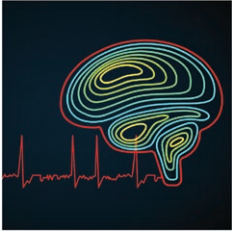


## Key Papers from the Most Recent Literature Relevant to Anesthesiologists



### Dexmedetomidine for reduction of atrial fibrillation and delirium after cardiac surgery (DECADE): A randomised placebo-controlled trial. *Lancet* 2020; 396:177–85. PMID: 32682483.

The sympatholytic, electrophysiologic, benzodiazepine and opioid sparing effects of dexmedetomidine have been speculated to influence the incidence of atrial fibrillation or delirium after cardiac surgery. The authors performed a randomized, placebo-controlled trial of dexmedetomidine in 798 patients undergoing cardiac surgery with cardiopulmonary bypass at six U.S. centers. The primary outcomes were atrial fibrillation and delirium occurrence up to postoperative day 5 or hospital discharge. Infusion of dexmedetomidine or saline began before incision (0.1 to 0.2  $\mu\text{g}/\text{kg}$  per hour during surgery) and increased to 0.4

$\mu\text{g}/\text{kg}$  per hour postoperatively for 24 h (with dose decreases permitted for safety issues). Additional sedation or analgesia was at the discretion of treating physicians. By intent to treat, 794 patients were analyzed. Atrial fibrillation occurred in 121 (30%) of 397 patients receiving dexmedetomidine and 134 (34%) of 395 placebo patients (relative risk 0.90 [97.8% CI, 0.72 to 1.15];  $P = 0.34$ ). Delirium occurred in 67 (17%) in the dexmedetomidine group versus 47 (12%) of the placebo cohort (relative risk 1.48 [97.8% CI, 0.99 to 2.23];  $P = 0.026$ ). Clinically significant hypotension was more common in the treated group (57% vs. 36%). (Article Selection: *BobbieJean Sweitzer, M.D.* Image: *M. Lane-Fall/Adobe Stock*.)

**Take home message:** An intraoperative dexmedetomidine infusion continued for 24 h after cardiac surgery did not reduce the incidence of postoperative atrial fibrillation or delirium.



### Effect of intraoperative dexamethasone on major complications and mortality among infants undergoing cardiac surgery: The DECISION randomized clinical trial. *JAMA* 2020; 323: 2485–92. PMID: 32573670.

The therapeutic effect of corticosteroids in pediatric cardiac surgical patients on reducing the systematic inflammatory response and reducing the incidence of postoperative complications remains uncertain. The authors randomized 394 infants younger than 12 months of age undergoing cardiac surgery with cardiopulmonary bypass to receive either 1 mg/kg of dexamethasone or a placebo after induction of anesthesia at four centers in China, Brazil, and Russia. The primary outcome was a composite of death, nonfatal myocardial infarction, need for extracorporeal membrane oxygenation, need for cardiopulmonary

resuscitation, acute kidney injury, prolonged mechanical ventilation, or neurological complications within 30 days after surgery. The primary outcome occurred in 38.1% in the dexamethasone group and 45.5% in the control group (absolute risk reduction 7.4% [95% CI, -0.8% to 15.3%]; hazard ratio 0.82 [95% CI, 0.60 to 1.10];  $P = 0.20$ ). The study may have been underpowered as the 95% CIs for the primary outcome included the prespecified minimal clinically important difference (15%). There were no statistical differences in 17 prespecified secondary outcomes. (Article Selection: *David Faraoni, M.D., Ph.D.* Image: *Adobe Stock*.)

**Take home message:** The prophylactic administration of dexamethasone does not reduce the risk of mortality and major postoperative complications in infants younger than 12 months of age undergoing cardiac surgery.



### Race, postoperative complications, and death in apparently healthy children. *Pediatrics* 2020; 146:e20194113. PMID: 32690804.

African American adults are known to be at higher risk of postoperative complications when compared to their white peers. A higher prevalence of comorbidities is implicated, a factor which should not be present in apparently healthy children. In this study, the authors reviewed data collected in the American College of Surgeons National Surgical Quality Improvement Program–Pediatric database between 2012 and 2017 focusing on children American Society of Anesthesiologists physical status I or II, undergoing inpatient surgery (120,991 white and 19,675 African American). The overall incidence of 30-day mortality, postoperative complications, and serious adverse events were 0.02%, 13.9%, and 5.7%, respectively. Using risk-adjusted

logistic regression, African American children had 3.43 times the odds of dying within 30 days after surgery compared to white children (odds ratio 3.43 [95% CI, 1.73 to 6.79]), 18% relative greater odds of developing postoperative complications (odds ratio 1.18 [95% CI, 1.13 to 1.23]) and 7% relative higher odds of developing serious adverse events (odds ratio 1.07 [95% CI, 1.01 to 1.14]). The site of care was not evaluated in this analysis. (Article Selection: *David Faraoni, M.D., Ph.D.* Image: *M. Lane-Fall/Adobe Stock*.)

**Take home message:** The risk of postoperative complications and mortality in apparently healthy African American children is increased compared to their white peers. Racial differences other than variation in preoperative comorbidities are likely a contributing factor.

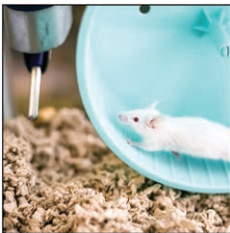


### Assessment of the prevalence of medical student mistreatment by sex, race/ethnicity, and sexual orientation. *JAMA Intern Med* 2020; 180:653–65. PMID: 32091540.

Medical students continue to experience discrimination and mistreatment during their education. The authors analyzed responses from the 2016 and 2017 Association of American Medical Colleges graduation surveys, given to all graduating students at 140 allopathic U.S. medical schools (27,504 surveys analyzed, representing 72.1% of graduating students), focusing on negative behaviors such as public humiliation, sex, race, ethnicity, and sexual orientation–based discrimination to characterize the prevalence of self-reported mistreatment. Overall, 35.4% of students reported at least one type of

mistreatment and were more likely to be female than male (40.9% vs. 25.2%,  $P < 0.001$ ), minority than white (31.9 to 38.0% vs. 24.0%,  $P < 0.001$ ), and lesbian, gay, or bisexual versus heterosexual (43.5% vs. 23.6%,  $P < 0.001$ ). Females reported more sex-based discrimination than males (28.2% vs. 9.4%,  $P < 0.001$ ), minority students more race/ethnicity-based discrimination than whites (11.8 to 23.3% vs. 3.8%,  $P < 0.001$ ), and lesbian, gay, and bisexual students more sexual orientation–based discrimination than heterosexuals (23.1% vs. 1.0%,  $P < 0.001$ ). (Article Selection: Marilyn D. Michelow, M.D. Image: M. Lane-Fall/Adobe Stock.)

**Take home message:** Discrimination and mistreatment are widespread in U.S. medical schools, and the burden is greater for women, Asian, underrepresented minority or multiracial, and lesbian, gay, or bisexual students.



### Blood factors transfer beneficial effects of exercise on neurogenesis and cognition to the aged brain. *Science* 2020; 369:167–73. PMID: 32646997.

Exercise may be capable of delaying or reversing the effects of age on cognition and neurodegenerative diseases. The authors evaluated the potential beneficial effects of exercise on memory in aged mice. Plasma from mice allowed to run on exercise wheels was intravenously injected into sedentary aged mice; memory testing as well as hippocampal neurogenesis were subsequently evaluated. Enhanced neurogenesis and improved memory function in the plasma-treated sedentary mice were demonstrated. Exercise plasma contained elevated concentrations of several liver-derived soluble proteins, including glycosylphosphatidylinositol (GPI)–specific phospholipase D1 (Gpld1), an enzyme that cleaves the GPI anchors of

several cell surface bound proteins. Similar increases in Gpld1 were noted in cohorts of sedentary versus healthy active elderly humans (8 to 12 per group, age 66 to 78 yr). Sedentary mice that received injections of expression constructs raising concentrations of Gpld1 displayed increased neurogenesis and improvements in memory much as the plasma-injected animals had. Enhanced Gpld1 was demonstrated to activate the coagulation and complement systems supporting the neurologic improvements. (Article Selection: J. David Clark, M.D., Ph.D. Image: Adobe Stock.)

**Take home message:** Exercise may enhance production of liver-derived peripherally circulating proteins that counter the effects of age on cognition by supporting the functioning of the hippocampus.



### Xenogeneic cross-circulation for extracorporeal recovery of injured human lungs. *Nat Med* 2020; 26:1102–13. PMID: 32661401.

Mortality among patients awaiting lung transplant remains high as many donor lungs are unsuitable due to injury and current *ex vivo* perfusion approaches are unable to salvage them. The authors used a novel swine extracorporeal circulatory platform to evaluate the effectiveness of xenogeneic cross-circulation for a period of 24 h of five pairs of acutely injured human lungs declined for transplantation. Immunosuppressive agents and recombinant cobra venom factor (for complement depletion) were administered to limit host immune responses. The regimen resulted in improved lung function (compliance and oxygenation) with reduced consolidation of lung tissue and lowered concentrations of airway secretions.

Histopathologic evaluation demonstrated a reduction in polymorphonuclear cells and reduced lung injury. Angiographic and histological analysis showed the absence of endovascular damage and thrombosis. The number of CD45+ leukocytes in the perfused human lungs declined over the course of the experiment. As an immunologic control, one additional lung not treated with immunosuppressive agents resulted in hemodynamic instability of the swine, pulmonary edema, and inflammatory evidence of hyperacute rejection. (Article Selection: J. David Clark, M.D., Ph.D. Image: M. Lane-Fall/Adobe Stock.)

**Take home message:** Xenogeneic cross-circulation can complement standard *ex vivo* lung perfusion techniques to recover human donor lungs declined for transplantation.

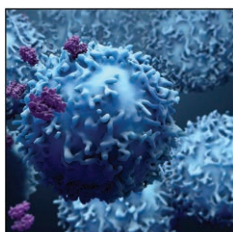


### Apgar score and risk of neonatal death among preterm infants. *N Engl J Med* 2020; 383:49–57. PMID: 32609981.

Preterm birth and low Apgar scores are both associated with increased neonatal morbidity, but their joint effects are unknown. This retrospective study estimated adjusted relative risks of neonatal death and absolute rate differences on neonatal mortality by Apgar scores at 5 and 10 min and its change in 113,300 preterm infants in Sweden. Neonatal mortality was 1.8%, ranging from 76.5% at 22 weeks of gestation to 0.2% at 36 weeks of gestation. In all gestational age strata, lower scores were associated with higher relative risk of neonatal death and greater absolute rate differences in neonatal mortality. Increases in low Apgar score-related relative risk were higher among infants with an older gestational age. When

compared to the gestational age-matched reference group of infants with scores of 9 to 10, adjusted relative risk of neonatal mortality in infants born between 25 and 27 weeks of gestation with a score of 4 to 6 was 2.7 (95% CI, 2.0 to 3.7) *versus* 20 (95% CI, 11.9 to 33.5) in infants born between 35 and 36 weeks of gestation. An increase between 5 and 10 min was associated with lower neonatal morbidity than a stable score. (Article Selection: Laszlo Vutskits, M.D. Image: Adobe Stock.)

**Take home message:** In preterm infants, Apgar scores measured at 5 and 10 min provide clinically meaningful prognostic information on neonatal survival.



### Marked T cell activation, senescence, exhaustion and skewing towards TH17 in patients with COVID-19 pneumonia. *Nat Commun* 2020; 11:3434. PMID: 32632085.

The complex expression of T-cell phenotypes and the functionality of these cells during an immune response varies in different populations and disease states. This single-center, case-control study in Italy compared blood samples from 39 COVID-19 pneumonia patients and 25 age- and sex-matched healthy controls to assess the proportion and function of different T-cell phenotypes and the associated plasma concentrations of 31 cytokines. COVID-19 pneumonia patients demonstrated lower absolute numbers of CD4+ and CD8+ T-lymphocytes, which displayed markers related to exhaustion,

senescence, and activation, as well as altered expression of master regulators and chemokine receptors. SARS-CoV-2 patients also had lower CD4+ T-cell proliferation but not mitochondria functionality. In COVID-19 patients, cytokine storm associated with increased plasma concentrations of tumor necrosis factor, interferon- $\gamma$ , and interleukin (IL)-2 was also associated with a skewing toward the CD4+ TH17 phenotype. IL-17 is crucial in recruiting and activating neutrophils that migrate to the lung and is likely involved in the pathogenesis of COVID-19 pneumonia. (Article Selection: Meghan E. Prin, M.D., M.S. Image: Adobe Stock.)

**Take home message:** T-cell expression and function differs in COVID-19 pneumonia patients compared to healthy controls, including increased T-cell production of IL-17, blockade of which may be a novel therapeutic strategy.

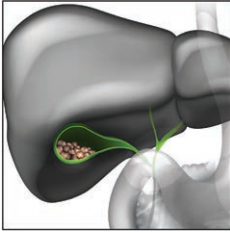


### Chronic pain diagnosis in refugee torture survivors: A prospective, blinded diagnostic accuracy study. *PLoS Med* 2020; 17:e1003108. PMID: 32502219.

Data suggest that up to 87% of torture survivors experience chronic pain, particularly brachial plexopathy or lumbosacral plexus injury. The United Nations Istanbul Protocol is the most widely used protocol for medical evaluation of torture victims but focuses primarily on psychologic therapies in contrast to multimodal pain therapies. This prospective, blinded study compared this standard tool to a validated pain screening tool (Brief Pain Inventory–Short Form survey) in the assessment of 20 male and female survivors of torture at the Weill-Cornell Center for Human Rights. The primary outcome was the diagnostic and treatment capability of the United Nations Istanbul Protocol *versus* the validated pain screen, compared to

the reference standard, evaluation by a pain medicine specialist. The specialist evaluation diagnosed 85% of the cohort with chronic pain. The Brief Pain Inventory–Short Form had a sensitivity of 100% (95% CI, 72 to 100%) and a negative predictive value of 100%, as compared to a sensitivity of 24% (95% CI, 8 to 50%) and a negative predictive value of 19% (95% CI, 5 to 46%) for the United Nations Istanbul Protocol ( $P < 0.001$ ). (Article Selection: Meghan E. Prin, M.D., M.S. Image: Adobe Stock.)

**Take home message:** A validated pain screen can supplement the current global standard assessment of torture survivors to increase the accuracy of pain diagnosis in torture victims.



### Urgent endoscopic retrograde cholangiopancreatography with sphincterotomy versus conservative treatment in predicted severe acute gallstone pancreatitis (APEC): A multicentre randomised controlled trial. *Lancet* 2020; 396:167–76. PMID: 32682482.

Patients with gallstone pancreatitis are at risk for cholangitis and life-threatening organ failure. Acute endoscopic retrograde cholangiopancreatographic biliary sphincterotomy is commonly performed for biliary decompression in such patients. It is unclear if endoscopic retrograde cholangiopancreatography improves outcomes in patients predicted to be at high risk for, but without current cholangitis. The authors randomized 232 patients at 26 hospitals in The Netherlands to either urgent endoscopic retrograde cholangiopancreatography with sphincterotomy or conservative treatment. The composite primary endpoint was mortality or development of major organ complications. Data from 230 patients were analyzed, of which 23% had an organ failure. Complications or death occurred in 50 of 113 patients in the control group, *versus* 45 of 117 patients in the sphincterotomy group (risk ratio 0.87 [95% CI, 0.64 to 1.18];  $P = 0.37$ ). Cholangitis was more common in the conservative treatment group (risk ratio 0.18 [95% CI, 0.04 to 0.78];  $P = 0.01$ ), but was not associated with adverse patient outcome. (Article Selection: Jamie W. Sleight, M.D. Image: M. Lane-Fall/Adobe Stock.)

**Take home message:** Urgent endoscopic retrograde cholangiopancreatography with sphincterotomy offers no benefit over conservative therapy in patients with predicted severe acute gallstone pancreatitis, with or without cholestasis, but without cholangitis. Its use should be reserved for patients with cholangitis or persistent cholestasis.



### Reduction of postoperative wound infections by antiseptica (RECIPE)? A randomized controlled trial. *Ann Surg* 2020; 272:55–64. PMID: 31599810.

Surgical site infection is commonly observed after abdominal surgery and is associated with significant morbidity and cost. The use of antiseptic wound irrigation could reduce surgical site infection compared to saline irrigation. The authors performed a single-center, single-blinded prospective randomized trial in Germany, comparing wound irrigation with 0.04% polyhexanide to 0.9% saline in patients undergoing elective laparotomy. The primary outcome was the rate of surgical site infection within 30 days postoperatively. A total of 393 patients were analyzed per protocol; 111 surgical site infections were recorded (28.2%), 70 in the saline group and 41 in the polyhexanide group ( $P = 0.004$ ). Logistic regression demonstrated that polyhexanide was associated with lesser surgical site infection (odds ratio 0.44 [95% CI, 0.27 to 0.72];  $P = 0.001$ ). Preoperative anemia and greater than 5 previous abdominal surgeries were associated with higher odds (odds ratio 2.08 [95% CI, 1.27 to 3.40];  $P = 0.004$ , and odds ratio 8.51 [95% CI, 2.57 to 28.21];  $P < 0.001$ , respectively). No difference in postoperative complications, allergic reactions, or serious adverse events were observed between groups. (Article Selection: Beatrice Beck-Schimmer, M.D. Image: Adobe Stock.)

**Take home message:** Wound irrigation with polyhexanide provides a safe and cost-effective way of reducing surgical site infection in patients undergoing abdominal surgery compared to saline irrigation.



### Timing of initiation of renal-replacement therapy in acute kidney injury. *N Engl J Med* 2020; 383:240–51. PMID: 32668114.

Initiation of renal replacement therapy in critically ill patients with acute kidney injury (AKI) before onset of major metabolic disorders or fluid overload is controversial. The investigators randomized 3,019 critically ill patients in 15 countries with AKI (stage 2 or 3 Kidney Disease: Improving Global Outcomes criteria) to an accelerated-strategy (within 12h) or standard-strategy group (metabolic or fluid disorders or AKI greater than 72h). The primary outcome was all-cause mortality at 90 days. A total of 2,927 patients were analyzed in an intent-to-treat analysis. Renal replacement therapy was instituted in 1,418 (96.8%) of the accelerated-strategy group and 903 (61.8%) of the standard group. In the accelerated-strategy cohort, 643 (43.9%) died at 90 days compared to 638 (43.6%) in the standard group (risk ratio 1.00 [95% CI, 0.93 to 1.09];  $P = 0.92$ ). In those surviving 90 days, renal replacement therapy dependence continued in 85 of 814 (10.4%) of the accelerated-strategy group and 49 of 816 (6.0%) of the standard group (risk ratio 1.74 [95% CI, 1.24 to 2.44]). Adverse events were more common in the accelerated-strategy group (23% vs. 16.5%,  $P < 0.001$ ). (Article Selection: BobbieJean Sweitzer, M.D. Image: Adobe Stock.)

**Take home message:** Accelerated renal replacement therapy for acute kidney injury in critically ill patients was not associated with lower death rates at 90 days compared to standard management.