The March issue of Shock continues to provide the latest update in clinical and basic science topics that will interest our readers. The issue begins with two excellent reviews that cover very timely topics for the treatment of shock. The first review by Roberts et al. (1) covers a topic that has been of interest for years—nitric oxide. It is clear that nitric oxide is involved in the pathophysiology of shock, but can nitric oxide be used to treat shock? The group from Camden, NJ, reviews the experience with using nitric oxide donors for the clinical treatment of shock by the mechanism of reducing reactive oxygen species. They reviewed 26 studies and found that only six were high-quality studies. Unfortunately, the only conclusion is that nitric oxide is safe, and further trials are needed. The second review, from Molina et al. (2), discusses the effects of alcohol abuse on the resuscitation of trauma and how the ability to fight infection is altered. This timely subject will help all caregivers of trauma patients because alcohol abuse has a high prevalence in surgical and trauma intensive care units. The authors provide a nice review of how alcohol affects the counterregulatory response to injury.

The next section in Shock covers clinical aspects in the management of sepsis in cancer and acute respiratory distress syndrome. The first article, from French investigators, evaluated the outcomes of cancer patients admitted to an intensive care unit for septic shock of pulmonary origin (3). They concluded that survival of cancer patients with pulmonary sepsis is still substantial even with organ dysfunction. Early and aggressive therapy may improve survival and quality of life. The second clinical study examines the genetic predisposition for acute respiratory distress syndrome in patients with sepsis (4). They followed patients with sepsis for the development of acute respiratory distress syndrome to determine whether one gene variant predominated. They investigated several genes but really focused on single-nucleotide polymorphisms in the angiotensin-converting enzyme gene. Of 149 patients, they investigated 35 who developed acute respiratory distress syndrome. They found that the presence of allele D of the angiotensin-converting enzyme gene was significantly associated with the diagnosis of acute respiratory distress syndrome. This knowledge could be used for screening patients with sepsis for a higher likelihood of developing acute respiratory distress syndrome. The remainder of the journal provides several topics covering the basic science of shock. The first five basic science articles focus on mechanisms of sepsis and shock in the lung. The first article comes from Taiwan and examines a potential mechanism of lung scarring in a bleomycin model that is a well-described inducer of pulmonary fibrosis. They used induced pluripotent stem cells lacking the reprogramming factor c-Myc (three-gene iPSCs) and its medium as treatment for fibrosis 24 h after the delivery of bleomycin (5). This is a promising potential therapy for the prevention of pulmonary fibrosis. The second pulmonary article, from Wisconsin, describes the development of a model of bronchiolitis obliterans organizing pneumonia (6). In their rat model, they created ischemia in a lung using an occlusive slip knot around the left main pulmonary artery. They also have started to examine the mechanisms involved in the production of bronchiolitis obliterans organizing pneumonia in their model. The third basic science article in this series examines the links between pulmonary artery reactivity and nitric oxide activity and the induction of inflammation after lung contusion (7). They investigated interactions between superoxide dismutase, catalase, and the activity of nitric oxide in a dependable model of pulmonary contusion. Continuing along the theme of acute lung injury, Uriarte et al. (8) examined the role of neutrophil exocytosis in a rat model of acute lung injury. Their goal was to inhibit secretory vesicle, gelatinase granule, and specific granule exocytosis in neutrophils using a TAT-fusion protein containing a SNAP domain from SNAP-23 (TAT-SNAP-23). This novel treatment inhibited the typical increase in vascular permeability in lungs without affecting neutrophil accumulation in the lungs. In the last of the series of mechanistic studies involving lung injury, investigators from Sweden attempted to inhibit streptococcal toxic shock syndrome from Streptococcus pyogenes of the M1 serotype (9). They investigated whether inhibition of geranylgeranyl transferase using GGTI-2133 would protect mice from lung injury induced by M1 protein injection. GGTI-2133 reduced the infiltration of neutrophils, edema, and tissue injury in the lung. We look forward to future studies with this compound.

The final four studies focus on mechanisms of shock in different organ systems. Investigators from China focused on a method of protecting the heart after ischemic injury (10). They sought to determine whether “postconditioning,” described as brief periods of ischemia just at the time of reperfusion, reduces cardiomyocyte apoptosis. They focused on p53 upregulated modulator of apoptosis (PUMA) as target of regulating apoptosis. Their results are very interesting, but I am not sure how postconditioning would be used in patients with recent myocardial infarctions. The next study examined the question of whether mitochondria can be infused as a source of energy to ischemic organs. Lin et al. (11) used a partial ischemia-reperfusion model in the liver of rats to test whether infusion of...
mitochondria into the spleen would reduce signs of injury. This novel concept seems to improve outcomes in these animals, but, again, translating this concept to the clinical world will be the big test. Right now, there is no way to deliver cells to a patient’s spleen. Hopefully, the development of an i.v. delivery system will be possible. The penultimate article examines the relationship between sepsis and aging using Klotho-knockout mice as a model of accelerated aging and shortened life span (12). They used a cecal ligation and puncture model in Klotho-knockout mice, where they found that there was a much higher mortality in the Klotho-knockout mice. The increased mortality was associated with increased levels of cytokines. It will be interesting to determine whether accelerated aging is a real model for being elderly. The final article for this issue examines the effects of salvianolic acid B, an active ingredient of Salvia miltiorrhiza, on the increase in permeability of lungs after lipopolysaccharide injection (13). Pretreatment with salvianolic acid B reduced the lipopolysaccharide-induced microcirculatory disturbance and may have potential therapeutic benefits for future trials in sepsis. Translating natural products for clinical use in the United States still has many challenges.

REFERENCES