DEAR COLLEAGUES,

I am pleased to present to you the current issue of the Operative Word, an electronic newsletter brought to you by the University of Chicago Medicine Phemister Society. In this e-newsletter, you will read about exciting updates and developments from the Department of Surgery.

In this issue of the Operative Word, we are proud to announce the recruitment of Thomas Lee, MD, an experienced pediatric general surgeon who joined us from Stony Brook Medicine in New York where he served for nearly 15 years. Dr. Lee, who completed his medical education right here at the University of Chicago Pritzker School of Medicine, is a valuable addition to our Section of Pediatric General Surgery. We are thrilled to welcome him back to the Hyde Park community.

We are also excited to share with you the latest developments from the laboratory of John C. Alverdy, MD, professor of surgery and executive vice chair of the Department of Surgery. His work over the last 15 years has led to the start of a groundbreaking clinical trial that relies on translational science to test innovative ways of treating anastomotic leaks.

Dr. Alverdy's leadership in this work exemplifies the impact of bench-to-bedside research on long-term patient care. Within this newsletter, we also provide an overview of our faculty's clinical and academic achievements, as well as their educational endeavors, over the last several months.

If ever you would like to learn more about our department's clinical, academic or educational efforts, please don’t hesitate to reach out to us. We look forward to communicating and engaging with our alumni around the globe.

Sincerely,

JEFFREY B. MATTHEWS, MD, FACS
Dallas B. Phemister Professor of Surgery
Chairman of the Department of Surgery
FROM THE BENCH TO BEDSIDE: MAKING LEAKS A THING OF THE PAST

It happens to even the most experienced and diligent surgeons. When a surgeon resects a portion of diseased intestine, continuity is reestablished by carefully suturing or stapling the remaining ends together, a connection termed “anastomosis.” No surgeon, no matter how much experience and training, is immune from this problem. If the anastomosis leaks, bacteria and toxins can seep out and cause peritonitis, sepsis and even death.

Surprisingly, such an event is not rare and has dogged gastrointestinal surgeons for decades. Although the mortality rate from anastomotic leak has gone down, the 12.1 percent incidence of leaks hasn’t changed, amounting to a $500-million burden on our healthcare system every year.

So, why do leaks occur, even when the anastomoses are performed perfectly? Researchers at the University of Chicago have been fervently investigating this very question and believe they may be on the cusp of uncovering the major role intestinal microbes play in the process of anastomotic leak. Such a discovery would pave the way to evidence-based protocols that could drastically lower the risk of anastomotic leaks forever.

Setting the stage in research

Leading the charge on this research is John C. Alverdy, MD, Sarah and Harold Lincoln Thompson Professor of Surgery and executive vice chair of the Department of Surgery at the University of Chicago Medicine. He has partnered with experts in colorectal surgery (Neil Hyman, MD, chief of Colon & Rectal Surgery, and Konstantin Umanskiy, MD, associate professor of surgery), microbiology (Jack Gilbert, PhD, and Olga Zaborina, PhD), biostatistics (Theodore Karrison, PhD) and research informatics (Samuel Volcenbourb, MD, PhD).

Pulling the brightest minds from each of these disciplines is a critical component to this research, Dr. Alverdy says.

“Anastomotic leaks continue to plague the most experienced and expertly trained surgeons and the human suffering is incalculable,” he says. “It is time to apply next-generation sequencing and precision medicine to understand and solve this devastating complication, which can lead to life-threatening infection, cancer recurrence and permanent colostomy.”

Over the last 15 years, Dr. Alverdy’s laboratory has been studying how intestinal bacteria shift their behavior to express enhanced virulence (harmfulness) when they “sense” factors released by host tissues during surgical injury. By understanding this process at the molecular level, they have developed novel, non-antibiotic compounds that can inhibit this process without disturbing the overall microbial ecology, thus preserving the health-promoting probiotic microbiota.

Using this line of reasoning, the Alverdy lab identified a species of intestinal bacteria that appears to play a direct role in the process of leakage, Enterococcus faecalis. Interestingly, this bacteria is normally present in the human intestine but behaves like a symbiont, meaning it shares resources and does not express harmfulness against its host.

Yet the lab demonstrated that this normal symbiont can turn into pathogenic bacteria (pathobiont) when it “senses” injury and stress and can shift its behavior from essentially a pacifist to an aggressive bacteria by activating genes that make the flesh-eating enzyme collagenase. This enzyme can then drill through healthy healing tissues and cause a leak.

“While we know that many of our so-called ‘normal microbiota’ can turn on us and cause harm, understanding this process at the species and molecular levels now equips us to think about strategies to interfere with the activating signals as opposed to simply taking a ‘shoot first, ask questions later’ approach with broad spectrum antibiotics,” Dr. Alverdy says. “This becomes especially important when we realize that many of the patients we operate on harbor antibiotic-resistant bacteria due to the promiscuous use of antibiotics. Understanding how and why these bacteria then become cued to cause harm during surgery is the key to prevention.”

Knowledge that leads to change

Armed with this new knowledge, Dr. Alverdy and his team are conducting preliminary clinical research — which is part of the larger multi-center trial called “Serial Endoscopic Surveillance & Direct Topical Antibiotics” (SES-DTA). In this trial, patients will undergo serial endoscopic examination of their anastomosis over three weeks with microbiologic sample analysis to examine which microbes are present in anastomotic tissues in order to determine how they behave over the course of healing.

In this preliminary research phase, the clinical team will enroll patients who are at the highest risk of experiencing anastomotic leak: patients undergoing low anterior colorectal resection where the anastomosis is 10 cm or less from the anal verge and a diverting loop ileostomy is performed.
The serial endoscopic surveillance will be performed three times, once in the operating room at the time of resection and twice in an inpatient endoscopy suite. Several important questions can be addressed by directly visualizing and examining anastomotic tissues for their microbial content and enzyme production.

- Are there flesh-eating microbes present on anastomotic tissues that have escaped the antibiotics routinely used by surgeons?
- How dangerous are these microbes, and what is their capacity to produce destructive enzymes?

- Are there molecules in the tissues that provoke these bacteria to produce tissue-destructive enzymes?
- Can antibiotics be locally applied to anastomotic tissues to keep them sterile without destroying all the normal bacteria by giving systemic or oral antibiotics in a manner that might actually aid the healing process?
- Can serial endoscopic surveillance and the development of biomarkers of bacterial enzyme production allow surgeons to predict which patients will leak?
- Can serial endoscopic surveillance be used to preemptively strike against an impending anastomotic catastrophe?

Dr. Alverdy and Dr. Hyman are performing this preliminary research in patients through a start-up grant from the American Society of Colorectal Surgeons to gain preliminary data for the larger SES-DTA multi-center trial.

So far, the results are highly encouraging that the procedure is safe and highly indicative of impending problems. Ultimately, the results from this initial planning phase of SES-DTA will allow Dr. Alverdy and Dr. Hyman to apply for R01 grant funding. This trial will be the largest of its kind in the department and a major benchmark for many more such trials in the future.
THOMAS K. LEE, MD
PROFESSOR OF SURGERY

Thomas K. Lee, MD, is an experienced pediatric general surgeon. His clinical interests include the surgical treatment of congenital anomalies, thoracic disease including chest wall anomalies, gastrointestinal conditions including inflammatory bowel disease, pediatric cancers and pediatric trauma.

As a dedicated academic surgeon, Dr. Lee has published more than 50 peer-reviewed articles, abstracts and book chapters on a diverse range of topics, including small bowel transplantation and pediatric trauma care. Dr. Lee serves as a reviewer for several journals, including the Journal of Pediatric Surgery, Transplantation Proceeding, American Journal of Perinatology and Pediatric Transplantation.

In addition to his clinical interests, Dr. Lee is a recipient of several teaching awards for surgical education and has expertise in healthcare administration specific to process and quality improvement. Dr. Lee also has been regularly featured as a Top Doctor in various publications, including Castle Connolly’s “Top Doctors: New York Metro Area,” Newsday’s “Top Doctors on Long Island” and New York Magazine’s “Best Doctors.”

Practice Locations
The University of Chicago Medicine
Comer Children’s Hospital
5721 S. Maryland Avenue
Chicago, IL 60637

Board Certifications
Surgery
Pediatric Surgery

Medical School
University of Chicago Pritzker School of Medicine

Internship and Residency
New York-Presbyterian Hospital-Weill Cornell Medical College

Fellowship
St. Louis University (Pediatric Surgery)

Memberships
American Academy of Pediatrics
American College of Surgeons
American Pediatric Surgical Association
Children’s Oncology Group

Clincial Interests
Pediatric Surgery
Neonatal Surgery
Minimally Invasive Surgery
Pediatric Cancer Surgery
Anorectal Malformation
Wilms’ Tumor
Chest Wall Deformities
Neuroblastoma
Inguinal Hernia
Undescended Testes
Soft Tissue Tumors

UPCOMING EVENT

12th Annual Dr. David B. Skinner Memorial Lecture

Keynote: Paul C. Kuo, MD, John P. Iguni Professor of Surgery, Chair, Department of Surgery, Loyola University Medical Center

Tuesday, September 29, 2015 from 5:00 p.m. - 6:00 p.m.
G-217 Mitchell Hospital, University of Chicago Medicine
The surgeons at the University of Chicago Medicine have reached a robotic milestone by performing more than 7,000 total cases, including robotic prostatectomies, nephrectomies and pediatric robotic urologic surgeries. About 5,000 of the procedures are urologic and the other 2,000 include cardiothoracic, OB/GYN and others.

Mohan Gundeti, MD; Alexander Langerman, MD; and Kevin Roggin, MD; received three of this year’s Distinguished Faculty Awards. Dr. Langerman received the Junior Award for Distinguished Leader in Program Innovation. Dr. Gundeti received the Senior Award for Distinguished Leader in Program Innovation. Dr. Kevin Roggin received the Senior Award for Distinguished Educator/Mentor for his excellence in clinical education.

Takeyoshi Ota, MD, Phd, has been named a co-director of the University of Chicago Center for Aortic Diseases, along with Ross Milner, MD. Dr. Ota is an assistant professor of surgery and an expert in the surgical treatment of aortic diseases. He also participates in the heart failure and ventricular assist device program, which includes heart transplantation.

Christopher Wigfield, MD, has been promoted to associate professor on the School of Medicine Track, effective July 1, 2015.

Konstantin Umanskiy, MD, has been promoted to associate professor on the School of Medicine Track, effective July 1, 2015.

Peter Angelos, MD, PhD, has been selected by his peers to serve as president-elect of the American Society of Endocrine Surgeons. His election took place earlier this month at the ASES annual meeting in Nashville. Dr. Angelos is the Linda Kohler Anderson Professor of Surgery, chief of endocrine surgery and the associate director of the MacLean Center for Clinical Medical Ethics.

At the 35th Annual Surgical Infection Society Meeting April 15-18, John Alverdy, MD, was inducted as the society’s president. He gave his first presidential address, one year after being made president-elect.

Ben Roitberg, MD, demonstrated pedicle screw placement at a junior resident bootcamp in Indianapolis using the department’s virtual reality system to teach the course. It is a simulation he developed with ImmersiveTouch, and this is the first time in this country that a virtual reality simulation of a neurosurgical procedure is part of a national basic training course to which all programs send their residents.

Irina Balyasnikova, PhD, has been promoted to a research associate (associate professor) for neurosurgery in the Lesniak Lab. Her promotion was effective May 1.

Jessica Kandel, MD, has been named a 2016 Hedwig van Ameringen Executive Leadership in Academic Medicine program fellow. As an ELAM fellow, Dr. Kandel will create an action project to address a need at the institution related to sustaining success of women who achieve leadership positions and changing the culture of academic health centers to value the contributions of women.

The University of Chicago Cleft Lip and Palate Clinic and Craniofacial Anomalies Multidisciplinary Program (CAMP) received accreditation from the American Cleft Palate-Craniofacial Association and the Cleft Palate Foundation. Russell Reid, MD, PhD, founded the CAMP program and serves as the director for both programs.

Julie Park, MD, has been promoted to associate professor on the School of Medicine track, effective July 1, 2015.

David Cronin, MD, will serve as a clinical associate for Transplant Surgery, effective May 1.

Piotr Witkowski, MD, PhD, has been promoted to associate professor on the School of Medicine track, effective July 1, 2015. Dr. Witkowski also serves as the director of the Pancreatic and Islet Transplant Program.

Mohan Gundeti, MD, has been promoted to professor on the School of Medicine Track, effective July 1, 2015.

Ross Milner, MD, was featured in a recent article in Endovascular Today. Dr. Milner discusses the Global Registry for Endovascular Aortic Treatment (GREAT), a system put together by Gore & Associates to monitor long-term device performance for improved clinical practice and patient outcomes.
RESEARCH AND CLINICAL TRIALS HIGHLIGHTS

Joel Collier, PhD, was invited by the National Institutes of Health to serve as a member of the Biomaterials and Biointerfaces Study Section at the Center for Scientific Review from July 1, 2015 to June 30, 2019. Study sections review grant applications submitted to the NIH, make recommendations on these applications to the NIH national advisory council or board and survey the status of research in their fields of science.

Mahesh Gupta, PhD, and associates discovered a new drug which mitigates preexisting cardiac hypertrophy/heart failure in mice by promoting cardiac mitochondrial functions. Their study was published in Nature.

John Alverdy, MD, and Neil Hyman, MD, hosted an information session at the American Society of Colon and Rectal Surgery meeting to promote their upcoming Systematic Endoscopic Surveillance & Direct Topical Antibiotics clinical trial. The physician researchers are currently recruiting other centers nationwide to take part in the study.

A paper penned by John Alverdy, MD, and his lab – titled “A microbial cause for intestinal anastomotic leak involving collagen degradation and MMP9 activation by Enterococcus faecalis” – was published in Science Translational Medicine.

The Journal of Neurology, Neurosurgery and Psychiatry’s impact factor was released in June at 6.807, the highest of all neurosurgery journals by far. The journal’s neurosurgical content is edited at the University of Chicago by Peter Warnke, MD, associate editor of the journal.

In May, the Awad Neurovascular Lab had a landmark paper published in the Nature Journal of Cerebral Blood Flow and Metabolism. Their research documented for the first time vascular hyperpermeability in the human brain of patients with cerebral cavernous malformations (CCM). The findings have profound implications for calibrating potential vascular permeability therapies in CCM, and also regarding vascular hyperpermeability in the aging brain. Issam Awad, MD, presented these findings as well as updates on the CLEAR and MISTIE trials at the European Stroke Symposium in Vienna, Austria.

Anita Chong, PhD, was chosen as this year’s recipient of the AST Basic Science Established Investigator Award by the American Society of Transplantation Board of Directors.

Scott Eggener, MD, recently had a study published in the Journal of Clinical Oncology delving into prostate cancer screening rates and determined they significantly declined among men older than 50 after the 2012 U.S. Preventative Services Task Force discouraged prostate-specific antigen-based prostate cancer screenings.

Scott Eggener, MD, has been awarded the Society of Urologic Oncology’s Young Investigator Award for 2015.

Researchers, led by Christopher Skelly, MD, have identified a biological process that an engineered strain of the Herpes simplex virus uses to prevent vein graft failure in bypass surgery. The paper was recently published in PLOS One.