnitude of DAMPs' removal is associated with mortality in patients with sepsis on CVVH.

Methods: We analyzed 26 AKI patients with sepsis and 10 without sepsis. The levels of circulating DAMPs (mitochondrial DNA, mtDNA; nuclear DNA, nDNA; heat shock

protein 70, HSP70) and cytokines (IL-1b, IL-6, IL-10, TNF-a, IFN-r) were measured at the beginning, 6h and 12h of CVVH at both inlet and outlet. MtDNA levels were quantified by using mtDNA genes D-loop and ND2. GAPDH and b-globin were used for nDNA levels quantifacation. Urinary DNA levels were analyzed at the beginning and the end of CVVH. Clearance rates during the initial 12 hours of CVVH were calculated. Clinical and laboratory data were acquired from patient's records data.

Results: Compared with AKI patients without sepsis, patients with sepsis showed older age(48.9±13.9 vs. 37.3±9.4, p=0.046) and a higher tendency in terms of APCHEII score and SOFA score (p=0.089; p=0.132). 18 sepsis patients (69.2%) and one patients (14.3%) without sepsis died (p=0.026). Baseline of cytokines and DAMPs levels were comparable. Reduction in circulating level of TNF-a (p=0.039) was found in both two groups, while there are no differences in other measured cytokines during the CVVH. MtDNA levels were increased (ND2 p=0.026; D-loop p=0.008) while the HSP70 level was decreased in sepsis patients (p=0.01). Comparing outlet with inlet, we also observed the mtDNA levels were rising after blood passing the filter. The ROC curve indicated that HSP70 clearance rate performed a considerable prediction efficiency for mortality (AUC=0.924, p=0.000). The Multivariable analysis showed that high level of HSP70 clearance rate was a significant independent predictor of mortality (OR=1.127, CI: 1.010-1.257, p=0.032). Urinary nDNA levels (b-globin) before CVVH was identified as an independent prognostic biomarker for duration of CVVH in sepsis patients in multivariate analysis (OR= -1.623, CI: -2.319- -0.928, p=0.000).

Conclusions: CVVH is valuable for sepsis patients with AKI in part via cytokine removal. However, mtDNA levels are increased after blood passing the filter and survival decreases significantly with higher HSP70 clearance rate. It provides novel mechanisms that allow physicians to improve the outcomes by interfering with it.

O38

Cross-Border Antibiotic Resistance Patterns in Trauma Patients

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Background: Antibiotic resistant bacteria are a growing problem worldwide, with differences in regional resistance patterns driven by local variance in antibiotic stewardship. Resistant gram-negative organisms are increasingly prevalent in Latin America and account for a higher percentage of infections than in the United States (USA) or Canada. Hospitals along the US-Mexico border increasingly identify resistance, raising concern for transfer of drug resistant (DR) organisms across the border.

Hypothesis: Patients transferred to a US trauma center after initial treatment by a healthcare facility in Mexico (MEX) will have a higher incidence of infections due to antibiotic-resistant organisms, including DR gram-negative bacteria.

Methods: The registry of an ACS verified Level-1 trauma center was queried for all trauma admissions between March 1, 2011 and August 30, 2015. Patients were included if at least 1 culture was sent during the first 3 days of hospitalization, to avoid analysis of hospital-acquired bacteria. Patients were divided into two groups based upon injury location: inside the USA or in MEX. Cultures were reviewed to remove duplicate results and for confirmation of clinical infection.

Results: A total of 127 MEX and 1149 USA patients were analyzed. MEX patients were younger (45.5 vs 60.4 years), more likely to be male (68.5% vs 60.1%) and Hispanic (64.6% vs 32.3%), had a higher median ISS (21 vs. 10), and longer hospital lengths of stay (11.1 vs 5.5 days). MEX patients most commonly had respiratory infections (53.9%), while urinary tract infections were most common in USA patients (43.4%). MEX patients were more likely to have any type of resistant infection (26.5% vs 7.1% of all organisms grown, $p<0.001$). Resistance was more common in MEX patients with Klebsiella (55.6% ESBL vs 0%, $p=0.01$) or any gram negative infection (39.3% vs 10.4%, $p=0.005$). 15.0% of MEX organisms were untreatable by both piperacillin-tazobactam and vancomycin, our empiric regimen, as compared to 4.8% of USA organisms ($p = 0.028$).

Conclusions: Antibiotic resistance is more common in patients initially treated in MEX healthcare facilities than those treated exclusively in the USA, despite close geographic proximity. MEX patients may require alternative empiric antibiotic regimens when presenting with infection. Global initiatives to improve antibiotic stewardship will be critical to limit the continued rise in drug-resistant infections.

O39

A Prospective Cohort Study on the Timing of Antimicrobial Prophylaxis for Post-Cesarean Surgical Site Infections

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Background: Sepsis is the leading cause of maternal death in Sub-Saharan Africa (SSA), a region that sees some of the highest rates of maternal mortality and morbidity in the world. As one of the most commonly performed surgical procedures in SSA and a proven risk factor for surgical site infection (SSI), cesarean section (CS) is an important operation to target due to its massive impact on maternal and neonatal health. There is currently insufficient published data available on the patient and facility based context around SSI following CS to establish a true and clear understanding of this infectious category. The objective of this study was to collect accurate and valid data on the incidence of SSI following CS and the circumstances around SSI in two Kenyan hospitals.

Hypothesis: Our primary analysis focused on the consequences of timing of perioperative antimicrobial prophylaxis. We hypothesized that patients who were administered pre-operative antibiotics would show lower SSI rates than those administered post-operative antibiotics.

Methods: This was an IRB-approved observational study of six hundred and nine women who had CS operations at two Kenyan hospitals from September to December 2015. Hospital A provided antimicrobial prophylaxis prior to incision for all patients and Hospital B provided only post-operative prophylaxis to all patients. It should be noted that this was due to a previous intervention at Hospital A, and was not a part of this observational study.

Results: Patients at the two hospitals had similar pre-operative characteristics indicating a relatively healthy population. The median age was 26±6 (18, 43) at Hospital A and 26±5 (18, 44) at Hospital B. Median parity was 1±1 (0, 7) at Hospital A and 1±1 (0, 10). Patients also went through a comparable number of antenatal care visits (median=4±1 at both hospitals). The number of patients with prolonged rupture of membranes was 103 (34.4%) at Hospital A and 99 (32.9%) at Hospital B. There were a slightly higher number of patients with meconium stained liquor at Hospital B Hospital (115) than Hospital A (74). The SSI rate was 4.0% (12/299; 11 superficial SSI, 1 deep SSI) at Hospital A and 9.3% (28/301; 18 superficial SSI, 7 deep SSI, 3 organ/space SSI) at Hospital B.

Conclusions: The data shows a striking difference between SSI rates in patients who were given properly timed pre-operative antibiotics and patients who were only given post-operative antibiotics. Administration of post-operative antibiotics is currently the norm in much of SSA and there is strong evidence that many of the infectious problems encountered in this population would be reduced by the provision of antibiotic prophylaxis prior to the incision.

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Burden of Pediatric Infections Requiring Surgery: Results from an Ugandan Tertiary Care Center

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Background: The burden of pediatric infections requiring operative intervention in low-middle income countries (LMIC) is poorly defined. The increased prevalence of infectious diseases necessitating operative intervention may tax the limited availability of surgical and intensive care resources.

Hypothesis: The operative volume resulting from pediatric infections represents a significant portion of the total surgeries performed in LMIC.

Methods: A retrospective review of all pediatric surgical patients (<14 years) presenting to an Ugandan tertiary referral hospital from Jan 2012 to Aug 2016. Infections present at admission treated by the pediatric surgery team were analyzed by operative intervention and overall mortality.

Results: Of 3,494 patients treated over the time period, 18.9% (n=662) were admitted with a surgical infection (Table 1). 46.9% were girls and 53.1% were boys with a median age of 2 years (IQR 0.24- 6.9 years). 63.5% (n=417) of patients presenting with an infection underwent an operation with an in-hospital mortality of 10.6% (n=70). This represented 20.1% of the total operative volume of the pediatric surgery department.

The most common infections included superficial infections and abscesses (47.2%), typhoid perforations (13.5%), appendicitis (10.7%) and abdominal sepsis (7.4%). The mortality for children presenting with abdominal sepsis was 59.1% (n=29/49), necrotizing enterocolitis was 50% (7/14), and neonatal sepsis was 28.6% (n=4/14). Surgical Infection n (%) Operation (%) Morality (%) Cellulitis/Abscess (total) 311 (47.2%) 64.7% 0.96% Phycomycosis 3 (0.5%) 33.3% 33.3% Necrotizing Fasciitis 30 (4.55%) 43.3% 10.0% Wound Sepsis 7 (1.1%) 0% 0% Surgical Site Infection 8 (1.2%) 62.5% 12.5% Primary Peritonitis 25 (3.79%) 72.0% 4.0% Appendicitis 71 (10.8%) 90.0% 0% Typhoid Bowel Perforation 89 (13.5%) 88.8% 16.9% Abdominal Sepsis 49 (7.4%) 28.6% 59.2% Thyroglossal Duct Cyst 7 (1.1%) 85.7% 0% Thoracic Empyema 2 (0.3%) 75.0% 0% Pneumonia 9 (1.4%) 11.1% 55.6% Septic Arthritis/Osteomyelitis 4 (0.6%) 75.0% 0% Necrotizing Enterocolitis 14 (2.1%) 28.6% 50.0% Neonatal Sepsis 14 (2.1%) 35.7% 28.6% Other 13 (2.0%) 23.1% 0% Other: Cervical Adenitis, Parotitis, Genital Warts, Cholangitis, Orchitis, Recurrent Urinary Tract Infection, Measles

Conclusions: The operative volume of pediatric infections was 20%, representing a significant proportion of the total surgery performed. This finding should inform resource allocation given the current limitation in access to essential surgical care in LMIC and that emergent cases can push back elective cases leading to backlog. The highest mortality rates were abdominal sepsis and neonatal sepsis, highlighting the need for pediatric intensive care in LMIC.

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Third generation cephalosporin resistance in Rwandan surgical patients

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Background: Antimicrobial resistance (AMR) is a significant barrier to effective treatment of infections across the globe. The World Health Organization has listed carbapenem and third generation cephalosporin resistance (3GCR) as areas of “critical priority”. The goal of this study was to determine the prevalence and types of AMR in surgical patients at a tertiary referral hospital in Rwanda.

Hypothesis: We hypothesized that 3GCR was common in Rwandan surgical patients and associated with increased mortality and prolonged length of stay.

Methods: Over a 6-month period (February – August 2017), samples were collected from all adult patients with an infection. We defined infection as any patient with temperature greater than 38 degrees Celsius or any patient undergoing operation for a suspected infectious process. Blood, tracheal aspirate, urine, and wound swabs were collected based on suspected etiology. All specimens were processed in the hospital microbiology lab. Data were collected on demographics, clinical presentation, operation, hospital course, microbiology, AMR, and in-hospital mortality.

Results: Over a 6-month period, we collected 54 surgical specimens. The mean patient age was 36 years, and 73% were female. Seven (13%) patients were positive for human immunodeficiency virus (HIV) infection. Most patients were transferred from another facility (n=37, 82%), underwent operation within the preceding 30 days (n=42,

78%), and received antibiotics within the preceding 30 days (n= 37, 82%). The most common diagnoses were obstetric complications (n=35, 65%) and necrotizing soft tissue infections (n=8, 15%). The most common operation was laparotomy (n=30, 56%). Most (n=37, 69%) patients were initially treated with ceftriaxone and metronidazole. In-hospital mortality was 7% (n=3) and median length of hospital stay was 17 days (Interquartile range: 9-34). Of the surgical specimens, 24 (53%) were culture positive. The organisms most commonly isolated included Escherichia coli (n=12) and Klebsiella sp (n=5). Thirteen (54%) isolates had 3GCR. One (5%) isolate was resistant to carbapenems. Of patients with 3GCR, 11 (85%) had empirically received ceftriaxone and 5 (38%) had antibiotics changed based on culture results. In patients with 3GCR versus sensitive isolates, there was no difference in mortality; however, median length of hospital stay for survivors was significantly longer (25 versus 9 days, p=0.0264).

Conclusions: We found a high rate of 3GCR in surgical patients at a referral hospital in Rwanda with antibiotics infrequently changed based on culture results. Patients with 3GCR had prolonged hospital stay.

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Osteomyelitis Recurrence with Open Femur Fractures among Combat Casualties from Iraq and Afghanistan

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Background: Combat trauma-related open fractures are frequently complicated by recurrent osteomyelitis and have identifiable predictors of increased risk.

Hypothesis: Characteristics of open femur fracture osteomyelitis cases among wounded U.S. military personnel (2003-2009) and risk factors for infection recurrence were assessed in a retrospective case-case comparison.

Methods: Open fractures were classified using a modified Gustilo-Anderson (GA) scheme (accounting for traumatic transfemoral amputations [TFA]) and Orthopaedic Trauma Association Open Fracture Classification (OTA OFC). Osteomyelitis diagnoses were classified as definite/probable or possible using standardized National Healthcare Safety Network diagnostic criteria. Recurrence was defined as an osteomyelitis diagnosis at the original site 30 days after the initial course of treatment was completed. Risk factors for osteomyelitis recurrence were assessed among subjects who had ≥30 days of follow-up.

Results: A total of 103 osteomyelitis cases were assessed, of which 32 and 71 were classified as definite/probable and possible, respectively. There was no significant

difference between the groups regarding GA (overall, 57% with GA-III, 40% with TFAs) and OTA OFC characteristics, timing of definitive surgery, and radiographic union (median: 128 days). A higher proportion of patients classified as definite/probable received vancomycin (75% vs 49%; p=0.018) and an extended duration of antibiotics (≥90 days; 34% vs 3%; p<0.001) compared to the possible group. Among 95 patients with ≥30 days of follow-up, 17 (18%) had an osteomyelitis recurrence with a median of 5 months (interquartile range: 3-8 months) from end of initial treatment to recurrence. Approximately 76% of patients with a recurrence received >21 days of antibiotics. Factors associated with fracture severity and management were assessed in a logistic regression model; however, only receipt of aminoglycosides for ≥5 days was independently associated with risk of osteomyelitis recurrence (odds ratio: 0.23; 95% confidence interval: 0.08-0.69). When timing of osteomyelitis recurrence was considered in a Kaplan-Meier plot, there was no significant association with injury severity or fracture classification.

Conclusions: No significant differences in clinical presentation or outcomes were observed based on osteomyelitis classification. Overall, disease recurrence is common among patients with combat-related open femur fractures diagnosed with osteomyelitis, so close monitoring is required as no independent risk factors for recurrence were identified except for use of aminoglycosides.

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Prevalence and source control of intraabdominal infection A single Indonesian hospital perspective

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Background: Intraabdominal infection (IAI) and complicated IAI (cIAI) remains a problem of surgical practice in our hospital. Such problem found to be different with those reported, predominately with delayed in management, both of prehospitally and in hospital due to many reasons; referred to difficult cases. A descriptive study run to find out the prevalence and output of source control management as the baseline to set a guideline for quality improvement.

Hypothesis:

Methods: Data of those with IAI of different etiology were collected during year 2017. Prevalence, etiology, epidemiology and outcome were noted and subjected to analysis descriptively.

Results: There were 945 abdominal surgeries managed during 2017. Out of these 110 (11.74%) were found to be IAI and cIAI; 74 (66.66%) were males and 36 (32.44%) were females. Median age was 48.5 years old (18–81). The predominant pathology was perforated gastroduodenal ulcer (13.5%), colonic perforation due to different etiology (10.8%), perforated appendicitis (8.1%), perforated ileum (5%) and perforated cholecystitis (5%). The remains were anastomosis leaks, trauma, etc. There were no comorbid noted but a case with hypertension. Surgical drainage preceded in 4 subjects (3.6%), surgical debridement in 14 subjects (12.6%), and the remains were preceded definitive source control including stoma (83.8%). Steps surgery intervention(surrogate surgery) were the strategy to overcome the abdominal sepsis cases. The epidemiology noted of most was Escherichia coli and Klebsiella penumoniae. The

mostly used antibiotic was amikacin sulphate in combination with metronidazole. Mortality was noted in 20 subjects (18%). Re-laparotomy were performed on 19 cases and 5 cases ended as operative mortality.

Conclusions: Prevalence of IAI in our hospital was 11.74% and op mortality was high. Definitive source control as surgeon's preference remain the most intervention preceded. Surrogate surgery most were be chosen during source control procedure