SCIENCE, MEDICINE, AND THE ANESTHESIOLOGIST

ANESTHESIOLOGY

Deborah J. Culley, M.D., Editor

Key Papers from the Most Recent Literature Relevant to Anesthesiologists

Prevention of early ventilator-associated pneumonia after cardiac arrest. N Engl J Med 2019; 381:1831–42.

The role of short-term preventive therapy for ventilator-associated pneumonia in adult mechanically ventilated patients undergoing targeted temperature management (32 to 34°C) after out-of-hospital cardiac arrest with shockable rhythm has not been demonstrated. This multicenter, double-blind, randomized control trial in 16 intensive care units in France included 198 patients randomized to either amoxicillin-clavulanate (1 gm/200 mg) administered three times a day for 2 days within 6 h of arrest (excluding patients with overt aspiration) or placebo. The primary outcome was ventilator-acquired pneumonia within the first 7 days of hospitalization. The incidence of early ventilator-associated pneumonia adjudicated in 51 patients was significantly lower with treatment than with placebo, 19% *versus* 34% (hazard ratio, 0.53; 95% CI, 0.31 to 0.92; $P = 0.03$). Despite this, no significant reductions were noted in the incidence of later ventilator-associated pneumonia, ventilator-free days, intensive care unit length of stay, serious adverse events, increase in antibiotic resistant bacteria on rectal swab at day 7, or 28-day mortality. *(Article Selection: Martin J. London. Image: Adobe Stock.)*

Take home message: A 2-day course of antibiotics reduced the incidence of ventilator-associated pneumonia in patients with an out-of-hospital cardiac arrest and a shockable rhythm without influence on other key clinical outcome variables.

Clinical presentation, treatment, and short-term outcomes of lung injury associated with e-cigarettes or vaping: A prospective observational cohort study. Lancet 2019; 394:2073–83.

Since 2019 there has been an eruption of lung injury associated with e-cigarettes or vaping. This multicenter, prospective observational study followed patients from an integrated health system between June and October 2019 with lung injury associated with e-cigarettes or vaping. The majority of the patients presented with constitutional (88%), respiratory (98%), and gastrointestinal (90%) symptoms and were young, with a median age of 27 yr (interquartile range, 22 to 36). Of the 60 patients who presented with lung injury, more than half were admitted to an intensive care unit. The majority of these received steroids (95%) and antibiotics (90%), but only 17% required mechanical ventilation. Interestingly, 18% of the patients developed a pneumothorax or pneumomediastinum. Among patients who were followed for 2 weeks, many had residual abnormalities on chest x-ray (67%) and pulmonary function tests (67%), and 10% were readmitted to the hospital or intensive care unit at least 2 weeks after hospital discharge. *(Article Selection: Beatrice Beck-Schimmer. Image: Adobe Stock.)*

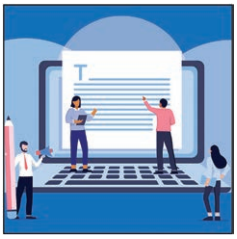
Take home message: E-cigarette use and vaping have been associated with constitutional, respiratory, and gastrointestinal symptoms in young patients that often require admission to an intensive care unit and are often associated with pulmonary abnormalities on chest x-ray and pulmonary function tests at least 2 weeks after hospital discharge.

Functional connectome of the fetal brain. J Neurosci 2019; 39:9716–24.

Although much is known about functional connectome in older children and adults, less is known about the functional connectome before birth. The purpose of this study was to evaluate the key characteristics of human connectome organization before birth and compare it to the mature adult brain. The authors performed functional magnetic resonance imaging examinations in 139 healthy pregnant women with singleton fetuses in their late second or third trimester of pregnancy. After exclusion of cases where there was high movement or detectable fetal health complications, the data of 105 fetuses were compared to data from 42 adult brains from a previous dataset. Imaging overlap was compared using the Rand index where 0 represents no overlap and 1 represents a complete overlap. Fetal and adult groups had a high Rand index of 0.730 ($P < 0.001$), suggesting significant overlap. *(Article Selection: Laszlo Vutskits. Image: Adobe Stock.)*

Take home message: This study suggests that key features of the functional connectome are present in the late second and third trimesters of pregnancy.

DOI: 10.1097/ALN.0000000000003183



Communities of practice in peer review: Outlining a group review process. Acad Med 2019; 94:1437–42.

Publication in a peer-reviewed journal is a cornerstone of scientific scholarship, but some consider peer review to be a negative experience due to lack of reviewer experience and inadequate mentoring. This manuscript reports on an Association of American Medical Colleges peer-review workshop from 2015. The authors of this manuscript worked with the editors of *Academic Medicine* to perform a group review of four manuscripts. The resultant group review process allowed the reviewers to learn and receive real-time feedback as peer mentors that they found enhanced their satisfaction with the peer review process. They believed that the group peer-review process provided robust feedback to the authors and journal editors. The authors propose that group peer review may serve as a unique opportunity to improve an individual's peer review skills and make mentorship more easily accessible. *(Article Selection: Cathleen Peterson-Lane. Image: Adobe Stock.)*

Take home message: Group peer review may be a viable way to improve an individual's peer review skills and make review mentorship more accessible.

Effect of stellate ganglion block treatment on posttraumatic stress disorder symptoms: A randomized clinical trial. JAMA Psychiatry 2019 Nov 6 [Epub ahead of print].

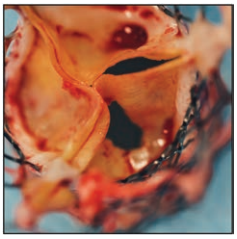
Posttraumatic stress disorder is common and difficult to treat. A number of case series have suggested that stellate ganglion block may effectively treat posttraumatic stress disorder (PTSD) but a larger study, with some potential limitations, found negative results. This prospective study was designed to determine the effectiveness of right-sided stellate ganglion blocks, when compared to sham control, on the past-month Clinician-Administered PTSD Scale for Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), at 8 weeks in active duty military personnel with a baseline past-month Clinician-Administered PTSD Scale for DSM-5 of 32 or higher. Participants who received stellate ganglion blocks had a greater reduction in their past-month Clinician-Administered PTSD Scale for DSM-5 score when compared with sham controls (Cohen d, 0.56; 95% CI, 0.38 to 0.73). Mean score reduction in the stellate ganglion block group was –12 ± 13 compared to –6 ± 8 in the sham control group. *(Article Selection: J. David Clark. Image: Adobe Stock.)*

Take home message: Stellate ganglion blocks may be effective for the treatment of posttraumatic stress disorder among active duty military personnel for up to 8 weeks; however, the long-term efficacy remains uncertain.

Comparing outcomes and costs of surgical patients treated at major teaching and nonteaching hospitals: A national matched analysis. Ann Surg 2019 Oct 15 [Epub ahead of print].

Although teaching hospitals are thought to offer higher quality care when compared to nonteaching hospitals, some question whether teaching hospitals actually improve outcomes and at what cost. This retrospective study used Medicare records from 340 teaching hospitals and matched controls from 2,444 nonteaching hospitals to determine the primary quality outcome of 30-day all-cause, all-location mortality. Value was determined by the difference in resource utilization cost between major teaching and nonteaching matched pairs divided by their difference in 30-day mortality. A total of 86,751 patients from teaching hospitals were matched with 86,751 nonteaching hospital patients. Overall 30-day mortality for general surgery in teaching hospitals was 4.6% *versus* 5.6% in nonteaching hospitals ($P < 0.001$) and was associated with a $915 cost difference ($P < 0.001$). For high-risk patients a 1% improvement in 30-day mortality was associated with a $1,682 increase in cost in teaching hospitals. Similar findings were noted with vascular surgery but may not be true in the setting of orthopedic surgery. *(Article Selection: Deborah J. Culley. Image: Adobe Stock.)*

Take home message: Care for Medicare beneficiaries at a teaching hospital was associated with decreased mortality in general and vascular surgery patients at marginally higher costs.



Reduced leaflet motion after transcatheter aortic-valve replacement. N Engl J Med 2020; 382:130–9.

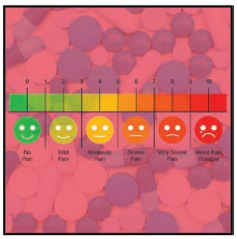
Subclinical aortic valve leaflet thickening and reduced motion after transaortic bioprosthetic aortic valve replacement has been described. However, it is unclear whether anticoagulation after valve replacement can reduce these occurrences. The authors report results of a preplanned substudy (GALILEO-4D) of a primary study (GALILEO) that evaluated the safety and efficacy of a rivaroxaban-based strategy (rivaroxaban [10 mg] plus aspirin [75 to 100 mg] once daily) compared with an antiplatelet-based antithrombotic strategy (clopidogrel [75 mg] plus aspirin [75 to 100 mg] once daily) after transcatheter aortic bioprosthetic implantation. The primary endpoint of this substudy was the percentage of patients with at least one prosthetic valve leaflet having reduced motion involving 50% or more of the leaflet at approximately 90 days after implantation. The secondary outcome was thickening of at least one valve leaflet. Twelve sites enrolled 231 patients for this analysis. At least one prosthetic valve leaflet with grade 3 or higher motion reduction was detected in 2 of 97 patients (2.1%) in the rivaroxaban group, as compared with 11 of 101 (10.9%) in the antiplatelet group (difference, −8.8 percentage points; 95% CI, −16.5 to −1.9; $P = 0.01$). Thickening of at least one leaflet was observed in 12 of 97 patients (12.4%) in the rivaroxaban group and in 33 of 102 (32.4%) in the antiplatelet group (difference, −20.0 percentage points; 95% CI, −30.9 to −8.5). Although these results were positive, in the main trial there were more adverse outcomes with the use of rivaroxaban. *(Article Selection: Martin J. London. Image: Adobe Stock.)*

Take home message: A rivaroxaban-based antithrombotic strategy was more effective than an antiplatelet-based strategy in preventing subclinical leaflet motion abnormalities but was associated with an increased risk of other adverse outcomes.

Effects of tranexamic acid on death, disability, vascular occlusive events and other morbidities in patients with acute traumatic brain injury (CRASH-3): A randomised, placebo-controlled trial. Lancet 2019; 394:1713–23.

Tranexamic acid has been shown to reduce surgical bleeding and decrease mortality in patients with extracranial trauma, but it is unclear whether administration of tranexamic acid is beneficial in the setting of traumatic brain injury. This study reports on 9,127 adult patients with a traumatic brain injury randomized to tranexamic acid or placebo. The primary outcome was head injury–related death that occurred in the hospital within 28 days of injury in patients who were treated within 3 h of injury. There were no differences in the primary outcome between those randomized to tranexamic acid (19%) when compared to placebo (20%; risk ratio 0.94; 95% CI, 0.86 to 1.02). However, on secondary analysis the risk of head injury–related death was reduced with tranexamic acid administration in patients with mild to moderate head injury (risk ratio 0.75; 95% CI, 0.64 to 0.95) but not in those with severe head injury (risk ratio 0.99; 95% CI, 0.91 to 1.28). There were no differences in vascular occlusive events or seizures between the groups. *(Article Selection: Beatrice Beck-Schimmer. Image: Adobe Stock.)*

Take home message: Overall, administration of tranexamic acid to patients with acute head injury did not increase survival, but a survival benefit may occur for patients with mild to moderate head injury without an increase in other adverse outcomes.



When a vital sign leads a country astray—The opioid epidemic. JAMA Surg 2019 Aug 14 [Epub ahead of print].

This publication is a viewpoint on how the addition of pain as the fifth vital sign and the belief by some that pain control was a patient's right led to an aggressive approach to pain and the opioid crisis. The viewpoint contains some important historical information, including the introduction of patient experience surveys that included documentation of a patient's experience of pain as a regulatory requirement, the belief that patients in pain do not become addicted to opioids, and the development of a subjective pain scale with an arbitrarily accepted cutoff that moved opioids from a treatment option for pain to the gold standard for pain control, resulting in an increased prevalence of substance use disorder. As a result, the authors note that 67% of the 70,000 deaths per year due to drug overdose involve opioids and that often the first exposure to opioids is through prescription drugs. Perhaps the most poignant statements included in the viewpoint was the role that physicians played as "unwitting accomplices in the opioid crisis" balanced with statements on how surgeons and anesthesiologists are working to mitigate the risk of opioid-naïve patients developing persistent opioid use after surgery. *(Article Selection: Deborah J. Culley. Image: Adobe Stock.)*

Take home message: Overaggressive treatment of pain due to regulatory requirements and the belief that pain relief was a patient's right may have contributed to the opioid crisis.

 DOI: 10.1097/ALN.0000000000003183

Assessment of jugular venous blood flow stasis and thrombosis during spaceflight. JAMA Netw Open 2019; 2:e1915011.

Little is known about the effect of spaceflight on cerebral venous blood flow despite an understanding that spaceflight results in chronic headward blood and body fluid shift. The purpose of this study was to assess internal jugular vein flow and morphology during spaceflight and determine whether application of lower body negative pressure reverses headward blood and body fluid shifts. This study was performed on 11 Space Station crew members participating in long-duration spaceflight missions. Internal jugular vein area increased from 10 mm^2 (95% CI, 1 to 21) preflight to 70 mm^2 (95% CI, 59 to 81) during spaceflight ($P < 0.001$). Similarly, mean internal jugular vein pressure went from 5 mmHg (95% CI, 3 to 8) preflight to 21 mmHg (95% CI, 19 to 24) during spaceflight ($P < 0.001$). Perhaps more interesting was the finding that seven crew members had stagnant or retrograde internal jugular vein blood flow and that one of these developed an occlusive thrombus. The application of negative pressure to the lower body improved the chronic headward blood and body fluid shift in 59%. *(Article Selection: Deborah J. Culley. Image: Adobe Stock.)*

Take home message: Spaceflight is associated with significant changes in internal jugular vein size and pressure and may lead to stagnant or retrograde internal jugular vein blood flow.

Randomized trial of three anticonvulsant medications for status epilepticus. N Engl J Med 2019; 381:2103–13.

The treatment of status epilepticus refractory to treatment with benzodiazepines is not well defined. This study compared safety and effectiveness of levetiracetam, fosphenytoin, and valproate on status epilepticus refractory to treatment with benzodiazepines in adults and children. The primary outcome was absence of seizures and improvement in consciousness by 60 min after drug initiation. The trial was stopped at a planned interim analysis due to futility. Among the patients randomized to levetiracetam (n = 145), fosphenytoin (n = 118), or valproate (n = 121), there were no differences in the primary outcome among the groups. The primary outcome occurred in 47% of patients randomized to levetiracetam (95% CI, 39 to 55), 45% of patients randomized to fosphenytoin (95% CI, 36 to 54), and 46% of patients randomized to valproate (95% CI, 38 to 55). Similarly, there were no statistically significant differences in any of the secondary outcomes. *(Article Selection: Laszlo Vutskits. Image: Adobe Stock.)*

Take home message: Treatment of benzodiazepine refractory status epilepticus with levetiracetam, fosphenytoin, or valproate are equally effective.

2019 American Heart Association focused update on advanced cardiovascular life support: Use of advanced airways, vasopressors, and extracorporeal cardiopulmonary resuscitation during cardiac arrest: An update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation 2019; 140:e881–94.

The American Heart Association advanced cardiovascular life support guidelines have had a focused update on a variety of issues of importance to anesthesiologists in particular. These include new recommendations on the use of advanced airways, vasopressors, and the growing interest in the use of extracorporeal cardiopulmonary resuscitation during cardiac arrest. It is now suggested that either bag mask ventilation or an advanced airway may be considered for adults requiring cardiopulmonary resuscitation, with assessments to verify effective placement in a manner that minimizes interruptions of chest compressions along with the use of capnography to confirm and monitor endotracheal tube placement. Emergency medical service systems that perform advanced airway management should ensure quality improvement processes to minimize complications and track success rates. It is considered reasonable to administer 1 mg of epinephrine every 3 to 5 min in cardiac arrest but the guidelines do not recommend the use of high-dose epinephrine for routine cardiac arrest. Vasopressin may be considered in cardiac arrest although current evidence suggests no advantage to it as a substitute for epinephrine. There is insufficient evidence to recommend the routine use of extracorporeal cardiopulmonary resuscitation, but it may be considered for selected patients as a rescue therapy. *(Article Selection: Martin J. London. Image: Adobe Stock.)*

Take home message: A focused update on advanced cardiovascular lift support from the American Heart Association has been published and contains clinical issues of particular importance to anesthesiologists.