

Quarterly Review of the Surgical Infection Literature

Michele M. Loor, MD

University of Minnesota Medical Center, Minneapolis, Minnesota

The use and knowledge of the literature is important for awareness of current findings and implementation of advances in surgical infection. To assist members of the Surgical Infection Society in this endeavor, the Scientific Studies Committee has embarked upon a program to identify the most important papers in the field of surgical infection, which we hope will be reported every quarter. These articles are selected by members of the Committee and submitted to the Executive Council for approval prior to appearance on the website of the organization. Each article will have a few sentences of commentary, and the reader is encouraged to consider and perhaps further explore the article at his/her convenience. It is hoped that this will further the knowledge of the membership, and provoke further conversation and investigation.

The process used was as follows. PubMed was used to search all publications between 1 April 2016 and 30 June 2016 with the search terms 'surgery' and 'infection'. The search yielded 1156 papers which were scanned for those with the most perceived impact. The search was repeated with the terms 'surgery' and 'sepsis', which yielded another 191 papers which were also scanned. Of these, 14 were selected as potentially the most useful for the membership, and are included below.

1. Chirurgia (Bucur). 2016 May-Jun; 111(3):242-50.

Effect of High Perioperative Oxygen Fraction on Surgical Site Infection Following Surgery for Acute Sigmoid Diverticulitis. A Prospective, Randomized, Double Blind, Controlled, Monocentric Trial.

Schietroma M, Pessia B, Colozzi S, Carlei F, Shehaj I, Amicucci G.

Propose: The clinical role of hyperoxia to prevent postoperative surgical site infection (SSI) remains uncertain since randomized controlled trials on this topic have reported different results. One of the principal reasons for such mixed results can be that previous trials have entered a heterogeneous population of patients and set of procedures. The aim of our study was to assess the influence of hyperoxygenation on SSI using an homogeneous study population. **METHODS:** We studied, in a prospective randomized study, extended on a time interval January 2009 to May 2015, 85 patients who underwent open intraperitoneal anastomosis for acute sigmoid diverticulitis. Patients were assigned randomly to an oxygen/air mixture with a fraction of inspiration (FiO₂) of 30% (n=43) or 80% (n=42). Administration was started after induction of anesthesia and maintained for 6 hours after surgery. **RESULTS:** The overall wound site infection rate was 24.7% (21 out of 85): 14 patients (32.5%) had a wound infection in the 30% FiO₂ group and 7 (16.6%) in the 80% FiO₂ group (p 0.05). The risk of SSI was 43% lower in the 80% FiO₂ group (RR, 0.68; 95% confidence interval, 0.35-0.88) versus 30% FiO₂. **CONCLUSIONS:** Therefore, supplemental 80% FiO₂ during and 6 hours after open surgery for acute sigmoid diverticulitis, reducing post-operative SSI, should be considered part of ongoing quality improvement activities related to surgical care, accompanied by few risk to the patients and little associated cost. PMID: 27452936 [PubMed - in process]

This study examined the effect of supplemental O₂ on the development of SSI following colorectal surgery. The findings of the study suggest that this would be an important adjunct for postoperative SSI-reduction bundles. As the addition of supplemental oxygen is a relatively easy, well-tolerated, and inexpensive intervention, this should be considered for all surgical patients.

2. J Arthroplasty. 2016 May 18. pii: S0883-5403(16)30157-7. doi: 10.1016/j.arth.2016.05.019. [Epub ahead of print]

Methicillin-Resistant and Methicillin-Sensitive Staphylococcus aureus Screening and Decolonization to Reduce Surgical Site Infection in Elective Total Joint Arthroplasty.

Sporer SM, Rogers T, Abella L.

BACKGROUND: Deep infection after elective total joint arthroplasty remains a devastating complication. Preoperative nasal swab screening for Staphylococcus aureus colonization and subsequent treatment of colonized patients is one proposed method to identify at-risk patients and decrease surgical site infections (SSIs). The purpose of this study was to determine whether a preoperative staphylococcus screening and treatment program would decrease the incidence of SSI in elective joint arthroplasty patients. **METHODS:** Since January 2009, a total of 9690 patients having an elective joint arthroplasty were screened before surgery for Methicillin-resistant Staphylococcus aureus (MRSA) and methicillin-sensitive Staphylococcus aureus (MSSA) with nares swabs. All patients with positive nares colonization for MSSA and MRSA were treated with mupirocin and chlorhexidine gluconate showers for 5 days before surgery. MRSA patients received vancomycin preoperatively and were placed in contact isolation. All elective arthroplasty patients used chlorhexidine gluconate antiseptic cloths the evening prior and the day of surgery. Perioperative infection rates were compared from 1 year before implementation to 5 years after implementation of this screening protocol. **RESULTS:** SSI rates have decreased from 1.11% (prescreening) to 0.34% (nasal screening; $P < .05$) after initiation of the process. Staphylococcus was identified in 66.7% of the SSI infections before nasal screening and in 33.3% of the SSI after routine screening ($P > .05$). **CONCLUSION:** The addition of MRSA and/or MSSA nares screening along with a perioperative decolonization protocol has resulted in a decreased SSI rate by 69%.

DOI: 10.1016/j.arth.2016.05.019

PMID: 27387479 [PubMed - as supplied by publisher]

This study focuses on orthopedic patients and the value of preoperative screening and intervention for Staphylococcus aureus. In comparison to the time period prior to intervention, they did show a reduction in SSI under this protocol. As SSI is a low incidence event in this population, the comparison to a preceding time period allowed for the large number of patients required to show an effect. However, future prospective studies would be helpful as this intervention is potentially costly and time-consuming.

3. Int J Colorectal Dis. 2016 Jun 29. [Epub ahead of print]

Preoperative inflammation increases the risk of infection after elective colorectal surgery: results from a prospective cohort.

De Magistris L, Paquette B, Orry D, Facy O, Di Giacomo G, Rat P, Binquet C, Ortega-Deballon P.

BACKGROUND: Septic complications after colorectal surgery are frequent and sometimes life threatening. It is well known that inflammation impairs the healing process. It has been suggested that preoperative ongoing inflammation could increase the risk of postoperative infections. This study aimed to elucidate the role of preoperative inflammation on postoperative infectious complications and to understand if, through biological markers, it is possible to identify preoperatively patients at higher risk of infection. **METHODS:** A prospective, observational study was conducted in three centers from November 2011 to April 2014. Consecutive patients undergoing elective colorectal surgery with anastomosis were included. Any ongoing infection was an exclusion criterion. C-reactive protein, albumin, prealbumin, and procalcitonin plasma levels were measured preoperatively. Postoperative infections were recorded according to the definitions of the Centers for Diseases Control. The areas under the receiver operating characteristic curve were analyzed and compared to assess the accuracy of each preoperative marker. **RESULTS:** Four-hundred and seventy two patients were analyzed. Infectious complications occurred in 118 patients (25 %) and mortality in 6 patients (1.3 %). In the univariate analysis, preoperative C-reactive protein and albuminemia were found significantly associated with postoperative infectious complications ($P = 0.008$ and $P = 0.0002$, respectively). Areas under the ROC curve for preoperative C-reactive protein and

albuminemia were 0.57 and 0.62, respectively. CONCLUSIONS: This study confirms the association between preoperative inflammatory activity, hypoalbuminemia, and the onset of infections after surgery. Trials aiming to decrease the inflammatory activity before surgery in order to prevent postoperative complications are warranted.

DOI: 10.1007/s00384-016-2620-8

PMID: 27357511 [PubMed - as supplied by publisher]

This is an interesting study in which elevations in preoperative markers of inflammation, namely CRP, were associated with increased risk of postoperative infectious complications. Previous studies had shown that early postoperative rises in CRP predict infectious complications, but this study focuses on elevated levels on the day prior to surgery. Interestingly, the group of patients who developed postoperative infectious complications was similar to the group of patients who did not have such complications with respect to comorbidities and surgical indications. This study also showed that low preoperative levels of albumin predict infectious complications, as has been shown in previous studies. Neither preoperative elevation of procalcitonin levels nor low prealbumin levels were associated with postoperative infectious complications.

4. Eur J Obstet Gynecol Reprod Biol. 2016 Jun 20; 203:232-238. doi: 10.1016/j.ejogrb.2016.06.003. [Epub ahead of print]

Surgical site infection in cesarean sections with the use of a plastic sheath wound retractor compared to the traditional self-retaining metal retractor.

Hinkson L, Siedentopf JP, Weichert A, Henrich W.

OBJECTIVE: A cesarean section rate of up to 19.4% is reported worldwide. Surgical site infection occurs with rates of up to 13.5%. Plastic-sheath wound retractors show reduced rates of surgical site infections in abdominal surgery. There is limited evidence in women having cesarean sections. This study evaluates the use of the Alexis[®] O C-Section Retractor in the prevention of surgical site infection in patients undergoing their first planned cesarean section compared to the traditional Collins self-retaining metal retractor. STUDY DESIGN: A single center, prospective, randomized, controlled, observational trial. The primary outcome is surgical site infection as defined by the Centers for Disease Control and Prevention. The secondary outcomes included intraoperative surgical parameters, postoperative pain scores and the short and long-term satisfaction with wound healing. From October 2013 to December 2015 at the Charité University Hospital, Berlin. 98 patients to the Alexis[®] O C-section Retractor group and 100 to the traditional Collins self-retaining metal retractor group. RESULTS: A statistically significant reduction in the rate of surgical site infections, when the Alexis[®] O C-section Retractor was used for wound retraction compared to the traditional Collins metal self-retaining wound retractor, 1% vs. 8% (RR 7.84, 95% CI (2.45-70.71) p=0.035). CONCLUSIONS: The use of plastic-sheath wound retractors compared to the traditional self-retaining metal retractor in low risk women, having the first cesarean section is associated with a significantly reduced risk of surgical site infection.

DOI: 10.1016/j.ejogrb.2016.06.003

PMID: 27352285 [PubMed - as supplied by publisher]

This study explores the use of the Alexis O C-section retractor as a means of reducing SSI. This is a randomized controlled trial with 100 patients in each arm (Alexis vs a traditional metal Collins retractor). While the retractors were donated to the study by the company, there was no other industry support or conflict of interest reported by the authors. Patients in the Alexis retractor arm had a significantly lower rate of SSI (1% vs. 8%). In addition, surgeons reported that the Alexis was easier to use, offered better visualization of the surgical field with less interference by bowel. Patients in this arm reported less scar pain and used less postop analgesics. All of these secondary findings were significant. The findings of this study suggest that similar retractors may be useful in reducing SSI in other types of wound class 2 cases.

5. Crit Care. 2016 Jun 24;20(1):203. doi: 10.1186/s13054-016-1380-8.

The value of polyurethane-cuffed endotracheal tubes to reduce microaspiration and intubation-related pneumonia: a systematic review of laboratory and clinical studies.

Blot SI, Rello J, Koulenti D.

BACKGROUND: When conventional high-volume, low-pressure cuffs of endotracheal tubes (ETTs) are inflated, channel formation due to folds in the cuff wall can occur. These channels facilitate microaspiration of subglottic secretions, which is the main pathogenic mechanism leading to intubation-related pneumonia. Ultrathin polyurethane (PU)-cuffed ETTs are developed to minimize channel formation in the cuff wall and therefore the risk of microaspiration and respiratory infections. **METHODS:** We systematically reviewed the available literature for laboratory and clinical studies comparing fluid leakage or microaspiration and/or rates of respiratory infections between ETTs with polyvinyl chloride (PVC) cuffs and ETTs with PU cuffs. **RESULTS:** The literature search revealed nine in vitro experiments, one in vivo (animal) experiment, and five clinical studies. Among the 9 in vitro studies, 10 types of PU-cuffed ETTs were compared with 17 types of PVC-cuffed tubes, accounting for 67 vs. 108 experiments with 36 PU-cuffed tubes and 42 PVC-cuffed tubes, respectively. Among the clinical studies, three randomized controlled trials (RCTs) were identified that involved 708 patients. In this review, we provide evidence that PU cuffs protect more efficiently than PVC cuffs against fluid leakage or microaspiration. All studies with leakage and/or microaspiration as the primary outcome demonstrated significantly less leakage (eight in vitro and two clinical studies) or at least a tendency toward more efficient sealing (one in vivo animal experiment). In particular, high-risk patients intubated for shorter periods may benefit from the more effective sealing capacity afforded by PU cuffs. For example, cardiac surgery patients experienced a lower risk of early postoperative pneumonia in one RCT. The evidence that PU-cuffed tubes prevent ventilator-associated pneumonia (VAP) is less robust, probably because microaspiration is postponed rather than eliminated. One RCT demonstrated no difference in VAP risk between patients intubated with either PU-cuffed or PVC-cuffed tubes, and one before-after trial demonstrated a favorable reduction in VAP rates following the introduction of PU-cuffed tubes. **CONCLUSIONS:** Current evidence can support the use of PU-cuffed ETTs in high-risk surgical patients, while there is only very limited evidence that PU cuffs prevent pneumonia in patients ventilated for prolonged periods.

DOI: 10.1186/s13054-016-1380-8

PMCID: PMC4921025

PMID: 27342802 [PubMed - in process]

This study compiles the available data comparing polyurethane endotracheal tubes (ETT) with the traditional PVC ETT with respect to risk of microaspiration and subsequent VAP. The authors site the current problem with the high volume, low pressure PVC ETTs being the fact that channels form due to folds on the cuff wall, and that these lead to accumulation of subglottic secretions, which contribute to the development of VAP. After an extensive literature search, the authors included 14 studies in this paper. In in vitro studies, the PU ETT performed better than PVC due to decreased leakage of fluid and a better seal regardless of PEEP levels. Three randomized controlled trials were included (708 patients), with the main finding that PU ETTs do not eliminate microaspiration but seem to delay it, which may have implications for the use of PU ETTs for patients undergoing short term intubation (ie., for surgery).

6. Infect Control Hosp Epidemiol. 2016 Aug; 37(8):888-95. doi: 10.1017/ice.2016.106. Epub 2016 Jun 7.

Frequency of Hand Decontamination of Intraoperative Providers and Reduction of Postoperative Healthcare-Associated Infections: A Randomized Clinical Trial of a Novel Hand Hygiene System.

Koff MD, Brown JR, Marshall EJ, O'Malley AJ, Jensen JT, Heard SO, Longtine K, O'Neill M, Longtine J, Houston D, Robison C, Moulton E, Patel HM, Loftus RW.

BACKGROUND Healthcare provider hands are an important source of intraoperative bacterial transmission events associated with postoperative infection development. **OBJECTIVE** To explore the efficacy of a novel hand hygiene

improvement system leveraging provider proximity and individual and group performance feedback in reducing 30-day postoperative healthcare-associated infections via increased provider hourly hand decontamination events. DESIGN Randomized, prospective study. SETTING Dartmouth-Hitchcock Medical Center in New Hampshire and UMass Memorial Medical Center in Massachusetts. PATIENTS Patients undergoing surgery. METHODS Operating room environments were randomly assigned to usual intraoperative hand hygiene or to a personalized, body-worn hand hygiene system. Anesthesia and circulating nurse provider hourly hand decontamination events were continuously monitored and reported. All patients were followed prospectively for the development of 30-day postoperative healthcare-associated infections. RESULTS A total of 3,256 operating room environments and patients (1,620 control and 1,636 treatment) were enrolled. The mean (SD) provider hand decontamination event rate achieved was 4.3 (2.9) events per hour, an approximate 8-fold increase in hand decontamination events above that of conventional wall-mounted devices (0.57 events/hour); $P < .001$. Use of the hand hygiene system was not associated with a reduction in healthcare-associated infections (odds ratio, 1.07 [95% CI, 0.82-1.40], $P = .626$). CONCLUSIONS The hand hygiene system evaluated in this study increased the frequency of hand decontamination events without reducing 30-day postoperative healthcare-associated infections. Future work is indicated to optimize the efficacy of this hand hygiene improvement strategy. Infect Control Hosp Epidemiol 2016; 37:888-895.

DOI: 10.1017/ice.2016.106

PMID: 27267310 [PubMed - in process]

In this study, the number of hand decontamination events (HDE) were increased in randomly selected operating rooms at the two participating hospitals through the use of personalized body-worn hand hygiene systems that dispense an alcohol-based hand cleanser. In these intervention groups the number of HDEs increased 8 fold. Nevertheless, the study did not detect any difference in hospital acquired infections between groups, and even noted a strong trend towards increased deep organ space infections in the treatment group. Financial support for the study was provided by the device/soap manufacturer (Sage).

7. Surg Infect (Larchmt). 2016 May 31. [Epub ahead of print]

Impact of Type of Health Insurance on Infection Rates among Young Trauma Patients.

Sawhney JS, Stephen AH, Nunez H, Lueckel SN, Kheirbek T, Adams CA Jr, Cioffi WG, Heffernan DS.

BACKGROUND: Many studies have described the detrimental effect of lack of health insurance on trauma-related outcomes. It is unclear, though, whether these effects are related to pre-injury health status, access to trauma centers, or differences in quality of care after presentation. The aim of this study was to determine if patient and insurance type affect outcomes after trauma surgery. METHODS: We conducted a retrospective chart review of prospectively collected data at the American College of Surgeons level 1 trauma registry in Rhode Island. All blunt trauma patients aged 18-45 observed from 2004 to 2014 were included. Patients were divided into one of four groups on the basis of their type of insurance: Private/commercial, Medicare, Medicaid, and uninsured. Co-morbidities and infections were recorded. Analysis of variance or the Mann-Whitney U test, as appropriate, was used to analyze the data. RESULTS: A total of 8,018 patients were included. Uninsured patients were more likely to be male and younger, whereas the Medicare patient group had significantly fewer male patients. Rates of co-morbidities were highest in the Medicare group (28.1%) versus the private insurance (16.7%), Medicaid (19.9%), and uninsured (12.9%) groups ($p < 0.05$). However, among patients with any co-morbidity, there was no difference in the average number of co-morbidities between insurance groups. The rate of infection was highest in Medicaid patients (7.7%) versus private (5.6%), Medicare (6.3%), and uninsured (4.3%) patients ($p < 0.05$). Only Medicaid was associated with a significantly greater risk of developing a post-injury infection (odds ratio 1.6; 95% confidence interval 1.1-2.3). CONCLUSION: The presence of insurance, namely Medicaid, does not equate to diagnosis and management of conditions that affect trauma outcomes. Medicaid is associated with worse pre-trauma health maintenance and a greater risk of infection.

DOI: 10.1089/sur.2015.210

PMID: 27244084 [PubMed - as supplied by publisher]

This study builds on previous literature which demonstrated that infections are associated with worse outcomes following trauma. The authors collected data on over 8000 trauma patients and grouped them by type of insurance coverage (private, Medicare, Medicaid, or uninsured). As expected, the presence of comorbidities increased the risk of developing an infection in all groups. After adjusting for several important factors, patients insured under Medicaid had significantly higher risk of post-injury infections. Interestingly, uninsured patients had no increased risk of infection.

8. *Medicine* (Baltimore). 2016 May; 95(21):e3704. doi: 10.1097/MD.0000000000003704.

Perioperative Standard Oral Nutrition Supplements Versus Immunonutrition in Patients Undergoing Colorectal Resection in an Enhanced Recovery (ERAS) Protocol: A Multicenter Randomized Clinical Trial (SONVI Study).

Moya P(1), Soriano-Irigaray L, Ramirez JM, Garcea A, Blasco O, Blanco FJ, Brugiotti C, Miranda E, Arroyo A.

To compare immunonutrition versus standard high calorie nutrition in patients undergoing elective colorectal resection within an Enhanced Recovery after Surgery (ERAS) program. Despite progress in recent years in the surgical management of patients with colorectal cancer (ERAS programs), postoperative complications are frequent. Nutritional supplements enriched with immunonutrients have recently been introduced into clinical practice. However, the extent to which the combination of ERAS protocols and immunonutrition benefits patients undergoing colorectal cancer surgery is unknown. The SONVI study is a prospective, multicenter, randomized trial with 2 parallel treatment groups receiving either the study product (an immune-enhancing feed) or the control supplement (a hypercaloric hypernitrogenous supplement) for 7 days before colorectal resection and 5 days postoperatively. A total of 264 patients were randomized. At baseline, both groups were comparable in regards to age, sex, surgical risk, comorbidity, and analytical and nutritional parameters. The median length of the postoperative hospital stay was 5 days with no differences between the groups. A decrease in the total number of complications was observed in the immunonutrition group compared with the control group, primarily due to a significant decrease in infectious complications (23.8% vs. 10.7%, $P=0.0007$). Of the infectious complications, wound infection differed significantly between the groups (16.4% vs. 5.7%, $P=0.0008$). Other infectious complications were lower in the immunonutrition group but were not statistically significantly different. The implementation of ERAS protocols including immunonutrient-enriched supplements reduces the complications of patients undergoing colorectal resection. This study is registered with ClinicalTrial.gov: NCT02393976.

DOI: 10.1097/MD.0000000000003704

PMCID: PMC4902354

PMID: 27227930 [PubMed - in process]

This study aimed to compare outcomes in elective colorectal surgery patients receiving immunonutritional supplements vs traditional nutritional supplements in the perioperative period (7 days pre-op to 5 days post op). The patients in this study were also treated by protocol on an enhanced recovery pathway. This is a prospective multicenter randomized single-blind study of 244 patients. The patients in the immunonutrition group had significantly less of any complication, less infectious complications, and lower rates of SSI.

9. *Surg Infect* (Larchmt). 2016 Jun 16. [Epub ahead of print]

Past, Present, and Future of Augmentation of Monocyte Function in the Surgical Patient.

Galbraith N, Walker S, Carter J, Polk HC Jr.

BACKGROUND: Patients who survive the early phases of major sepsis and trauma can have greater susceptibility to nosocomial infection later. One cause may be impaired monocyte function, which can leave the patient at risk of overwhelming sepsis and multi-organ dysfunction. Efforts to target this immune defect have been fraught with challenges, with many questions unanswered. We summarized the past and current and likely future therapeutic

approaches to augmentation of monocyte function in the surgical patient. METHODS: A literature search was conducted using PubMed to determine the evidence to date for immunoadjuvant therapy specifically for monocyte impairment. The search terms were "monocyte," "immunoparalysis," "tolerance," and "deactivation" cross-referenced with "trauma," "major surgery," and "sepsis." We supplemented our search with "interferon- γ ," "granulocyte colony-stimulating factor" (G-CSF), and "granulocyte-macrophage colony-stimulating factor" (GM-CSF), known agents used for this purpose. We limited our findings to clinical trials in human beings. Relevant currently registered trials relating to impaired monocyte function also were included. RESULTS: Interferon- γ appears to be the most commonly studied therapeutic agent to augment monocyte function, followed in decreasing order by GM-CSF and G-CSF. Studies were heterogeneous, generally under-powered, and enrolled few target patients with documented monocyte impairment. Finally, current studies are focusing on personalized therapy in order to treat those with monocyte impairment, with attention to programmed cell death protein 1 (PD-1) and programmed cell death ligand (PD-L1) as both markers and therapeutic targets. CONCLUSION: Early studies have been promising in identifying patients who are likely to benefit from monocyte augmentation; i.e., those with low HLA-DR or ex-vivo tumor necrosis factor (TNF)- α production. The surgeon remains incompletely equipped to enhance monocyte function consistently and specifically in order to reduce the mortality rate. Although there is little evidence to support the routine use of any of these immunotherapies, the issues of patient selection, timing of administration, and treatment duration have hampered any true answers to this important clinical problem. The challenge remains in identifying the right patients, at the right time, to receive the right therapy.

DOI: 10.1089/sur.2016.014

PMID: 27309382 [PubMed - as supplied by publisher]

This is a nice review of the literature on different monocyte augmentation therapies and which groups of patients benefit from such treatment. The authors reported on three main therapies: Interferon- γ , GM-CSF, and G-CSF. Many of the studies cited in this paper demonstrate equivocal outcomes, and this is likely related to the heterogeneity of the populations and differences in timing of follow up and administration of therapy.

10. Shock. 2016 May 11. [Epub ahead of print]

Gastrointestinal Leakage Detected by Serum (1 \rightarrow 3)- β -D-Glucan in Mouse Models and a Pilot Study in Patients with Sepsis.

Leelahavanichkul A(1), Worasilchai N, Wannalerdsakun S, Jutivorakool K, Somparn P, Issara-Amphorn J, Tachaboon S, Srisawat N, Finkelman M, Chindamporn A.

Gastrointestinal (GI) leakage is believed to exacerbate sepsis and new, validated markers of GI barrier performance might benefit clinical decision-making. Serum (1 \rightarrow 3)- β -D-glucan (BG) was evaluated as a potential GI leakage marker. Serum BG was tested in several mouse models of GI leakage, including dextran sulfate solution (DSS) administration, endotoxin (LPS) injection, and cecal ligation and puncture sepsis (CLP). Serum BG titer was also evaluated in patients with sepsis and septic shock, for comparison. With 0.75% DSS administration, BG increased only after oral administration of heat-killed *C. albicans*, but increased spontaneously with 1.5% DSS. In the LPS and CLP models, BG increased as early as 1 h and at 12 h after LPS administration and surgery, respectively. GI leakage was confirmed by orthogonal validation methods including FITC-dextran oral administration in the DSS, LPS and CLP models and, in the DSS model, with urine sucralose after oral administration and serum endotoxemia. IL-6 increased in parallel with serum BG. Serum BG or IL-6, at 18 h, anticipated sepsis mortality in the CLP model. Analysis of serum BG from patients with febrile neutropenic sepsis (N = 49) and febrile non-neutropenic sepsis (N = 39) demonstrated BG elevation. Patients with bacterial septic shock had serum BG titers similar to levels observed in invasive fungal disease, regardless of febrile neutropenia. Serum BG was lower in less severe cases of bacterial sepsis. Elevated serum IL-6 was associated with GI leakage and elevated serum BG. Serum BG may have potential as a sepsis/septic shock biomarker and further study in this context is warranted.

DOI: 10.1097/SHK.0000000000000645

PMID: 27172153 [PubMed - as supplied by publisher]

This is an interesting study on the use of serum levels of (1→3)-β-D-glucan (BG) as a marker of GI leakage using a mouse model. BG is normally found within the lumen of the intestine, with low serum levels. As such, the authors hypothesized that elevations in serum levels may be indicative to a disruption of the gut barrier. Using several different mouse models, the authors did demonstrate this to be the case. They also examined blood samples from neutropenic patients to confirm elevated BG levels in the setting of sepsis. Moreover, higher BG levels were associated with higher mortality. These interesting initial findings require further investigation, but may lead to a clinically useful marker of GI leakage.

11. Cytokine. 2016 Jul; 83:206-9. doi: 10.1016/j.cyto.2016.05.004. Epub 2016 May 6.

Reduction in circulating level of HMGB-1 following continuous renal replacement therapy in sepsis.

Ueno T, Ikeda T, Yokoyama T, Kihara Y, Konno O, Nakamura Y, Iwamoto H, Shimizu T, McGrath MM, Chandraker A.

Early recovery from shock improves prognosis in patients with severe sepsis and septic shock. During this period, cytokine imbalances mediate the development of organ damage and mortality. In Japan, we have access to hemoperfusion using an immobilized polymyxin B fiber column for endotoxin removal (PMX-DHP) and continuous hemodiafiltration (CHDF) as artificial support for patients with septic shock, with the aim of improving hemodynamics and organ dysfunction caused by elevated inflammatory cytokines and mediators. In this Short communication, we discuss recent findings showing anti-inflammatory treatment following these continuous renal replacement therapies in sepsis.

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DOI: 10.1016/j.cyto.2016.05.004

PMID: 27155819 [PubMed - in process]

In this study, the authors propose the use of continuous hemodiafiltration (CHDF) as an anti-inflammatory treatment in sepsis. The authors published previous studies on the use of endotoxin removal during CRRT in severe sepsis, demonstrating improvements in tissue oxygenation and hemodynamics. They also reported on the use of HMGB-1 as a prognostic biomarker in sepsis-induced organ failure. In the current study, they saw a reduction in HMGB-1 levels in patients who underwent CHDF. This was an initial observational study of 60 patients, and requires further investigation, but may lead to additional therapeutic options for patients with severe sepsis.

12. J Gastrointest Surg. 2016 Jun; 20(6):1123-31. doi: 10.1007/s11605-016-3142-y. Epub 2016 Apr 12.

Probiotics and Synbiotics Decrease Postoperative Sepsis in Elective Gastrointestinal Surgical Patients: a Meta-Analysis.

Arumugam S, Lau CS, Chamberlain RS.

BACKGROUND: The health benefits of probiotics and synbiotics are well established in healthy adults, but their role in preventing postoperative sepsis remains controversial. This meta-analysis assesses the impact of probiotics and synbiotics on the incidence of postoperative sepsis in gastrointestinal (GI) surgical patients. **METHODS:** A comprehensive literature search of all published randomized control trials (RCTs) was conducted using PubMed, Cochrane Central Registry of Controlled Trials, and Google Scholar (1966-2015). Inclusion criteria included RCTs comparing the use of any strain or dose of a specified probiotic/synbiotic with placebo or a "no treatment" control group. The incidence of postoperative sepsis (within 1 month of surgery) and postoperative mortality were analyzed. **RESULTS:** Fifteen RCTs involving 1201 patients (192 receiving probiotics, 413 receiving synbiotics, and

596 receiving placebo) were analyzed. Overall, probiotic and synbiotic uses significantly reduced the risk of developing postoperative sepsis by 38 % (relative risk (RR) = 0.62, 95 % confidence interval (CI) 0.52-0.74, $p < 0.001$). CONCLUSIONS: The use of probiotic/synbiotic supplementation is associated with a significant reduction in the risk of developing postoperative sepsis in patients undergoing elective GI surgery. Probiotic/synbiotic supplementation is a valuable adjunct in the care of patients undergoing GI surgery. Additional studies are required to determine the optimal dose and strain of probiotic/synbiotic.

DOI: 10.1007/s11605-016-3142-y
PMID: 27073082 [PubMed - in process]

A previous meta-analysis on this topic focused on post-operative infectious complications in patients receiving probiotics and/or symbiotics. In this current study, the authors focus instead on the development of sepsis in patients undergoing elective GI surgery who receive probiotics/symbiotics versus placebo or no supplement. This is a meta-analysis which includes 15 studies or 1201 patients. Significantly fewer patients in the probiotic/symbiotic group developed sepsis (13 vs. 24%, $p < 0.001$), but no difference in perioperative mortality was detected.

13. Shock. 2016 May; 45(5):475-82. doi: 10.1097/SHK.0000000000000534.

The Shift of an Intestinal "Microbiome" to a "Pathobiome" Governs the Course and Outcome of Sepsis Following Surgical Injury.

Krezalek MA, DeFazio J, Zaborina O, Zaborin A, Alverdy JC.

Sepsis following surgical injury remains a growing and worrisome problem following both emergent and elective surgery. Although early resuscitation efforts and prompt antibiotic therapy have improved outcomes in the first 24 to 48 h, late onset sepsis is now the most common cause of death in modern intensive care units. This time shift may be, in part, a result of prolonged exposure of the host to the stressors of critical illness which, over time, erode the health promoting intestinal microbiota and allow for virulent pathogens to predominate. Colonizing pathogens can then subvert the immune system and contribute to the deterioration of the host response. Here, we posit that novel approaches integrating the molecular, ecological, and evolutionary dynamics of the evolving gut microbiome/pathobiome during critical illness are needed to understand and prevent the late onset sepsis that develops following prolonged critical illness.

DOI: 10.1097/SHK.0000000000000534
PMCID: PMC4833524 [Available on 2017-05-01]
PMID: 26863118 [PubMed - in process]

This is a nice review article describing the late onset of sepsis as a conversion of the microbiome to a pathobiome, with the authors concluding that sepsis is related not only to microbial virulence but also to immune dysregulation driving ongoing inflammation and organ failure.

14. Ann Surg. 2016 Jun; 263(6):1207-12. doi: 10.1097/SLA.0000000000001342.

Postoperative Interleukin-6 Level and Early Detection of Complications After Elective Major Abdominal Surgery.

Rettig TC(1), Verwijmeren L, Dijkstra IM, Boerma D, van de Garde EM, Noordzij PG.

OBJECTIVE: To assess the association of systemic inflammation and outcome after major abdominal surgery. BACKGROUND: Major abdominal surgery carries a high postoperative morbidity and mortality rate. Studies suggest that inflammation is associated with unfavorable outcome. METHODS: Levels of C-reactive protein (CRP), interleukin-6 (IL-6), and tumor necrosis factor- α and the systemic inflammatory response syndrome (SIRS) were

assessed in 137 patients undergoing major abdominal surgery. Blood samples were drawn on days 0, 1, 3, and 7, and SIRS was scored during 48 hours after surgery. Primary outcome was a composite of mortality, pneumonia, sepsis, anastomotic dehiscence, wound infection, non-cardiac respiratory failure, atrial fibrillation, congestive heart failure, myocardial infarction, and reoperation within 30 days of surgery. RESULTS: An IL-6 level more than 432 pg/mL on day 1 was associated with an increased risk of complications (adjusted odds ratio: 3.3; 95% confidence interval [CI]: 1.3-8.5) and a longer median length of hospital stay (7 vs 12 days, $P < 0.001$). As a single test, an IL-6 cut-off level of 432 pg/mL on day 1 yielded a specificity of 70% and a sensitivity of 64% for the prediction of complications (area under the curve: 0.67; 95% CI: 0.56-0.77). Levels of CRP started to discriminate from day 3 onward with a specificity of 87% and a sensitivity of 58% for a cut-off level of 203 mg/L (AUC: 0.73; 95% CI: 0.63-0.83). CONCLUSIONS: A high IL-6 level on day 1 is associated with postoperative complications. Levels of IL-6 help distinguish between patients at low and high risk for complications before changes in levels of CRP.

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This study investigates the use of IL-6 level on postoperative day 1 as a marker of patients at high risk for complications. The study includes 137 patients. Patients with high levels of IL6 on day 1 had significantly higher rates of sepsis, anastomotic dehiscence, and respiratory insufficiency. In addition, this group of patients had 3 fold risk of complications and increased length of stay. Further studies on the clinical use of this biomarker would be useful in the interpretation of high values for surgical patients.