New Faculty

Microbes and Gut Health: Can bacteria help us recover from trauma and sepsis as we age?

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Physicians can predict some of what happens to the heart, the lungs, the kidneys and even the joints as we age, but we know very little about what happens to the gut. Early studies show that the intestinal wall becomes more permeable over time because the strong connections between the cells break down. We also know that the bacteria in our stool change as we age, whether in response to our diet, antibiotics, or where we live. Does the integrity of our intestine change based on what bacteria are present, or are they a byproduct of the increased permeability and the nutrients that leak out?

How does that gut permeability affect the patient in a stressful situation like emergency surgery, trauma, or sepsis? We know that there is a large inflammatory cascade in response to stress, but perhaps it can be modulated by these bacteria in the gut, and perhaps they worsen the response. Previously scientists have used a mouse model to study inflammation, but much of the inflammatory response has been questioned in recent studies. Also, caged mice tend to have a homogenous gut microbiome, which isn’t true for humans. We would like to study the inflammatory response in a rat model that we are developing, as well as in surgical patients.

I also suspect that the known reductive and oxidative pathways of the bacteria in the gut may change the way the patient responds, especially because the bacteria outnumber us billions to one and those products are the result of an enzymatic cascade. Once we know these inflammatory and redox mediators in the intestine – can we use them to predict which patients will have a difficult postoperative recovery? Can we even predict which patients will form that dreaded postoperative leak or fistula?

Ultimately, we hope to bring this knowledge back to the patients to help them recover from their surgery by changing the gut microbiome pre- or post-operatively. There are many ‘probiotics’ commercially available, some of which are FDA approved, and fecal transplants have become an accepted treatment for recalcitrant *C. difficile* colitis. Perhaps it is as simple as taking healthy bacteria for a week before your colon surgery.
With Humble Hearts

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We are approaching various holidays, a new year, and anticipated time with family and friends giving time and cause for introspection, retrospection, and circumspection. At this time of year there are innumerable references to our hearts; at least metaphorically. Dr. Schwann and I have the daily privilege of caring for patients with heart disease and often, quite literally, holding their hearts in our hands. It gives one pause to consider as we are surrounded by science and evidence-based medicine how little we really know fundamentally about whom we are and how we work. Do we have souls and if so where is it? Descartes postulated that it was in the pineal gland. Mahler compels the heart and Bach makes it clear it exists in some extra-anatomic location. These are some of the thoughts that occur, at least to me, peering deep into the hearts of our patients, performing what is the most-studied operation in the world. And there is the irony. One would think that with a database from over 1000 participating sites, with over 3 million patients with an additional 300,000 cases added yearly that we would really know what we’re doing. I have described to you the Society of Thoracic Surgeons (STS) database. In tribute to science and innovation, it is amazing that an operation just invented in the mid 1960s, that had a >10% mortality rate in 1971, now has a mortality of 2% in a patient population that is over 10 years older than just a decade ago. In spite of this, fundamental questions such as, what is the best bypass conduit? best pattern of grafting? best way to close the sternum and care for the wound? who should get blood thinners? etc, remain unanswered.

The Division of Cardiothoracic Surgery at UTMC is trying to answer some of these questions. We have ongoing research projects in multiple areas and over twenty publications in the past two years. The following are areas of focus.

1. Factors influencing outcomes in cardiac surgery. We have reported data supporting the use of the radial artery as a bypass conduit and its superiority to vein grafts both in patency rates and overall mortality. While currently only utilized in 5% of coronary artery bypass graft operations nationally, UTMC uses the radial artery in about 80% of our patients. We have reported outcomes in the elderly, diabetics, triple vessel disease, compared it to percutaneous coronary intervention (stents) and to other grafting configurations.

2. The impact, risks, and safety of blood transfusions in cardiac surgery. While increasing oxygen carrying capacity is good, it comes at a high price; financially and physiologically. We have ongoing projects studying the impact of blood products on outcomes, graft patency, deep venous thrombosis, and the age of transfused blood and implications of old blood transfused in cardiac surgery patients.

3. Patterns and best practices for anticoagulation after valve replacement operations. There remains tremendous variability nationally and we are collaborating with the STS database to examine practice patterns and outcomes.

4. Functional outcomes and quality of life after Left Ventricular Assist Device (LVAD) implantation. Congestive heart failure is an enormous health issue and number one expense for Medicare. The field of mechanical circulatory support is growing and number of LVAD implants is increasing exponentially. Collaborating with Dr. Haines, a neuropsychologist at UTMC, we have been the first to report improvement in cognitive function after LVAD implant. We have also explanted 10% of our patients with their own hearts recovered while the national rate remains just below 1%. We have ongoing projects looking at factors influencing myocardial recovery and continue to study cognitive function in this population.

5. Guidelines for the care of LVAD patients. As this population grows exponentially, we must be prepared societally to deal with this. Through our own experience and representation on the guidelines committee of the Heart Failure Society of America, we are proposing guidelines for LVAD patients with other needs, i.e trauma and ambulatory non-cardiac surgery.

6. Sternal Fixation. We have been, and continue to be involved in multi-center trials looking at innovative platforms for sternal closure. Articles in press.

In addition to the various research projects and practice of cardiac and thoracic surgery, we also have the only LVAD program and in northwest Ohio. We have implanted over 30 patients two of whom have been successfully transplanted and three of whom have been successfully explanted with cardiac recovery. We also have the only Extracorporeal Membrane Oxygenation program in the region to support acute cardiopulmonary failure with suspected reversible cause. We have successfully supported patients with cardiac arrest, profound pneumonia, flu, traumatic lung injury, and pulmonary embolism with this technology.
Clinical care and research are team sports. We have a fantastic team here at UTMC. In addition to Drs. Schwann and Bonnell, we have two nurse practitioners, Jennifer Davis and Connie Mueller, data base, quality, and administrative support from Lori Beck and Dianne Anaya, and research support from Christina Eisenhauer. We are indebted to them for all their hard work.

So it is with humble hearts that Dr. Schwann and I revere the great privilege of caring for these patients, accepting their trust, and contemplating all we don’t know while trying to answer a few questions. It is a season…and a world full of wonder to be sure. Keep wondering.

Selected Publications:

   Everolimus-Eluting Stents or Bypass Surgery for Coronary Disease. 
   Role of blood transfusion product type and amount in deep vein thrombosis after cardiac surgery. 
   Equipoise between radial artery and right internal thoracic artery as the second arterial conduit in left internal thoracic artery-based coronary artery bypass graft surgery: a multi-institutional study. 
   Eur J Cardiothorac Surg 03/2015
5. Fang JC et al. (2015) 
   Advanced (Stage D) Heart Failure: A Statement From the Heart Failure Society of America Guidelines Committee. 
   J Card Fail 21(6):519-534.
6. Haynesp et al. (2014) 
   Transmural Heterogeneity of Cellular Level Power Output Is Reduced in Human Heart Failure. 
   Neuropsychological Functioning, Pre- and Post-Placement of Left Ventricular Assist Device: A Pilot Study. 
   Clin Neuropsychol 27(4):584-584

Dr. Schwann, recent LVAD patient, Dr. Bonnell

Clinical Snippets

Series Editors: Anand Mutgi, MD & Sadik Khuder PhD

Time to Rethink Treatment of Iron Deficiency States

Basil Akpunonu, MD
Anu Garg, MD
Andrew Jeter, BS

Anemia is a common disease and contributes to 9% of global disability. Iron deficiency is the common cause
and is associated with low hemoglobin and symptoms of weakness, dizziness, exercise intolerance. Iron deficiency is currently treated with oral supplementation of ferrous sulphate 325 mg 3 times daily for 3 to 6 months. This month we present a study which radically changes our approach in treating iron deficiency.

This study included 54 non-anemic but iron deficient women, with plasma ferritin of ≤ 20 mcg/L who were treated with different doses of iron daily. Iron absorption was assessed by several parameters including plasma ferritin, soluble transferrin receptor, C reactive protein, plasma iron, and total iron binding capacity. Iron absorption was reduced when daily iron dose exceeded 40 mg per day. This reduced absorption was associated with increased hepcidin levels, which lasted for up to 48 hours.

Current understanding is that iron absorption is linked to serum hepcidin level. High levels of hepcidin inhibit iron uptake in the gut, and prevent the release of iron for use in synthesis of hemoglobin.

So what does this mean for a practicing physician in 2015?

1. Current practice of prescribing high doses of iron at 325 mg, 3x times a day may not be the best way to treat iron deficiency. Provision of smaller doses (≤ 40 mg daily) maximizes absorption.
2. Multiple daily doses do not improve iron absorption.
3. Doses higher than 40 mg would work best if used on alternate days.

Based on the study we suggest a modest dose of 40 mg of iron daily or higher doses on alternate days as the optimal treatment of iron deficiency status.

New Clinical Trials

A Cerebrospinal Fluid and Salivary Biomarker in Moderate to Severe Traumatic Brain Injury.
Dr. Gaudin - Surgery

A Prospective, Multi-Center Study Designed to Evaluate the Positive Predictive Value of WOUNDCHECK Protease Status on Venous Leg Ulcers (VLUs) and Diabetic Foot Ulcers (DFUs) by Testing Wound Fluid Swab Samples Collected from Two Types of Chronic Wounds.
Dr. Nazzal - Surgery

High Pressure vs. Cutting Balloon in the Treatment of Neo-intimal Hyperplasia in Patients with Arterio-venous Dialysis Grafts.
Dr. Nazzal - Surgery

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