Having just returned from the 2016 Shock Society Annual Congress in Austin, Texas, I am constantly reminded by the vitality, the breadth, and the expertise of the Shock Society membership. This year’s annual congress once again exceeded my expectations, and I return full of enthusiasm, new ideas, and more potential collaborations. Congratulations to the organizers, the participants, and all who attended. Although sitting in Atlanta’s Hartsfield-Jackson International Airport Terminal D, I now have the opportunity to peruse the upcoming September issue of Shock. It is a no more fitting way to end a most satisfying week.

This month’s issue of Shock continues the rich tradition of the journal established by the Editor, Dr Chaudry, and the Publications Committee of the Society. Contained are 14 articles including 2 contemporary reviews, 1 brief report, and 11 clinical and basic sciences reports covering a multitude of facets surrounding shock, trauma, and sepsis research.

The first article is a review by Burke, Karlstad, and Collier from LSU summarizing our current state of knowledge regarding the islet cell response to trauma and inflammation (1). This is a timely and important review, as the role of substrate metabolism in regulating the inflammatory response has taken center stage both in clinical terms of maintaining glycemic control of the critically ill patient and the role of intermediary metabolism on immunological function. Here, the authors provide a current and applicable overview of the mechanisms behind insulin resistance in trauma and the compensatory changes that occur in the islet cells. I direct the reader to the conclusions and the last figure where the authors provide a very coherent and important argument for the adaptive responses by the pancreas and islet cells to injury-associated insulin resistance. A must read for both the clinician and the basic scientist.

The second review comes from Hongpeng Jia at Johns-Hopkins University and is focused on the role of angioten-sin-converting enzyme 2 (ACE2) in inflammatory lung disease (2). Although the role of the renin-angiotensin system in lung inflammation has been previously well described, and angiotensin 1, angiotensin 2, an angiotensin converting enzyme have been well studied, our understandings of the contribution of ACE2 in the lung inflammatory response is much less well known. Dr Jia argues very effectively that it is the soluble form of ACE2 that has the primary catalytic activity and could be a primary target for therapeutic interventions in acute lung injury. Kudos to Dr Jia for his “Conclusions and Perspectives” section which is both rich and detailed, and provides a strong roadmap for future research and discovery in this exciting field.

Celeste Finnerty and David Herndon’s laboratory has the first “Clinical Aspects” paper in this issue of the journal, and it is a retrospective analysis of two different clinical approaches for measuring cardiac output in burned children (3). For the nonclinicians, hemodynamic monitoring of cardiac output in children primarily relies on pulmonary artery catheters which are an invasive procedure with a very small but measurable rate of complications. Recently, less invasive thermal dilution approaches and transthoracic echocardiography of the heart have been promulgated as alternatives to pulmonary artery catheters. This article reviews the Galveston experience with both the transthoracic echocardiography and the pulse index continuous cardiac output (PICCO) methods in 54 pediatric burn patients over 2 years. In this retrospective analysis, the authors conclude that echocardiography may underestimate cardiac output in this population, and that PICCO can offer multiple analyses to assess trends over time. Although the authors promulgate the use of PICCO over echocardiography, they rightfully remind the reader that a direct comparison between PICCO and measurements made with a pulmonary artery catheter are required. Still, the article is a must read for clinicians requiring cardiac output measurements for their clinical management.

Takahashi et al. (4) have examined the value of plasma IL-6 concentrations as a diagnostic for infection and a prognostic for injury in ICU patients. Although IL-6 concentrations have been frequently used in similar populations, this article discriminates itself from others in its effort to compare IL-6 with procalcitonin, presepsin, and C-reactive protein as both a diagnostic and prognostic. The data from a total of 172 patients in two cohorts argue that IL-6 may have better sensitivity and specificity than these other markers for infection and organ injury. It is reassuring to me that IL-6 remains a viable biomarker as we move forward in efforts to better describe and assess our critically ill patients.

Along the same lines, Wagner et al. (5) have examined how alcohol intoxication alters the IL-6 and inflammatory responses in 74 trauma patients with traumatic brain injury from Frankfurt, Germany, compared with 27 nonintoxicated patients. Using a blood alcohol concentration threshold of what they
define as 0.5% (corresponding to what I believe is a 0.05 g/dL concentration), the authors demonstrate (see their Table 1) that intoxicated traumatic brain injury patients (mean 0.19 g/dL or approximately 2.5 times the legal limit in the United States) manifested a much reduced IL-6 and leukocyte numbers than traumatic brain injury patients with blood alcohol concentrations less than 0.05 gm/dL. The authors conclude that this level of intoxication may blunt inflammatory responses. It will be interesting to know whether the blunting of inflammatory responses is alcohol concentration-dependent, or whether a threshold exists.

Moving in a different direction Suzuki et al. (6) from Kanegawa, Japan, have examined B-cell function in two groups of patients with severe sepsis, those over 64 years of age and those under. T-cell function is known to be reduced in aging individuals after trauma and sepsis, but less is known about the B-cell response. In fact, it has been assumed that the B-cell response to sepsis is dramatically different from the T-cell response in both sepsis and in the ageing. However, in this report, the authors convincingly demonstrate that both in vivo immunoglobulin M (IgM) concentrations and ex vivo production are reduced in elderly patients. In the elderly septic patients, serum IgM concentrations are inversely correlated with the APACHE score. Although these results demonstrate that the elderly IgM response is attenuated in sepsis, future studies will need to confirm whether other functions are similarly affected, as well as their implication for the clinical response.

The last “Clinical Aspects” paper comes from Ray et al. (7) in London. The authors conducted a 7-year retrospective study to examine the value of the shock index (SI) as a prognostic for pediatric patients transferred to a centralized pediatric intensive care unit. In 474 patients who survived transport, the SI (systolic blood pressure/heart rate) was significantly higher in nonsurvivors than in survivors. Moreover, in survivors, there was a significant decline in SI over time. Although statistically significant as a group, the authors were unable to show that the individual patient’s SI was a better predictor of outcome than heart rate or blood pressure alone. Although disappointing, the findings are not surprising and the search for predictive biomarkers that have the specificity and sensitivity for clinical use in this patient population continues.

Ghanpur et al. (8) from Melbourne, Australia, bring us a “Rapid Communication” that shows us the unintended consequences of advancements in our technology. As the authors note, plastic syringes have all but replaced glass syringes in most clinical applications, but common plastics are permissible to air. The authors examined the ramifications of this in the measurements of central venous oxygen from blood samples. In a very simple study from 21 patients, blood samples collected in plastic syringes were allowed to stand for periods up to 20 min either at rest or being mixed. Oxygen concentrations were determined, and it was shown that in both tubes, oxygen tensions increased over time, dramatically more when the samples were constantly mixed. The recommendations are simple and straightforward: blood samples drawn in plastic should be measured as rapidly as possible, within 5 min. If longer storage is planned, glass syringes should be used.

Moving to the “Basic Sciences Aspects” of this issue of the journal, Leite et al. (9) previously reported that endothelin-1 (ET-1) reduced the frequency of spontaneous excitatory currents in vasopressinergic cells through the activation of endothelin endothelin A receptor (ETA) receptors in rat brain slices. Here they asked whether blockade of the ETA or endogenous cannabinoid receptors during severe sepsis improved survival during the period of enhanced ET-1 expression. The authors clearly show that blockade of central cannabinoid and ETA receptors in the late phase of sepsis increased the survival rate, reduced body temperature, and increased circulating arginine vasopressin levels. However, the authors were unable to conclude whether changes in host protective immunity or the magnitude of the inflammatory response were responsible for the improved outcomes. A great start and an area of research that needs more attention.

Along similar lines, selective beta-blockers have been shown to improve outcomes in pediatric burn populations and some adult inflammatory conditions. Here Wei et al. (10) from INSERM have examined whether heart rate reduction with ivabradine, an I channel inhibitor, can improve outcome in a rat model of peritonitis induced septic shock. The authors compared rats infused with antibiotics, analgesics, and crystalloids with the same intervention with added ivabradine. The authors achieved their goal of blocking the sepsis-induced heart rate increase, but had no effect on mortality or the inflammatory response. The authors concluded that reductions in heart rate alone do not influence outcomes from septic shock.

Zanella et al. (11) from Milan, Italy, have examined a novel extracorporeal technique for regional anticoagulation based on calcium removal by ion exchange chromatography. Using a swine model, the authors used a venous to venous extracorporeal circuit that removed calcium from the blood and provided anticoagulation, as confirmed by thromboelastography analysis. Although the authors could demonstrate that the procedure was effective and safe over 2 h, they did not look at either longer-term anticoagulation or other effects of the procedure. In addition, the studies were conducted in healthy swine, and not those hypercoagulable due to trauma or sepsis. In particular, inflammatory responses were not evaluated. This is an excellent start and proof of principle, but there is obviously a long way to go.

Wang et al. (12) from Chongqing, China, have explored the potential benefit of inhaled hydrogen gas in patients with cardiac arrest. Rats were subjected to asphyxia-induced cardiac arrest and were then resuscitated with 98% oxygen and either 2% nitrogen or hydrogen gas, with and without hypothermia (nitrogen gas). Surprisingly, small amounts of hydrogen gas were more effective than nitrogen gas with or without hypothermia in improving survival and protecting against neurological injury. Unfortunately, the authors could provide no direct mechanism for the protection. Good start, much more to do.

In another report from Chongqing, the investigators have demonstrated that the aryl hydrocarbon receptor (AhR) plays an important role in the maintenance of the function of the intestinal barrier in patients with inflammatory bowel disease and in mouse models. Here they ask whether the AhR also plays a role in intestinal obstruction (13). Using both an animal model
and intestinal epithelial cells, the authors clearly show that in response to intestinal obstruction or hypoxia, AhR expression is reduced. Using an agonist for AhR actually improved tight junction activity and endothelial barrier function. These findings provide convincing preliminary support for targeting the AhR, and better understanding its protective mechanisms.

The final article in this month’s issue comes from Wu et al. (14) in Hunan, China. The authors have examined the role of pyroptosis in the acute lung injury associated with endotoxemia. In this report, the authors provide more evidence that endotoxin-induced Toll-like receptor (TLR4) signaling through interferon-response factor (IRF-1) drives caspase-1-mediated pyroptosis and lung injury. Although it is well known that TLR4 signaling through MyD88 can lead to IRF-1 activation, and TLR4 signaling can play a role in activating the inflammasome, this and earlier work by the authors confirms that lipopolysaccharide can directly stimulate caspase 1 activation and pyroptosis in alveolar macrophages through IRF-1. It does not appear a second signal for the inflammasome directly is required. This is an important observation.

My flight to Gainesville from Atlanta is finally getting ready to depart and I find myself queuing up to board. The past week in Austin at the Shock Society annual meeting and the opportunity to preview the September issue of the journal has reinvigorated me. I am comfortable that the Society and its journal remain on a high trajectory with only the best publications of its membership. This issue reveals again the international nature of the journal, the quality of the work, and the impact it has on the field. Congratulations to all of the contributors for their fine work.

REFERENCES