O01.
Biological analysis and therapeutic application of a de novo synthesized polyphosphorylated triblock polymer ABA-PEG20-Pi20 to prevent anastomotic leak

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Background:

We have previously shown that anastomotic leak can be caused by collagenolytic strains of *Enterococcus faecalis* that colonize anastomotic tissues. Clinical studies have demonstrated that despite purgative cleansing, oral and intravenous antibiotics (i.e., full bowel prep), intestinal *E. faecalis* persists in the stool of patients undergoing anastomotic surgery suggesting that strategies other than antibiotics are needed to prevent the deleterious effect of this pathogen. The aim of this study was to synthesize a polymer compound capable of suppressing collagenase production in *E. faecalis* and improve healing in a mouse model of *E. faecalis* – mediated anastomotic leak.

Hypothesis:

We hypothesized that drugs affecting bacterial collagenolytic activity are potent to improve anastomotic healing.

Methods:

We synthesized a polyphosphorylated triblock PEG based polymer (ABA-PEG20-Pi20) with specific composition of matter to deliver phosphate to the anastomotic site following oral ingestion. ABA-PEG20-Pi20's biological activity was tested *in vitro* by examining collagenase activity in *E. faecalis* and *in vivo* in C57BL/6 male mice drinking the solution following a low colorectal anastomosis contaminated by *E. faecalis* via enema. Briefly, mice were randomly assigned to drink 5% dextrose or 5% dextrose supplemented with 1% ABA-PEG-Pi20. At POD7, anastomotic healing was assessed and the total amount of *E. faecalis* present at the anastomotic site and the percentage of *E. faecalis* expressing the collagenolytic phenotype were determined.

Results:

We successfully achieved a defined ABA architecture and a precise level of phosphorylation (20 Pi per molecule) in the synthesized ABA-PEG20-Pi20. Overnight incubation of two different *E. faecalis* collagenolytic strains with 2 mM of ABA-PEG20-Pi20 led to near complete inhibition of collagenase production in both strains (from 18,000 to 1,000 and from 68,000 to 5,000 (n=6, P<0.001)) without suppressing bacterial growth. Based on calculated anastomotic healing scores, leak rates were decreased from 80% to 20% in mice drinking 1% ABA-PEG20-Pi20 (n=10, p<0.01). In ABA-PEG20-Pi20 drinking mice, the mean population of *E. faecalis* at the site of anastomosis was decreased 12 fold with the percentage of collagenolytic colonies in entire populations decreased from 20% (no ABA-PEG20-Pi20) to 1% (with ABA-PEG20-Pi20) (n=5, p<0.05).

Conclusions:

ABA-PEG20-Pi20 may be an effective adjunct to the bowel prep to prevent anastomotic leak due to collagenolytic bacteria such as *E. faecalis.*

O02.
Fecal Microbiota Transplantation Rescues the Gut Microbiome and Improves Symptoms in Pediatric Inflammatory Bowel Disease

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Background:

Fecal microbiota transplantation (FMT) is an effective treatment for refractory C. difficile colitis. It has been studied with conflicting results to treat adults with inflammatory bowel disease (IBD). However, few studies have evaluated FMT in the pediatric IBD population. The aim of this study is to determine the efficacy of FMT in treating pediatric IBD patients and the corresponding impact on the gut microbiota.

Hypothesis:

We hypothesize that FMT will correct intestinal dysbiosis in pediatric IBD patients.

Methods:

Twenty-one pediatric patients with refractory IBD underwent FMT via upper and lower endoscopy using stool obtained from a healthy related donor. Validated disease activity index (PCDAI / PUCAI) scores were calculated before FMT, at 1 week, 1 month, and 6 months after FMT. Bacterial 16S rRNA genes in each sample including donor samples were sequenced on the Illumina MiSeq. QIIME / LEfSE were used for microbiome analyses.

Results:

Ten patients with ulcerative colitis and 11 patients with Crohn's disease participated (mean age 12.4y). Alpha diversity, a species richness index, was reduced in patients before FMT relative to healthy donors, but increased at 1 week and 1 month following FMT before returning to baseline by 6 months (p< 0.05). Pre-FMT samples were enriched with pathogens from the Enterobacteriaceae family and depleted of beneficial taxa from the Lachnospiraceae family (p<0.05).
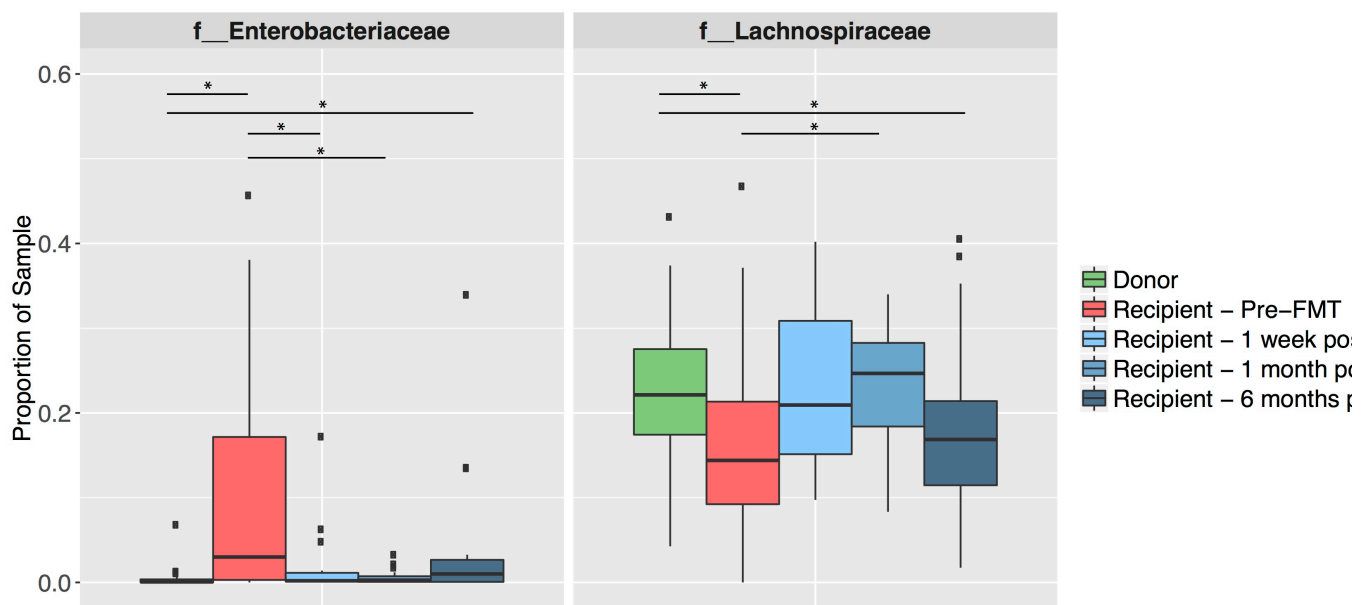
These patterns reversed in 100% and 88% of patients, respectively, at 1 month after transplant. Clinical response rates at 1 and 6 months were 65% and 53%, respectively, and these responses correlated with durable changes in the microbiome after FMT. Retrospective analysis revealed that pre-FMT samples distinguished responders and

non-responders by a higher abundance of Enterobacteriaceae and lower abundance of Lachnospiraceae in the responder group.

Conclusions:

FMT drives the gut microbiome of pediatric IBD patients towards increased species diversity and a healthier microbial configuration marked by decreased pathogens and increased protective species. The high success rate in this pilot study serves as a basis for future randomized trials of FMT in pediatric IBD, possibly examining the role of serial FMT.

O03.
FER Electroporation-mediated Gene Delivery Enhances Immune Response and Improves Survival in Murine Model Gram-Negative Pneumonia

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Background:

Alternative treatments against antibiotic-resistant bacteria are being strongly investigated. Potentially, transient manipulations of the genome can potentiate our immune response against infection. Recently, our laboratory demonstrated that electroporation-mediated delivery of the FER gene can improve survival in a lethal model of trauma-related pneumonia (PNA). The exact mechanism of protective FER-mediated lung inflammatory response is still unknown

Hypothesis:

We propose that FER lung gene expression induces signaling and recruitment of enhanced immune cells primed to remove bacteria

Methods:

C57/BL6 mice were inoculated with 500 CFU of *Klebsiella pneumoniae*. At 1-hr they received a DNA plasmid encoding human FER (PNA/*p*FER-EP) via pharyngeal drop followed by 8 electroporation pulses (EP) inducing expression in the lung. We recorded survival in treatment and control groups (PNA-only; PNA/EP-empty vector). In parallel experiments, bronchial alveolar lavage (BAL) and lung samples were processed and cellular subpopulations, bacterial CFUs, histology, gene and protein expression, and cytokines were analyzed at specific time points (24, 48, 72-hr)

Results:

After PNA/*p*FER-EP; 5-day survival was markedly improved as compared to controls (80 vs 20 vs 0%; $p < 0.05$). Earlier abundant numbers of macrophages, inflammatory monocytes and neutrophils with Toll-Like Receptor-2/4 markers were seen in the BAL and lungs of FER animals, whereas controls had much smaller and delayed peaks. BAL cells from the FER group had better phagocytic and MPO activity. FER increased activation of transcription factor STAT3, which correlated with expression of downstream CXCL2, CCR2, IL-1β, TNFα, Nitric Oxide Synthase-2, Resistin-like molecule-1 and IFNγ genes. Interestingly, FER group had increased secretion of CCL-2, KC, TNFα, IFNβ and IFNy cytokines being counterbalanced by higher levels of RAGE and IL-1RA in BAL. Finally,

at 72-hr, HSP90 (STAT3 chaperone) and inflammasome NRLP3 had significant increase of expression whereas pro-inflammatory genes fell back to baseline only in the FER group, with recovery from infection confirmed with CFUs and histology

Conclusions:

Lung gene delivery of FER improves survival by activating STAT3 pathway with early upregulation of CCL-2, KC and IFNy promoting fast recruitment of primed inflammatory cells. After infection, this inflammatory response is able to shut down using HSP90 and NLRP3 counter-regulation. This constitutes a novel therapeutic strategy against severe Gram-negative pneumonia.

O04.
Biomarker Evidence to Support Persistent Inflammation Immunosuppression and Catabolism Syndrome (PICS) in Surgical Patients with Chronic Critical Illness Following Sepsis

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Background:

The PICS paradigm was initially proposed to provide a unifying mechanistic explanation for the adverse clinical outcomes associated with chronic critical illness (CCI) which develops after sepsis in surgical ICU patients. We now seek to identify biochemical alterations which support the hypothesis that PICS exists and underlies clinically observable CCI.

Hypothesis:

We hypothesize that septic patients who develop CCI will exhibit persistent alterations in biomarkers of inflammation, immunosuppression, and catabolism consistent with PICS pathophysiology.

Methods:

This single-center prospective observational study enrolled surgical ICU patients treated for sepsis. Patients were divided into 2 groups: those who developed CCI (defined as ICU length of stay > 14 days plus persistent organ dysfunction) and those who did not. Two patients (3%) died within 14 days of protocol onset and were excluded from this analysis. Patient blood and urine samples were collected at 1, 4, 7, 14, and 28 days after sepsis protocol onset and analyzed for biomarkers of inflammation, immunosuppression, and catabolism. Non-parametric rank tests were performed to determine significant differences between groups ($p < 0.05$). Graphical representation of the means over time with standard error bars are provided in Figure 1.

Results:

Over 20 months, 73 surgical ICU patients were enrolled, of which 30 (41 %) developed CCI. In comparison to non-CCI patients, CCI patients demonstrated sustained elevations in IL-6, IL-10, and TNF-α during index hospitalization to suggest ongoing inflammation ($p < 0.05$) (Figure 1). Absolute lymphocyte count, used as a marker

of immunosuppression, was found to be lower in the CCI subjects, particularly around a week after sepsis onset. Levels of insulin-like growth factor-binding protein 3 (IGFBP-3), which is thought to play a role in catabolism, also significantly differed between CCI and non-CCI subjects. Finally, mean urinary 3-methylhistidine (3-MH) to creatinine ratios were higher in CCI patients, supporting a greater degree of protein catabolism and lean muscle wasting in this group.

Conclusions:

Surgical ICU patients who develop CCI after sepsis exhibit persistent alterations in biomarkers to suggest ongoing inflammation, immunosuppression, and protein catabolism consistent with PICS.

O05.
Microbiology of Necrotizing Soft Tissue Infections in Immunocompromised Patients

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Background:

The organisms involved in NSTIs are well-described and consist most commonly of mixed polymicrobial infections, followed by group A *streptococci*, *S. aureus*, and more rarely *V. vulnificus*. There is a paucity of research regarding the types of pathogens between patients who are immunocompromised versus those who are immunocompetent.

Hypothesis:

We hypothesize that there will be a difference in the microbiology seen in immunocompromised versus immunocompetent patients diagnosed with NSTI.

Methods:

We performed a retrospective cohort study of NSTI patients admitted from 1995 to 2014 to a tertiary-care, academic hospital with a major cancer center. Immunocompromised patients were identified and microbiology findings were compared between immunocompromised and immunocompetent patients using Fisher's exact test. Multivariate logistic regression was performed to assess if a particular pathogen was an independent predictor of in-hospital mortality.

Results:

Table 1. Comparison of microbiology findings between immunocompromised and immunocompetent patients with NSTI

Variable	All patients (N=81)	Immunocompromised Patients (n=53)	Immunocompetent Patients (n=192)	P Value
Staphylococcus aureus	35 (15.0)	5 (11.1)	30 (15.9)	0.49
Coagulase-negative Staphylococcus species	65 (27.8)	7 (15.6)	58 (30.7)	**0.04**
Gram-negative rods	81 (34.5)	17 (37.0)	64 (33.9)	0.73
β-hemolytic streptococcal species	50 (21.4)	4 (8.9)	46 (24.3)	**0.025**
Anaerobes	110 (47.0)	20 (44.4)	90 (47.6)	0.74
Diphteroids	22 (9.4)	0	22 (11.6)	**0.01**
Enterococcus species	49 (20.9)	11 (24.4)	38 (20.1)	0.54
Polymicrobial wound culture	152 (64.7)	27 (60.0)	125 (61.8)	0.49

245

patients with complete data were included. The most common pathogens in both patient groups are shown in Table 1. Polymicrobial infections were the most common in both groups (60% vs. 61.8%, p=0.49). Coagulase-negative Staphylococcus species and β-hemolytic streptococcal species were significantly more prevalent in immunocompetent patients (p = 0.04 and p=0.025, respectively). More immunocompromised patients had positive blood cultures within 24 hours of admission (34.0% vs. 18.9%, p = 0.03). There was no difference in the rate of receiving the appropriate antibiotics (90.6% vs. 94.3%, p=0.35) in both groups. On multivariate analysis, no pathogen was found to independently predict in-hospital mortality.

Conclusions:

Polymicrobial infections are still the most common finding in NSTI patients regardless of their immune status. While coagulase-negative Staphylococcus species and β-hemolytic streptococcal species were significantly more prevalent in immunocompetent patients, the type of microbial infection is not an independent risk factors for in-hospital mortality after adjusting for immunologic status. Therefore, the initial broad spectrum antibiotic regimen does not need to be altered in immunocompromised patients.

O06.

A novel role of TLR9 in peritoneal B cell in regulating host defense during polymicrobial sepsis

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Background:

TLR9 is known to play important roles in sepsis.TLR9 deficient (TLR9$^{-/-}$)mice are resistant to polymicrobial sepsis.

Hypothesis:

However, the mechanisms and biological pathways by which TLR9 regulates host defense are yet to be identified.

Methods:

To investigate this, mice were subjected to a clinical relevant polymicrobial sepsis model, cecal ligation and puncture(CLP), for 18 hours.

Results:

As expected, global deletion of TLR9 increased survival and decreased bacterial load in peritoneal as well as systemic inflammation after CLP. The number of peritoneal PMNs in TLR9$^{-/-}$ mice was significantly higher than in WT mice after CLP (WT CLP 9.26±1.03*10^6;TLR9 KO CLP 16.2±5.08*10^6), suggesting that TLR9 may regulate host defense via PMN recruitment. However, specifically knockout of TLR9 in myeloid cells was not phenocopy of global TLR9$^{-/-}$ after CLP; suggesting that TLR9 on myeloid cell did not play critical roles in host defense. Interestingly, the number of peritoneal B cells assessed by flow cytometry was significantly higher in TLR9$^{-/-}$ mice than their control at baseline as well as after CLP (Number of peritoneal B cells: WT Control 4.85±1.46*105; TLR9 KO Control 33.8±5.44*105;WT CLP 1.39±1.12*105;TLR9 KO CLP 6.42±3.07*105).Importantly, the circulating level of natural antibody IgM, which is important for opsonization of bacteria for PMN phagocytosis, was significantly increased in TLR9$^{-/-}$ mice than their control at baseline and after CLP.

Conclusions:

Our data suggest an unrecognized role of TLR9 in B cells in regulation of host defense via modulation of IgM secretion from B cell.

O07.

Recent Antimicrobial Exposure Is Associated With Increased Complications Following Elective Surgery

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Background:

Recent antimicrobial exposure has been associated with poor outcomes following infection in a mixed population. The microbiome plays a key role in modulating the inflammatory response and may be susceptible this exposure.

Hypothesis:

Recent antimicrobial exposure would be associated with poorer outcomes following elective surgery.

Methods:

From August 2015 to August 2016, all elective surgical patients were questioned about antimicrobial exposure in the previous 3 months. These data were matched to our ACS NSQIP sample from the same period. Data were recorded for general surgery and gynecologic cases. Standard univariate techniques were employed. Risk models for major outcomes were created using the 2014 ACS NSQIP Participant Use File. These models were used to calculate risk-adjusted odds ratios for antimicrobial exposure controlling for surgeon influence. Primary outcomes included any serious complication, any complication, any infection, and surgical site infection. Secondary outcomes included length of stay, *C. difficile* infection, and mortality. A separate analysis excluding colorectal patients who had undergone an oral antibiotic bowel preparation was also performed.

Results:

Ninety-four percent of eligible patients (n = 1543) answered the exposure question with a 3-month antimicrobial exposure rate of 32.6%. Colorectal patients had the highest exposure rate while hernia patients had the lowest (69.4% vs. 19.9%). Exposed patients had higher rates of serious complication (6.1% vs. 11.1%; p-value = 0.0005), any complication (6.7% vs. 11.1%; p-value 0.003), and any infection (5.7% vs. 8.7%; p-value = 0.02). Exposed patients had a median 2-day longer hospital stay (p-value <0.0001). There were no differences in SSI, *C. difficile*, or mortality rates between groups. Exposure was independently associated with any serious complication and any complication in non-colorectal surgery (Table 1).

Conclusions:

Recent antimicrobial exposure is associated with increased complications following elective surgery. Antimicrobial induced alterations in microbiome-related inflammatory responses may play a role, highlighting an opportunity for pre-surgical intervention in this at-risk population.

Table 1:

	Antimicrobial Exposure Odds Ratios (95% CI)		
	Unadjusted	***Risk Adjusted: All Patients**	***Risk Adjusted: Excluding Colorectal**
Any Serious Complication	1.94 (1.33-2.83)	1.46 (0.98-2.17)	1.64 (1.03-2.59)
Any Complication	1.74 (1.2-2.51)	1.27 (0.87-1.89)	1.60 (1.02-2.51)
Any Infection	1.59 (1.06-2.39)	1.19 (0.77-1.84)	1.53 (0.95-2.50)
Any Surgical Site Infection	1.46 (0.88-2.41)	0.94 (0.55-1.62)	1.32 (0.70-2.47)
C Statistics	0.53-0.58	0.68-0.70	0.68-0.69

* C Statistic for PUF Risk Models = 0.73–0.75

O08.
Extrathoracic Trauma Decrements the Pulmonary Antimicrobial Response in a Murine Model of Post-Trauma Pseudomonas Pneumonia.

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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 injury affects the pulmonary response to infection, we measured the inflammatory response to pneumonia in a murine model of non-lethal polytrauma.

Hypothesis:

Injury induces a defective immune response to subsequent pneumonia.

Methods:

C57BL/6 mice were subjected to polytrauma comprised of a 15% blood volume hemorrhage, bilateral lower extremity pseudofracture and a liver crush injury, a modification of our previously described protocol. To induce pneumonia, 48 hours after injury the animals underwent intratracheal injection of 5×10^6 cfu of *Pseudomonas aeruginosa*. 24 hours after induction of pneumonia we isolated plasma, lungs, and spleens. Inflammatory cytokines in the blood and lung homogenates were assayed by cytometric bead array (BD) and compared by t-test. Bacterial burden was measured by plating serial dilutions of blood, lung, or spleen homogenates on agar plates and compared by Mann-Whitney U test.

Results:

Injury alone resulted in no mortality; similarly pneumonia after sham injury (sham→ pneumonia) resulted in less than 10% mortality. However, pneumonia 48 hours after polytrauma resulted in 60% mortality (p<0.05 vs. sham→pneumonia by Log-Rank test). As compared to pneumonia after sham, pneumonia after injury was associated with a significant increase in both lung and blood bacterial counts (lung: 1.5×10^5 vs. 2.5×10^7. Pneumonia after injury was also associated with an exaggerated systemic inflammatory response characterized by significant elevations in plasma levels of TNF-alpha, MCP-1, IL-6 and IL-10 (Table 1). In spleen and lung tissue, only MCP-1 was significantly elevated (Table 1).

	Lung		Spleen		Plasma	
	Sham	Trauma	Sham	Trauma	Sham	Trauma
TNF-α	1211±605	1705±957	ND	ND	26±9	184±150*
IL-6	2736±2080	5690±4723	ND	113±178	65±66	3889±4097*
MCP-1	2375±1667	4500±1749*	52±11	315±263*	72±46	1751±1807*
IL-10	25±13	115±137	ND	ND	ND	68±58*

Table 1. Cytokine levels in indicated tissues; values are listed as pg/organ (lung/spleen) or pg/ml (plasma). *p<0.05 vs. Sham by Mann-Whitney U

Conclusions:

Extrathoracic polytrauma leads to a significant defect in both the local and systemic antimicrobial response to *Pseudomonas* pneumonia. This is associated with an exaggerated systemic inflammatory response and a dramatic increase in mortality from pneumonia.

O09.
Pre-Operative Antibiotics for Facial Fractures: Is More Than One Day Necessary?

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Background:

Despite a paucity of evidence, patients with facial fractures (fx) often receive long courses of preoperative (pre-op) antibiotics. We sought to compare the effect of a short vs long course of pre-op antibiotics on the development of head or neck infections (H/N infxs) following surgical management of facial fx.

Hypothesis:

There will be no difference in the incidence of H/N infxs between patients who receive a short vs long course of pre-op antibiotics. Mandible fx may benefit from a long pre-op course.

Methods:

This study included all adult patients admitted (2010–2015) to a level 1 trauma center with isolated head/neck injuries who underwent surgery for facial fx. Patients with infections prior to surgery were excluded. Our primary analysis compared H/N infx between patients given a short course of pre-op antibiotics (≤ 24 hours) to those given a long course (>24 hours). Bivariate analysis and multivariate logistic regression (MLR) were performed to determine risk factors for H/N infxs.

Results:

This study included 188 patients; mean age was 41 yrs, 83% were male, and 81% had blunt injuries. The midface was the most common fx location. 83 patients had an open fx and 92 required ICU admission. 86.2% underwent open reduction. The overall rate of H/N infx was 19.7%. 125 patients received a short course and 63 received a long course of pre-op antibiotics, their demographics and outcomes are compared in Table 1a. H/N infx were higher in the long course group, but median days to infection were similar. Factors associated with H/N infx are shown in Table 1b. MLR found mandible fx (OR:2.9, p=0.01) and ICU admission (OR:3.3, p=0.003) to be independent predictors of H/N infx (ROC=0.706). Subgroup analysis of patients with mandible fx, comparing 57 short and 46 long course patients, resulted in similar demographics and hospital outcomes, as well as similar rates of H/N infx (25% vs 30%, p=0.51). However, evaluation of 42 patients with isolated mandible fx demonstrated higher rates of

H/N infxs in the long group (4% vs 29%, p=0.03), despite similar demographics.

Table 1a. Comparison of Short vs Long Course of Pre-op Antibiotics			
	Short course n=125	Long course n=63	p
Mean age	41.2	40.4	0.77
Male	86%	76%	0.10
Blunt injury	82%	78%	0.44
ISS	10.7	11.0	0.83
Fracture location(s)			
Upper Face	28.0%	33.3%	0.50
Midface	78.4%	73.0%	0.47
Mandible	45.6%	73.0%	<0.01
Fx in multiple facial thirds	47.2%	60.3%	0.12
ICU admission	45%	57%	0.12
Median LOS, days	2.0	4.0	<0.01
Median ICU days	0	2	<0.01
Median days to fx reduction	5.0	5.0	0.84
Any H/N infx	15.2%	28.6%	0.03
Median post-op days to H/N infx	14.0	18.0	0.78
Table 1b. Factors Associated with H/N Infxs			
	No H/N infx n=151	H/N infx n=37	p
Mean age, years	41.9	37.1	0.06
Male	84.8%	75.7%	0.22
Mean ISS	10.5	12.3	0.19
Penetrating injury	15.2%	35.1%	0.01
Mandible fx	49.7%	75.7%	<0.01
Fx in multiple facial thirds	46.4%	73.0%	0.01
Long pre-op antibiotic course	29.8%	48.6%	0.03
ICU admission	43.0%	73.0%	<0.01
Median LOS, days	3.0	4.0	0.02
Median ICU days	0	2.0	<0.01
Median days to fx reduction	5.0	4.0	0.93

Conclusions:

Long courses of continuous pre-op antibiotic prophylaxis, >24 hours before surgery, for facial fx does not reduce the development of H/N infx.

O10.
Similar outcomes despite wide variability in utilization of bowel preparation before elective colon surgery at children's hospitals

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Background:

The utility of mechanical bowel preparation (MBP) to minimize infectious complications in elective colorectal surgery is contentious. Recent data in the adult population suggests a benefit to MBP when administered with oral antibiotics (OAB). There is a paucity of data in children on the benefit of MBP±OAB.

Hypothesis:

We assess the current utilization of bowel preparation prior to elective colon operations in young children and hypothesize that patients receiving MBP with OAB will have fewer complications.

Methods:

The Pediatric Health Information System (PHIS) was queried for children <10 years of age undergoing elective procedures involving a colonic anastomosis from 2011-2014. Patients were divided into 3 groups: no bowel preparation (Group 1), MBP alone (Group 2), and MBP with OAB (Group 3). Statistical significance was determined using univariate and multivariate analysis using GEE models accounting for clustering by hospital.

Results:

Among 1581 patients who met study criteria, 63.7% were in Group 1, 27.1% in Group 2, and 9.2% in Group 3. In univariate analysis, surgical complication rate was higher in Group 1 (23.3%) compared to Groups 2 and 3 (14.2% and 15.5%; p<0.001). Likewise, length of stay was longer in Group 1 (11.127.8 days) compared to Group 2 (7.04.9) and Group 3 (7.15.5; p=0.002). 30 day readmission rates were similar for all groups. In subgroup analysis of 988 colostomy closures, surgical complication occurred in 17.3% in Group 1, 8.5% in Group 2, and 15.6% in Group 3 (p=0.002). LOS and 30 day readmission rates were not significantly different. In multivariate analysis accounting for clustering by hospital, the odds ratio (OR) for surgical complication was 0.72 (95% CI 0.40 – 1.29, p=0.28) in Group 2 and 1.79 (95% CI 1.28 – 2.52, p=0.0008) in Group 3 compared to the referent Group 1. When patients who received MBP with or without OAB were combined, the odds of surgical complication was 1.13 (95% 0.81 – 1.58, p=0.46) compared to patients who received no preparation.

Conclusions:

There is large variability in the utilization of MBP across children's hospitals in the U.S., with no preparation being the most commonly used strategy. While univariate analysis suggested a benefit to MBP, there was no significant difference in multivariate analysis. Given the discrepancy with the current adult literature, a three-armed pediatric-specific randomized controlled trial is needed to answer this important question.

O11.
PCR-Electrospray Ionization Mass Spectrometry in Identifying Microbial Infections in Burn Wounds

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Background:

Infection remains the major complication associated with burn injury and remains a cause of death. Managing burn wound infection is challenging and would benefit from early detection of microbes so as to initiate appropriate therapy. There is a yet unmet need for rapid identification of burn wound pathogens beyond standard culture.

Hypothesis:

We hypothesized that molecular examination of the microbial DNA contents of burn wounds may be able to better and more speedily identify burn wound bacteria/pathogens versus routine culture-based methods.

Methods:

Burn wound tissues were obtained from 141 patients that underwent first time surgical debridement at more than one body site (n=316). Tissues were analyzed by standard microbiological culture and compared to a novel culture-independent PCR/electrospray-ionization-mass spectrometric (PCR/ESI-MS) assay after genomic DNA isolation. Demographics, complications, and outcome data were prospectively collected during recruitment and also from the electronic medical records. Parametric and non-parametric analyses were used along with logistic regression. All tests were two sided with $\alpha=0.05$.

Results:

PCR/ESI-MS analyses identified far greater numbers of microbial organisms resident in burn wounds compared to standard culture methods. Demographics of the patient population are as follows: age (48.03±18.12), sex (females 71.6%), weight (69.4-100), BMI (28.84 ±7.46) and the mean value for Injury Severity Score was 4 with interquartile range1-5. Of the 316 patient samples analyzed, 80 derived from sites with clinical evidence of burn wound infection, of which 10 showed microbiological concordance between PCR/ESI-MS and standard culture methods, approaching statistical significance (p=0.07). Univariate and multivariate analyses results are presented in Table 1. The result of multivariate logistic regression showed that a model with six independent variables was statistically significant P<0.0001. The strongest predictor of burn wound infection was PCR/ESI-MS, OR=8.6, p=0.007, followed by concordance in microbiological identification between PCR/ESI-MS and culture. Wound culture alone is also a statistically significant predictor, along with degree of burn and high age-adjusted Charlson Comorbidity Index.

Conclusions:

Our results indicate that using PCR/ESI-MS in identifying microbial pathogens could be a test of merit to complement standard culture that can be developed to identify patients that are at high risk for burn wound infection.

O12.
Fungal Infection is Associated with a Three-fold Increase in Mortality in Necrotizing Soft Tissue Infection

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Background:

Necrotizing soft tissue infections (NSTI) result in significant morbidity and mortality, with up to 14% of patients dying during their index admission. Data on fungal involvement in NSTI is limited to isolated case reports. However, clinical experience suggests that NSTI involving fungus may be increasing in frequency.

Hypothesis:

Fungal infection frequently complicates NSTI and is associated with increased morbidity and mortality.

Methods:

A prospectively maintained Acute and Critical Care Surgery (ACCS) database spanning 2008-2015 and including over 11,000 patients was queried for patients with NST. Microbiologic data, demographics and clinical outcomes were abstracted. Risk factors and outcomes associated with NSTI with positive operative fungal culture were determined. Frequencies were compared by χ^2 and continuous variables by the Student's T-test using SPSS.

Results:

A total of 230 patients were diagnosed with NSTIs; 197 had intraoperative cultures; 21/197 (10.7%) of NSTIs had positive intraoperative fungal cultures. Fungal infection was more common in women (71% vs. 44%, p=.019) and patients with higher BMI (41.36 ±18.14 vs. 34.36±12.69 , p=.025). There were no significant differences in other patient demographics, comorbidities or site of infection.

The majority of patients had mixed bacterial and fungal infections (18/21); in 3/21 patients, fungi were the only species isolated. Of positive fungal cultures, 12/21 grew Candida albicans, 1/21 grew candida dubliniensis, 1/21 grew Apophysomyces trapeziformis, and 8/21 grew unspeciated yeast. On average, fungal cultures were collected on hospital day 3.5. Patients with positive fungal cultures required more operations (5±3.4 vs 3±2.1 p=.042) and had increased mortality (24% vs 7% p=.014) than patients without fungal involvement.

Conclusions:

To our knowledge, this is the largest series to date describing the impact of fungal infection in NSTIs. Our data demonstrates a three-fold increase in mortality and need for 2 additional operations. Further research is needed to determine risk factors for fungal involvement. Consideration should be given to starting patients on empiric antifungal therapy in high risk cases.

O13.
Very Early (Prehospital) Antibiotics and Fluids in the Treatment of Sepsis: A Murine Trial

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Background:

Antibiotics and fluid resuscitation are mainstays of sepsis therapy and are time-sensitive. Timely delivery of these therapies remains an important clinical challenge. Protocolized sepsis care in the prehospital setting may offer an added benefit, with potential to gain two or more hours of lead time in the initiation of therapy. Whether or not this incremental advancement in time improves outcome is unknown. We propose to test two-hour advancements in therapy delivery in a physiology-based murine sepsis model.

Hypothesis:

Incremental advancements of two hours in the delivery of antibiotics and fluids (e.g. prehospital sepsis care) will improve mortality, inflammation, and organ dysfunction in murine cecal ligation and puncture (CLP) sepsis.

Methods:

C57BL/6 mice (8-12 weeks) were subjected to 1cm, 21-gauge double puncture CLP with simultaneous implantation of a HD-X11 wireless biotelemetry device (DSI), which enables continuous monitoring of heart rate and core temperature. Mice were monitored until reaching a previously defined and validated threshold for acute physiologic deterioration. Mice received antibiotics (imipenem 25 mg/kg) or antibiotics and fluid resuscitation (0.9% saline 30cc/kg SQ) at the time of meeting criteria, at a two hour delay, or at a four hour delay. Survival time was quantified for each group. For the antibiotics group we sacrificed a second set of mice at 24 hours after meeting criteria for acute deterioration; plasma and tissue were harvested. Cytokines (IL-6, IL-10, TNF-α) and Cystatin C, a marker of renal injury, were quantified by ELISA. Continuous variables were compared using a Kruskal-Wallis test. Survival was compared using the Mantel-Cox test and the logrank test for trend.

Results:

Each two hour delay to antibiotic therapy resulted in a stepwise decrease in median survival (3969 vs. 3485 vs. 2619 minutes, p<0.001). Median IL-6 increased with each two hour delay (8672 vs. 13224 vs. 38597 pg/mL, p=0.04). Median survival for combination antibiotic and fluid therapy was 3945.5 vs. 4467.5 vs. 2519.5 minutes for therapy given at the time of meeting criteria for deterioration, two hours later, or four hours later (p=0.046).

Conclusions:

Hourly delays in sepsis treatment increase mortality and inflammation in our model. Additional biomarker analysis is ongoing. Prehospital protocols for sepsis will allow treatment to begin at an earlier time point, with the potential to improve mortality and rates of organ dysfunction. A human trial of prehospital sepsis care is indicated.

O14.
Bacterial Burden in Critically Injured Ventilated Patients: does burden define pneumonia

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Background:

The development of pneumonia during mechanical ventilation (VAP) is the most common healthcare-associated infection in severely injured patients, accounting for substantial morbidity and increased mortality. Trauma ICUs have the highest rates of VAP among all surgical units, in part related to the high incidence of aspiration during and after trauma. The relationship of the bacterial burden within the lungs early after severe trauma to the subsequent development of clinical pneumonia is poorly understood.

Hypothesis:

We hypothesize that critically injured, mechanically ventilated patients who develop pneumonia have a progressive increase in pathogen burden over the course of ventilation until a threshold for symptomatic pneumonia is reached and VAP is suspected clinically.

Methods:

Critically injured adults ventilated for > 2 successive days without planned extubation for whom surrogate consent was obtained were enrolled. Patients underwent daily surveillance mini-bronchoscopic alveolar lavage (miniBAL) while ventilated for 14 days or until extubation. Standard semi-quantitative cultures were performed in the lab, results were blinded from clinical use. Standard patient management was performed by the clinical team. Patients suspected of VAP by the clinical team underwent bronchoscopic-BAL (bBAL) and semi-quantitative culture, VAP defined as > 10^4 CFU bacteria.

Results:

37 patients enrolled were ventilated a median of 9 days. 21 bBALs were performed for suspicion of VAP, 13 (35%) positive with > 10^4 CFU of one or more pathogens and treated. Surveillance miniBAL revealed that in 14 of 37, burden remained < 10^4 CFU during ventilation. None were suspected of VAP. 23 had a burden of > 10^4 CFU, 18 of these within 2 days of enrollment. Only 13 of 23 developed clinical VAP and confirmation by bBAL. In all 13, pathogens were those identified by miniBAL. Of 18 patients with positive miniBAL within 2 days, only 6 had suspicion of VAP at the time. 10 of the 23 patients cleared their bacterial burden without clinical suspicion VAP.

Conclusions:

Contrary to our hypothesis, a significant percentage of critically injured, ventilated adults develop high bacterial burden within the lungs early during their course. A significant number clear these bacteria without suspicion of VAP during ventilation. Defining patient characteristics that separate these two groups requires further study.

O15.
The Adipose Tissue: a Neglected Pro-Inflammatory Reservoir during Hypermetabolic and Septic States.

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Background:

Traumatic injury, including burns, leads to considerable alterations in plasma proteins, a reaction commonly referred to as "the acute phase response" (APR). These acute phase proteins include Serum Amyloid A (SAA), a pro-inflammatory protein that also functions as a damage-associated molecular pattern (DAMP). Severely burned patients display a strong acute phase response in the first hours to days after burn injury, the purpose of which is to mobilize immune cells. However, prolongation of the APR response and its attendant inflammatory processes may have damaging consequences for post burn outcome. While the inflammatory potential of adipose derived SAA has been described in the context of obesity and neonatal sepsis, whether this acute phase protein is also directly involved in the chronic hypermetabolic and pro-inflammatory state observed in burns is unclear.

Hypothesis:

We hypothesized that adipose derived SAA may be the culprit that facilitates chronic systemic inflammation post burn injury.

Methods:

Twenty patients with burns admitted to our burn centre and ten healthy individuals undergoing elective surgeries were consented for blood and subcutaneous white adipose tissue (sWAT) collection. SAA serum levels, gene and adipose secretion were all measured. The damaging effects of chronic SAA in post burn outcome was investigated using C57BL/6 mice subjected to both a 30% total body surface area (TBSA) thermal injury and a sub-lethal Pseudomonas aeruginosa (PA) infection (1 x 10^4 CFU).

Results:

Serum SAA levels increased significantly during the acute phase (0-3 days) in burn as well as in septic burn patients. Interestingly, SAA production increased and persisted post the acute phase (>7days) in both subgroups, with septic burn patients showing a greater increase in magnitude. Chronic SAA levels in septic burn patients were associated with an increased systemic inflammatory cytokine profile. SAA treatment of both human and mouse macrophages markedly elicited a pro-inflammatory response. Equally, daily injections of recombinant SAA in post burn infected mice increased mortality. We also demonstrate for the first time that SAA is highly and selectively expressed in the sWAT of burn patients. Moreover, ex-vivo fat explants from burn patients results showed increased SAA secretion.

Conclusions:

The increased expression and secretion of SAA by adipocytes in burns suggests that it maybe the culprit that sustains chronic systemic inflammation linked to sepsis and poor outcome in these patients.

O16.
Use of Crowdsourcing to Triage Surgical Site Infections

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Background:
Surgeons can use wound photographs to monitor for surgical site infections (SSI). mHealth apps that allow patients to securely transmit photos to providers may facilitate remote wound surveillance, but can increase the burden of data that must be interpereted by surgeons and may not be a scalable method for wound triage.

Employing internet users to rapidly perform discrete tasks (crowdsourcing) may facilitate real-time wound triage, but the ability of the crowd to accurately assess wound photographs is unknown.

Hypothesis:
Crowdsourced wound photo triage will provide accurate surveillance for SSI.

Methods:

Ten case scenarios (6 SSI, 4 non-SSI), presented as 4-6 sequential days of surgical wound photographs and symptoms, were administered as a survey through Amazon Mechanical Turk (mTurk), a global crowdsourcing platform. Participants provided demographics and prior experience with SSI; each completed at least 3 cases. SSI was defined, but no additional diagnostic training was provided. For each scenario day, they indicated if they felt SSI was present, their level of confidence, and their triage recommendation for continued observation, treatment or follow-up. Triage appropriateness was defined as escalation of care when SSI was suspected or non-escalation of care in the absence of SSI. SSI and non-SSI cases were analyzed to determine diagnostic accuracy and appropriateness of recommendations.

Results:

1171 participants completed the survey within 6 hours. After quality control for survey completion, data from 993 participants (3311 cases) were analyzed. 530 (53%) of participants were female, mean age was 35.5 years (SD±11.38), and 741 (74.6%) had prior experience with surgical wounds. Overall diagnostic accuracy was 34.6%; 18.1% of SSIs and 59.6% of non-SSI were correctly identified. Personal history of SSI was associated with improved accuracy in both SSI (19.8% v 16.2%,p=0.037) and non-SSI cases (62.9% v 55.8%,p=0.008). Higher levels of confidence were associated with higher accuracy in non-SSI cases (OR 1.34 [1.28-1.43],p<0.001), but lower accuracy in SSI cases (OR 0.84 [0.80-0.86],p<0.001). Triage recommendations were appropriate in 52.8% of cases; 45.7% of non-SSI cases were over-triaged and 57.6% of SSI cases were under-triaged.

Conclusions:

Crowdsourcing without training demonstrated poor performance in the detection of SSI using wound photography. SSI surveillance via crowdsourcing may be enabled by development of standard wound image features of SSI and associated training tools.

O17.
Are Antibiotics Directed Against MRSA Necessary in Patients with Negative MRSA Nasal Screening Swabs?

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Background:

MRSA infections are associated with high morbidity and mortality, as well as increased healthcare costs related to antibiotic therapy. Much of the use of anti-MRSA agents is empiric for suspected infection, exposing a large number of patients to toxicities related to the medications and collateral damage related to the use of broad-spectrum antimicrobials. This study was undertaken to determine if SICU patients with negative nasal screening swabs for MRSA could have empiric MRSA coverage safely withheld when they had a suspected infection.

Hypothesis:

Patients with negative MRSA nasal swabs are at sufficiently low risk for MRSA infection that empiric antibiotics directed against MRSA are unnecessary.

Methods:

The study was approved by the Washington University Investigational Review Board. All SICU patients who had a positive clinical culture for MRSA starting in 2007, when admission nasal swabs for MRSA became mandatory, were reviewed. It was determined whether the patients had positive or negative MRSA screen on admission, or converted to a positive MRSA nasal swab prior to the positive clinical MRSA culture. Patients who had a positive clinical culture obtained before a screening nasal swab were excluded from the analysis.

Results:

There were 361 patients admitted to the SICU from 2007-2016 who had at least one positive clinical culture for MRSA. The majority of the MRSA-positive cultures were from respiratory sites, followed by multiple sites, blood, and wounds. Approximately 7% of patients (24 patients) did not have a nasal swab performed before the clinical culture was obtained. Of the remaining 337 patients, 228 (68%) had a positive MRSA nasal swab obtained before the positive clinical culture. However, 109 patients (32%) had negative MRSA nasal swabs before the positive culture was obtained. Of these, 60 patients converted to a positive nasal swab but 49 patients (15%) continued to have a negative MRSA nasal swab even after a positive clinical culture had been obtained.

Conclusions:

Nasal screening swabs for MRSA remained negative in a significant number of patients with positive clinical cultures for MRSA. Moreover, with current screening practices, 32% of patients with a positive clinical culture for MRSA culture were considered negative for MRSA by nasal swab at the time the clinical culture was obtained. Withholding empiric antibiotic coverage against MRSA in such patients would have resulted in inadequate initial antimicrobial therapy in a substantial number of patients.

O18.
Same-hospital readmission rate is not reliable for measuring postoperative infection incidence

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Background:

Postoperative infections cause morbidity, use resources, and are an important measure to
assess hospitals. Commonly-used metrics do not account for readmission to a different hospital. The Nationwide Readmissions Database (NRD) tracks readmissions across US hospitals. Infection-related readmission across hospitals has not been previously studied nationally.

Hypothesis:

The incidence of postoperative infection-related readmission to different hospitals after common procedures is significant.

Methods:

The 2013 NRD was queried for admissions with a primary International Classification of Diseases, 9th version, Clinical Modification code for the most frequently performed surgeries. Unplanned all-cause, infection-related, and different hospital 30-day readmission rates were calculated, using All Patient Refined Diagnosis Related Groups codes. Multivariate logistic regression identified risk factors for readmission.

Results:

Of 826,836 patients surviving to discharge, 39,281 (4.8%) had an unplanned readmission within 30 days, occurring at a different hospital 20.5% of the time. The most common reason for readmission was infection (25.1%). Of infection-related readmissions, 17.4% occurred at a different hospital. Postoperative infections after extra-abdominal procedures were more likely to admitted to a different hospital. Risk factors for infection-related different hospital readmission include: non-elective procedures, age ≥ 65 years, Charlson Comorbidity Index > 1, length of stay > 30 days, and index admission at an urban academic medical center.

Procedure	n	Readmission, all-cause (%)	Different hospital readmission, all-cause (%)	Different hospital readmission, all-cause (OR [95% CI])	p	Readmission, infection (%)	Readmission, infection (OR [95% CI])	p	Different hospital readmission, infection (%)	Different hospital readmission, infection (OR [95% CI])	p
Knee arthroplasty	176,808	2.9	26.7	--	--	20.8	--	--	20.5	--	--
Hip replacement	140,442	4.3	23.6	0.85 [0.78-0.93]	<0.01	21.8	1.53 [1.41-1.66]	<0.01	22.8	1.15 [0.94-1.39]	0.18
Spinal fusion	99,984	4.4	26.1	0.97 [0.88-1.06]	0.48	25.8	1.89 [1.74-2.05]	<0.01	23.3	1.18 [0.96-1.44]	0.12
Appendectomy	70,109	4.1	11.8	0.37 [0.32-0.42]	<0.01	41.5	2.85 [2.62-3.09]	<0.01	8.6	0.36 [0.28-0.47]	<0.01
Cholecystectomy	61,556	6.2	15.7	0.51 [0.46-0.57]	<0.01	17.3	1.78 [1.62-1.97]	<0.01	11.4	0.50 [0.38-0.66]	<0.01
Laminectomy	59,269	4.6	24.0	0.87 [0.78-0.96]	0.01	25.7	1.95 [1.77-2.14]	<0.01	21.6	1.07 [0.85-1.35]	0.58
Hip/femur reduction/fixation	57,982	7.7	22.1	0.78 [0.71-0.85]	<0.01	27.4	3.54 [3.26-3.85]	<0.01	22.3	1.11 [0.91-1.36]	0.30
Lysis of adhesions	50,778	8.0	14.1	0.45 [0.40-0.50]	<0.01	24.7	3.31 [3.04-3.61]	<0.01	10.8	0.47 [0.37-0.60]	<0.01
Leg reduction/fixation	45,579	4.4	22.3	0.79 [0.70-0.89]	<0.01	24.6	1.78 [1.60-1.98]	<0.01	18.1	0.86 [0.65-1.13]	0.27
Oophorectomy	36,345	3.7	17.7	0.59 [0.51-0.69]	<0.01	30.7	1.87 [1.67-2.10]	<0.01	14.8	0.67 [0.50-0.92]	0.01
Colectomy	28,975	8.1	11.5	0.36 [0.31-0.41]	<0.01	27.8	3.76 [3.41-4.15]	<0.01	11.1	0.48 [0.36-0.64]	<0.01

Risk factor	Readmission, all-cause (OR [95% CI])	p	Different hospital readmission, all-cause (OR [95% CI])	p	Readmission, infection (OR [95% CI])	p	Different hospital readmission, infection (OR [95% CI])	p
Elective	0.58 [0.57-0.59]	<0.01	1.46 [1.39-1.54]	<0.01	0.88 [0.84-0.92]	<0.01	0.73 [0.65-0.81]	<0.01
Female	0.95 [0.93-0.97]	<0.01	0.96 [0.91-1.01]	0.12	0.95 [0.91-1.00]	0.03	1.01 [0.90-1.13]	0.88
Age ≥ 65 years	1.08 [1.05-1.11]	<0.01	1.18 [1.11-1.26]	<0.01	1.00 [0.95-1.06]	0.97	1.38 [1.21-1.58]	<0.01
Charlson Comorbidity Index > 1	1.94 [1.89-1.98]	<0.01	1.05 [1.00-1.11]	0.07	1.06 [1.00-1.11]	0.04	1.14 [1.01-1.28]	0.03
Length of stay > 30 days	2.31 [2.06-2.58]	<0.01	1.80 [1.43-2.26]	<0.01	1.25 [1.00-1.55]	0.05	1.70 [1.13-2.56]	0.01
Lowest median household income quartile	1.07 [1.04-1.09]	<0.01	1.11 [1.05-1.17]	<0.01	1.02 [0.97-1.08]	0.45	1.02 [0.90-1.15]	0.80
Public insurance	1.59 [1.55-1.64]	<0.01	1.16 [1.09-1.24]	<0.01	1.00 [0.94-1.06]	0.96	0.94 [0.81-1.08]	0.39
Low-volume hospital	0.89 [0.81-0.99]	0.03	1.51 [1.22-1.87]	<0.01	1.10 [0.88-1.39]	0.39	1.25 [0.84-1.87]	0.28
Small hospital	0.86 [0.83-0.89]	<0.01	1.92 [1.79-2.06]	<0.01	0.98 [0.91-1.05]	0.55	1.01 [0.87-1.18]	0.85
Public hospital	1.01 [0.97-1.04]	0.78	0.96 [0.89-1.04]	0.31	1.08 [1.01-1.16]	0.03	0.93 [0.78-1.10]	0.39
Urban academic medical center	1.08 [1.05-1.10]	<0.01	0.86 [0.81-0.90]	<0.01	1.08 [1.03-1.13]	<0.01	1.20 [1.07-1.33]	<0.01

Conclusions:

A significant number of postoperative readmissions, particularly for infection, are missed by same-hospital readmission data. Readmission rates to a different hospital, including for postoperative infection, are affected by patient and institution-specific factors. This has implications for coordination of care, resource allocation, and quality metrics.

O19.

The non-thyroidal illness syndrome is associated with poor postoperative outcomes in enterocutaneous fistula

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Background:

The non-thyroidal illness syndrome (NTIS) is common in critically ill patients and associated with poor outcomes. Although, many enterocutaneous fistula (ECF) patients have rehabilitated from critical illness, most of them still suffered NTIS when receiving the definite digestive tract reconstruction surgery.

Hypothesis:

This study was designed to investigate the association between preoperative presence of NTIS and postoperative outcomes in ECF patients.

Methods:

A total of 264 ECF patients who underwent definite digestive tract reconstruction surgery from April 2014 to November 2016 were collected. The thyroidal hormones were tested for each patient before surgery, and all the patients were divided into NTIS group and non-NTIS group according to the presence of NTIS. Demographic, surgery related data and complications until postoperative days 30 were recorded and analyzed.

Results:

Among the ECF patients preparing for definite surgery, the prevalence of NTIS was 31.4%(83/264). The most common presentation of NTIS was low FT3 (26.5%), followed by low TSH (4.9%) and FT4 (2.7%). The percentage of multiple ECF and use of enteral nutrition shorter than 3 months, and incidence of postoperative surgical site infections(SSIs) in NTIS group were higher than those of non-NTIS group (P<0.05). The levels of FT3 correlated with the occurrence rates of postoperative SSIs, especially for superficial and deep SSIs. Receiver operating characteristic curve analysis showed the diagnostic effectiveness of FT3, suggesting the optimal cut-off value was 3.5 pmol/L with area under curve, sensitivity and specificity of 0.75, 72.6% and 68.7%, respectively.

Conclusions:

The ECF patients with NTIS before definite surgery associated with more risk of poor outcomes. Whether they need thyroid hormone replacement therapy or delay of the definite surgery should be further studied.

O20.
Utility of Sepsis Scores for Identifying Infection in Surgical Intensive Care Unit Patients

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Background:

In 2016, the Sepsis Definitions Task Force provided updated definitions of sepsis and septic shock. The new definitions use the Sequential Organ Failure Assessment (SOFA) and quickSOFA (qSOFA) scores to define sepsis based on changes in these scores. This methodology is meant to replace the Systemic Inflammatory Response System (SIRS) criteria as identifiers of septic patients. However, these new metrics have not been well tested in post-surgical or trauma populations.

Hypothesis:

SOFA score, qSOFA score, and SIRS criteria do not predict infection in surgical intensive care unit patients

Methods:

Over a ninety day period, data were prospectively collected on all patients in the surgical/trauma intensive care unit and cardiothoracic surgical intensive care unit. For each patient-day, qSOFA, SOFA, and SIRS scores were calculated. Trauma as well as treatment for an active infection was noted. SOFA, qSOFA, and SIRS scores were calculated. SOFA scores were evaluated using Wilcoxon rank sum, while qSOFA and SIRS criteria were evaluated using chi-square.

Results:

Data from 1942 patient-days were included in our study (see table). Ongoing infection was noted for 437 (24%) patient-days, and 120 new episodes of ICU-acquired infection where treatment was started on the day of survey were identified. Eighty five percent of new infectious episodes had an associated qSOFA score greater or equal to 2, and 93.3% had 2 or more SIRS criteria. However even in non-infected patients, 81.3% had either qSOFA or SIRS (91.9%) scores of 2 or more. On univariate analysis, there was no association between SOFA, qSOFA, or SIRS criteria with episodes of new infection (p-values 0.21, 0.6, and 0.95 respectively). While controlling for trauma and the presence of active infection using multivariable analysis, no statistically significant correlation between SOFA, qSOFA, or SIRS criteria and infection was observed. (p-values 0.22, 0.57, 0.81 respectively)

	Trauma	Non-trauma	Cardiothoracic	Uninfected	Ongoing infection	New infection
Number	534	653	749	1375	439	116
SIRS citeria (avg)	2.7	2.4	2.7	2.6	2.5	2.7
SOFA (avg)	6.5	6.9	7.8	7.0	7.3	7.4
qSOFA (avg)	2.2	2.0	2.2	2.2	2.1	2.2

Conclusions:

Neither SOFA, qSOFA, or SIRS criteria correlated with new infection in a population of critically ill surgical patients. Further research is needed to determine applicability of the new sepsis definitions to post-surgical and trauma populations.

O21.
A Pilot Randomized Controlled Trial of Video Education versus Skill Demonstration: Which is More Effective in Teaching Sterile Surgical Technique?

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Background:

Video education has many advantages over traditional education including efficiency, convenience, and individualized learning. Learning sterile surgical technique is imperative for medical students as proper technique helps prevent surgical site infections.

Hypothesis:

We hypothesized that video education is as effective or superior to traditional skill demonstration in educating first year medical students on sterile surgical technique.

Methods:

A video series was created to demonstrate sterile surgical technique. A pilot randomized controlled trial was designed to assess which education method best teaches sterile surgical technique: video education or skill demonstration (Figure 1).

First year medical students (n=131) were consented and randomized into two groups: 1) those who attended a skill demonstration session {control group; n=70}, and 2) those who watched the video series {experimental group; n=61}. The control group attended a 90-minute nurse-educator led skill demonstration. Participants then completed a 30-item multiple choice quiz to test their knowledge.
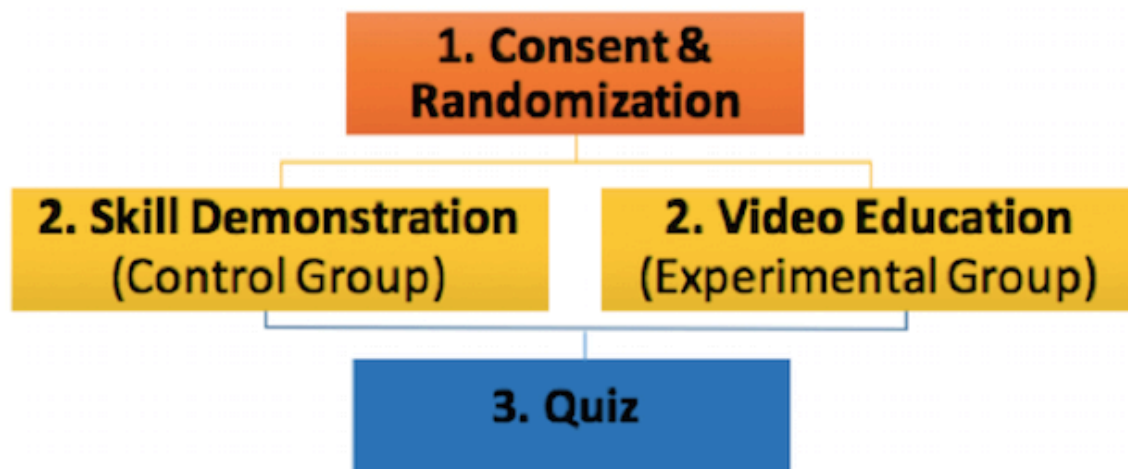

Figure 1. Study Design

Results:

Seven 2-6 minute videos (30 minutes total) were created to educate students on surgical attire, scrubbing, gowning and gloving, and maintaining sterility. On average, each video was viewed 1.6 times, and the videos on surgical attire and maintaining sterility had the most views.

Preliminary quiz results showed significant difference between control (n=49) and experimental (n=46) groups (21.8±0.4 vs 26.6±0.5, p<0.0001, Figure 2).
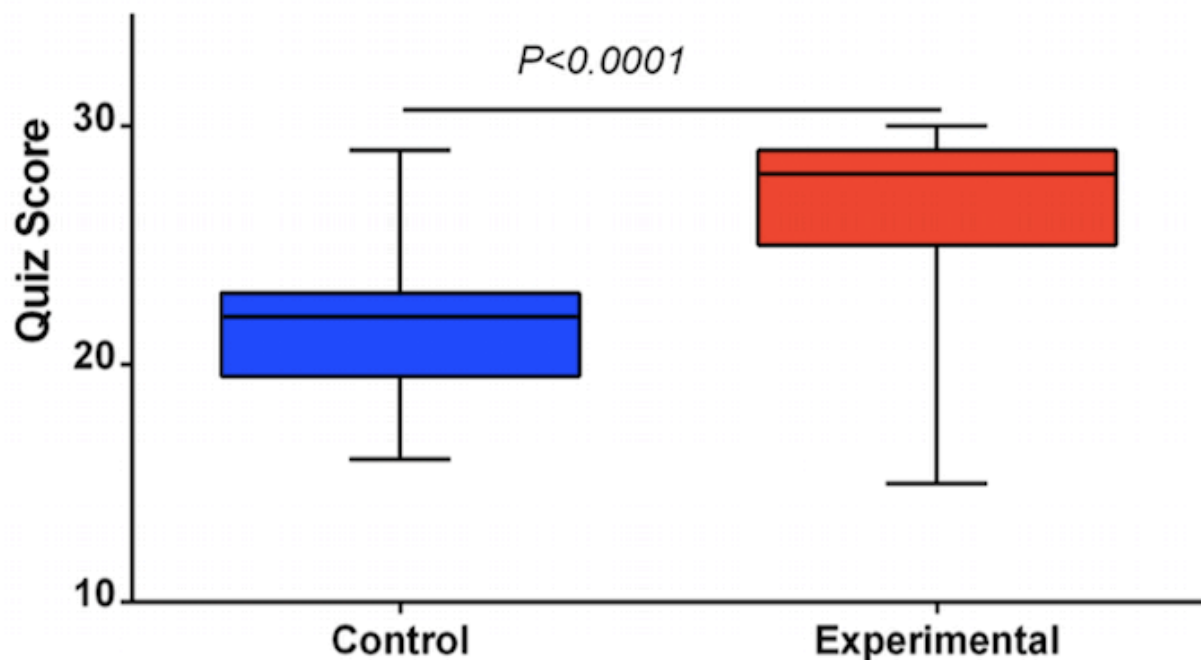
Figure 2. Box plot of control and experimental participant quiz scores. The maximum score was 30.

Conclusions:

Video education is superior to skill demonstration in providing medical students with knowledge on sterile surgical technique. In an era of duty hour restrictions and limited resources, video education can augment medical students' knowledge prior to their operating room experience to ensure that a sterile environment is maintained for patients. The ultimate goal is to reduce surgical site infections.

O22.
Lactobacillus murinus Protects Against Necrotizing Enterocolitis Caused by Cronobacter muytjensii

Mubina Isani, Children's Hospital of Los Angeles;Jordan Bowling, Chlidren's Hospital of Los Angeles;Melissa Elizee, Children's Hospital of Los Angeles;Chioma Moneme, USC, Children's Hospital of Los Angeles;Brandon Bell, Children's Hospital of Los Angeles;Laura Illingworth, Children's Hospital of Los Angeles;Jamie Golden, Children's Hospital of Los Angeles;Jin Wang, Children's Hospital of Los Angeles;Anatoly Grishin, Children's Hospital of Los Angeles;Henri Ford, Children's Hospital of LA, University of SC

Background:

Necrotizing enterocolitis (NEC) is a leading cause of morbidity and mortality in premature infants. *Lactobacillus* probiotics have been shown in a number of studies to protect against NEC. However, trials remain inconclusive due to the use of different species and doses of bacteria. Furthermore, whether the lactobacilli are colonizing the intestine remains unknown. Our lab has isolated naturally occurring *Lactobacillus* species that are efficient colonizers of the neonatal rat intestine.

Hypothesis:

We propose that an efficient probiotic strain is not only a naturally occurring species capable of colonizing the neonatal intestine, but also one that protects the intestine against NEC.

Methods:

Animal experiments were approved and neonates were obtained from pregnant rats and subjected to formula feeding and hypoxia every 8 hours for 4 days. The animals were sacrificed and intestinal contents were plated to isolate the lactobacilli. Three species were identified: *L.reuteri, L.murinus*, and *L.acidophilus.*

Lactobacillus species were introduced in our NEC model at the 10^7 and 10^8 CFU/animal with the first feed. Next, to determine if the *Lactobacillus* species protect animals against a known NEC pathogen, *Cronobacter muytjensii*, we introduced the *Lactobacillus* with the first feed and the *Cronobacter* with the second feed. Terminal ileum sections were stained with H&E and examined to determine NEC score. Sections were also immunostained to determine if COX-2 and iNOS levels were changed in the presence of the *Lactobacillus* species and *C.muytjensii*. Real time PCR was done to determine if COX-2 mRNA and iNOS mRNA levels changed.

Results:

L.reuteri, L.murinus, and *L.acidophilus* were isolated from neonatal rat intestine. All three species were able to colonize the intestine. However, NEC scores were only lower in groups that received *L.murinus* ($p= 0.05$ at 10^7 CFU/animal n=25 and $p=0.03$ at 10^8 CFU/animal, n=35). Furthermore, *L.murinus* was able to protect against NEC when animals were challenged by a known NEC pathogen, *C.muytjensii* ($p=0.03$, n=6). *L.murinus* decreased COX-2 protein and mRNA expression in tissue induced by *C.muytjensii* ($p=0.0001$, n=4).

Conclusions:

L.murinus is a naturally occurring species that is able to colonize the intestine of neonatal rats and protect them against NEC. It can also protect against NEC when animals are challenged by *C.muytjensii* and it decreases expression of COX-2 induced by *C.muytjensii*. Our results show that protective effects of lactobacilli in NEC may be species-specific.

O23.
Blue Light Reduces Neutrophil Influx in Acute Lung Injury

John Griepentrog, University of Pittsburgh;Anthony Lewis, ;Xianghong Zhang, University of Pittsburgh;Matthew Rosengart, University of Pittsburgh

Background:

Acute lung injury is arguably the most common organ dysfunction experienced by critically ill patients and imparts additional attributable mortality. The underlying causal mechanisms of acute alveolar damage include an excessive accumulation of neutrophils in the lung and the subsequent production of inflammatory mediators and neutrophil-mediated oxidant damage. Previous work from our lab demonstrated that blue light reduces organ injury from ischemia/reperfusion. However, the ramifications of manipulating light spectrum on the outcomes of sterile and septic lung injury are unknown.

Hypothesis:

We hypothesize that blue light enhances regional control of a septic focus and thereby reduces bacterial dissemination and attenuates acute lung injury in a murine model of pulmonary sepsis.

Methods:

Male C57BL/6 mice were administered Ultrapure LPS (1.5mg/kg) or Klebsiella pneumoniae (8000 CFUs) intratracheally and were treated with blue (442nm, 1400 lux), red (617nm, 1400 lux), or ambient (400 lux) white light. Mice were sacrificed at 6, 24, 48 hours for LPS and at 24 hours for Klebsiella. The left lung was isolated and four sequential lavages of 0.5mL bronchoalveolar lavage (BAL) fluid (0.9% saline with 0.6mM EDTA) were instilled into the right lung. ELISA was performed on BAL fluid, lung tissue homogenate, and serum. Comparisons between groups were performed by Kruskal-Wallis or rank sum tests with α = 0.05.

Results:

During Klebsiella pneumonia, Blue light, by comparison to Red and Ambient light, reduced total BAL cell count, primarily by reducing the influx of neutrophils: Blue vs. Red: 3.8×10^5 vs. 1.2×10^6 (p=0.004) vs. Ambient: 1.2×10^6 (p=0.01). Similarly blue light reduced BAL neutrophil concentration in a sterile model of LPS-induced acute neutrophilic lung injury. Despite reduced alveolar neutrophils, the lungs and blood of blue light mice exhibited reduced bacteria, though this did not attain statistical significance. Lung MPO activity was slightly decreased after blue light. Levels of plasma and lung cytokines (IL-6, IL-10, TNF-alpha) and BAL chemokines (CXCL1/KC, CCL3/MIP-1a) were decreased with blue light, but not statistically significant.

Conclusions:

Blue light attenuates neutrophil influx into the lung after sterile and infectious insults, and promotes clearance of the infection. Further studies are required to elucidate the circadian clock mechanisms and determine if blue light reduces bacterial dissemination at longer time points and improves survival.

~~O24.~~
~~**Elevated Levels of Plasma Mitochondrial DNA Are Associated with Clinical Outcome in Intra-abdominal Infections Caused by Severe Trauma**~~

Qiong-yuan Hu, Department of Surgery, Jinling Hospital;Jianan Ren, Nanjing General Hospital of Nanjing;Gefei Wang, Department of Surgery, Jinling Hospital;Guosheng Gu, Department of Surgery, Jinling Hospital

Background:

Mitochondrial DNA (mtDNA) damage-associated molecular patterns (DAMPs) accumulate in the circulation after severe trauma, however, little is known concerning the relationship between serum mtDNA levels and intra-abdominal infections (IAIs) after trauma.

Hypothesis:

The purpose of our study was to prospectively determine relationships between plasma mtDNA concentration and clinical outcome in IAIs patients induced by severe abdominal trauma.

Methods:

DNA was isolated from serum samples taken from IAIs patients at hospital days 0, 1, 2. Plasma mtDNA concentration was assessed by real-time PCR within *Human Cytochrome B*, *COX1*, *MT-ND2*, and *D-Loop* genes. The study population's clinical and laboratory data were analyzed.

Results:

MtDNA DAMPs were expressed as PCR threshold cycle (Tc) number. Lower Tc indicated increased plasma mtDNA concentration. IAIs patients had significant higher plasma mtDNA than healthy controls. Patients with sepsis had apparently elevated mtDNA levels in 4 selected sequences examined (30.9±2.0 vs 28.7±2.4; 33.3±2.6 vs 28.9±2.4; 32.9±1.6 vs 31.2±2.2; 33.1±3.6 vs 28.1±2.2, respectively). Patients who developed MODS also had increased mtDNA concentration compared with those who did not (31.0±1.8 vs 27.9±1.8; 32.9±2.4 vs 27.8±1.7;

32.9±1.5 vs 29.8±1.7; 32.0±3.8 vs 27.1±2.1, respectively) /submission/image.axd?id=dd7b34a3-4455-4113-85d3-494d8d0731af&t=636157288945270000. Baseline mtDNA concentration had high effectiveness in predicting mortality for IAIs patients with severe abdominal trauma using ROC analysis. Furthermore, serum mtDNA levels on admission correlated with the lactate concentration, however, no significant correlations were found between mtDNA levels and WBC, C-reactive protein and procalcitonin /submission/image.axd?id=dd7b34a3-4455-4113-85d3-494d8d0731af&t=636157288945270000.

Conclusions:

Plasma mtDNA was associated with the occurrence of sepsis, MODS, and mortality in IAIs patients caused by severe abdominal trauma.

O25.
The role of PD-1 in sepsis induced alterations in splenic PD-L1 and PD-L2 expression

Daithi Heffernan, ;Eleanor Fallon, Rhode Island Hospital;Chun Chung, Brown University;Alfred Ayala, RI Hospital

Background:

Program Death Receptor-1 (PD-1) is a central component of the immune response to a variety of chronic (cancer) and acute (including sepsis) illnesses in both humans and murine models. PD-1, a regulatory check point protein, functions by modulating the excessive inflammation and immune storm induced by acute sepsis. However less is known about PD-L1 and PD-L2, the two ligands for PD-1. Specifically there is a dearth of knowledge pertaining to the surface expression of PD-L1/PD-L2 following sepsis and how PD-1 may affect changes in ligand expression.

Hypothesis:

Given the central role for PD-1 in modulating the immune response to sepsis, we hypothesize that alterations in surface expression of PD-L1/PD-L2, across a variety of innate immune cells, will be affected by the presence/absence of PD-1.

Methods:

Sepsis, induced by Cecal Ligation and Puncture(CLP), versus sham laparotomy, in 8-12 week old C57BL/6 background control/wild type(WT) and PD-1 knockout (PD-1$^{-/-}$) mice. 24 hours later spleens were harvested. Flow cytometry was used for phenotyping using mAbs to CD11b, F4/80, PD-L1 and PD-L2.

Results:

Sepsis induced decreased total spleen cell counts in both WT and PD-1$^{-/-}$ mice. Specifically, counts for both F4/80^{+} and CD11b^{+} cells were decreased following sepsis in both WT and PD-1$^{-/-}$ mice. In WT, compared to sham, sepsis increased expression of PD-L1 on both F4/80^{+} cells (78% vs 94%;$p<0.05$) as well as CD11b^{+} cells (75% vs 86%;$p<0.05$). This effect was unchanged in PD-1$^{-/-}$ mice with sepsis increasing PD-L1 expression upon both F4/80^{+} and CD11b^{+} cells. However, PD-1$^{-/-}$ did affect PD-L2 expression following sepsis. Within WT mice, sepsis induced a decline in %PD-L2^{+}F4/80^{+} cells (14.8% vs 8%;$p<0.05$) but no change in %PD-L2^{+}CD11b^{+} cells (5.1% vs 6.2%;$p=0.4$). Accounting for cell numbers, this led to an absolute decline in PD-L2^{+}F4/80^{+} and CD11b^{+} cells in WT. However, within PD-1$^{-/-}$ mice, following sepsis there was no change in %PD-L2^{+}F4/80^{+} (14% vs 12%;$p=0.7$) but an increase in %PD-L2^{+}CD11b^{+} (6 vs 11%$p<0.05$). Accounting for total cell counts, within PD-1$^{-/-}$ mice, numbers of both PD-L2^{+}F4/80^{+} (2.5 vs 1.4x10^{4}/ml;$p=0.1$) and PD-L2^{+}/CD11b^{+} (8.4 vs 7x10^{4}/ml;$p=0.5$) cells were preserved following sepsis.

Conclusions:

Counter to our hypothesis, PD-1 did not appear to play a role in the alteration of PD-L1 expression across innate immune cell following sepsis. However PD-1 did play a role in PD-L2 expression, suggesting PD-1 may mediate the loss of PD-L2$^+$ innate splenocytes seen in sepsis.

O26.
The septic spleen: impacts of Programmed cell death receptor-1 (PD-1) gene expression in murine neonatal and adult polymicrobial infection.

Eleanor Fallon, Brown University / Rhode Island Hospital;Daithi Heffernan, Brown University;Chun-Shiang Chung, Brown University / Rhode Island Hospital;William Cioffi, Rhode Island Hospital;Alfred Ayala, RI Hospital

Background:

The spleen is an important tertiary lymphoid immune organ. In response to acute events splenic cellular composition and functions change with age. We previously demonstrated that Programmed cell death receptor-1(PD-1) contributes to septic mortality in pups and adults, and its inhibition alters immune responses.

Hypothesis:

PD-1 differentially alters septic innate and adaptive cellular composition between pups and adults.

Methods:

Cecal Ligation and Puncture(CLP) and Cecal Slurry(CS) for intra-abdominal polymicrobial sepsis in adult and neonatal mice, respectively. Splenocytes were harvested at 24 hours for flow cytometry(phenotyping) and ELISA(cytokine). Cell counts are reported per ml.

Results:

Sepsis induced cell depletion in both WT and PD-1$^{-/-}$ adults, versus increased splenic cell counts in WT pups and decreased counts in PD-1$^{-/-}$ pups. In septic adults, PD-1 did not affect CD3$^+$ responses with declines in both CD3% and number in both WT and PD-1$^{-/-}$. Despite increased %CD8$^+$ in adult WT and PD-1$^{-/-}$, total number of CD8$^+$cells was decreased in both WT and PD-1$^{-/-}$. Conversely WT pups demonstrated increased CD3$^+$(4.2 vs 5.0x10^5) and CD8$^+$(0.7 vs 1.33x10^5) cells. This was reversed in septic PD-1$^{-/-}$ pups with loss of CD3$^+$(5.2 vs 2.9x10^5) and CD8$^+$(0.9 vs 0.53x10^5) cells. Regarding adult innate responses, the %F4/80$^+$ cells was unchanged in WT and decreased in PD-1$^{-/-}$ mice, whereas %CD11b$^+$ cells was decreased in both WT & PD-1$^{-/-}$. Adjusting for cell count this led to reductions in both F4/80$^+$ & CD11b$^+$ across both WT and PD-1$^{-/-}$ adults. Conversely, in WT pups following sepsis there was an increase in % and absolute number of F4/80$^+$(0.6 vs 1.33 x10^5) and no change in the CD11b$^+$ population(0.74 vs 0.73x10^5). In PD-1$^{-/-}$ pups, sepsis induced a loss of both F4/80$^+$ and CD11b$^+$. With respect to PD-1 expression, in adult WT mice, sepsis induced increases in PD-1$^+$F4/80$^+$(27% vs 40%), but no change in PD-1$^+$CD11b$^+$(17% vs 19%). Conversely, in pups, there was no change in PD-1$^+$/F4/80$^+$cells(13.6% vs12.3%) and a decrease in PD-1$^+$CD11b$^+$ cells (29% vs 20%). In pups, sepsis decreased splenic tissue lysate TNF-α and IL-2 in WT, but did not alter cytokines in PD-1$^{-/-}$ pups. In adults sepsis induced increases in IL-6 in WT mice.

Conclusions:

In contrast to adults, the neonatal spleen is sensitive to the effects of PD-1, wherein PD-1 exerts a differential effect upon cellular (lymphocytic/innate) population shifts in sepsis. Our data highlights potentially differing immune priorities for PD-1 between adults and neonates in sepsis.

O27.
Antibiotic management of surgical patients with peritonitis at a tertiary referral hospital in Rwanda

Jennifer Rickard, ;Christian Ngarambe, ;Leonard Ndayizeye, ;Blair Smart, ;Robert Riviello, ;Jean Paul Majyambere, ;Stephen Rulisa, ;Rahel Ghebre,

Background:

Antibiotic usage and antimicrobial resistance impact surgical patient outcomes and there is growing recognition of the worsening problem of antibiotic resistance and need for antibiotic stewardship in low resource settings. We report results of antibiotic usage in patients undergoing surgery for peritonitis at a tertiary referral hospital in Rwanda.

Hypothesis:

We hypothesize that there is a substantial number of patients at high risk for treatment failure and current antimicrobial therapy is inadequate.

Methods:

Patients undergoing surgery for the indication of peritonitis at a tertiary referral hospital in Rwanda were included in this study. Post Caesarean section peritonitis was excluded. Prospective data were collected on epidemiology, clinical features, operative procedure and outcomes. Antibiotics were prescribed and intraoperative cultures were collected according to surgeon discretion. We compared antibiotic usage with current Surgical Infection Society (SIS) guidelines.

Results:

Over a 6-month period, 280 patients underwent a laparotomy for peritonitis. Data on antibiotic usage was available for 244 patients. The most common diagnoses were intestinal obstruction (N=97), appendicitis (N=36) and trauma (N=35).

229 (93.9%) patients received antibiotics with the most common antibiotics being third-generation cephalosporins (N=215, 88.1%) and metronidazole (N=188, 77.1%). The mean duration of antibiotics was 4.5 days (range: 0, 14) with longer mean duration seen in patients with typhoid intestinal perforation (7.8 days) and cholecystitis (7.0 days) compared with liver abscess (3 days), tumor (3.4 days) and intestinal obstruction (3.6 days). Based on SIS guidelines, 94 (38%) patients were a high-risk for treatment failure and 113 (46%) patients received the proper initial antibiotic.

Surgical specimens were collected on 33 (12%) patients and 7 (21%) patients had an organism isolated. The most common organism isolated was *Escherichia coli*, identified in 5 surgical specimens, 1 urine culture and 1 blood culture.

Conclusions:

Broad antibiotic coverage with third-generation cephalosporins and metronidazole is common in Rwandan surgical patients with peritonitis. Areas for improvement should focus on choice of and duration of antibiotics, tailored to underlying diagnosis and risk factors for treatment failure. Given the number of patients at high-risk for treatment failure, more data is needed on antibiotic resistance patterns to guide antimicrobial therapy.

O28.
CaMKIV regulates mitochondrial function during sepsis

Xianghong Zhang, University of Pittsburgh;Li Xu, University of Pittsburgh; Union hospital,Tongji Medical College, Huazhong University of Science and Technology China;Anthony Lewis, University of Pittsburgh;John Griepentrog, UPMC;Brian Zuckerbraun, University of Pittsburgh School of Medicine;Matthew Rosengart, University of Pittsburgh

Background:

Sepsis-induced organ failure is associated with oxidative stress and mitochondrial damage. We previously observed that kidney function was worse in mice lacking CaMKIV and noted a loss in mitochondrial architectural integrity in the renal cortex of CaMKIV knockout mice subjected to CLP sepsis. These data suggest that CaMKIV may regulate mitochondrial function during sepsis.

Hypothesis:

CaMKIV regulates mitochondrial function during sepsis.

Methods:

We used CaMKIV$^{-/-}$ and C57BL/6 wild-type control mice. Mice were subjected to CLP, and at various times, were euthanized and the blood and organs were harvested. Oxygen Consumption Rate was determined by Seahorse. Complex protein expression (OXPHOS) was determined by immunoblot. The activities of mitochondrial complexes I, II and IV were assessed by Complex Enzyme Activity Microplate Assay. Protein peroxidation was evaluated by an Oxyblot Assay. Lipid peroxidation was assessed by 4-hydroxy-2-nonenal (4-HNE) immunostaining. PGC1a was determines by immunoblot. Real time PCR was used to detect the mtDNA in serum.

Results:

After LPS exposure, WT peritoneal macrophage exhibited a reduction in basal OCR at 12 hours followed by a rebound to baseline OCR levels by 24 hours that was not observed in CaMKIV$^{-/-}$ peritoneal macrophage. There were less Complex I in CaMKIV$^{-/-}$ mice subjected to CLP by comparison to WT mice. And the activities of Complex I and II also decreased significantly. More peroxided protein and lipid were found in the kidney lacking CaMKIV. To correspond with damaged mitochondria observed in renal cortex in EM, mitochondrial biogenesis was also suppressed due to the inhibition of PGC1a, and more mtDNA were released to blood in CaMKIV$^{-/-}$ mice.

Conclusions:

Collectively, these observations suggest that CaMKIV regulates mitochondrial function during sepsis. The loss of CaMKIV exacerbates oxidative stress, which may underlie the increase in cellular damage and organ dysfunction.

O29.
COX-2 upregulation following LPS injection is attenuated in EP2 receptor knockout mice

Jamie Golden, Children's Hospital Los Angeles;Laura Illingworth, Children's Hospital Los Angeles;Oswaldo Escobar, Children's Hospital Los Angeles;Mubina Isani, Children's Hospital Los Angeles;Christopher Gayer, Children's Hospital Los Angeles;Anatoly Grishin, Children's Hospital Los Angeles;Henri Ford, Children's Hospital Los Angeles

Background:

EP2 is a pro-inflammatory prostanoid receptor that is activated by high levels of prostaglandin E2 (PGE2). Cyclooxygenase-2 (COX-2) is the rate limiting enzyme in the production of PGE2. Previous work in our lab suggests that the EP2 receptor is involved in PGE2-induced upregulation of COX-2 during intestinal inflammation and may play a key role in gut-origin sepsis.

Hypothesis:

We hypothesized that EP2 receptor knockout would attenuate upregulation of COX-2 and prevent intestinal barrier breakdown in experimental peritonitis.

Methods:

C57Bl/6 mice (WT) and congenic EP2 receptor knockout mice (EP2KO) were orally gavaged with fluorescein isothiocyanate (FITC)-dextran and injected intraperitoneally with saline as a control or with 30mg/kg lipopolysaccharide (LPS) to induce experimental peritonitis. Mice were sacrificed 16 hours later. Blood samples were collected and analyzed for levels of FITC-dextran to determine barrier breakdown. Terminal ileum was evaluated for COX-2, IL-6, and iNOS mRNA using real-time PCR.

Results:

WT and EP2KO mice showed no significant difference in intestinal barrier breakdown in response to LPS injection (4.9±0.6 versus 5.6±1.6 fold change from saline, p=0.7). At baseline, EP2KO mice had 1.6±0.8 fold higher COX-2 levels than WT mice. However, COX-2 mRNA levels after LPS injection were significantly lower in EP2KO mice compared with WT mice (0.5±0.1 versus 2±0.4 fold change from saline controls, p<0.001). EP2KO mice did not significantly differ from WT mice in LPS-induced expression of IL-6 mRNA and iNOS mRNA (548±314 and 2.9±0.8 fold change from saline, respectively).

Conclusions:

EP2 receptor knockout did not protect against intestinal barrier breakdown or upregulation of IL-6 and iNOS mRNA following LPS injection, but abrogated LPS-induced COX-2 upregulation. This suggests that EP2 may specifically alter COX-2 mediated inflammation but does not protect against concomitant inflammatory pathways activated by LPS. This may have important therapeutic implications in the treatment of COX-2 mediated inflammation and gut-origin sepsis.

O30.
Establishment of a specialty ventral hernia clinic decreases surgical site infections

Deepa Cherla, University of Texas Health Science Center at Houston;Julie Holihan, University of Texas Health Science Center at Houston;Juan Flores, University of Texas Health Science Center at Houston;Debbie Lew, University of Texas Health Science Center at Houston;Rick Escamilla, University of Texas Health Science Center at Houston;Cristina Viso, University of Texas Health Science Center at Houston;Tien Ko, University of Texas Health Science Center at Houston;Lillian Kao, University of Texas Health Science Center at Houston;Mike Liang, University of Texas Health Science Center at Houston

Background:

The association among volume, specialization, and improved outcomes has been shown in multiple surgical fields, but the need for specialized centers for ventral hernia repair(VHR) remains controversial.

Hypothesis:

We hypothesized that establishment of a specialty hernia clinic would decrease surgical site infections (SSI).

Methods:

Databases of patients undergoing elective VHR at 1 academic institution were reviewed prior to (2010-2011) and following the establishment of a specialty hernia clinic (2015-2016). All general surgeons (n=17) performed VHR in the 2010-2011 period; following establishment of the specialty clinic, 3 surgeons managed all VHRs and related visits. Patient demographics, comorbidities, operative details, and SSI rates at 1-month postoperatively were compared.   Demographic variables and outcomes were compared using Chi Square for categorical variables and

Mann-Whitney U for continuous variables. Stratified analysis was performed using the European Hernia Society(EHS) Ventral Hernia Classification.

Results:

Patients who underwent VHR preceding and following the establishment of a specialty hernia clinic differed significantly (Table). Following implementation of the specialty hernia clinic, patients treated were more likely to be older, have higher ASA scores, and have larger, incisional, and recurrent hernias. In addition, patients were less likely to be obese or smoke. Laparoscopic repair and mesh reinforcement was more likely to be utilized. SSI rates were reduced following the implementation of the specialty hernia clinic (29/399,7.3% versus 9/237,3.8%, p=0.074). This difference persisted following stratification for case complexity (Table 1)

Table 1: Comparison Before and After Implementation of a Specialty Hernia Clinic

	Pre- (n=399)		Post- (n=237)		p value
Age (median, IQR)	45 (37-53)		49.5 (40.0-58.1)		<0.001
BMI (median, IQR)	31.9 (28.3-36.0)		30.7 (27.9-32.7)		<0.001
History of tobacco use	77 (19.3%)		25 (10.5%)		0.004
COPD	11 (2.8%)		4 (1.7%)		0.390
Diabetes	59 (14.8%)		46 (19.4%)		0.101
ASA					<0.001
1 & 2	331 (83.0%)		144 (60.8%)		
3 & 4	68 (17.0%)		93 (39.2%)		
Hernia defect size (median, IQR)	4 (1.0-15.0)		9 (2-48)		0.017
Hernia type					<0.001
Primary	167 (41.9%)		54 (22.8%)		
Incisional	232 (58.1%)		183 (77.2%)		
Recurrent	51 (12.8%)		49 (20.7%)		0.008
Case type					<0.001
Laparoscopic	94 (23.6%)		192 (81.0%)		
Open	292 (73.2%)		40 (16.9%)		
Hybrid	13 (3.3%)		5 (2.1%)		
Wound Classification					0.212
1 & 2	393 (98.5%)		230 (97.0%)		
3 & 4	6 (1.5%)		7 (3.0%)		
Mesh reinforcement	314 (78.7%)		225 (94.9%)		<0.001
Hernia Type	**N**	**%SSI**	**N**	**%SSI**	-
Primary	7/167	4.2%	1/54	1.9%	
Incisional Small	10/147	6.8%	2/52	3.8%	
Incisional Medium	4/64	6.3%	1/73	1.4%	
Incisional Large	8/21	38.1%	4/15	26.7%	

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Conclusions:

Despite repairing larger and more complex hernias, utilization of a specialty hernia clinic decreased SSI rates postoperatively. Reductions in SSIs were observed across all levels of case complexity. Improvements in improving SSI rates may be attributed to careful patient selection, preoperative optimization, adherence to evidence based guidelines, and successful use of laparoscopy in complex cases. Further studies should investigate the cost-effectiveness and long-term outcomes of specialty hernia clinics.

O31.
Mitochondrial Antiviral Signaling (MAVS) Protein is a Novel Anti-Inflammatory Mediator in Liver Ischemia/Reperfusion

Menachem Ailenberg, St. Michael's Hospital;Chung Ho Leung, St. Michael's Hospital;Phil Williams, Schulich School of Medicine & Dentistry, Western University;Ori Rotstein, St. Michael's Hospital

Background:

Oxidative stress contributes to the pathogenesis of ischemia/reperfusion (I/R) injury, in part through induction of signaling pathways leading to NF-κB activation and elaboration of pro-inflammatory cytokines. *In vitro*, we have previously shown that oxidative stress induces activation of a mitochondrial protein, Mitochondrial Antiviral Signaling protein (MAVS), a molecule central to the innate antiviral response. In the present study, we examine the role of MAVS in the pathogenesis of liver I/R injury in a murine model.

Hypothesis:

Oxidative stress resulting from liver I/R activates MAVS, which participates in downstream signalling pathways in response to hepatocellular injury.

Methods:

Wildtype and MAVS KO mice were subjected to 45 min warm liver ischemia to the median and left lateral lobes and were sacrificed at 1 and 4 hr post reperfusion. Mito-TEMPO, a mitochondria specific oxidant scavenger, was administered prior to ischemia to investigate the role of mitochondrial ROS in the activation of MAVS. Protein expression of the MAVS monomer and aggregates were used to measure activation of MAVS. Hepatic injury was evaluated by serum levels of ALT and TNF-α. The anti-inflammatory response to I/R was evaluated by the expression of heme oxygenase-1 and IL-10.

Results:

Liver I/R activated MAVS as indicated by a significant reduction in the expression of MAVS monomers and increased expression of MAVS aggregates. Mito-TEMPO significantly reduced the activation of MAVS, demonstrating the role of mitochondria ROS in its activation. Compared to WT mice, MAVS KO mice exhibited significantly elevated hepatocellular injury and inflammation as indicated by serum ALT and TNF-α (Table 1). In contrast, the mRNA levels of the antioxidant enzyme heme oxygenase-1 and the anti-inflammatory cytokine IL-10 were notably higher in liver tissue of WT mice versus MAVS KO mice (Table 1).

	Serum ALT (U/L; 4 hr)	Serum TNF-α (pg/ml; 4 hr)	HO-1 mRNA (RQ; 1hr)		IL-10 mRNA (RQ; 1hr)	
	I/R	I/R	Sham-I/R	I/R	Sham-I/R	I/R
WT	8890±2295	10.26±2.86	1±0.04	5.57±0.45 [#]	1±0.10	41.7±1.6 [#]
MAVS KO	17707±1363 *	21.4±0.94 *	1.6±0.04	3.78±0.15	1.46±0.02	25.8±1.1
Statisical Analysis	* ttest P<0.05 vs WT, n=4		# ANOVA Tukey Kramer P<0.05 vs MAVS KO I/R, n=4			

Conclusions:

Mitochondrial ROS resulting from I/R lead to the activation of MAVS. MAVS appears to be hepatoprotective, following I/R through its influence on the balance between pro- and anti-inflammatory cytokines. This heretofore unrecognized role for the antiviral protein MAVS suggests a novel target for therapies aimed at lessening I/R injury.

O32.
Early Results of a Preoperative Decontamination Protocol to Reduce Surgical Site Infections in Patients Undergoing Elective Oncologic Resections

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Adigun, Michael E. DeBakey VAMC;Samir Awad, Baylor College of Medicine

Background:

Surgical site infections (SSIs) are associated with greater healthcare costs and higher rates of patient morbidity and mortality. In cancer patients, SSIs can lead to delay or omission of adjuvant therapy and have been associated with a decrease in overall survival. Recent efforts have focused on SSI prevention through preoperative decontamination, but to date, this has not been reported in surgical oncology patients.

Hypothesis:

We hypothesize that implementation of a preoperative decontamination protocol (PDP) will decrease the SSI rate among cancer patients undergoing elective curative resections.

Methods:

A PDP was implemented as a quality improvement initiative in October 2014 at our institution. The PDP consists of using chlorhexidine gluconate (CHG) wipes, CHG oral rinse, and intranasal povidone-iodine the night before and morning of surgery. Patients who underwent elective primary tumor resection between Oct 2013 to Aug 2016 were identified. Data including protocol compliance, tumor site, wound class, SSI rate, SSI type, and culture results were obtained through retrospective chart review. Patients who performed decontamination (decon) were compared to those who did not (control) using univariate analysis with significance set at $p<0.05$.

Results:

A total of 445 patients were identified (control: n=290, decon: n=155) with no difference in tumor site between groups ($p=0.10$). Compliance increased from 57% in 2015 to 67% in 2016 ($p=0.12$). SSI rates were 14% in the control group and 8% in the decon group, $p=0.08$. SSI rates remained lower for decon compared to control when stratifying by wound classification, without reaching significance (clean: control 13% vs. decon 5%, $p=0.24$; clean-contaminated: control 15% vs. decon 10%, $p=0.27$). Cultures were obtained for 28 of the 54 SSI cases. 3 resulted in no growth. From the remaining 25 SSIs (20 control, 5 decon), the predominant organisms were *Enterococcus* (36%), *Escherichia coli* (28%), and *Staphylococcus epidermidis* (20%). *S. aureus* was not isolated from the decon group, but was present in 5 of the 20 control group cultures (25%), with 1 being MRSA ($p=0.55$).

Conclusions:

Our preliminary results demonstrate a trend toward reduction of SSIs with a PDP among patients undergoing elective oncologic resections. Although not statistically significant, continued efforts at patient enrollment and compliance may impact future SSI rates. In SSIs where cultures were taken, PDP may be effective against *S. aureus*. Further study is warranted.

O33.
Reduced Macrocytocic Migration in Oncostatin M Receptor Deficient Mice Provides Beneficial Effects Against Sepsis

Saad Salim, University of Alberta;Nour AlMalki, University of Alberta;Thomas Churchill, University of Alberta;Rachel Khadaroo, University of Alberta

Background:

Vulnerable, elderly populations are at increased risk for septic related mortality. High levels of oncostatin M, an IL-6 family cytokine, has been found in patients suffering from septic shock; however, little is known about its

mechanistic role in the evolution of sepsis.

Hypothesis:

We hypothesized that oncostatin M receptor (OSMR) knockout would provide protection against sepsis in a murine model of sepsis.

Methods:

Cecal slurry (C/S) injected into the peritoneum was used as a model of sepsis. C/S was prepared from cecal contents of healthy 9-13 weeks old wildtype mice. C/S at a dose of 1.3mg/g was injected into OSMR knockout and control mice older than 55 weeks. After 18 hours, surviving mice were euthanized via exsanguination and the organs were harvested. Peritoneal lavage was anaerobically cultured. Endotoxin assay was performed on blood. Additionally, peritoneal macrophages were isolated from thioglycollate injected mice. Isolated macrophages were stained with CD11b, F4/80, Ly6c for flow cytometry, or gentamycin protection assay was performed for assessing bacterial killing.

Results:

Old OSMR knockout mice had better survival and clinical score than their aged-matched controls. Despite a significant increase of peritoneal bacterial cultures in the knockout mice, there was no difference in serum endotoxin concentrations compared to controls. Peritoneal isolated macrophages from OSMR knockouts had better live *E.coli* killing capacity than controls. Flow cytometry revealed that old knockout mice had reduced recruitment of CD11b$^+$ F4/80$^+$ Ly6c^{high+} macrophages into the peritoneal than controls, but no difference in resident CD11b$^+$ F4/80$^+$ Ly6c^{low+} macrophages.

Conclusions:

OSMR deficiency provides protection against sepsis in old mice by decreasing macrocytic migration into the peritoneum. This reduces the perpetuation of the inflammatory cascade. OSMR knockout macrophages have better bacterial killing capacity, lowering potential of serum endotoxicity. Inhibition of OSM signaling may provide a novel treatment strategy for abdominal sepsis, especially in the elderly.

O34.
Consequences of Implementing a "Better" Blood Culture System

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Background:

Blood cultures (BCx) are the gold standard for diagnosing blood stream infections, identifying organisms, and guiding treatment. However, contamination remains a challenge and can increase cost, hospital days, and unnecessary antibiotic use. National goals are to keep overall BCx contamination rates to ≤3%. Our hospital recently moved to a BCx system with better performance in organism recovery, especially for gram negative, fastidious, and anaerobic bacteria.

Hypothesis:

A more sensitive BCx system will significantly increase hospital contamination rates and pathogen recognition.

Methods:

The electronic health record was queried for all BCx from April 2015 to October 2016. April 2016 was the transition period, so these BCx were excluded. Cultures were divided into those obtained 12 months before and 6 months after the new system. A positive BCx was defined as one with any growth. Contaminated BCx were defined as coagulase-negative Staphylococcus, Corynebacterium, Bacillus, Micrococcus, or Propionibacterium acnes. Cultures with Staphylococcus aureus, Klebsiella pneumoniae, or Escherichia coli were said to contain a true pathogen. Results based on hospital location of blood culture draw were also determined.

Results:

A total of 20,978 blood cultures were included, 13,292 before and 7,686 after the new system. Positive BCx increased from 7.5% to 15.7% (p<0.001). Contaminants increased from 2.3% to 5.4% (p<0.001). Pathogens increased from 2.5% to 5.8% (p<0.001). Contaminated BCx significantly increased in Surgical/Trauma Intensive Care Unit (STICU), Emergency Department (ED), and Medical ICU (MICU), while pathogen BCx increased on the surgical floor, ED, and MICU (Table 1).

Table 1: Number of contaminated and pathogen blood cultures by location	Contaminants			Pathogens		
	Before	After	P-value	Before	After	P-value
STICU	16 (1.8%)	28 (6.3%)	<0.001	17 (1.9%)	14 (3.2%)	0.174
Surgical Floor	8 (1.3%)	11 (3%)	0.091	8 (1.3%)	18 (4.9%)	0.001
Burn ICU	1 (0.8%)	2 (2.2%)	0.573	2 (1.6%)	0 (0.0%)	0.511
ED	171 (4.8%)	195 (9.1%)	<0.001	156 (4.4%)	153 (7.1%)	<0.001
MICU	13 (1.1%)	35 (4.8%)	<0.001	28 (2.4%)	77 (10.7%)	<0.001

Conclusions:

A new blood culture system resulted in significant increases in the rates of positive, contaminated, and pathogen BCx. The new system resulted in the STICU, ED, and MICU having contamination rates >3%. This data suggests that a "better" BCx system may not be superior in regards to overall infection rates, and may affect quality-based measures and reimbursements. More research is needed to determine the impact of identifying more contaminants and pathogens with the new system, as well as missing pathogens with the old system.

O36.
Relationship of Measured Vital Capacity and Pneumonia Following Traumatic Cervical Spinal Cord Injury

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Center;John Como, Metrohealth Medical Center

Background:

Pulmonary function testing has previously been used to characterize the degree of respiratory dysfunction and risk of pneumonia (PNA) following traumatic rib fractures. Literature regarding the utility of early pulmonary function testing in cervical spinal cord injuries (C-SCI) is sparse.

Hypothesis:

Inpatient vital capacity performed early during trauma hospitalization will be predictive of the risk for developing pneumonia in patients with acute traumatic C-SCI.

Methods:

All patients with an acute traumatic C-SCI admitted to our level one trauma center from January 2013-June 2016 were identified. The primary outcome evaluated was pneumonia. Additional information including demographics, mechanism of injury, level and ASIA grade of cord injury, pulmonary function testing, co-existing chest injuries, and other key clinical data was obtained from the electronic medical record and trauma registry.

Results:

A total of 93 patients with acute C-SCI was identified; of these, 83 (89%) had inpatient vital capacity recorded. Mean population age was 55 years (SD±16), ISS was 17 (IQ±5), and blunt mechanism represented 96% of injuries. Of 83 patients, 12 (14.5%) developed pneumonia. Patients diagnosed with pneumonia were younger, more severely injured, and with more associated chest injuries than those who did not develop pneumonia (Table 1). C-SCI at C4 had the highest rate of pneumonia (58.3%). Percent of predicted vital capacity was statistically lower in patients who developed pneumonia. A logistic regression analysis of key variables was performed and demonstrated younger age (OR 0.95, CI 0.903-0.998, p = 0.040), higher ISS (OR 1.21, CI 1.061-1.386, p = 0.005), and lower percent of predicted VC (OR 0.95, CI 0.891-0.999, p= 0.045) were significant for the development of pneumonia (area under the curve = 0.93).

Table 1. Factors Associated with Pneumonia in Traumatic C-SCI

	No PNA (n = 71)	PNA (n = 12)	p
Mean age, yrs	57.7 (SD±15.3)	41.7 (SD±15.9)	0.001
Male	55 (77.5%)	10 (83.3%)	1.0
Median ISS	16.5 (IQ±5.0)	27.0 (IQ±16.8)	0.001
Hemothorax/Pneumothorax	3 (4.2%)	4 (33.3%)	0.003
Pulmonary Contusion	2 (2.8%)	4 (33.3%)	0.007
ASIA A	12 (16.9%)	7 (58.3%)	0.012
Diag. of COPD	3 (4.2%)	1 (8.3%)	0.471
History of smoking	43 (60.6%)	7 (58.3%)	1.0
Mean predicted VC%	46.3% (SD±22.4)	22.9% (SD±12.7)	0.001

Conclusions:

Decreased vital capacity during trauma hospitalization increases the odds of developing pneumonia.
Early pulmonary function testing can be utilized to help identify at risk patients and institute appropriate preventive therapy.

O37.
Comparison of various sepsis clinical criteria for burn patients

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Background:

Although sepsis is one of the leading causes of morbidity and mortality in burn patients, the identification and definition of sepsis represents an ongoing challenge, as the signs of sepsis are ubiquitously present during the post-burn stress period with profound inflammatory and hypermetabolic responses. Burn-specific sepsis criteria have been developed to identify sepsis, but none have been successful. The aim of this study was to evaluate the sensitivity of current sepsis criteria in burn patients.

Hypothesis:

We hypothesized that a prospective clinical assessment will be more sensitive than the burn-specific definitions.

Methods:

We enrolled and studied 420 adult burn patients admitted to a tertiary burn centre between 2006-2014. Sepsis was identified by prospective clinical diagnosis made by attending burn surgeons based on clinical signs. Sensitivities of the American Burn Association (ABA) sepsis criteria, Mann-Salinas (MS) burn sepsis predictors, and Sepsis-3 Consensus (S3C) definition were compared. To determine sensitivity, sepsis criteria were applied using records from a 48-hour period prior to clinical diagnosis. Patients were stratified based on total body surface area (TBSA) burn size into two groups: <20% and ≥20% TBSA. Chi-square test was used to compare sensitivities between the two TBSA groups, and McNemar's test was used to compare sensitivities within each TBSA group.

Results:

In our study, 92 of the 420 patients (22%) were identified as having sepsis. In the <20% TBSA burn group (n=37) the ABA, MS and S3C criteria were positive in 60%, 27%, and 81% respectively. For patients with ≥20% TBSA burn (n=55) the ABA, MS and S3C criteria were positive in 56%, 27%, and 83% respectively. There was no significant difference between the two TBSA groups with respect to the 3 criteria. Sensitivities of the tests overall showed a statistically significant difference between any two criteria (p<0.0001).

Conclusions:

The S3C outperformed both burn-specific sepsis criteria, with the ABA sepsis criteria coming in second, and the MS criteria performing the least consistently. However, no one defining criterion of sepsis was found to be sensitive enough to be used as a diagnostic standard within the burn patient population. The clinical picture is the gold standard and sepsis should be prospectively documented. The S3C is the best definition to identify sepsis retrospectively, though this may underestimate the incidence of sepsis in burns.

O38.
Primary Closure after Surgical Drainage of Complicated Intra-abdominal Infections Does Not Require a Longer Regimen of Antibiotic Therapy

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Background:

The duration of antibiotic usage in the treatment of complicated intra-abdominal infections (CIAIs) has recently been reported by a prospective, multi-center, randomized controlled trial. Similar outcomes were reported for a four-day and a longer regimen of antibiotic use once adequate source control was obtained.

Hypothesis:

We hypothesized that primary surgical wound closure techniques would not increase the risk of infectious complications in patients treated with a short-course of antibiotics compared to a longer course.

Methods:

The STOP-IT trial database of patients with a CIAI who received surgical drainage with primary closure were analyzed. Patients were randomized to receive a longer regimen of antibiotics (2 days after the resolution of fever, leukocytosis, and ileus, with a maximum of 10 days) or a fixed course of antibiotics (4 ± 1 days). Outcomes included incidence of and time to, surgical site infection (SSI), recurrent intra-abdominal infection (RIAI), extra-

abdominal infections (EAI), and Clostridium Difficile infection (CDI). Hospital length of stay (LOS) and mortality were also reported.

Results:

Of the 588 STOP-IT database patients, 191 met inclusion criteria. With respect to short vs longer antibiotic regimen the incidence of infectious complications were as follows: SSI (8.0% vs 14.6%, P=0.15), RIAI (12.5% vs 11.7%, P=0.86), and EAI (11.4% vs 3.9%, P=0.05). Time to onset of complications were 7.7 + 6.1 vs 11.3 + 7.7 days (P= 0.30) for RIAI, 10.5 + 7.3 vs 13.9 + 6.1 days, (P= 0.83) for SSI,13.9 + 7.4 vs 15.3 + 4.8 (P= 0.15) for EAI, and 3.4% vs 1% (P=0.241) for CDI. Overall outcome measures of LOS and death were similar (9.5 + 8.3 vs 8.6 + 7.2 days, P= 0.232) and (1.1% vs 0%, P=0.278).

Conclusions:

Our results suggest that CIAIs in which surgical source control was obtained and closed in a primary fashion can safely be treated with a short-course of antibiotics. No difference was observed between a short regimen of antibiotic therapy compared to a long regimen in patients with primary wound closure.

O39.
Development of a surgical infection surveillance program at a tertiary hospital in Ethiopia: lessons learned from two follow up strategies in separate operating theater environments

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Background:

The World Health Organization Surgical Safety Checklist is proven to decrease morbidity and mortality but remains difficult to implement, particularly in low resource settings. We developed CLEAN CUT - Checklist Expansion for Antisepsis and Infection Control: Customization, Use, and Training - with two goals: (1) increase adherence to evidence-based perioperative infection prevention measures and (2) establish a sustainable surgical infection surveillance program. Here we describe our infection surveillance program and lessons learned from two distinct follow up strategies.

Hypothesis:

A chart review strategy will underestimate surgical complications.

Methods:

CLEAN CUT was piloted at a 432 bed tertiary hospital in Ethiopia. Data were collected in main (n=3), obstetric (n=2) and pediatric (n=1) operating theatres (OT). Infection prevention measures included skin decontamination, gauze tracking, antibiotic use and timing, instrument sterility, gown/drape integrity, and checklist compliance. Outcome measures included hospital length of stay, SSI, reoperation, and discharge disposition. Two surveillance methods were used. In the first, we reviewed the written hospital charts of all patients whose operation occurred in the main and pediatric OT. An on-site surgical fellow attended semi-structured weekly rounds on general surgical patients to evaluate charting accuracy. In the second, we directly observed all post-surgical patients in obstetrics over one week.

Results:

We reviewed 79 patient charts in the chart review group and followed 55 obstetric patients in the direct observation group. There was a marked difference in the rate of post-operative infectious complications between

the two groups: 16.5% in main OT (6.3% SSI) versus 25.5% in obstetric OT (7.3% SSI). Multiple inconsistencies in documentation were noted in the chart review group including failure to record wound opening by staff, antibiotic prescription practices, and complications such as wound dehiscence and surgical site infections. All complications from the obstetric unit were directly recorded using standardized definitions for complications.

Conclusions:

Surgical site infections were poorly captured in documentation, but direct observation and prospective follow up is possible in a resource limited setting. However, this second method is time-intensive and requires substantial clinical skill and training. For accurate surgical infection surveillance, a tool that incorporates direct observation of patients on rounds is essential.

O40.
Is Less More? Undetectable Estradiol Level a Predictor of Survival in the Critically Ill and Injured

Nathan Elwood, University of Virginia;Puja M. Shah, ;Addison May, Vanderbilt University Medical Center;Christopher Guidry, UVA Health System;Robert Sawyer, University of Virginia HSC

Background:

The role of sex hormones in the stress and immune response is unclear. Animal data suggest that higher estradiol levels are protective in infection, while human data have been inconclusive. In a large cohort of critically ill patients with infections, it has been noted that a significant number of patients produce undetectable levels of sex hormones.

Hypothesis:

We hypothesized that among critically ill patients with infections, those who produce undetectable levels of estradiol, testosterone, or DHEA (phenotypic nulls) have a higher mortality rate than those who produce higher levels of these hormones.

Methods:

A prospective, multi-institution cohort of critically ill trauma and surgical patients who experienced 1,241 infectious episodes was retrospectively evaluated. Infections were analyzed on a per-episode basis. Descriptive comparisons were performed using Chi-square, Fisher's exact, and Kruskal-Wallis tests as appropriate. Multivariable analysis using demographic and clinical variables selected *a priori* was also performed. The primary outcome was death.

Results:

1,241 infectious episodes captured in this data set were analyzed. Overall, 44% were phenotypic nulls for estradiol, 17% for testosterone, and 37% for DHEA. For estradiol, phenotypic nulls had a decreased risk of mortality (13% vs 24%, p= <0.0001). There was no difference for testosterone (21% vs 18%, p=0.37), while phenotypic nulls for DHEA had an increased risk of death (23% vs 16%, p=0.001). Men and women were equally likely to produce undetectable levels of estradiol (45% vs 43%, p=0.40) and testosterone (17% vs 19%, p=0.26), while women were more likely to be phenotypic nulls for DHEA (50% vs 30%, p= <0.0001). Phenotypic nulls for estradiol were younger than those producing higher hormone levels (46 vs 50, p= <0.0001), while phenotypic nulls for DHEA were older (54 vs 45, p= <0.0001). After controlling for age, sex, and APACHE II score, having an undetectable level of estradiol was associated with decreased odds of mortality (OR 0.51, p= 0.0001), while no significant effect was detected for testosterone or DHEA. The c-statistic of this model was 0.77.

Conclusions:

In this cohort, critically ill patients with infectious processes who produce undetectable levels of estradiol had better survival than those with higher levels, after controlling for both age and sex. Since mortality was associated with a DHEA phenotypic null response, it is possible that decreased conversion of DHEA to estradiol is an infection survival mechanism.

O41.

Exosomes in Post-Shock Mesenteric Lymph Act as Danger Signals Triggering the Systemic Inflammatory Response via Toll-like Receptor 4

Mitsuaki Kojima, University of California-San Diego;Todd Costantini, University of California-San Diego;Theresa Chan, University of California-San Diego;Andrew Baird, University of California-San Diego;Brian Eliceiri, University of California-San Diego;Raul Coimbra, University of California-San Diego

Background:

Toll-like receptor 4 (TLR4) is the primary recognition receptor for inflammatory responses mediated by endogenous ligands signaling danger. TLR4 is believed to play a critical role in the development of remote organ injury after trauma/hemorrhagic shock (T/HS). Recently, gut-derived exosomes were identified in mesenteric lymph (ML) that initiate immune cell activation and acute lung injury after T/HS in experimental models.
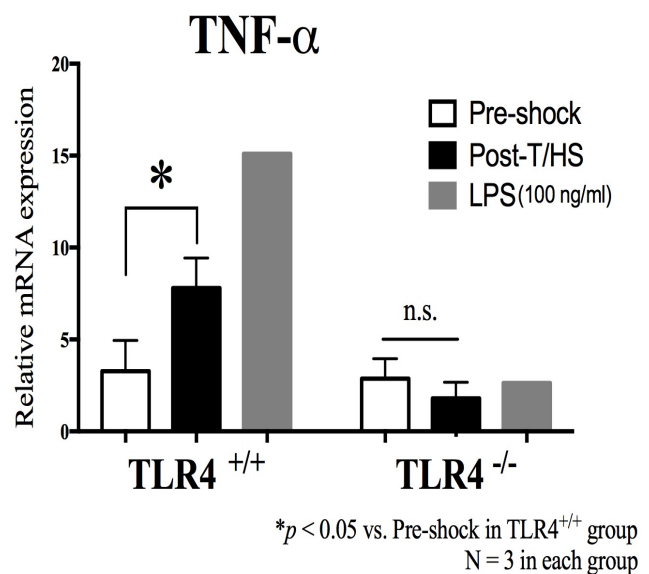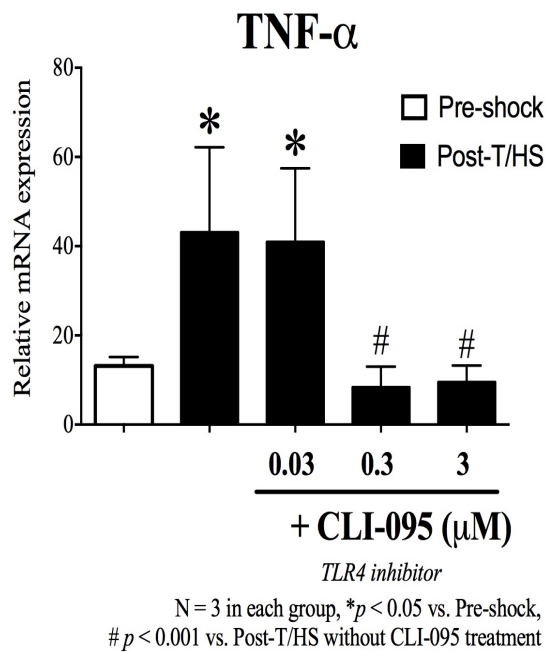
Hypothesis:

We hypothesized that exosomes secreted into ML promote a systemic inflammatory response through macrophage TLR4 activation after T/HS.

Methods:

Male rats underwent cannulation of the femoral artery, jugular vein, and ML duct before trauma/hemorrhagic shock (T/HS; mean arterial pressure 35 mmHg for 60 min), followed by resuscitation with shed blood and two times normal saline. ML was collected before HS (pre-shock) and after T/HS (post-T/HS) for isolation of exosomes by differential centrifugation. ML exosomes harvested during pre-shock or post-T/HS were then exposed to macrophage cell lines in vitro. The inflammatory activities of ML exosomes in each phase were measured by TNF-α and NF-κB production in rat macrophage cell line by qRT-PCR at 6 hours after stimulation. Exosome uptake in $TLR4^{+/+}$ and $TLR4^{-/-}$ murine macrophages was measured by flow cytometry. Macrophage cell lines pre-treated with a specific inhibitor or genetic deficiency in TLR4 were used to determine the relevance of TLR4 on ML exosomes-induced TNF-α production.

Results:

The pro-inflammatory activity of post-T/HS ML exosomes was demonstrated by increased TNF-α (2.6-fold increase; $p<0.05$) and NF-κB mRNA production (4.8-fold increase; $p<0.001$) compared to pre-shock. $TLR4^{-/-}$ macrophages did not differ with regards to ML exosome uptake compared to TLR4-suficient macrophages (94.5±3.4 vs. 96.1±3.3 %; p=ns). Both pharmacologic inhibition and genetic knockout of TLR4 completely abolished post-T/HS ML exosome-induced TNF-α production (See figure).

TNF-α (left graph)

Relative mRNA expression

Pre-shock
Post-T/HS

* * # #

0.03   0.3   3

+ CLI-095 (μM)

TLR4 inhibitor

N = 3 in each group, *p < 0.05 vs. Pre-shock,
# p < 0.001 vs. Post-T/HS without CLI-095 treatment

TNF-α (right graph)

Relative mRNA expression

Pre-shock
Post-T/HS
LPS (100 ng/ml)

* n.s.

TLR4 $^{+/+}$ TLR4 $^{-/-}$

*p < 0.05 vs. Pre-shock in TLR4$^{+/+}$ group
N = 3 in each group

Conclusions:

TLR4 is involved in ML exosome-mediated inflammatory signaling in macrophages but not their uptake mechanism. Our findings define the essential role of TLR4 as a recognition receptor of immune cell activation by gut-derived exosomes after severe injury.

O42.
An Evidence-Based Care Protocol Decreases Length of Stay and Cost in Pediatric Appendicitis

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Background:

Appendicitis remains one of the most frequently encountered pediatric surgical diagnoses. In an effort to improve patient care, we implemented an evidence-based treatment protocol that prioritized limited IV narcotic and fluid use, early postoperative enteral feeding and ambulation, decreased central lines and Foley catheter usage, as well as timely preoperative and reduced postoperative antibiotic administration.

Hypothesis:

We hypothesized that a standardized, evidence-based perioperative care protocol would result in decreased hospital length of stay and a lower overall cost of care without compromising patient outcomes.

Methods:

Data from patients treated surgically for appendicitis after protocol initiation was prospectively collected from January 2015 to September 2016. We compared this cohort with historical control patients treated from November

2013 to December 2014, prior to the initiation of our protocol. We examined length of stay (LOS), surgical site infection (SSI), readmission, and cost data. Continuous variables were compared with a Wilcoxon rank-sum test. Categorical data was compared using Fisher's Exact Test. All tests were two-sided with alpha=0.05. Statistical analysis was performed using Stata 14.2.

Results:

The protocol group containing 810 patients was compared to the historical control group of 506 patients. There were no significant differences in age or sex between the two groups. Median LOS decreased from 39.9 [IQR 29.0-87.0] hours to 35.5 [IQR 24.2-62.2] hours after protocol implementation (p<0.001). There were no significant differences in the rate of SSI (control 0.7% vs. protocol 0.2%; p=0.24) or readmissions between groups (control 4.8% vs. protocol 3.4%; p=0.33). Cost analysis showed a 10.4% decrease in average cost per patient treated after protocol initiation. Subgroup analysis of patients with complicated appendicitis (defined as patients found at the time of surgery to have a perforated appendix ± abscess formation) showed a significant reduction in LOS (147.4 [IQR 128.4-219.1] vs. 110.5 [IQR 77.1-159.1] hours; p<0.001) and average cost per patient (-19.7%) after initiation of the protocol.

Conclusions:

Initiation of an evidence-based protocol to treat pediatric patients with appendicitis resulted in a significant decrease in LOS and cost per patient without negatively affecting SSI and readmission rates. Continued use and development of data-driven standardized treatment protocols may prove beneficial to patients and cost-effective for health-care systems.

O43.
Nonoperative Management of Appendicitis is more Frequent in Elderly Patients with Comorbidities.

Isaiah Turnbull, Washington University in Saint Louis;Christopher Horn, Washington University School of Medicine;Dajun Tian, Washington University School of Medicine;Grant Bochicchio, Washington University School of Medicine;John Mazuski, Washington University School of Medicine

Background:

Appendicitis is the most common intraabdominal surgical emergency in the United States, with over 250,000 cases each year. Several European studies have evaluated the efficacy of nonoperative management of appendicitis in adults, and it has become an accepted option for a previously uniformly surgical disease. To determine the role of non-operative management of acute appendicitis in the US, we evaluated treatment patterns for acute appendicitis in 2012 National Inpatient Sample.

Hypothesis:

Patients at increased risk for appendectomy will be more frequently managed nonoperatively.

Methods:

The 2012 NIS was queried for patients with a principal diagnosis of appendicitis. Exclusion criteria where age<18, elective admission, peritoneal abscess. We compared demographics of patients who underwent early operation vs. those who underwent no intervention. We identified controls for the no-intervention group within those who underwent early operation and case-matched for age, gender, number of comorbidities and inpatient diagnosis. Frequencies were analyzed by Chi^2 and continuous variables by T-Test.

Results:

31730 cases of appendicitis were identified. 94.3% of patients underwent early operation. 3.4% underwent no intervention. 1.6% underwent a delayed operation and 0.7% underwent a percutaneous drainage procedure. As

compared to the early operation group, the no-intervention group was significantly older (48.5 vs. 41.0 years, p<0.05), had more comorbid conditions (2.4 vs. 1.5, p<0.05), and more inpatient diagnosis (5.6 vs. 3.8, p<0.05). After controlling for these factors, we found that nonoperative management was associated with a longer length of stay (3.0 vs. 2.6 days, p<0.05) but was significantly less expensive as indicated by total hospital costs ($21,691.01 vs. $26,049.05, p<0.05). Before case-matching, nonoperative management was associated with a significantly high risk of mortality (0.4% vs. 0.1%, p<0.05). However, as compared to case-matched controls there was no difference in mortality (0.3 vs. 0.4%).

Conclusions:

Nonoperative management is associated with an increased length of stay but decreased costs. Elderly patients with multiple comorbidities are more likely to undergo nonoperative management than younger, healthier patients. The increased mortality in patients managed non-operatively likely reflects the increased age and comorbidity in this cohort. However, when age and comorbidities are controlled for, there is no difference in mortality between operative and nonoperative management.

O44.
Does isolation of Enterococcus affect outcomes in intraabdominal infections?

James Sanders, JPS Health Network;Jeffrey Tessier, JPS Health Network;Billy Moore, JPS Health Network;Robert Sawyer, University of Virginia HSC;Therese Duane, JPS Health Network

Background:

Enterococcus constitutes a pathogen isolated in intraabdominal infections (IAIs), most commonly in health-care associated/postoperative infection, and may predict poor clinical outcomes. It remains controversial whether this pathogen warrants an altered treatment approach in regards to empiric and definitive treatment.
Hypothesis:

Patients with *Enterococcus* isolated will have worse clinical outcomes compared to patients without *Enterococcus* isolated.

Methods:

The cohort studied included patients previously comprised in the STOP-IT trial database. Through post hoc analysis patients were stratified based on isolation of *Enterococcus* with 50 patients out of the cohort (n=518) having *Enterococcus* isolated from at least one culture site. Univariate and multivariate analyses were conducted to determine if the isolation of *Enterococcus* constitutes an independent predictor of the pre-defined STOP-IT composite outcome (surgical site infection, recurrent IAI or mortality) and the individual components.

Results:

From the cohort of 50 patients, 52 isolates of *Enterococcus* spp. resulted with a predominance of *E. faecalis* (40%) followed by other *Enterococcus* spp. (37%) and *E. faecium* (17%). Baseline demographic characteristics were statistically similar between the two groups. Antibiotic utilization distribution remained balanced between the *Enterococcus* and no *Enterococcus groups* with the majority of the patients receiving piperacillin-tazobactam, 64% and 54%, respectively. The groups had comparable infection characteristics including setting of acquisition (>50% community-acquired) and site of infection (predominantly colon or rectum). Individual and composite clinical outcomes were not statistically different between the *Enterococcus* and no *Enterococcus* groups: surgical site infection [4.0 vs. 8.1%; p=0.41], recurrent IAI [12% vs. 15%;p=0.57], death [0% vs. 1.1%;p=1.00] and composite of all three [16% vs. 23%;p=0.29], respectively. Multivariate analysis revealed that isolation of *Enterococcus* did not independently predict the incidence of the composite outcome (OR 0.56 [95% CI=0.21-1.49];p=0.24; c-statistic=0.81).

Conclusions:

Isolation of *Enterococcus* did not independently predict surgical site infection, recurrent IAI, mortality or the composite outcome in our post hoc analysis. This suggests that isolation of *Enterococcus* may not warrant an altered treatment approach of IAIs.

O45.
Surgery versus Antibiotics for Uncomplicated Appendicitis: What Would a Medical Student Want?

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Background:

In the last two decades, data have shown that treatment of acute, uncomplicated appendicitis (AUA) with antibiotics may be as effective as surgery. Recent literature has suggested over 50% of patients would choose antibiotic therapy for acute appendicitis. Medical students (MS) represent a unique population of potential patients with greater medical knowledge than the general public but possibly less bias than practicing physicians; therefore, we aimed to evaluate what their treatment choice for AUA would be and what factors may influence their decision.

Hypothesis:

We hypothesized that MS would be more likely to choose surgery over antibiotics and that students interested in a procedure-oriented specialty would be more inclined to select surgery.

Methods:

We conducted a survey of current MS at a single institution. Survey data included demographics, interest in surgery or a procedure-related specialty, knowledge of and experience with surgery and antibiotics, and concerns about treatments. A summary of literature regarding the efficacy and safety of antibiotics and surgery was presented. Each participant then indicated a treatment preference if they personally were diagnosed with AUA.

Results:

255 MS completed the survey (mean age 24.8±2.4 years, 51.5% female). The majority (41.2%) were second year students, followed by 32.9% first, 13.3% third and 12.2% fourth. 54.2% reported an interest in a procedure-related specialty. 93% had prior antibiotic use (19% reporting adverse effects), and 50% had prior surgery (20% reporting adverse events). When given the scenario of how they would treat their own AUA, 66.3% selected surgery, 24.3% selected antibiotics, and 9.4% were unsure. Specialty of interest (procedural vs. non-procedural) and year of training had no significant relationship to treatment choice (both p>0.5). More students reported having no concerns about taking antibiotics than about having a surgery (24% vs. 2%). When asked to choose concerns regarding each treatment choice, "surgical complications" was selected most frequently (82%) for surgery and "adverse events and side effects" was selected most frequently for antibiotics (57%). History of adverse effects related to antibiotics or surgery was not significantly related to treatment choice (both p>0.1).

Conclusions:

When informed of the benefits and risks of surgery vs. antibiotics to treat AUA medical students are more likely than the general population to choose surgery.