The Department of Anesthesiology
proudly presents its 10th Annual

Research Exposition

February 12, 2015

Weill Cornell Medical College

NewYork-Presbyterian Hospital
Weill Cornell Medical Center

Welcome to the Anesthesiology Research Exposition February 12, 2015

Oral Presentations

"Effects of of isoflurane on presynaptic voltage – gated calcium channels coupled to exocytosis in hippocampal neurons"

Daniel Cook, MS IV

Weill Cornell Medical College

3:00pm – 3:45pm, M309

"HCN channels and neuropathic pain: Science and serendipity"

Peter Goldstein, M.D

Professor of Anesthesiology
Associate Professor of Medical Ethics, Weill Cornell Medical College
Faculty Member - Neuroscience Graduate Program,
Weill Cornell Graduate School of Medical Sciences
Attending Anesthesiologist, NewYork-Presbyterian Hospital

Guest Speaker

Alan Van Poznak, MD

Professor Emeritus of Anesthesiology

Special Research Seminar

"How anesthetics prevent learning- from molecules to memory"

Robert A. Pearce, MD, PhD

Ralph M. Waters Distinguished Chair of Anesthesiology
University of Wisconsin-Madison School of Medicine and Public Health

4:00pm – 4:30pm, M309

Reception

4:30pm – 5:00pm

Poster Presentations

To Immediately Follow

Department of Anesthesiology
525 East 68th Street

Department of Anesthesiology Research Department

Hugh C. Hemmings, Jr, MD, PhD, FRCA
Chairman of Anesthesiology

Cynthia A. Lien, MD
Vice Chair for Academic Affairs

Kane O. Pryor, MD
Director of Clinical Research

Anesthesiology Clinical Research

Michele Steinkamp, RN	Elizabeth Lemoine, BA
Emma Rogers, BA	Farrell Cooke, BS
Sean Till, BA	Mariya Redko, BS
Bryce Petty, BA	Lindsay Pharmer, MD
Deirdre Kelleher, MD	Asha Mellor, M.A
Ronit Sternberg, DDS, MD	Alan Wang, BA

Center for Perioperative Outcomes Research

Peter M. Fleischut, MD	Gregory Giambrone, MS
Susan L. Faggiani, RN	Hugh C. Hemmings, M.D.,PhD, FRCA
Christian Tope, BS	Kane O. Pryor, MD
Zachary A. Turnbull, MD	Virginia Tangel, MA
Akshay U. Bhat, MEng	Ramin Zabih, PhD
Andrew N. Lazar, MS	Matthew Alexander, B.S
Licia Gaber-Baylis, BA	

Laboratory of Molecular Anesthesiology

Hugh Hemmings, Jr, MD, PhD	Rheanna Sand, PhD
Zhenyu Zhou, PhD	Christina Bonvicino, BS
Daniel Cook, BS	Kerry Purtell, BA
Karl Herold, MD, PhD	Jimcy Platholi, PhD
Kenneth Johnson, BS	

Neuromuscular Relaxant Research.

Matthew Belmont, MD	Peter Savard, MD
Paul Heerdt, MD, PhD	John Savarese, MD
David Kopman, MD	Ralph Slepian, MD
Daniel Lahm, MD	Hiroshi Sunaga, MD
Cynthia Lien, MD	Matthew Murrell, MD, PhD
Jaideep Malhotra, MD	

CV Starr Laboratory for Molecular NeuroPharmacology

Alessio Accardi, PhD	Anna I. Adamo, BS
Peter Goldstein, MD	Alessandra Picollo, PhD
Crina Nimigean, PhD	David Posson, PhD
Byoungcheol Lee, PhD	Vikrant Upadhyay, PhD
Mattia Malvezzi, BS	Dorothy Kim, PhD
Malvin Vien, BA	Lacey Ferraro, BS

Cardiovascular & Cerebrovascular Laboratory

Paul Heerdt, MD, PhD	Harrison Peprah-Mensah, BS

Cardiac Clinical Research

Meghann Fitzgerald, MD	James Osorio, MD
Shanna Hill, MD	Lingesh Sivanesan, MD
Natalia Ivascu, MD	Nikolaos Skubas, MD
Gregory Kerr, MD, MBA	Ralph Slepian, MD
Shreyajit Kumar, MD	Fun-SunYao,MD
Arun Jayaraman, MD, PhD	

Pain Clinical Research

Neel Mehta, MD	Roniel Weinberg, MD
Shakil Ahmed, MD	Lisa R. Witkin, MD
Maryam Jowza, MD	David Zylberger, MD
Shenella Bourne, RN	Julie Huang, MD, MBA

Neuroanesthesia Clinical Research

Kingsley Storer, MD, PhD	Alexander Proekt, MD, PhD
Peter Goldstein, MD	Kane Pryor, MD
David Kopman, MD	Patricia Fogarty-Mack, MD

General Clinical Research

Eric D. Brumberger, MD	Jon Samuels, MD
Mary Casciano, MD	Aarti Sharma, MD
Ralph Slepian, MD	Jill Fong, MD
Kingsley Storer, MD, PhD	Tiffany Tedore, MD
Vinod Malhotra, MD	Matthew Murrell, MD, PhD
Anup Pamnani, MD	

Obstetrics/Gynecological Clinical Research

Sharon Abramovitz, MD	Klaus Kjaer, MD, MBA
Alaeldin Darwich, MD	Jeremy Pick, MD
Farida Gadalla, MD, ChB	Angela Selzer, MD
Michael Kiselev, MD	Jamie Aaronson, MD
Steven Beaudry, DO	

Global Health

Gunisha Kaur, MD	Eric D. Brumberger, MD
Gregory Kerr, MD, MBA	Lee Rasamny, MD
Michelle Shirak, MD	

Poster Award Finalists

Clinical Research

Evaluation of Diastolic Dysfunction in Patients Undergoing Transcatheter Aortic Valve Replacement

Authors: June M, Chan, Polydoros N. Kampaktsis, Fay Y. Lin, Ingrid M. Hriljac, Richard B. Devereux, Arash Salemi, Nikolaos J. Skubas

A Multistate Analysis of Readmission for Invasive Cardiac Surgeries

Authors: Zachary A. Turnball, Natalia S. Ivascu, Gregory P. Giambrone, Xian Wu, Licia Gaber-Baylis, Elizabeth Lemoine, Jonathan Eskreis-Winkler, Akshay U. Bhat, Ramin Zabih, Peter M. Fleischut

Laboratory Research

Recovery of Consciousness from Isoflurane Anesthesia is Mediated by a Structured Network of Discrete Intermediate Brain States

Authors: A.Hudson, D.P Calderon, D.W. Pfaff, A. Proekt

Calcium-dependent Gating in MthK K^+ Channels Occurs at the Selectivity Filter

Authors: David J. Posson, Radda Rusinova, Olaf S. Andersen, Crina M. Nimigean

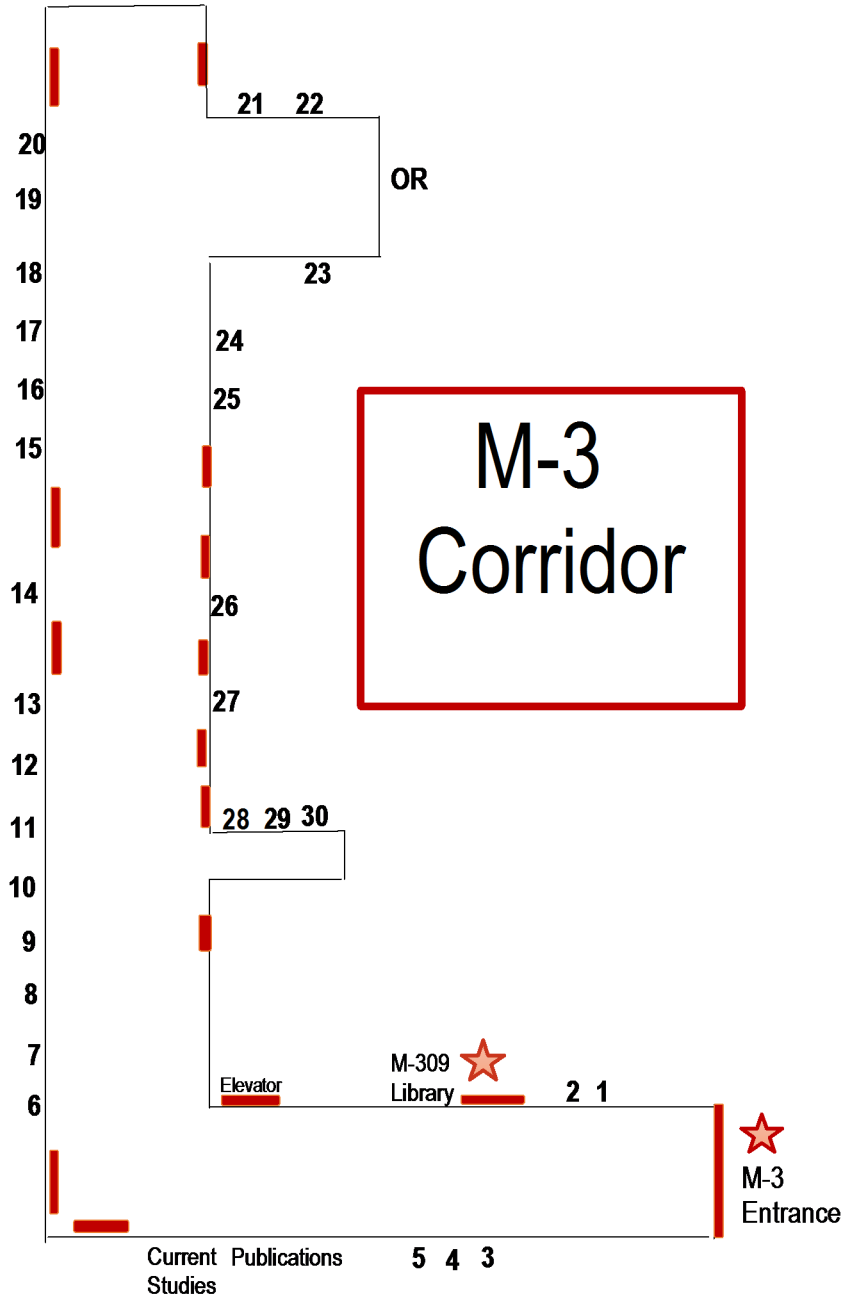

TABLE OF CONTENTS

EVALUATION OF DIASTOLIC DYSFUNCTION IN PATIENTS UNDERGOING TRANSCATHETER AORTIC VALVE REPLACEMENT

June M. Chan[§], Polydoros N. Kampaktsis[#], Fay Y. Lin[#,*], Ingrid M. Hriljac[#,*], Richard B. Devereux[#,*], Arash Salemi[¶,*], Nikolaos J. Skubas[§,*]

*Departments of [§]Anesthesiology, [#]Cardiology and [¶]Cardiothoracic Surgery, Weill Cornell Medical College, New York, NY, and *William Acquavella Heart Valve Center, NewYork-Presbyterian Hospital, New York, NY*

Introduction: Diastolic dysfunction in patients with aortic stenosis is associated with increased mortality. Echocardiographic evaluation of diastolic dysfunction may be challenging due to interpretative differences and conflicting parameters, despite the use of established practice recommendations.

Objective: To assess the applicability of the American Society of Echocardiography (ASE) recommendations for evaluating diastolic function in patients who are undergoing transcatheter aortic valve replacement (TAVR)

Methods: The ASE recommendations were used to retrospectively assess the pre-operative transesophageal and transthoracic echocardiogram examinations of 229 consecutive patients who underwent TAVR with the Edwards SAPIEN balloon-expandable prosthetic valve. Patients with mitral or aortic regurgitation >1+ were excluded. Inclusion criteria were those associated with diastolic dysfunction: decreased septal (<8 cm/s) and lateral (<10 cm/s) early (e') diastolic myocardial velocity, and elevated left atrial volume index (LAVI ≥ 34 ml/m2). Grading of diastolic dysfunction was performed using at least two of the ASE-recommended parameters: transmitral early (E) to late (A) filling velocity (E/A) ratio, E deceleration time (DT), E/e' ratio, pulmonary vein flow (PVF) atrial reversal-A duration (Ar-A). In addition, we considered the PVF systolic / diastolic velocity (S/D) ratio.

Results: 91 patients were included in the analysis. 64 patients (70%) were diagnosed with diastolic dysfunction of any severity, while 25 patients (27%) could not meet the ASE diagnostic parameters for diastolic dysfunction. 27 (42%) patients with diastolic dysfunction had decreased ejection fraction (defined as <55%) and 10 (16%) had atrial fibrillation. Not all patients with diastolic dysfunction had sufficient data to allow for full grading of severity. The E/e' ratio was recorded in 95% of examinations, the DT in 89%, and the E/A in 83%. When combined together, 77% had 3 recommended severity criteria, and 53% had all 5 recommended criteria. When E/A, DT and E/e' were used to grade severity, only 8% of patients were graded. No patient was gradable using all 5 criteria. Using 2 of 3 criteria, or 3 of 5 criteria expanded the number of gradable patients to 50% and 45%, respectively. Of those who could be graded using the methods described, the majority had grade I dysfunction. There was reasonable agreement between any of the diastolic dysfunction severity criteria and the overall severity grade, except for the E/e', which was heavily skewed towards grade III dysfunction.

Conclusion: Using the ASE recommendations, the majority of our TAVR patients met diagnostic criteria for diastolic dysfunction. A large portion of our patients had unclassifiable diastolic function due to discordant data, despite the conduct and interpretation of the examination by a small, core group of experienced echocardiographers. Severity assessment of diastolic dysfunction was limited by conflicting criteria when applied according to the recommendations. This is consistent with experience reported in other centers4,5. Altering the recommended grading criteria to include fewer parameters allowed significantly more patients to be graded for severity. This method suggests that the majority of patients with diastolic dysfunction had Grade I-II diastolic dysfunction. When assessed individually, E/e' data appears to suggest severe diastolic dysfunction across the majority of our patients. The importance of E/e' as a reproducible parameter, and in prognosticating short and long term outcomes is well established. The relationship of this outlier with our other data requires further examination. The ASE recommendations for diastolic function evaluation should be studied in larger TAVR cohorts to explore which criteria may be associated with perioperative risk and outcomes.

RAPID AND IMMEDIATE ANTAGONISM BY L-CYSTEINE OF THE NEW ULTRA-SHORT ACTING NONDEPOLARIZER CW 1759-50: PAIRED STUDIES IN RHESUS MONKEYS GIVEN CONTINOUS DOSAGE TO MAINTAIN 100% BLOCK OF TWITCH

John J. Savarese, MD[§]; Hiroshi Sunaga, MD[§], Matthew Belmont, MD[§]; Paul M Heerdt, MD, PhD[§], Douglas L. Cohn, DVM[#]

§ Department of Anesthesiology, Weill Cornell Medical College, New York, NY, #Albany Medical College, Albany, NY

Introduction: CW1759-50 shows ultra-short duration (6-8 mins from injection at ED99 bolus dosage to return of twitch and TOF to 95% of control values) in the Rhesus Monkey. The block is rapidly antagonized by exogenous L-cysteine. The drug is rapidly degraded by endogenous L-cysteine. The following study was performed to document rapid antagonism of CW 1759-50 blockade by L-cysteine at the end of continuous infusions of varying length where CW 1759-50 block was maintained at very deep levels (100% twitch block) by administering 2x ED99 dosage throughout the infusion. These experiments were meant to simulate clinical scenarios where a continuous overdose of CW 1759-50 may have been administered over a lengthy period of time, yet rapid recovery may nevertheless be desired.

Methods: Adult male Rhesus monkeys weighing 10-20 kg were studied under isoflurane (1.5 – 2.0%) and N2O/O2 (70/30 mixture) anesthesia. The study was approved by the IACUC of Albany Medical Center, where the experiments were performed. Arterial pressure, twitch, and TOF were measured continuously. Temperature and SpO2 were monitored continuously. Ventilation was controlled at 20 BPM, 15mL/kg.

Results: Data are shown in Table I. All comparisons are highly significant ($p < 0.01$). There was no significant difference between the durations of infusions C and D.

Discussion: The data show that a standard dose of L-cysteine (30 mg/kg) given 1 min after discontinuation of infusion rapidly antagonizes deep CW 1759-50 block where infusions have been given at high dosage (2x ED99) to maintain 100% twitch block. Reversal is nearly as rapid (3.7 ± 0.6 min vs. 2.1 ± 0.5 min) as following infusions where 99% block (ED99) has been maintained. Rapid antagonism of CW 1759-50 immediately following deep block may be clinically advantageous.

3

OPTIMIZATION OF NANODISC PLATFORM FOR EXPLORATIONS OF LIPID EFFECTS IN CNG CHANNELS

Alexis Jaramillo Cartagena[1,2,3], Julia Kowal[4], Sourabh Banerjee[2,3], Crina M. Nimigean[1,2,3]

Tri-Institutional Training Program in Chemical Biology. Weill Cornell Medical College/ The Rockefeller University/ Memorial Sloan-Kettering Cancer Center, New York, NY. 2. Department of Anesthesiology, Weill Cornell Medical College, New York, NY. 3. Center for Cellular Imaging and NanoAnalytics, Biozentrum, University of Basal, Switzerland. 4. Department of Physiology and Biophysics. Weill Cornell Medical College, New York, NY.

Introduction: The lipid membranes of cells are elaborate and dynamic environments that can potentially alter the three dimensional structure and function of membrane proteins including cyclic nucleotide-gated (CNG) ion channels. Such environments can contain cohorts of specific types of lipids and membrane proteins serving as anchors for other proteins; this phenomena is observed in lipid rafts. CNG ion channels play important roles in sensory signal transduction and their activity is modulated by the binding cyclic nucleotides. To study the lipid modulation of CNG channels we have optimized the incorporation of a model CNG channel into nanoscale apolipoprotein bound bilayers (nanodiscs) of precise lipid compositions. The incorporation of ion channels into nanodiscs permits the thermodynamic study of cAMP binding to the channel in the presence of a native lipid environment using isothermal titration calorimetry (ITC). To examine the lipid modulation of CNG channels, we used a chimeric channel (KC) previously engineered in our laboratory.

Nanodisc Optimization: Top: coomassie blue stained 12% SDS- PAGE. Unboiled KC sample (lane 2) runs as a tetramer above the 115 kD marker. Zap1 (lanes 3 and 7) runs as a series of bands around 26 kD; expected MW: 24.5 kD. Unboiled nanodiscs (lanes 4 and 5) contain both KC and Zap1. Upon boiling, KC runs as a monomer (lane 6) above the 26 kD marker, expected MW 27.9 kD. KC runs as a monomer in in the boiled nanodiscs (lanes 8 and 9) Bottom: 300 nm absorbance from TMR-labeled Zap1. Optimization of nanodisc formation by adjusting molar ratios of the components of the nanodiscs. 40-50 uL of 100-200 uM sample were filtered and injected into an ÄKTApurifier core system, where it was loaded into a Superose 6 (GE Healthcare) with a bed volume of 2.4 mL. Starting from conditions containing 45 lipids per Zap1 protein, a large peak was observed around 1 mL. This elution volume corresponds to species of > 700 kD, and thus was assumed to be liposomes or aggregates. Reducing the equivalents of lipids and KC lead to a monodispersed species with a peak maximum at 1.8 mL, which was assumed to be the size of nanodiscs containing one channel per disc. Deconvolution of nanodisc absorbance spectra. Since the nanodisc 550 nm signal is attributed solely to the TMR used to label Zap1, and since Zap1 has an specific 280 nm to 550 nm ratio,we can use this information to obtain its corresponding 280 nm signal and corresponding to the KC, from which the exact concentration of KC in the nanodiscs is calculated.

Nanodisc Optimization/IFC: Transmission electron microscopy imaging of KC incorporated into nanodiscs. Negatively stained samples were imaged using electron microscopy. Purified samples were adsorbed for 1 min to carbon-coated copper grids previously rendered hydrophilic by glow discharging. Grids were washed with 4 drops of nanopure water and stained twice for 12 s with 5 µL of 2% uranyl acetate. Single particles were imaged with a transmission electron microscope Phillips CM-10 operated at 80 kV. Electron micrographs of specimens were recorded at magnification of 130,000×, using a 2k×2k CCD camera. Data were collected using a MicroCal AutoITC200 (GE Healthcare). Samples were dialyzed in 10 mM HEPES, 100 mM KCl, 5 mM DM, pH 7.6 and degassed. cAMP was dissolved in dialysis buffer. Data were collected at 25 °C. The protein concentration was 60–160 µM and titrated with ~ 30 injections of cAMP to cover a ligand-to-sample molar ratio of 1-1.5. Results were analyzed using MicroCal. The binding stoichiometry (n), enthalpy change (ΔH), and equilibrium dissociation constant (KD) were determined by fitting a one-site model to the results.

Discussion: The different equilibrium disassociation constants for the binding of cAMP to our chimeric channel indicates that the channel is indeed affected by the lipid composition of its local environment. This could be due to local depletion of cAMP concentration in the vicinity of the nanodiscs due to charge repulsions encountered in anionic bilayers. To test this hypothesis, we're looking into incorporating the channel into other cationic and neutral lipids: Increasing the salt concentration of the ITC buffer could further screen the negative charges in POPG bilayers and thus lead to less repulsion of cAMP. Additionally, other research groups have began to acquired detailed electrophysiology data of ion channel activities inlipid bilayers of lipid composition. Moving forward, we could conduct experiments to observe how this change in affinity for cAMP translates to channel activity (Faure ,2014).

4

A DUAL FUNCTION TMEM16 HOMOLOGUE IS A Ca^{2+}- DEPENDENT ION CHANNEL AND A PHOSPHOLIPID SCRAMBLASE

Mattia Malvezzi[1,2], Madhavan Chalat[3], Radmila Janjusevic[1], Alessandra Picollo[1], Hiroyuki Terashima[4], Anant Menon[3], and Alessio Accardi[1,2,3]

[1]Department of Anesthesiology, [2]Department of Physiology and Biophysics, [3]Department of Biochemistry, [4]Osaka University (JAPAN)

Abstract: Ca2+-dependent phospholipid scramblases collapse the plasma membrane lipid asymmetry, externalizing phosphatidylserine and triggering blood coagulation. Externalization of phosphatidylserine is also a mark of apoptotic cells ready for phagocytic clearance. The molecular identity of the phospholipid scramblases has eluded researchers for decades. Recently TMEM16F, a cation-selective member of the TMEM16 family of Ca2+-gated channels, was shown to be critical for scrambling. Mutations in TMEM16F cause Scott syndrome, a bleeding disorder associated with defective lipid scrambling in platelets, and deletion of the TMEM16F gene in mice leads to uncontrolled bleeding and impaired scrambling. It is controversial whether TMEM16F itself is the long awaited phospholipid scramblase or a channel regulating scrambling. To resolve this controversy we screened different TMEM16 homologues for over-expression, purification and functional reconstitution purposes. Here we show that a purified TMEM16 homologue from Aspergillus fumigatus, afTMEM16, has two transport functions: it is a Ca2+-gated channel and a Ca2+-dependent scramblase. Two other TMEM16 homologues, including the Ca2+-activated Cl- channel TMEM16A, do not mediate lipid transport. This suggests that the TMEM16 family has diverged into channels and dual function channels/scramblases. Remarkably, we find that a single Ca2+ site regulates separate transmembrane pathways for ions and lipids, as simultaneous charge-neutralization of two highly conserved acidic residues affects both ion and lipid movement. We propose that the spatial separation of the ion and lipid pathways underlies the evolutionary divergence, and suggest that other homologues, such as TMEM16F, might also be channels and scramblases. afTMEM16 is the first Ca2+-dependent lipid scramblase identified at the molecular level and its dual function opens intriguing scenarios on how a single protein is able to directly couple Ca2+, membrane and electrical signaling.

5

PURIFICATION AND CHARACTERIZATION OF CLC-mt1: A CHLORIDE CHANNEL FOR CRITICAL FOR *MYOBACTERIUM TUBERCULOSIS* HOST COLONIZATION

Malvin Vien[1], Shumin Tan[4], Neelima Sukumar[4], David G. Russell[4], and Alessio Accardi[1,2,3]

[1]Weill Cornell Medical College, Department of Anesthesiology, New York, NY USA, [2]Weill Cornell Medical College, Department of Physiology and Biophysics, New York, NY USA, [3]Weill Cornell Medical College, Department of Biochemistry, New York, NY USA, [4]Cornell University, College of Veterinary Medicine, Department of Microbiology and Immunology, Ithaca, NY USA

Abstract: The macrophage serves as a primary host cell during My-cobacterium tuberculosis (Mtb) infection. The successful colonization by Mtb requires that the bacterium senses and responds to intraphagosomal signals. It has been previ-ously shown that chloride concentration ([Cl-]) and pH are inversely correlated during phagosome maturation, and that Cl-, like pH, can act as an environmental cue for Mtb, with the bacterium responding to these signals both in vitro and in vivo. Here, we identify CLC-mt1 as encoding a ClC channel in Mtb that is critical for successful colonization of its host cell. Futhermore, with biochemical and physiological character-ization of purified ClC-mt1 we show that the channel is able to mediate Cl- transport in a pH-dependent manner withou H+ antiport. Activity levels of purified ClC-mt1 could further be modulated by site-directed mutagenesis of key residues. These results are a first indication of the importance of Cl- sensing and/or the maintenance of Cl- homeostasis during Mtb's colonization of its host, and illustrate an important biological role of a ClC Cl-channel for a bacterium in the context of infection.

6

VOLATILE ANESTHETICS INHIBT VOLTAGE-GATED SODIUM CHANNELS DIRECTLY WITHOUT ALTERING BULK LIPID BILAYER PROPERTIES

Karl F. Herold[1], William Lee[1], R. Lea Sanford[3], Olaf S. Andersen[3], Hugh C. Hemmings Jr.[1,2]

Departments of Anesthesiology[1], Pharmacology[2], and Physiology, Biophysics and Systems Biology[3]. Weill Cornell Medical College, New York, NY

Introduction: General anesthetics were introduced over 160 years ago, but our understanding of their molecular mechanisms remains incomplete. Recent studies indicate that anesthetics can interact directly with transmembrane ion channels, but indirect effects mediated through the lipid bilayer have not been ruled out. To address this question, we examined how the fluorobenzene (FB) model anesthetics alter the function of voltage-gated sodium channels (Na_v), which are one of the classes of ion channels that are inhibited by anesthetics.

Design: We compared the effects of hour FB anesthetics and the clinically sued volatile anesthetic isoflurane on Na_v function with their ability to alter bulk lipid bilayer properties, as sensed by a bilayer-spanning reporter channel. We also examined the bilayer-perturbing effects of a range of other anesthetics (diethyl ether, desflurane, sevoflurane, halothane, chloroform, cyclopropane, F3, F5, flurothyl, ketamine, etomidate, and propofol).

Methods: Effects on Na_v function were tested using whole-cell voltage-clamp electrophysiology on mammalian neuronal cells (ND7/23). Effects on lipid bilayer properties were tested using a gramicidin channel-based stopped flow fluorescence assay for lipid bilayer perturbation.

Results: At clinically relevant concentrations, equivalent to 1 MAC (minimum alveolar concentration), the FBs and isoflurane significantly and reversibly inhibited peak Na^+ current ($/_{Na}$). None of the model FB or other anesthetics affected lipid bilayer properties at 1 MAC. Even at supra-therapeutic concentrations (2 and 4 times MAC), only minimal bilayer effects were observed.

Conclusions: Our results show that general anesthetics *do not* alter lipid bilayer properties at clinically relevant concentrations, where they produce large changes in Na_v function. They do alter bilayer properties at higher concentration, which highlight the importance of choosing appropriate physiological concentrations for studies involving general anesthetics to avoid nonspecific effects mediated by perturbations of lipid bilayer properties. We conclude that the anesthetics tested exert their actions by interacting directly with membrane proteins, such as Na_v.

7

RECOVERY OF CONSCIOUSNESS FROM ISOFLURANE ANESTHESIA IS MEDIATED BY A STRUCTURED NETWORK OF DISCRETE INTERMEDIATE BRAIN STATES

A. Hudson, D.P. Calderon, D.W. Pfaff, A. Proekt

Introduction: How does the brain transverse the vast space of potential neuronal activity states to recover those compatible with consciousness after a gross perturbation? There are several distinct possibilities. The simplest possibility is that the trajectory is a random walk through the parameter space. Another possible trajectory is a smooth directed path towards the region in the parameter space compatible with consciousness. Finally, it is possible that en route to recovery, brain activity abruptly jumps between several distinct individually stabilized intermediate states. To distinguish among these possibilities, we analyzed cortico-thalamic local field potentials (LFPs) recorded from rats during recovery of consciousness from isoflurane anesthesia. The titratability of isoflurane allowed us to parametrically perturb ongoing brain dynamics. Our results suggest that, en route to recovery, brain activity is confined to a low dimensional subspace defined by characteristic spectral signatures of the LFPs. Futhermore, differences between states are associated with changes in the global coherence among multiple cortical and thalamic electrodes. Within this subspace, spectral characteristics of the LFPs cluster into discrete metastable states that persist for minutes. Transitions between these metastable states are structured such that some states from "hubs" that connect groups of otherwise disconnected "spur" states. This, this network architecture suggests that the brain must pass through one or more of the hub states to reach wakefulness. These observations begin to characterize the intrinsic dynamics that allow recovery of the consciousness from a large perturbation resulting in loss of consciousness and characterized by burst suppression.

Methods: Adult Sprague Dawley rats were anesthetized with isoflurane. A single dose of SC flunixin was administered. A craniotomy was made over thalamus, the wound edge infiltrated with local anesthetic, and earbars were withdrawn after the skull was fixed to the stereotaxic frame. The animal was taken through a slow stepwise decrease in inhaled anesthetic concentration until purposeful limb or tail movement. The delivered anesthetic concentration then increased to 1.5%. Animals spontaneously ventilated throughout. Respiratory rates (determined via QRS modulation) were not significantly altered by anesthetic concentration ($p=0.83$, repeated measures ANOVA).

We recorded wideband (0.2Hz-20 KHz) cortical and thalamic activity with a custom 24 channel microarray (Alpha Omega, Alpharetta, GA) via a commercial multichannel op-app system (Plexon, Dallas, TX). Local field potentials (LFPs) were extracted (acausal 4^{th} order Butterworth filter, 500Hz low pass). Evolving spectral activity was determined with the Thomson multi-taper method, using 17 tapers on a sliding 60s window (frequency resolution 0.15Hz). The mean power at ach frequency was subtracted to examine variations in powers over time Global Coherence was calculated following Mitra and Bokil. The global coherence estimate is the ratio of the largest singular valve of the SVD to the sum of all singular values of the cross spectral matrix. The spatial eigenmode then indicates the contribution of particular channels to the coherence estimate.

8

CALCIUUM-DEPENDENT GATING IN MthK K^+ CHANNELS OCCURS AT THE SELECTIVITY FILTER

David J. Posson, Radda Rusinova, Olaf S. Andersen, Crina M. Nimigean

Dept. of Physiology and Biophysics and Dept. of Anesthesiology Weill Cornell Medical College, New York, NY

Project Summary: Does Ca^{2+} regulate the K^+ conductance of MthK by opening a tight gate (the 'bundle crossing') near the intracellular entryway into the channel? Here we provide evidence that such a tight closure likely does not occur by measuring closed-state channel block by quaternary ammonium compounds using a stopped-flow-based Tl^+-flux assay with MthK prteoliposomes. The results support a model where Ca^{2+} ions alter the channel conformation at the entryway while also opening a gate at the selectivity filter.

Ca^{2+} - DEPENDENT PHOSPHOLIPID SCRAMBLING BY A RECONSITUTUED TMEM16 ION CHANNEL

Mattia Malvezzi[1,2], Madhavan Chalat[3], Radmila Janjusevic[1], Alessandra Picollo[1], Hiroyuki Terashima[4], Anant Menon[3], and Alessio Accardi[1,2,3]

Weill Cornell Graduate School of the Medical Sciences and Weill Cornell Medical College, New York, NY

[1]Dept. Of Anesthesiology, [2]Dept. of Physiology and Biophysics, [3]Dept. of Biochemistry, [4]Osaka Univ. (Japan)

Abstract: Phospholipid scramblases collapse the plasma membrane lipid asymmetry, externalizing phosphatidylserine to trigger blood coagulation and mark apoptotic cells. Despite their importance in cell physiology, the molecular identity of the scramblases has eluded researchers for decades. TMEM16F, a member of the TMEM16 family of Ca2+-gated channels, has been shown to be involved in lipid scrambling. The function of TMEM16F remains controversial, as it has been also reported to be a Ca2+-dependent cation channel and three different Cl- channels. Two other members of the TMEM16 family, TMEM16 A and B, are Ca2+-activated Cl- channels and they do not seem to be involved in lipid scrambling. Whether TMEM16F, and possibly other members of the family, are phospholipid scramblases or ion channels that regulate scrambling activity remains unclear. To differentiate between these hypotheses we expressed, purified and reconstituted several TMEM16 family members and discovered that purified afTMEM16, from Aspergillus fumigatus, is a dual-function protein: it is a Ca2+-gated channel, with characteristics of other TMEM16 homologues, and a Ca2+-dependent scramblase, with the expected properties of mammalian phospholipid scramblases. Remarkably, we find that a single Ca2+ site, conserved among the TMEM16 homologues, regulates separate transmembrane pathways for ions and lipids. Two other purified TMEM16 -channel homologues do not mediate scrambling, suggesting that the family diverged into channels and channel/scramblases. Our results demonstrate for the first time that a member of the TMEM16 family is simultaneously a Ca2+dependent ion channel and a Ca2+ dependent lipid scramblase. We propose that the spatial separation of the ion and lipid pathways underlies the evolutionary divergence of the TMEM16 family, and that other homologues, such as TMEM16F, might also be dual-function channel/scramblases.

A MULTISTATE ANALYSIS OF READMISSION FOR INVASIVE CARDIAC SURGERIES

Zachary A. Turnball[1], Natalia S. Ivascu[1], Gregory P. Giambrone[1], Xian Wu[2], Licia Gaber-Baylis[1], Elizabeth Lemoine[1], Jonathan M. Eskreis-Winkler[1], Akshay U. Bhat[3], Ramin Zabih[3], Peter M. Fleischut[1]

[1]Department of Anesthesiology, New York-Presbyterian/Weill Cornell Medical College, New York, NY, [2]Department of Healthcare and Policy and Research, Division of biostatics and Epidemiology, Weill Cornell Medical College, New York, NY, [3]Cornell University, Ithaca, NY

Background: With the ever-growing focus on pay for performance, readmission has become an important metric in quality care. Prevention of readmission is an opportunity to maximize patient outcomes and minimize lost revenue.

Objective: We sought to examine the frequency and determinants of 30-day and 90-day readmission after cardiac surgery.

Methods: Analyzed the State Inpatient Databases (SID) from 2007-2011 in CA, FL and NY. Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality Created 7 mutually exclusive groups of cardiac surgeries. Groups: Coronary Artery Bypass Graft (CABG); Aortic Valve Surgeries (AVS); Mitral Valve Surgeries (MVS); AVS/CABG; MVS/CABG; AVS/MVS; AVS/MVS/CABG. Outcome: 30-day and 90-day readmission
Variables of interest: Length of stay (LOS) [low, medium, high]; Hospital [very low, low, medium, high, and very high]; discharge disposition; payer. Multivariable logistic regression analyses were performed

Results: 263,333 discharges met inclusion criteria CABG = 64%; AVS = 14%; MVS = 8%; AVS/CABG = 9%; MVS/CABG = 3%; AVS/MVS = 2%; AVS/MVS/CABG = 1% AVS/MVS/CABG had the highest readmission rate (27%). AVS had the lowest readmission rate (18%). LOS is a significant predictor of 30-day readmissions across all surgical group models, except AVS/CABG. Analyses of 90-day readmission yielded similar results.

Conclusions: Longer LOS increased odds of readmission. The significance of insurance type & discharge disposition for individual procedures remains uncertain. Hospital volume was not found to play a significant role in readmission among most groups. The current study assessed all cause readmission & did not evaluate if readmission was related to the procedures of interest. Further investigation is needed to analyze additional contributory factors.

11

INCIDENCE AND IMPLICATIONS OF RE-INTUBATION AFTER CARDAIC SURGERY

Zachary A Turnball[1], Natalia S. Ivascu[1], Gregory P. Giambrone[1], Jonathan M. Eskreis-Winkler[1], Akshay U. Bhat[2], Ramin Zabih[2], Peter M. Fleischut[1]

[1]Department of Anesthesiology, New York-Presbyterian/Weill Cornell Medical College, New York, NY, [2]Cornell University, Ithaca, NY

Background: Re-intubation, after cardiac surgery can significantly effect a patient's hospital length of stay (LOS).

Objective: Examine the incidence of re-intubation after cardiac surgery to determine predictive patient characteristics. Secondary endpoints included the effect on hospitalization & discharge

Methods: Population: Patients undergoing aortic valve replacement, mitral valve replacement, coronary artery bypass, or a combination, between 2007 & 2011 in NY, FL, and CA. State Inpatient Databases, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality Comparison of group outcomes: In-hospital mortality, LOS. Additional variables of interest: Age, Deyo Index, post-operative complications.

Results: 266,585 patients underwent cardiac surgery [Table 1] 6.3% required re-intubation postoperatively. Re-intubation records increased in-hospital mortality (16.0% vs. 1.0%, $p<0.0001$) and prolonged LOS (17 days vs. 8 days, $p<0.0001$) [Table1] Of patients requiring re-intubation, 66.9% were >65 years old. Re-intubated patients had a higher Deyo Index ($p <.0001$) & a higher frequency of all complications analyzed [Table 2]

Conclusions: Re-intubation is an important risk factor for increased morbidity and mortality, and prolonged LOS. Post-operative re-intubation can occur for many reasons. Has a significant prognostic impact on overall outcomes. Further investigation is needed to determine which cardiac procedures have the highest likelihood of postoperative re-intubation and comorbid risk factors. SID has important limitations, further analyses are necessary to identify additional contributory factors

12

VASOPRESSIN FOR POST-INDUCTION HYPOTENSION REFRACTORY TO CATECHOLAMINES

Klaus Kjaer, MD

Department of Anesthesiology, Weill Cornell Medical College, New York, NY

Case: A 60 year-old presented for breast reconstruction under general anesthesia. She had no history of cardiovascular disease. Her weight was 113 kg, height 165 cm, and BMI 41.5. Her medications included losartan/hydrochlorothiazide (Hyzaar) 100/25 mg, which she did not take on the morning of surgery and had been taking at the time of two previous uneventful surgeries. She was NPO.

Intraoperative Course: Prior to induction, the patient received 700 mL Lactated Ringer's solution and has an immediate pre-induction blood pressure of 140/70 and pulse of 90. Induction at 13:20 pm was with midazolam 2 mg, fentanyl 200 mcg, lidocaine 80 mg, propofol 180 mg, and succinylcholine 120 mg. Intubation was easy with a McGrath 3 video laryngoscope. Following induction, she became hypotensive to a blood pressure of 60/30. Due to the temporary unavailability of ephedrine, phenylephrine boluses (400 mcg) and the epinephrine boluses (72 mcg) were given over the next 30 min in an attempt to restore blood pressure. The blood pressure briefly returned to 105/60, but then fell again to 58/26. The patient was on less than one MAC of volatile anesthetic agent during this time, and there was no evidence of anaphylaxis. ECG and ETCO2 were normal at all times. Eventually, phenylephrine infusion at 80 mcg/min was started at 13:58 and vasopressin 1 unit was given at 13:59. This successfully restored blood pressure to 135/80. The effect lasted approximately 30 minutes, after which hypotension refractory to epinephrine recurred. A second dose of vasopressin 1 unit was given at 14:37 with good response. The patient was extubated at 15:17. She had uneventful recovery with no post-operative complications.

Discussion: This case illustrates that vasopressin can be an effective intervention in the management of post-induction hypotension refractory to exogenous catecholamines. Having patients hold their dose of renin-angiotensin system antagonists on the day of surgery may not be adequate to prevent post-induction hypotension. Effective rescue interventions include intravenous fluids, phenylephrine, ephedrine, epinephrine, norepinephrine, vasopressin, and terlipressin (a precursor of lysine-vasopressin). Terlipressin 1 mg IV may be more effective than norepinephrine infusion at 0.1mcg/kg/min. Side effects of vasopressin and terlipressin may include decrease in cardiac index, decrease in gastric mucosal perfusion, and regional cerebral oxygen desaturation.

13

A NOVEL MODEL FOR GLOBAL HEALTH EDUCATION: INCORPERATING MEDICAL ANTHROPOLOGY INTO GLOBAL HEALTH TRAINING

Gunisha Kaur, M.D[1], Eric Brumberger, M.D[1]
Department of Anesthesiology[1], Weill Cornell Medical College, New York, NY

Overview: The current scope of global health work is limited and its paradigm has been constrained by a separation of concrete clinical patient care and the abstract concepts of how medical anthropology influences health and healthcare. Here we present an educational model that considers anthropological forces such as education, economics, and access to natural resources, which are intimately linked to health.

Our flagship training program is a global health elective based in Punjab, India that connects health care providers not only to individual patients, but also to communities, health care systems, and the anthropologic forces that permeate this region. With guidance from experts in both medical and global health education as well as activists on the ground, we created a rigorous curriculum that allows for physicians to both act as clinical practitioners in providing medical care to local Punjabis during the mornings, and receive on-the-ground global health training in the afternoons.

One educational module, for example, is dedicated to drug addiction and rehabilitation because in Punjab, substance abuse is a major cause of morbidity and mortality. The epidemic influences the practice of medicine as there is apprehension and avoidance of obtaining narcotics licenses even at major health care centers; this means that intra-operative and post-operative care is provided in the absence of opioid medications.

In and of itself, providing anesthesia for surgery without opioids is an educational and unique experience; to have the opportunity to understand the sociologic factors that influence this paradigm is significantly more powerful. In learning about such issues, physicians receive a pre-elective primer on the problem, are exposed to patients that suffer from substance abuse in the hospital, and then meet one of the leading addiction specialists in the state who takes them through the largest government rehabilitation facility. A visit to one of Punjab's most impoverished localities, Maqboolpura, where elective participants meet children of drug addicts in a school run by a non-profit organization, rounds out the experiential learning.

14

POPULATION-BASED TRENDS OF PANCREATICODUODENECTOMY: TEMPORAL AND AGE-RELATED OUTCOMES

Cheguevara Afaneh[1], Paul O'Mahoney[1], Gregory P. Giambrone[2], Jonathan Eskreis-Winkler[2], Akshay U. Bhat[3], Ramin Zabih[3], Fabrizio Michelassi[1], Peter M. Fleischut[2]
[1]Surgery & [2]Anesthesiology, New York-Presbyterian Hospital/Weill Cornell Medical center, New York, NY, [3]Cornell University, Ithaca, NY

Background: Pancreaticoduodenectomy (PD) remains a technically challenging procedure with significant morbidity and mortality. Medical and technological advancements have lead to an ageing patient-population and advanced disease associated with increasing technical challenges and taxing postoperative management. We report outcomes of PD across three major states over a 6-year period.

Endpoints: Our primary end-points were 30-day mortality and length of stay (LOS).

Materials and Methods: Using the State Inpatient Databases (SID), Healthcare Cost and Utilization Project (HCUP), Agency for Healthcare Research and Quality, we retrospectively reviewed the outcomes of all PDs performed from 2006 to 2011 in the states of California, Florida, and New York. Patient variables of interest included gender, age distribution, admission and disposition stratification, and payer distribution.

Conclusions: Mortality rates and LOS continue to improve following pancreaticoduodenectomy despite an increasingly ageing patient population. Mortality rates and LOS remain lowest for younger patients. The SID has important limitations; therefore, further analyses are necessary to identify the full impact of these findings.

15

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16

A THREE STATE ANALYSIS OF BARIATRIC PROCEDURES: TRENDS AND OUTCOMES

Cheguevara Afaneh[1], Gregory P. Giambrone[2], Jonathan Eskreis-Winkler[2], Akshay U. Bhat[3], Ramin Zabih[3], Gregory Dakin[1], Alfons Pomp[1], Peter M. Fleischut[2]

[1]Surgery & [2]Anesthesiology, New York-Presbyterian Hospital/Weill Cornell Medical center, New York, NY, [3]Cornell University, Ithaca, NY

Background: The popularity of bariatric surgery has continued to grow over the last decade. The safety and efficacy of bariatric surgery has been previously established. Nevertheless, trends as well as patient characteristics continue to evolve and change in bariatric surgery. We report trends and outcomes following bariatric surgery from 3 major states over a 6 year interval using the State Inpatient Databases (SID), Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality.

Methods and Materials: Using SID data from California, Florida, and New York, we retrospectively reviewed outcomes of all laparoscopic adjustable gastric bandings (LGB), laparoscopic sleeve gastrectomies (LSG), and laparoscopic roux-en-y gastric bypasses (LRYGB) performed on obese patients from 2006 to 2011. Discharges were analyzed by age & Deyo Comorbidity Index by procedure. Furthermore, morbidity and mortality rates were compared and reported.

Conclusions: Bariatric surgery remains safe and feasible. LSG is becoming more popular than LGB, especially for older patients with significantly more comorbidities; however, morbidity remains higher for LSG compared to LGB. The SID has important limitations; therefore, further analyses are necessary to identify the full impact of these findings.

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TOTAL INTRAVENOUS ANESTHESIA WITHOUT MUSCLE RELAXANT FOR LAPROSCOPIC DIAPHRAGMATIC PACEMAKER INSERTION IN A PATIENT WITH AMYOTROPIC LATERAL SCLEROSIS

Kevin J. Walsh, MD[§,*], Simin S. Frisk, MD[§]

Department of Anesthesiology[§], Weill Cornell Medical College

Introduction: ALS is a progressive neuromuscular disease of unknown etiology characterized by degeneration of upper and lower motor neurons, resulting in atrophy, weakness, and hyperreflexia. ALS affects about 30,000 people in the United States, and death usually results from hypercarbic respiratory failure. Direct diaphragm pacing stimulation (DPS) is a technique used to stimulate a patient's intra-abdominal phrenic nerves, in an attempt to produce and ultimately strengthen diaphragmatic contraction. Initially used in patients with spinal cord injuries, diaphragm pacing has demonstrated some benefit in patients with ALS.

Patient Presentation: A 39 year old female was admitted for diaphragmatic pacemaker implantation. Her weight was 43 kg and height 157 cm. She had a history of endometriosis previously treated with laparoscopic uterine cauterization and ALS diagnosed eight months prior to the present admission with dysarthria, dysphagia, generalized weakness and shortness of breath with minimal exertion. Preoperative evaluation demonstrated weakness, dysarthria, and difficulty moving independently. Vital signs and laboratory findings were within normal limits. She had a small mouth opening and airway examination revealed a Mallampati I classification. She was classified as an American Society of Anesthesiologists (ASA) class III physical status.

Intra-Operative Management: The pt. did not receive any preanesthetic medications. Standard monitors were applied and 60 mg lidocaine was administered to block injection pain. A remifentanil infusion was started at 0.03 mcg/kg/min. Anesthesia was induced with 200 mg of propofol in divided doses. She was not ventilated due to the increased aspiration risk, and her trachea was intubated with a 7 mm ID endotracheal tube. There was no movement on intubation. She was ventilated with 50% oxygen with a respiratory rate of 10 per minute, tidal volume of 7-10 ml/kg and PEEP of 4 cm H2O. Anesthesia was maintained with remifentanil (0.1-0.25 mcg/kg/min) and propofol (100-200 mcg/kg/min) infusions. There was no hemodynamic instability. Blood pressure was 85-110/50-70 with heart rate 50-75. She received no vasopressors and the procedure finished uneventfully. At the conclusion of the procedure the propofol and remifentanil infusions were discontinued, her oropharynx was suctioned and the back of the operating room table elevated. Her trachea was extubated after she regained consciousness and demonstrated adequate strength (hand grip, head lift and spontaneous unassisted tidal volume >5 ml/kg). She breathed spontaneously without any discomfort, was eventually discharged to the floor, remained comfortable with a normal oxygen saturation and was discharged home without complication.

Specific Concerns for Diaphragmatic Pacemaker Insertion:

- Capnothorax: signs include increased airway pressure, increased $EtCO_2$, hemodynamic instability and decreased O_2 saturation. Resolution is accelerated using PEEP and hyperventilation.
- Upper Airway Collapse: In patients with bulbar muscle weakness, negative airway pressure created by activation of the pacemaker can cause upper airway collapse.

Regional Anesthesia in ALS: Regional anesthesia including spinal and epidural is generally avoided in patients with motor neuron disease due to fear of disease exacerbation. Reports of successful use of epidurals with no evidence of disease exacerbation suggest epidural anesthesia may be useful in patients with ALS.

Conclusions: A useful strategy for anesthetizing patients with ALS includes:
minimizing the use of neuromuscular blockers, avoiding succinylcholine, optimizing time to awakening after surgery, use of short acting opioids and hypnotics, minimization of inhalational anesthetics at the conclusion of the procedure, avoidance of antiemetic medications with QT prolongation, infiltration of local anesthetic at incision sites, careful titration of long-acting opioids.

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Conclusions: A useful strategy for anesthetizing patients with ALS includes:

REPEAT CESAREAN DELIVERY UNDER GENERAL ANESTHESIA WITH BILATERAL TAP BLOCKS IN A PATIENT WITH TYPE IV OSTEOGENESIS IMPERFECTA

Jeremy Pick, MD[1], Milica Markovic, MD[1], Alaeldin Darwich, MD[1]

[1]Department of Anesthesiology, New York Presbyterian Hospital, Weill Cornell Medical College, New York, NY

Background: 22 yo F G4P1, 144cm and 44kg, with type IV osteogenesis imperfecta (OI) presented at 34 weeks with preterm labor. She was wheelchair bound, had severe scoliosis, and restrictive lung disease. Physical examination included a Mallampati class II airway, limited neck flexion with pectus excavitum and an inability to lie supine. Her PSH included bilateral femoral rod placement and a prior cesarean section (CS1) under general anesthesia (GA) with successful airway management using a C-MAC®. A dilaudid intravenous (IV) patient controlled analgesia (PCA) was used for post-op pain control.

Case Management (CS2): Endotracheal intubation was successfully managed with a McGrath® video laryngoscope. Transversus abdominal plane (TAP) block was performed under ultrasound guidance using 20mL of 0.25% bupivacaine with 5mg preservative free dexamethasone. A T5-T12 dermatome level sensory block was achieved. A dilaudid IV PCA was instituted as a supplemental pain control modality.

Results (CS2 v CS1): 20% less dilaudid utilized when a TAP block was performed in CS2. Patient reported much better pain control with use of bilateral TAP block in CS2. 38% fewer attempts made via IV PCA within first 12 hours of use after TAP block in CS2.

Conclusions: Anesthetic management of OI cases are complicated by difficulty with airway management and regional technique. We successfully managed a patient with two different forms of portable video laryngoscopy. Our patient benefitted from the use of TAP block as demonstrated by less dilaudid IV PCA use in comparison to her previous CS.

WEST AFRICAN EBOLA VIRUS RESPONSE PLAN: SINGLE-USE AIRWAY MANAGEMENT (UAMK) AND UNIT VASCULAR ACCESS (UVAK)

Jon Samuels, M.D[1], Nicholas Cavalieri, Cert. AT, NREMT-P[1]
Department of Anesthesiology[1], Weill Cornell Medical College, New York, NY

Introduction: On August 8, 2014, the World Health Organization declared the West African Ebola crisis a "public health emergency of international concern." Under the 2005 International Health Regulations (IHR), countries must implement national preparedness capacities, such as those seen in 2009 with influenza H1N1 and in 2014 with poliomyelitis. The Ebola epidemic has become the latest international public health concern requiring rapid development of procedures and policies necessitated by this infectious disease.

Features of Ideal Airway Devices for Highly Infectious Patients: Portable and disposable kits should be manufactured with one size for most adults at an affordable cost (under $1000). These kits will need to tolerate vibrations and extreme weather conditions during transport, operates on alkaline batteries, no use of chargers or electrical outlets, easy to operate with a short learning curve to deliver treatment more effectively, Intubation should be performed with no line of sight required at greatest distance from patient, eliminating the need to place hands within the oral cavity, intubation should allow adequate optics in presence of secretions, aspirate, or blood. The "Improved Channel" of King VisionTMhas the longest distance from laryngoscopistto patient. The J-curve facilitates tracheal tube advancement while the shorter channel allows for blade removal without the need for the operator's hands to be inside the oral cavity. The optical inlet and light source is distal for wider visual angle and a "fish eye" lens allows cleaning if secretions soil optical inlet.

Discussion: Of the 3 common Ebola virus disease (EVD) strains (Zaire, Sudan, and Bundibugyo), this most recent outbreak has been identified as a new strain of Zaire. Infection symptoms include fever, vomiting, diarrhea, and generalized bleeding as well as death with a reported fatality rate of 55%. Contraction of Ebola in humans occurs only through close contact with bodily fluids of those who are infected. Presently, there no vaccines or treatments for those who have either contracted the virus or for post-exposure prophylaxis. First response health care workers are at increased risk of contracting the virus. As of early August, 140 African health care workers have been infected during this epidemic, resulting in 80 deaths. Optimal clinical care involves intravenous access for fluids, antiviral and nutritional support, and airway management for highly infected patients. Personal protective equipment (PPE) and disposable kits should be utilized for vascular access and airway management. This equipment has to have the ability to be transported to third world countries and be used by local health care providers, including the first responders.

After examination of numerous airway devices and differing technologies, the following conclusions were reached: A single-use Macintosh laryngoscope should be included as back-up. Device technology should be simple and robust, such as an optical scope or optical light-emitting diode (OLED). Trained users of the device should have minimize need for "rescue devices". Insertion in a neutral neck position with minimal mouth opening is helpful in managing patients with difficult airways. Disadvantages of alternative devices considered:

- AirtraqOptical Disposable LaryngoscopeTM(*ProdolMeditec*, Vizcaya, Spain): Need to get close to device
- *GlideScope*TMVideolaryngoscope(Bothell, WA): Need to get close to the patient
- Unique LMA-FastrachTM(*Teleflex Medical*, San Diego, CA): Long learning curve, requires hands in mouth
- McGrath MAC VideolaryngoscopeTMAircraft MedicalTMSeries 5 (Edinburgh, United Kingdom): Expensive, fragile, scope gets soiled.

Conclusion: Single-use airway management and vascular access kits facilitate delivery of healthcare in third world countries with suboptimal environments. When providing critical care services to highly infectious patients, the safety of the healthcare worker must be prioritized. The King VisionTMappears to be an ideal airway device for healthcare management of patients infected with Ebola virus, maintaining protection for those delivering treatment.

HIGH STAKES ANESTHESIA IN THE AMBULATORY SETTING: ANESTHETIC MANAGEMENT AND IMPLICATIONS FOR COMPLETE DENTAL EXTRACTION IN A 57-YEAR-OLD PATIENT WITH MULTIPLE COMPLEX COMORBIDITIES

Rohan K. Panchamia, MD, Jon D. Samuels, MD, Daniel Garcia[§], PhD, Min-Hee Sur*, DMD
§ Weill Cornell Medical College, New York, NY *Dept. of Surgery, Division of Dentistry, Oral & Maxillofacial Surgery, Weill Cornell Medical College, New York, NY

Introduction: Dental procedures are performed under general anesthesia for certain patients and clinical situations in which local anesthesia is not an option. A frail middle-age woman with multiple comorbidities, notably multi-valvular insufficiency and severe asthma, was scheduled to undergo extraction of 20 remaining teeth in anticipation of quadruple valve intervention. Preoperative dental exam revealed generalized gross caries of remaining dentition, multiple fractured teeth, and generalized chronic periodontitis. Per TEE, she had severe valvular MR and moderate AS/AR/PR/PS/TR with resulting biventricular failure and WHO group II severe pulmonary hypertension. Her asthma was classified as severe persistent, interfering with daily activities secondary to increased work of breathing. She was intubated several times in the past for asthma exacerbations. CT chest without contrast showed marled enlargement of the main pulmonary artery and mild dilatation of the ascending aorta, as well as diffuse ground-glass opacities and pulmonary nodules. Most recent PFTs were significant for FEV1 L (29%), $FEF_{25-75\%}$ 0.51 L (23%), and DLCO 50% predicted.

Case Details: Comprehensive airway evaluation revealed a Mallampati class 4 airway along with decreased thyromental and inter-incisor distances.Pre-induction radial arterial line was inserted for hemodynamic monitoring and frequent arterial blood gases. Induced with 3 µg/kg of fentanyl , lidocaine 2 mg/kg, and etomidate 0.2 mg/kg; cisatracurium was given for skeletal muscle relaxation only after mask ventilation was established. Gentle laryngoscopy with the indirect optical laryngoscope Airtraq™ was successfully performed with insertion of oral 6.5 ETT. Physiological stability was maintained with a low dose infusion of phenylephrine and periodic administration of glycopyrrolate.Ventilation parameters incorporated a high FiO2, RR titrated to mild hypocapnia, optimum level of PEEP, reasonable tidal volume, and allowed for adequate time in expiration. Arterial blood gases were unremarkable for acidosis, hypercarbia, hypoxia, or electrolyte abnormalities. In all, the operative course, including extubation, was uneventful.

Discussion: We selected general anesthesia as our surgical anesthetic for two main reasons: 1. the patient's inability to tolerate procedural sedation in the past, and 2. her multiple comorbidities.Perioperative goals in the management of pulmonary HTN:
Ventilation strategy that avoids atelectasis or hyperinflation, Maintaining SR and RV coronary perfusion; preventing RV under filling or overdistension, and Avoidance of stressors, such as hypoxemia, hypercapnia, acidosis, pain, and anxiety.

In patients with MR, forward flow can achieved with a vasopressor +/- inotropic agent. Bradycardia and/or a high afterload can lead to exacerbations in volume overload.Risk of pulmonary complications is greater in asthmatics with recent exacerbations, prior postoperative pulmonary complications, recent hospitalizations, or intubations for asthma. Airway instrumentation may lead to life-threatening bronchospasm, which may be prevented with the use of agents that suppress airway reflexes (opioids), cause bronchodilation (sevoflurane), and avoid reflex bronchospasm (LTA). A carefully crafted general anesthetic plan, without the use of invasive monitoring techniques, was successfully performed.

AN INTERDISCIPLINARY APPROACH TO IMPROVING HAND HYGIENE: GREENBERG 3RD FLOOR RECOVERY

A. Schuyler Alsop, RN, BSN, PCCN; Zachary A. Turnball, MD; Susan L. Faggiani, RN, BA, CPHQ

Background: Healthcare workers' hands are the most common source of transmission of healthcare-associated pathogens. Hand hygiene is the easiest and most effective way of preventing hospital acquired infections.

Literature Review: Studies have shown the effectiveness of a multimodal approach to improving hand hygiene compliance.1Interventions such as signage, education, incentives, changing dispenser locations, and creating a culture of safety and accountability have all been shown to be effective ways of improving hand hygiene compliance at other institutions.

Problem:

PACU hand hygiene scores for the 1stquarter of 2014 ranged from 76 to 82%, which was well below the hospital goal of 98%.

The Department of Anesthesiology also had scores well below the hospital goal for hand hygiene, with one of the lowest compliance rates of any physician-based department in the hospital.

Creating A Culture Change: The most significant intervention, and principal change in culture, involved peer-to-peer accountability. Both nurses and physicians consistently reminded one another about hand hygiene before and after patient contact. Nurses were welcomed to remind residents, fellows and attendings, in a professional manner, of the importance of hand hygiene, and vice-versa, creating a powerful culture.

Goals: Increase PACU compliance to greater than 90%

Increase Department of Anesthesiology compliance to greater than 90%

Create a culture of safety where all staff were encouraged to work together to improve patient care

Strategies:

Increased signage to reinforce hand hygiene:

Held educational meetings with all perioperative staff

Did a walkthrough, with Epidemiology and Environmental Services, maximized workflow, optimized Purell dispenser locations, and highlighted other obstacles to compliance.

Gave Anesthesiology residents their own individual Purell bottles.

Incentivized staff for collaborative scores greater than 90%

Notified the Housestaff Quality Council© representatives from the surgical services about the shared initiative to maximize efforts to improve hand hygiene

Outcomes: Nursing compliance increased to well above the 90% goal, reaching 100% compliance
within the first month. By June 2014, the Department of Anesthesiology had surpassed their goal of 90% compliance for the month.

Next Steps: Sustain the culture change by continued perioperative collaboration and Continue monthly re-evaluations.

CROSSOVER STUDIES IN MONKEYS SUGGESTS THAT THE NEW ULTRA-SHORT ACTING NONDEPOLARIZER, CW 1759-50, IN CONTRAST WITH GANTAXURIUM, HAS DIRECT CIRCULATORY MECHANISMS AND ELICITS NO HISTAMINOID PHENOMENA

John J. Savarese, MD[§], Matthew R. Belmont, MD[§], Hiroshi Sunaga[§], MD, Matthew T. Murrell, MD, PhD[§], Jeff McGilvra, PhD[*], Paul M. Heerdt MD, PhD[§], Jaideep Malhotra, MD[§], Erin Jeannotte, V[#], Jingwei Zhang, BS[§], Bryce Petty, BA[§]

[§]Dept. of Anesthesiology, Weill Cornell Medical College, New York, NY. [#]Albany Medical College, Albany, NY, [*]Cederburg Hauser Pharm, Inc.

Introduction: The Weill Cornell NMB Development Program has sought to reduce the side-effect profile of Gantacurium (GW 280430A, AV 430A) with respect to histaminoid phenomena. CW 1759-50 has been chosen as a candidate compound.

Methods: With IACUC approval, severn animals weighing 9-18kg, known to show increasing dose-related histaminoid phenomena to gantacurium, were selected for a crossover comparison with CW 1759-50 under isoflurane (1.2-2.0%) and N_2O/O_2 (70:30). Ventilation was controlled at 20 BPM. SpO2 and T were maintained between 96-100% and 99-101.5°F. Twitch, TOF, BP, and HR were recorded continuously. Gantacurium or CW 1759-50 (2.0-4.0 mg/kg, or 30 to 80x ED95) were given as the "first dose of the day". One data point per day therefore was obtained from each experiment. Animals were studied at 4-6 week intervals.

Dose-response curves for MAP and HR were constructed. Facial flushing was evaluated. Tachyphylaxis: Two (1759-50) or three (gantacurium) doses of 3.0 mg/kg of each compound were given at 15 minute intervals to ascertain whether MAP, HR, and skin changes decreased during sequential dosing. $H_1 + H_2$ prophylaxis: Diphenhydramine 5 mg/kg and ranitidine, 5 mg/kg were given 30 min prior to dosing with the NMBS. Changes in MAP and HR and presence of facial flushing following doses of 3.0 mg/kg of each NMB were compared with data from experiments where prophylaxis was not given.

Results: Gantacurium caused increasing tachycardia, hypotension, and facial flushing as dosage increased from 2.0-4.0 mg/kg. Three successive doses of gantacurium 3.0 mg/kg resulted in marked tachyphylaxis to MAP decrease and HR increase MAP decrease, HR increase and facial flushing were abolished by H1 + H2 prophylaxis. CW 1759-50 caused gradual reductions of both MAP and HR over the dose range 2.0-4.0 mg/kg. MAP reduction developed slowly, peaking in 3-5 min, in contrast with gantacurium, where MAP decrease was sudden and followed by a sudden increase in HR. Tachyphylaxis did not occur. Repetitive dosing caused HR and MAP changes which were qualitatively similar, and the peak changes did not differ significantly. Antihistamine prophylaxis had no effect on circulatory changes. Facial flushing did not occur. There was no relation of HR to dose of 1759-50.

Conclusion: Development of tachyphylaxis and the effectiveness of antihistamine prophylaxis suggest an indirect mechanism, i.e. histamine release, for gantacurium. CW 1759-50 has lesser circulatory effects than gantacurium in the monkey. Lack of tachyphylaxis and failure of $H_1 + H_2$ prophylaxis suggest that CW 1759-50 does not cause histaminoid side effects at dosage up to 80 x ED 95(4.0 mg/kg) in the monkey. Additional unpublished data. [1,2] suggest that direct autonomic mechanisms, such as blockade of autonomic ganglia, may cause moderate decreases of blood pressure after 80xED95 of 1759-50.

INTRATHECAL CATHETER PLACEMENT & BEDSIDE FATE EXAM FOR MANAGEMENT OF HIP FRACTURE IN PATIENT WITH SAM PHYSIOLOGY

Daniel O'Neill, MD[§], ***Tiffany Tedore, MD***[§]
Department of Anesthesiology[§], *Weill Cornell Medical College, New York, NY*

Case Summary: A 101 year old woman with HTN, mitral regurgitation, known systolic anterior motion (SAM) physiology of the mitral valve presents for surgical correction of a right intertrochanteric femur fracture with a long-stem intramedullary femoral nail.**ROS**: Negative for dyspnea, fatigue, chest pain, palpitations, syncope/pre-syncope. **PMH:** Dobutatmine Stress Echo 1999/TTE 2005. Severe inducible SAM of mitral leaflets and moderate/severe MR, with increased LVOT velocity (3.9 m/s) consistent with severe subaortic gradient, EF 60-65% Medications: None, EKG: NSR 77, LAFB, +LVH, CXR: pulmonary edema, enlarged cardiac silhouette and small bilateral effusions, Physical exam notable for 3/6 holosystolic murmur at the left apex, radiating to axilla, Bedside FATE exam reveals hyperdynamic and under filled left ventricle.

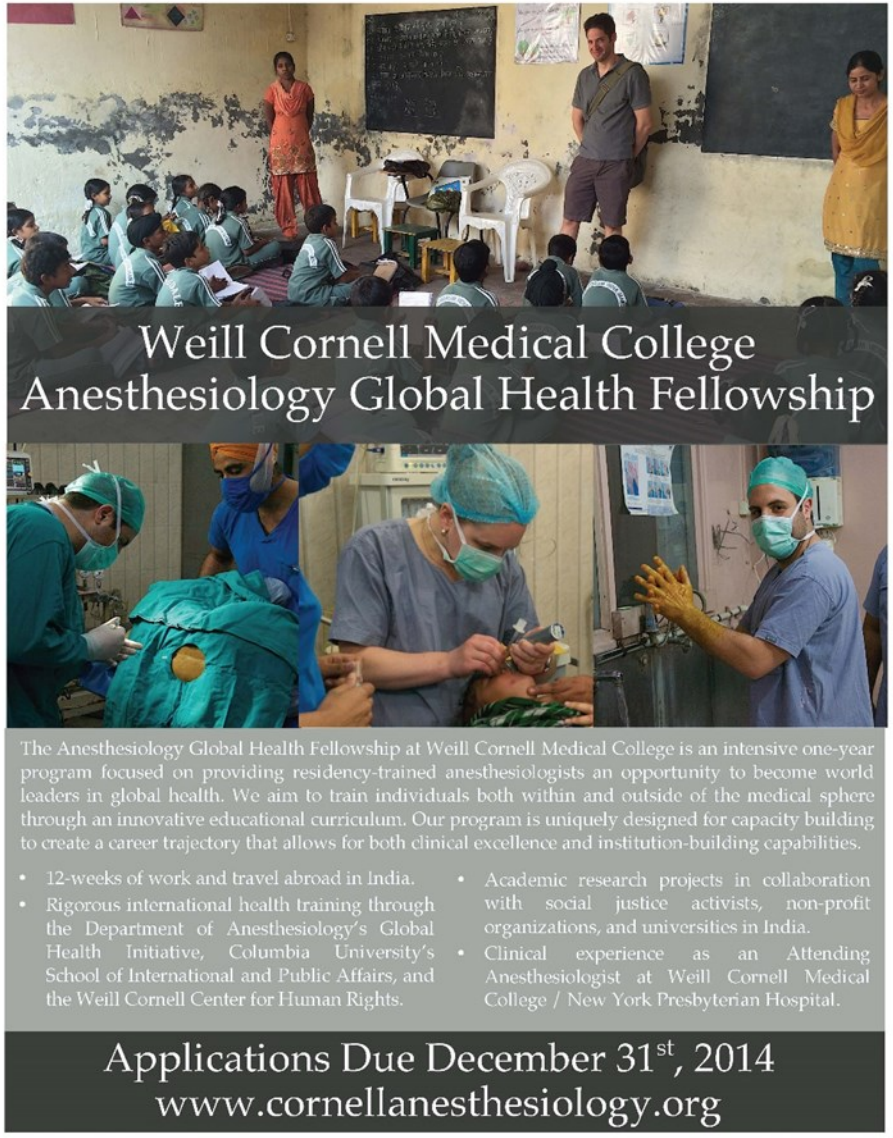
Focus Assessed Transthoracic Echocardiography (FATE): Truncated ultrasound cardiac examination ***–not meant to replace TTE***. Considered an ultrasound assisted extension of the physical exam. Prospective observational study –POC in pts>65yo scheduled for emergency non-cardiac surgery. Cardiac disease found in 75% of patients with a change in cardiac diagnosis in 67% and change in management in 44%(Canty, et al. 2012).

- Delay for cardiology referral
- Change in surgical technique
- Request for ICU care postoperatively
- Invasive monitoring
- Fluid management

Hypertropic Cardiomyopathy (HCM): HCM is a genetically determined heart muscle disease most often (60-70%) caused by mutations in one of several sarcomere genes encoding the contractile apparatus. Characterized by left ventricular hypertrophy (LVH) of various morphologies – ovoid, ellipsoid, cresentic. Left Ventricular Outflow Tract (LVOT) obstruction characteristically demonstrated by hyperdynamic LV function with a small (underfilled) LV cavity, and SAM of mitral leaflets, often associated with mitral regulation. Obstruction in 20-30% of patients with HCM and inducible obstruction in an additional 20-30%. Mechanism of obstruction-LVOT narrowed by a combination of septal hypertrophy and anterior displacement of the mitral valve. Inward movement of the interventricular septum during systole further narrows the LVOT, resulting in high LVOT blood velocities which pull the mitral valve leaflet toward the septum via the Venturi Effect. Precipiants- withdrawal of a beta blocker of CCB; decreased preload (dehydration, diuretics, acute blood loss); decreased afterload (vasodilation); arrhythmia (SVT, AF/flutter, sinus tachycardia).

Anesthetic Plan: Based on bedside FATE exam, patient received 500cc LR fluid bolus, Pre-induction arterial line and 2ndlarge bore PIV,Single shot femoral block to facilitate positioning & provide postoperative pain control, Intrathecal catheter incrementally dosed with 0.5cc of 0.5% bupivacaine to patient comfort and optimal hemodynamics, Minimal sedation with 25mcg fentanyl prn for discomfort/agitation Patient taken to OR, with uncomplicated surgical course. HR maintained between 60-90 bpm and SBP between 120-140 mmHg with a phenylephrine infusion at 10-50 mcg/min and x1 dose of esmolol10mg

Post Op Course:
IT catheter removed in OR and phenylephrine weaned off in PACU. Post-op EKG normal and patient asymptomatic; troponins peaked at 0.32 on POD 3. Formal repeat TTE noted concentric LVH with severe subaorticgradient and increased LVOT velocity (4.7 m/s) suggestive of HCM with normal global ventricular function. Patient was started on ASA and a statin and discharged to rehab POD 4.



27

ANESTHESIA FOR OPTHALMIC ARTERIAL CHEMOSURGERY FOR RETINOBLASTOMA: FIVE YEAR EXPERIENCE WITH SEVERE INTRA-OPERATIVE RESPIRATORY COMPLIANCE CHANGES

Meredith Kato[1], Nicole Green[1], Kelli O'Connell[1], Sean Till[1], Daniel J. Kramer[1], Mashael Al-Khelaifi[1], Jung Hee Han[1], Kane O. Pryor[1], Yves-Pierre Gobin[2], Alex Proekt[1]

Department of Anesthesiology[1], Department of Interventional Neuroradiology[2], Weill Cornell Medical College, NewYork-Presbyterian Hospital, New York City

Background: Ophthalmic arterial chemosurgery (OAC) is a powerful tool against retinoblastoma. OAC cases are associated with acute decreases in lung compliance. We investigated the incidence of severe respiratory compliance changes (SRCC) and short term outcomes in patients undergoing this procedure.

Methods: IRB approval was obtained. OAC patients between 9/2006 and 7/2013. Retrospective analysis of data collected from electronic anesthesia and medical records. Peak inspiratory pressures, positive end expiratory pressures, and tidal volumes collected at 15s intervals were analyzed and compliance ($\Delta V/\Delta P$) was determined. Three consecutive compliance values that were $\leq(\mu-2*\sigma)$ were identified. The magnitude of the change was the ratio of the peak to the mean of the 30 measurements prior to the change. Changes in compliance were plotted as a function of probability to assess their distribution and severity. Changes in end tidal CO2 and SpO2. corresponding to changes in compliance were extracted and plotted. Comparisons between groups were assessed with the X2 test or Fisher's exact test for categorical data. Continuous data were assessed with univariate logistic regression. Anesthesiologists were polled and their management strategies summarized.

Conclusions: Severe respiratory compliance reactions happen during OAC at a rate of 29.2% and 68% of patients have the reaction at some point during their multiple treatments. SRCC occurs at a predictable stage of the procedure and is self-limited. The reaction is more likely to happen on the second or subsequent procedure, but can happen on the first procedure in as many as 18.1%. No child in our series suffered morbidity, longer recovery room times, or was admitted as a result of SRCC. We conclude that anesthesia for this procedure can be safely administered to children. Fear of SRCC should not prevent children from being treated with OAC.

Results: 122 patients, 468 cases of OAC, mean 3.8 per child. Respiratory compliance changes fell into mild and severe groups, with severe meeting a minimum reduction in compliance of 40%.
Median onset was 750s , median duration was 90s. SRCC occurred in 136/468 cases (29%). 78/122 (68%) of children had SRCC at some point during their treatment. 18.1% of children had SRCC on their first exposure to the procedure, but this was poorly predictive of SRCC on subsequent procedures. Incidence of desaturation below 90% during SRCC was 0.199, that of a drop in EtCO2 by 30% or more was 0.343. No variables including age, weight, allergies or medical problems were significant with respect to SRCC. SRCC was not associated with longer recovery room times or admissions. All anesthesiologists increased FiO2 to 1.0 at the start of the case. 8/10 gave small boluses of 0.5-1 mcg/kg epinephrine at the first sign of decreased tidal volumes on pressure controlled ventilation.

28

MEDICALLY CHALLENGING CASE REPORT: BOWEL PERFORATION IN LABOR

Mary So, M.D., Klaus Kjaer, M.D

Department of Anesthesiology, Weill Cornell Medical College, New York, NY

Abstract: Acute abdominal pain in a pregnant patient can be challenging to evaluate. A wide range of etiologies can be the culprit and despite a thorough physical exam, blood work and even the use of imaging modalities it still may be difficult to pinpoint a diagnosis. Among the differentials, intestinal obstruction is a rare but dangerous diagnosis that cannot be overlooked. Delay or misdiagnosis of intestinal obstruction can lead to bowel perforation which poses significant maternal and fetal mortality.
We herein present a rare case of bowel perforation in a 33-year old gravida 1, para 0, woman at 37 weeks gestation with a history of ulcerative colitis who required emergent cesarean section and exploratory laparotomy under general anesthesia.

Case: A 33-year old gravida 1, para 0, woman at 37 weeks gestation with a history of ulcerative colitis (status post ileostomy) and three prior bowel obstructions during this pregnancy presented with crampy abdominal pain and no ostomy output for several hours. Physical exam was significant for a tense abdomen with guarding and diffuse abdominal pain. General surgery was consulted who recommended endoscopic decompression by gastroenterology (GI) and a chest x ray to rule out perforation. They agreed with the obstetrical team that the patient should undergo induction of labor (IOL) and be given a 12 hour trial of labor after decompression. The plan was to proceed with a cesarean section (C/S) if patient failed IOL. The anesthesiology team was consulted for pain/labor analgesia management. A lumbar epidural (L4/5) was placed since the initial plan coordinated between the obstetrical and general surgery team had been for IOL after endoscopic decompression. A chest x-ray to rule out free air under the diaphragm was negative. The gastroenterology team performed a limited endoscopic decompression and left a decompression foley through the ileostomy. The patient was then induced with pitocin and monitored for several hours with serial abdominal exams. However, the patient's pain became increasingly intense despite the epidural and her nausea worsened. The decision was made to bring the patient to the operating room for emergency cesarean section (C/S) under general anesthesia given history of extensive gastrointestinal pathology and possible need for airway protection. Upon arrival to the operating room, the patient developed bilious vomiting and a nasogastric tube was placed for gastric decompression prior to induction. The patient was preoxygenated with 100% oxygen and a rapid sequence induction was performed with succinylcholine and propofol. The patient was successfully intubated on the first attempt without aspiration and was maintained on desflurane for maintenance of anesthesia. A phenylephrine drip was started as the patient became hypotensive upon opening the abdomen. The obstetrical team found that the patient's bowel obstruction had perforated and worked quickly to extract the baby and called for general surgery to assist in an exploratory laparotomy. Eventually, the perforation was located and a small bowel resection was performed. The patient was successfully extubated at the end of the case and brought to the surgical intensive care unit for further monitoring. Both the mother and baby recovered well and were discharged a week later from the hospital to home.

Discussion: Bowel Perforation in labor is an exceedingly rare event; however, it poses significant risk to both the mother and fetus. The incidence of intestinal obstruction in pregnancy is about 1:66,000 deliveries and the incidence of bowel perforation is even less. It is important in patients with a history of prior abdominal surgery, intestinal obstruction, or inflammatory bowel disease to have a high index of suspicion for perforation. Special attention should be paid to the physical exam, keeping in mind that the location of abdominal pain may be altered by pregnancy and thus it is important to do serial exams. Any change in abdominal exam should be investigated further with ultrasound, abdominal x-ray or even magnetic resonance imaging studies.

Communication and early involvement of the different specialties such as general surgery, gastroenterology and anesthesiology by the obstetrical team is key. The management of these patients is complex and timing is crucial. Therefore it is essential to have scheduled multidisciplinary meetings to discuss the progress of the patient. Roles need to be delegated to different members of the multidisciplinary team in anticipation of both medical management and emergency surgical intervention.

POLYMYXIN –INDUCED RECURARIZATION REQUIRING POSTOPERATIVE REINTUBATION

Vikram Bhasin and Jon Samuels
Department of Anesthesiology, Weill Cornell Medical College, New York, NY

Introduction: Polymyxin antibiotics are effective against most gram-negative bacteria. Concerns regarding nephrotoxicity, neurotoxicity and neuromuscular weakness manifesting as respiratory distress have limited their use. The global problem of advancing antimicrobial resistance has led to a resurgence in their use

Case Presentation: 45-year-old male with a history of HTN, HL, right femoral vein DVT (s/p IVC filter insertion, on anticoagulation), cholecystitis (s/p cholecystectomy), admitted to the hospital with post-ERCP pancreatitis complicated by multiple polymicrobial abscesses. He was scheduled to undergo debridement of necrotic tissue to be done under general anesthesia. Prior drainage of one of the abscesses grew Klebsiella pneumonia, Enterococcus faecalis, and Candida. He was started on polymyxin, meropenam, and fluconazole, one week prior to the procedure.

In the operating room, immediately prior to surgery, he received his regularly scheduled doses of meropenam and polymyxin. His induction, intubation, and intraoperative course were uneventful. Prior to extubation he received full reversal with neostigmine 5mg, and atropine 1.8mg. A nerve stimulator showed 4 twitches with no visible fade after reversal. He was alert, oriented, following commands, and breathing spontaneously with good tidal volumes and was extubated. Two minutes after extubation he had difficulty breathing which was initially thought to be due to partial laryngospasm and resolved with positive ventilation. He was responsive and his vital signs remained stable, but he reported feeling weak and had discoordinated movements. The nerve twitch stimulator showed zero twitches indicating recurarization. He received neostigmine 2mg with atropine 0.6mg. Due to persistent need for positive pressure ventilation, he was re-intubated and transferred to the ICU and extubated a few hours later.

Discussion: The differential diagnosis for postoperative respiratory distress is very broad, but in this case, there was objective evidence that the patient had neuromuscular weakness after he had initially showed evidence of return of neuromuscular function. After reviewing his medications, it was deemed that the polymyxin most likely contributed to his recurarization. Although he had received polymyxin during his hospital course, this was the first time he had received it alongside a neuromuscular blocking agent.
Overall, the incidence of neuromuscular blockade with polymyxin use has been very low, but it has been noted that the incidence has decreased significantly when comparing data from 1962 to 1977 and 1995 to 2005.

PEDIATRIC MAGNETIC RESONANCE IMAGING WITHOUT AN ANESTHESIA MACHINE: AVOIDING TRIGGERS OF MALIGNANT HYPERTHERMIA WITH KETAMINE- A POTENTIAL TECHNIQUE FOR DEVELOPING NATIONS

Mohammad Piracha, M.D., Franklin Chiao, M.D
Department of Anesthesiology, Weill Cornell Medical College, New York, NY

Introduction: Pediatric patients often require sedation or general anesthesia to remain still for MRI scans. It is a standard of care to have an anesthesia machine available to provide general anesthesia particularly in the event of failed sedation. In developing nations, this can prove to be challenging as the cost for an anesthesia machine and MRI compatible machine can be over $100,000. Furthermore, for patients at risk for malignant hyperthermia (MH), placing an intravenous catheter in an awake patient may be challenging and stressful for the patient, parents, and physicians. We present an MRI case where an anesthesia machine was not required. This technique can also be used to avoid all triggers of MH. This technique could potentially be used in developing nations where an anesthesia machine is too costly to purchase.
Malignant hyperthermia is a life threatening disorder involving skeletal muscle via the release of calcium from the sarcoplasmic reticulum which leads to a cascade of hypermetabolism and has a mortality rate as high as a 70% .The release of the massive stores of calcium is mediated via the ryanodine receptor, the calcium-release channel of the sarcoplasmic reticulum. Genetic predisposition to malignant hyperthermia usually involves mutations in the genes that code for the ryanodine receptor$_1$.
Ketamine is a dissociative anesthetic and most importantly, preserves respiratory drive. Additionally, it is a bronchodilator, and avoids cardiovascular depression. It is a blocker of N-methyl-D-aspartate (NMDA) receptors and mu opioid receptors$_2$. These characteristics make ketamine a great option for analgesia, and anesthesia; particularly in children. It is not a trigger for malignant hyperthermia.

Case History: A 3 year old male child with an autism spectrum disorder (ASD) for evaluation of a neck mass presented for MRI. It has been estimated that 5% of ASD is secondary to definite mitochondrial disease and as a result extremely sensitive to general anesthesia$_3$. Recent studies have shown that patient with mitochondrial dysfunction may not be more prone to malignant hyperthermia; however; precautionary avoidance of malignant hyperthermia triggering agents is still practiced by many practitioners.

Case Plan: Options included an awake or sedated intravenous (IV) catheter placement. We believe an awake IV placement is a technique for cases where avoiding inhalational gas is desirable. This is associated with challenges though particularly in autistic patients, where limited cooperation and patient movement makes IV placement difficult.
An alternate anesthetic plan was performed. 45 minutes before the MRI, topical 2.5% lidocaine and 2.5% prilocaine was applied to hands, antecubital areas, feet and one shoulder. Ten minutes before MRI, 4mg/kg intramuscular ketamine was applied to the shoulder.
Adequate anesthesia was achieved and an intravenous catheter placement was successful performed without any movement. Additionally all utilization of inhalational anesthetic was completely avoided.

Conclusion: This case describes an alternative approach to an awake intravenous catheter placement in any pediatric patient at risk for malignant hyperthermia. We realize the potential for intramuscular injections in developing countries with limited resources and/or no anesthesia delivery system.