Clinical ICU

Giora Netzer (<u>GNetzer@som.umaryland.edu</u>): Dr. Netzer is formally trained in pulmonary and critical care medicine and clinical epidemiology and is Director of Clinical Research for the Pulmonary and Critical Care Medicine Division. His past research focused on risk factors associated with worse outcomes in ARDS. His current research is focused on identifying sources of morbidity among family members of patients in the intensive care unit, concentrating on using validated measures to quantify potential deficits potentially compromising effective decision-making. He serves as Vice President of Patient Experience for the University of Maryland Medical Center.

Highlighted Publications:

 Sullivan DR, Liu X, Corwin DS, Verceles AC, McCurdy MT, Pate DA, Davis JM, Netzer G. "Learned Helplessness Among Families and Decision-makers of Patients Admitted to Medical, Surgical, and Trauma Intensive Care Units." *Chest.* 142(6): 1440-1446, 2012. PMID: 22661454.
Afshar M, Smith GS, Terrin ML, Barrett M, Lissauer MD, Mansoor S, Jeudy J, Netzer G. "Blood Alcohol Content, Injury Severity and Acute Respiratory Distress Syndrome." *The Journal of Trauma and Acute Care Surgery*. 76(6): 1447-1466, 2014. PMID: 24854314.

3. Fusaro MV, Nielsen ND, Nielsen A, Fontaine MJ, Hess JR, Reed RM, DeLisle S, **Netzer G**. "Restrictive Versus Liberal Red Blood Cell Transfusion Strategy Following Hip Surgery: A Decision Model Analysis of Healthcare Costs." *Transfusion*. 57(2):357-366, 2017. PMID: 28019009.

4. Leiter N, Motta M, Reed RM, Adeyeye T, Wiegand DL, Shah NG, Verceles AC, **Netzer G**. "Numeracy and Interpretation of Prognostic Estimates in Intracerebral Hemorrhage Among Surrogate Decision Makers in the Neurologic ICU." Critical Care Medicine. 2018, 46:264-71, PMID:29215368.

Links:

Faculty webpage: http://www.medschool.umaryland.edu/profiles/Netzer-Giora/

PubMed publications:

http://www.ncbi.nlm.nih.gov/sites/myncbi/16itinuBusjkB/bibliography/49607537/public/?sort=dat e&direction=ascending

<u>Carl Shanholtz</u> (<u>Cshanhol@som.umaryland.edu</u>): Dr. Shanholtz has had a longstanding interest in improving management of critically ill patients and has a long and successful record of clinical research in critical illness in general, and acute respiratory distress syndrome specifically. Together Dr. Roy Brower, Dr. Shanholtz conducted the phase II clinical trial of low tidal volume ventilation in ARDS on which the ARDSNet ALVEOLI study was based and he has been site director for ARDSnet-I and II. Dr. Shanholtz also studies methods to reduce fluid administration to critically ill patients, and is a co-investigator and Director of the Clinical Coordinating Center for Dr. Hasday's CHILL trial of therapeutic hypothermia in ARDS patients.

Highlighted Publications:

1. Netzer G, Dowdy DW, Harrington T, Chandolu S, Dinglas VD, Shah NG, Colantuoni E, Mendez-Tellez PA, Shanholtz C, Hasday JD, Needham DM. Fever is associated with delayed ventilator liberation in acute lung injury. Ann Am Thorac Soc. 2013 Dec;10(6):608-15. PubMed PMID: <u>24024608</u>; PubMed Central PMCID: <u>PMC3960965</u>.

2. Shah NG, Cowan MJ, Pickering E, Sareh H, Afshar M, Fox D, Marron J, Davis J, Herold K, Shanholtz CB, Hasday JD. Nonpharmacologic approach to minimizing shivering during surface cooling: a proof of principle study. J Crit Care. 2012 Dec;27(6):746.e1-8. PubMed PMID: <u>22762936</u>; PubMed Central PMCID: <u>PMC3494806</u>.

3. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. N Engl J Med. 2000 May 4;342(18):1301-8. PubMed PMID: <u>10793162</u>.

4. Brower RG, Shanholtz CB, Fessler HE, Shade DM, White P Jr, Wiener CM, Teeter JG, Doddo JM, Almog Y, Piantadosi S. Prospective, randomized, controlled clinical trial comparing traditional versus reduced tidal volume ventilation in acute respiratory distress syndrome patients. Crit Care Med. 1999 Aug;27(8):1492-8. PubMed PMID: <u>10470755</u>.

5. Slack DF, Corwin DS, Shah NG, Shanholtz CB, Verceles AC, Netzer G, Jones KM, Brown CH, Terrin ML, Hasday JD. Pilot Feasibility Study of Therapeutic Hypothermia for Moderate to Severe Acute Respiratory Distress Syndrome. Crit Care Med. 2017 45:1152-59;PubMed PMID: <u>28406814</u>.

<u>Links</u>:

Med School faculty page: http://www.medschool.umaryland.edu/profiles/Shanholtz-Carl/

PubMed publications:

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/47839782/?sort=date&direction=ascending

Michael Terrin (MTERRIN@som.umaryland.edu): Dr. Terrin is a pulmonologist and formally trained epidemiologist and clinical trialist who has mentored multiple physicians in the design and execution of large clinical trials. He has been Principal Investigator of the Administrative and Data Coordinating Centers for several large and successful NIH studies including the NHLBI-sponsored Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED), the Multicenter Study of Hydroxyurea in Sickle Cell Anemia (MSH), and the NHLBI-sponsored Functional Outcomes in Cardiovascular Patients Undergoing Surgical Hip Fracture Repair (FOCUS) Clinical Trial, the NIA-sponsored AZIP trial, and the NHLBI Progenitor Cell Biology Consortium (PCBC) Administrative Coordinating Center. He is an internationally recognized expert in study design, study organization and management, data management, and data analysis.

Highlighted Publications:

1. Gore J, Sloan M, Price T, Randall AMY, Bovill E, Collen D, Forman S, Knatterud G, Sopko G, Terrin ML and the TIMI Investigators. Intracranial hemorrhage, cerebral infarction, and subdural hematoma following acute myocardial infarction and thrombolytic therapy in the Thrombolysis in Myocardial Infarction Study (TIMI II Pilot and Randomized Clinical Trial). Circulation 1991;83:448-459.

2. Schulman SP, Becker LC, Kass DA et al. L-Arginine Therapy in Acute Myocardial Infarction. JAMA 2006; 295:58-64.

 Charache S, Terrin ML, Moore RD, Dover GJ, Barton FB, Eckert SV, McMahon RP, Bonds DR and the Investigators of the Multicenter Study of Hydroxyurea in Sickle Cell Anemia. Effect of hydroxyurea on the frequency of painful crises in sickle cell anemia. NEJM 1995;332:1317-1322.
Hassan H, Othman AA, Eddington ND, Duffy L, Xiao L, Waites KB, Kaufman DA, Fairchild KD, Terrin ML, Viscardi RM. Pharmacokinetics, Safety, and Biologic Effects of Azithromycin in Extremely Preterm Infants at Risk for Ureaplasma Colonization and Bronchopulmonary Dysplasia. J Clin Pharmacol 2011; 51:1264-1275. [PMCID:PMC4240745]

5. Baxter TB, Matsumura J, Curci J, McBride R, Blackwelder WC, Liu X, Larson L, and Terrin ML. Non-Invasive Treatment of Abdominal Aortic Aneurysm Clinical Trial(N-TA³CT): Design of a Phase IIb, Placebo-Controlled, Double-Blind, Randomized Clinical Trial of Doxycycline for the

Reduction of Growth of Small Abdominal Aortic Aneurysm. Contemporary Clinical Trials 2016; 48:91-98. doi: 10.1016/j.cct.2016.03.008. Epub 2016 Mar 25.

<u>Links</u>:

Med School faculty page: http://www.medschool.umaryland.edu/profiles/Terrin-Michael/

PubMed publications:

http://www.ncbi.nlm.nih.gov/sites/myncbi/collections/bibliography/48077438/

Jeffrey Hasday (ihasday@som.umaryland.edu): The Hasday lab has focused on how febrilerange hyperthermia and hypothermia modify biological processes relevant to disease pathogenesis with emphasis on acute lung injury/ARDS and fibrosis. Using approaches that span structural biology, gene and protein expression, cell culture, animal models and human trials, the Hasday laboratory has shown that hyperthermia worsens and hypothermia improves lung injury by modifying endothelial permeability, neutrophil recruitment, epithelial injury, and cytokine and heat shock protein expression. The p38 MAP kinase pathway appears to be a major contributor to the temperature-dependence of endothelial barrier function and expression of proinflammatory cytokines. The Hasday laboratory is currently has three areas of research: (1) the DoD-funded Cooling to Help Injured Lungs (CHILL) randomized clinical trial of mild hypothermia plus neuromuscular blockade vs. standard temperature management in patients with moderate to severe ARDS, a 14-center trial for which we serve as both the Data Coordinating Center and Clinical Coordinating Center; (2) expansion of our exciting data showing that the structure and function of p38alpha, the proinflammatory p38 family member, but not p38beta is temperaturedependent in the 33° to 39°C range; and (3) the computer-assisted design of a novel class of substrate- and function-selective inhibitors of p38alpha for treatment of acute lung injury; one of these novel drugs has just completed Phase 1 studies and will begin Phase 2 studies in the near future. Dr. Hasday also directs the University of Maryland Cytokine Core Laboratory (www.cvtokines.com).

Highlighted Publications:

1. Shah NG, Tulapurkar ME, Ramarathnam A, Brophy A, Martinez R 3rd, Hom K, Hodges, T, Samadani R, Singh IS, MacKerell AD Jr, Shapiro P, Hasday JD. Novel Noncatalytic Substrate-Selective p38α-Specific MAPK Inhibitors with Endothelial-Stabilizing and Anti-Inflammatory Activity. J Immunol. 2017; 198(8):3296-3306. Pubmed PMID: 28298524.

2. Slack DF, Corwin DS, Shah NG, Shanholtz CB, Verceles AC, Netzer G, Jones KM, Brown CH, Terrin ML, Hasday JD. Pilot Feasibility Study of Therapeutic Hypothermia for Moderate to Severe Acute Respiratory Distress Syndrome. Crit Care Med. 2017 45:1152-59;PubMed PMID: <u>28406814</u>.

3. Tulapurkar ME, Ramarathnam A, Hasday JD, Singh IS. Bacterial lipopolysaccharide augments febrile-range hyperthermia-induced heat shock protein 70 expression and extracellular release in human THP1 cells. PLoS One. 2015;10(2):e0118010. PubMed PMID: <u>25659128</u>; PubMed Central PMCID: <u>PMC4320107</u>.

4. Gupta A, Cooper ZA, Tulapurkar ME, Potla R, Maity T, Hasday JD, Singh IS. Toll-like receptor agonists and febrile range hyperthermia synergize to induce heat shock protein 70 expression and extracellular release. J Biol Chem. 2013 Jan 25;288(4):2756-66. PubMed PMID: <u>23212905</u>; PubMed Central PMCID: <u>PMC3554941</u>.

5. Tulapurkar ME, Almutairy EA, Shah NG, He JR, Puche AC, Shapiro P, Singh IS, Hasday JD. Febrile-range hyperthermia modifies endothelial and neutrophilic functions to promote extravasation. Am J Respir Cell Mol Biol. 2012 Jun;46(6):807-14. PubMed PMID: <u>22281986</u>; PubMed Central PMCID: <u>PMC3380289</u>.

6. Shah NG, Tulapurkar ME, Damarla M, Singh IS, Goldblum SE, Shapiro P, Hasday JD. Febrilerange hyperthermia augments reversible TNF-α-induced hyperpermeability in human microvascular lung endothelial cells. Int J Hyperthermia. 2012;28(7):627-35. PubMed PMID: <u>22834633</u>.

7. Deredge, D., Wintrode, P., Tulapiurkar, M. E., Nagarsekar, A., Zhang, Y., Weber, D. J., Shapiro, P., and Hasday, J. D. (2019) A temperature-dependent conformational shift in p38 MAP kinase substrate binding region associated with changes in substrate phosphorylation profile. *J. Biol. Chem.* 2019;294:1264-37. PubMed PMID 31073086.

<u>Links</u>:

Med School faculty page: http://www.medschool.umaryland.edu/profiles/Hasday-Jeffrey/

PubMed publications:

https://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40776367/?sort=date&direction=ascending