# Missouri ACP 2014 Abstract Winners



July 9, 2016

The abstracts below represent the winners in the Residents and Medical Students categories at the 2014 Missouri ACP Chapter meeting.

**Winner, Research Poster for Missouri ACP 2014.**

**Evaluation of the reporting process of the tests pending at discharge in an academic hospital.**

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**Introduction:** A patient's hospital stay involves multiple diagnostic tests done for various indications. Not uncommonly, the final results of diagnostic tests including lab tests, radiology, pathology and microbiology come back after a patient is discharged. A number of times, these results might not be clinically significant but sometimes they are. These results are to be discussed with the patients, and action taken, in a timely manner. Not uncommonly, these results go unreported and are missed. We aim to study how the reporting process is working in our hospital focusing on medical inpatients, and to find solutions to any problems that may exist.

**Methods:** We performed a retrospective chart review of all medical in-patients at Truman Medical Center-Hospital Hill (TMC-HH) who were discharged in the month of July 2014 and had tests pending at the time of discharge (TPADs). Appropriate descriptive statistics were used for nominal and ordinal data.

**Results:** A total of 229 instances of TPADs were identified. Fifty percent belonged to chemistry, 34% belonged to pathology, 12% belonged to radiology and 4% to microbiology. Twenty eight percent of TPADs were clinically actionable. Discharge summaries included actionable TPADs in 82% of the cases. Appropriate action was taken in 92% of the actionable TPADs. Action was taken in 52% of the cases within one week and 82% of the cases within one month after results arrived.

**Conclusion:** The discharge process is a critical step in a patient's hospital course. Our data gives us insights into our discharge process and the reporting of TPADs. Most of the TPADs were acted upon with the patients and in a timely manner. The majority of the discharge summaries documented actionable TPADs. There is still room for improvement.

**Nutritional Knowledge in Internal Medicine Residents.**

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**Introduction:** Malnutrition affects approximately 30% of inpatients world-wide and is strongly associated with adverse outcomes, but is often poorly addressed by house-staff. The purpose of our study was to identify educational deficiencies in the knowledge base of internal medicine resident physicians.

**Methods:** For 2.5 months, nutrition competency was assessed by comparing inpatient diet orders made by medicine residents with dietician recommendations. Information collected included diet orders, patient age and gender, and resident year of training. Diet orders made by residents were classified as “concordant” or “discordant” depending on agreement with dietician recommendations. Malnutrition was defined using ASPEN criteria. The students’ t-test, chi-square test, and z-tests of proportions were used where appropriate.

**Results:** Of 1,419 patients reviewed, 17% were evaluated by dietitians for diet alone, and 8% for malnutrition. Of patients identified as malnourished, residents made the diagnosis of malnutrition in only 40% (45/111). Futhermore, only 17% of house-staff orders were concordant with dietitian recommendations (19/111). Concordance of diet orders was related to resident ability to diagnose malnutrition ($p=0.08$). Discordant orders were more common in resident-identified patients than resident-missed patients ($p=0.045$). Overall, results did not differ with respect to age and gender.

**Conclusion:** Resident physicians perform poorly in diagnosing malnourished patients, a population at need for early appropriate intervention. Similarly, residents were poor at prescribing appropriate diets in the vast majority of patients. Graduate programs should improve training in identifying malnourished patients and promote a better understanding of factors involved in selecting an appropriate diet.

**Extracorporeal photopheresis as second-line treatment for acute graft-versus-host disease: Impact on six month freedom from treatment failure.**

**Li Zhou**, Emma Das-Gupta, Hildegard Greinix, Ryan Jacobs, Bipin N. Savani, Brian G. Engelhardt, Adetola Kassim, Nina Worel, Robert Knobler, Nigel Russell, Madan Jagasia.

Extracorporeal photopheresis (ECP) is a promising treatment for corticosteroid-refractory or dependent acute graft-vs-host disease (GVHD). However, traditional clinical endpoints used in studies to evaluate treatments of this complication incompletely capture a patient’s clinical response. Six-month freedom from treatment failure (FFTF) has been proposed as a novel clinical trial endpoint and is defined by the absence of death, malignancy relapse/progression, or addition of next line of systemic immunosuppressive therapy within 6 months of intervention and prior to diagnosis of chronic GVHD. In this study, we analyzed 128 patients enrolled from 3

centers treated with ECP as second-line therapy for acute GVHD. Our study demonstrated that 6 month FFSF correlates strongly with overall survival at 1 year (78.9%), 2 years (70.8%), and 3 years (69.5%). Furthermore, the incidence of 6 month FFTF was 77.3% with a 2-year survival of 56%. Grade of aGVHD (grade 2 vs. 3-4) at onset of second-line therapy was an important determinant of outcome, as measured by survival (HR 2.78, P<0.001), non-relapse mortality (HR 2.78, P=0.001) and 6 month FFTF (HR 3.05, P<0.001). Our study supports the use of 6 month FFTF as a clinical trial endpoint for evaluating second line treatments in steroid refractory/dependent acute GVHD, and demonstrates the efficacy of ECP in this patient population.

**Winner: 2014 ACP-Missouri Chapter Medical Student Competition**

**Targeted Delivery of Phosphodiesterase Inhibitors to Erythrocytes: Implications for the Treatment of Vascular Disease in Type 2 Diabetes.**

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In skeletal muscle, when erythrocytes (RBCs) are exposed to low $O_2$, they release both $O_2$ and the potent vasodilator, ATP, permitting these cells to alter distribution of perfusion to meet tissue $O_2$ need. However, in humans with Type 2 Diabetes (DM2), ATP release from RBCs in response to low $O_2$ is lost. This defect could contribute to the associated peripheral vascular disease (PVD). A signaling pathway for low $O_2$-induced ATP release from RBCs that requires increases in cAMP that are regulated by Phosphodiesterase 3 (PDE3) has been defined. Although the use of the PDE3 inhibitor cilostazol (CILO) in DM2 is attractive, side effects limit its use. In addition PDE3 can also be inhibited by cGMP, a cyclic nucleotide that is regulated by PDE5. The aims of this study were to 1) construct liposomes containing the PDE3 inhibitor, CILO, and determine if the directed delivery to DM2 RBCs restores low $O_2$-induced ATP release and 2) determine if the PDE5 inhibitors, zaprinast (ZAP) or tadalafil (TAD), also rescue low $O_2$-induced ATP release from DM2 RBCs. RBCs from healthy humans and humans with DM2 were exposed to both normal and reduced $pO_2$ using a thin-film tonometer in the presence of either empty dimyristoylphosphatidylcholine liposomes or liposomes containing CILO, ZAP, or its vehicle dimethylformamide (DMF). In healthy human RBCs, ATP release increased from 13.6±2.3 to 25.2±4.6 with exposure to low $O_2$ (P<0.01). In contrast, when RBCs of humans with DM2 were incubated with empty liposomes ATP levels did not increase (15.4±1.4 to 14.7 ± 1.1). The defect in ATP release was rescued by incubation with liposomes containing the PDE3 inhibitor, CILO, with ATP increasing from 14.8±1.2 to 23.1±3.8 (P<0.01). Similarly, incubation of DM2 RBCs in the absence of liposomes with the PDE5 inhibitors, ZAP or TAD, also rescued low $O_2$-induced ATP release with increases of 9.2±0.9 to 18.7±1.7 (P<0.01) and 14.6±5.0 to 21.1±4.8 (P<0.05), respectively. In summary, both directed delivery of a PDE3 inhibitor to RBCs by liposomes and the administration of PDE5 inhibitors alone rescue low $O_2$-induced ATP release from DM2 RBCs. These results provide new support for the hypothesis that PDE5 is a component of a signaling pathway for low $O_2$-induced ATP

release from RBCs along with PDE3. Restoration of this function permits DM2 RBCs to participate in the regulation of perfusion to meet tissue $O_2$ need and suggests new approaches to the treatment and/or prevention of peripheral vascular disease in patients with DM2.

**Developing a model for FGF and Notch Signaling Hierarchy in Sensory Neurogenesis reveals potential pathway for malignancy.**

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**Introduction:** The ophthalmic trigeminal (opV) placode exclusively gives rise to sensory neurons, making it a good model to study the molecular regulation of sensory neurogenesis. A number of signaling pathways including Wnt, PDGF, FGF, and Notch have been shown to be involved in the process of opV placode cell development. However, the regulatory relationship between these signaling pathways is still unknown, and has been difficult to study experimentally. Using a novel multifactorial approach in chick embryos that allows for inhibition of FGF throughout the tissue or in individual cells, with simultaneous inactivation of Notch signaling, we investigated the potential interaction between the FGF and Notch signaling pathways in trigeminal sensory neurogenesis.

**Methods**: To determine if FGF activation acts to modulate Notch signaling in the sensory neurogenesis pathway, FGF signaling was first inhibited globally with a FGF chemical antagonist while simultaneously inactivating Notch signaling. FGF signaling was then inhibited in individual cells via electroporation with a secreted-FGF receptor while concurrently inhibiting Notch signaling in order to define the interaction between the signaling pathways cell-autonomously. FGFR4 expression was also analyzed by *in situ hybridization* after Notch inhibition to determine if Notch downregulation allows for broadened FGFR4 expression. Finally, the role of FGF and Notch signaling on basement membrane integrity was examined by inhibiting both pathways individually or collectively and staining for laminin.

**Results:** FGF pathway inhibition resulted in few cells delaminating from the opV placode and a statistically significant decrease in the number of cells contributing to ganglion formation. Conversely, Notch pathway inhibition resulted in a robust expansion of these cells. Simultaneous FGF and Notch pathway inhibition also resulted in a reduction of cells delaminating from the opV placode and contributing to the ganglion producing a similar phenotype to embryos in which the FGF pathway alone was inhibited. Further, Notch inhibition did not lead to broad enhancement of FGFR4 expression, but instead resulted in a highly fragmented basal lamina, which was reversed when blocking FGF signaling.

**Conclusions and Discussion**: Cumulatively, these results do not support a model of Notch/FGF interdependence, but rather a relationship where FGF and Notch act in parallel to promote sensory neurogenesis. These conclusions suggest a model where FGF activation with parallel Notch downregulation lead to basement membrane fragmentation and

subsequent differentiation of opV placode cells. This proposed model of basement membrane regulation by FGF and Notch will be a focus of ongoing research and may provide significant insight as to how some cancer cells become malignant in various cancer cells lines.