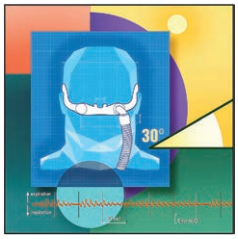
THIS MONTH IN
ANESTHESIOLOGY®



15 Combination Therapy of High-flow Nasal Cannula and Upper-body Elevation for Postoperative Sleep-disordered Breathing: Randomized Crossover Trial

Obstructive sleep apnea (OSA) is an independent risk factor for postoperative respiratory and cardiovascular complications. Continuous positive airway pressure therapy decreases OSA frequency but postoperative adherence is low in newly diagnosed OSA patients. Use of high-flow nasal cannula (HFNC) at a 20 l · min^{-1} flow rate improves the OSA severity of patients with mild to moderate OSA. Sleep in the upper-body elevation position decreases the apnea index by more than 50% in patients with moderate to severe OSA. The hypothesis that 30-degree head-of-bed elevation effectively improves the modified apnea hypopnea index based on the air flow signal (AHI-flow) was tested in a randomized crossover study of 19 patients with moderate to severe OSA receiving HFNC therapy during the first and second postoperative nights. The baseline mean ± SD AHI-flow of 60 ± 12 events · h^{-1} was reduced by 15 (95% CI, 6 to 30) events · h^{-1} with upper-body elevation, 11 (1 to 21) events · h^{-1} with HFNC therapy, and 23 (13 to 32) events · h^{-1} with combined upper-body elevation and HFNC therapy. *See the accompanying Editorial on* ***page 1****. (Summary: M. J. Avram. Image: A. Johnson, Vivo Visuals Studio.)*

28 Constrained Functional Connectivity Dynamics in Pediatric Surgical Patients Undergoing General Anesthesia

Functional connectivity, the statistical covariation between two brain signals, has been used to study neural activity across states of consciousness. Changes in functional connectivity discriminate between anesthetic-mediated changes in states of consciousness. The hypothesis that changes in functional connectivity patterns reflect anesthetic-induced changes in states of consciousness in the developing brain and that they would undergo dynamic shifts during the stable maintenance phase of general anesthesia as they do in adults was tested in a preplanned analysis of a previously reported study of 50 healthy 8- to 16-yr-old children undergoing surgery with general anesthesia. Cortical functional connectivity was estimated using weighted phase lag index, a measure of the phase synchronization of two signals. A cluster analysis method was used to identify dynamic changes in functional connectivity across the perioperative period. Changes in functional connectivity were associated with anesthetic state transitions across multiple regions and frequency bands, but functional connectivity changes in late childhood and early adolescence appeared stable rather than dynamic as they are in adults. *See the accompanying Editorial on* ***page 4****. (Summary: M. J. Avram. Image: J. P. Rathmell/A. Johnson, Vivo Visuals Studio.)*

41 Mechanical Power during General Anesthesia and Postoperative Respiratory Failure: A Multicenter Retrospective Cohort Study

Postoperative pulmonary complications predispose patients to respiratory failure and reintubation and are associated with increased postoperative mortality. Retrospective studies in mechanically ventilated patients suffering from acute respiratory distress syndrome reported higher mortality when a higher mechanical power was applied. Mechanical power is a concept that integrates ventilator-delivered inspiratory work (calculated from inspiratory pressures and tidal volume) and cyclic repetition (derived from respiratory rate) to estimate the energy delivered to the respiratory system and the lung in joules per minute. The hypothesis that higher mechanical power applied during intraoperative mechanical ventilation is associated with postoperative respiratory failure requiring reintubation was tested in a retrospective cohort study of 230,767 records of patients undergoing general anesthesia for noncardiac surgical procedures. Within 7 postoperative days, 2,024 (0.9%) patients required reintubation for respiratory failure. The median (interquartile range) intraoperative mechanical power in patients with postoperative respiratory failure was 7.7 (5.6 to 10.1) J · min^{-1} and that in those without respiratory failure was 6.6 (4.6 to 9.1) J · min^{-1}. *See the accompanying Editorial on* ***page 6****. (Summary: M. J. Avram. Image: J. P. Rathmell.)*

55 Personalized Surgical Transfusion Risk Prediction Using Machine Learning to Guide Preoperative Type and Screen Orders

Accurate estimation of the likelihood of surgical transfusion has implications for patient safety and cost. A common approach for estimating a patient's likelihood of transfusion is the procedure-specific transfusion rate, which does not consider patient-specific factors associated with an increased likelihood of transfusion. This study tested the hypothesis that a machine learning model incorporating both patient- and surgery-specific variables would provide better discrimination of transfusion risk across a diverse set of surgical procedures than a baseline model, which used only the historic procedure-specific transfusion rate. Four machine learning models trained on a large national cohort of surgical cases were developed to predict transfusion risk. Compared with a baseline model, the gradient boosting machine model had the best discriminative performance with the highest C-statistic and average precision. When tailored specifically to guide preoperative type and screen decision-making, the gradient boosting model required one-third fewer type and screen orders, while maintaining 96% sensitivity to detect transfusion, compared to the baseline model in both internal and external validation datasets. *See the accompanying Editorial on* ***page 9****. (Summary: M. J. Avram. Image: J. P. Rathmell.)*

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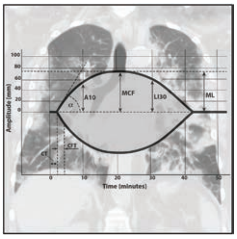
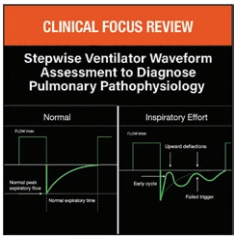


67 Suppression of Fibrinolysis and Hypercoagulability, Severity of Hypoxemia, and Mortality in COVID-19 Patients: A Retrospective Cohort Study

The coagulopathy produced by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection is marked by thrombotic events, especially in critically ill patients requiring life support measures in the intensive care unit (ICU). The hypothesis that severity of coagulopathy would be associated with worse clinical outcomes including acute respiratory distress syndrome (ARDS) severity, major thrombotic events, and mortality in patients requiring ICU-level care was tested in a prospective observational cohort study of 55 SARS-CoV-2–positive patients admitted to an ICU in 2020. Fifty-three (96%) patients required mechanical ventilation, 9 (16%) required extracorporeal membrane oxygenation (ECMO), 14 (25%) had clinically significant thrombotic events, and 13 (23%) died during hospitalization. Elevated plasminogen activator inhibitor 1 (PAI-1) concentrations were associated with severe ARDS. Patients experiencing a clinically significant thrombotic event had elevated PAI-1 and von Willebrand factor (vWF) concentrations and factor VIII activity despite prophylactic anticoagulation. Patients who survived their hospitalization were less likely to have higher concentrations of procoagulant acute phase reactants including microparticle bound tissue factor (MP-tissue factor). *See the accompanying Editorial on* ***page 13****.* *(Summary: M. J. Avram. Image: J. P. Rathmell.)*

81 Savoring Uncertainty (Classic Papers Revisited)

This Classic Paper Revisited is a brief account of the life and career of Thomas F. Hornbein, M.D., described in Wikipedia as "an American mountaineer" but perhaps better known in the anesthesia community for his research on the chemical control of breathing. Fascinated with mountains since his early teens, in medical school he explored the scientific literature on how humans adapt to high altitude. In his senior year he sought to discover whether the higher blood hemoglobin concentrations in high-altitude natives of Peru might explain why they breathed less vigorously than lowlanders acclimatized to the same high altitude. The resulting publication in the *Journal of Applied Physiology* in 1958 had one subject. As a National Institutes of Health–supported research trainee he studied whether diminished breathing with polycythemia could be explained by decreased discharge from peripheral chemoreceptors in a Classic Paper published in the *Journal of Neurophysiology* in 1961. He went on to serve as chairman of the Department of Anesthesiology at the University of Washington, where he helped shape anesthesia resident training. *(Summary: M. J. Avram. Image: From original article.)*



85 Stepwise Ventilator Waveform Assessment to Diagnose Pulmonary Pathophysiology (Clinical Focus Review)

Electronically displayed ventilator waveforms provide considerable insight into the physiology of the respiratory system. In the equation of motion, the pressure applied to the patient's respiratory system is the sum of ventilator pressure, a positive pressure, and the patient's respiratory muscle pressure, a negative pressure. The combination of these must overcome the patient's intrinsic resistance to flow, elastic response to volume, and retained positive end-expiratory pressure to deliver a ventilated breath. The equation of motion can be implemented at the bedside by assessing the flow and pressure waveforms over time in the context of patient and ventilatory activity. This Clinical Focus Review provides a stepwise approach that can be taken to diagnose pulmonary pathophysiology using ventilator waveforms in patients receiving pressure control ventilation or volume control ventilation assuming a one-compartment lung model with a linear response to a range of tidal volumes. *(Summary: M. J. Avram. Image: From original article.)*

93 Gut Microbiome in Anesthesiology and Pain Medicine (Review Article)

The human microbiome is a complex ecosystem that is constantly shaped by the host and its environment and plays critical roles in human health and disease. The microbiome is in a state of constant interaction with its host *via* a variety of mechanisms, including bidirectional interactions with the immune system and secretion of biologically active metabolites, which are only beginning to be understood. A growing body of evidence suggests an association between gut-microbiome compositional changes and a variety of clinical conditions in humans, although the association of specific microbiome compositions to a medical condition does not establish a causal relationship. Evidence regarding the causal role of gut bacteria, the mechanisms by which they exert their pathophysiologic effects, and the clinical applications of these observations is largely limited to studies in animal models. This review summarizes key findings in preclinical and clinical studies on the interaction of the gut microbiome with four distinct clinical domains, including effects of anesthetics and opioids on microbiome composition, postoperative outcomes, intensive care, and pain. *(Summary: M. J. Avram. Image: From original article.)*