Cardiopulmonary bypass universally elicits a complex inflammatory response in neonates, infants, children and adults. This immune response may be responsible for mortality and morbidity after cardiac surgery. Although multiple trials have demonstrated that steroids have diverse effects on this immune response, they have typically been limited in design due to factors such as lack of power and absence of important clinical endpoints.

This SCA session will examine the role of steroids from three perspectives: the effects of steroids on the inflammatory response to cardiopulmonary bypass; the evidence for steroids in adult cardiac surgery; and, the evidence for steroids in pediatric cardiac surgery. Definitive conclusions about the effects of steroids on meaningful clinical outcomes after cardiac surgery will depend on data from pivotal large randomized trials.

(A) Steroids and the Systemic Inflammatory Response to Cardiopulmonary Bypass

The systemic inflammatory response syndrome (SIRS) to cardiopulmonary bypass (CPB) has an early and late phase. The early phase develops from the contact activation of blood interacting with nonendothelial surfaces. The late phase is dominated by ischemia-reperfusion injury and endotoxemia. The early phase of SIRS involves protein and
cellular components. The protein components are the contact system, the intrinsic and extrinsic coagulation cascades, complement, and the fibrinolytic system. The cellular components are the endothelial cells, the neutrophils, the monocytes, the lymphocytes, and platelets.

The evidence thus far shows that steroid therapy affects SIRS in a variety of ways. Studies have demonstrated that steroids reduce complement activation, cytokine levels, endotoxin release, and expression of endothelial adhesion molecules. Although steroids inhibit the release of pro-inflammatory cytokines, interlekin-6 and interleukin-8, they also boost levels of the anti-inflammatory cytokine, interleukin 10. Furthermore, steroids suppress circulating concentrations of C-reactive protein while augmenting levels of long pentraxin 3, a novel mediator that may be cardioprotective. Interlekin-6 and interleukin-8 levels after CPB have been correlated with significant increases in transfusion and intensive care unit stay after cardiac surgery with CPB.

Although steroids appear to dampen the SIRS response to CPB, the key question is whether these anti-inflammatory effects translate into meaningful outcome improvement after cardiac surgery with CPB. The subsequent sections review the recent outcome evidence related to this question in both adult and pediatric cardiac surgery.

(B) The Evidence for Steroids in Adult Cardiac Surgery

Three large recent meta-analyses (cumulative N = 8205) have demonstrated that perioperative steroid exposure significantly decreases atrial fibrillation, bleeding, and length of stay. Although steroids had no effect on mortality and infection, they were associated with perioperative hyperglycemia. A recent Cochrane meta-analysis (cumulative N = 3615: 54 randomized trials) demonstrated that steroid therapy had no
effect on mortality, cardiac and pulmonary complications. These studies will be examined in further detail during the panel discussions.

To address the lack of power in the adult steroid CPB studies, 2 large randomized controlled trials are currently underway in adult cardiac surgery: the SIRS (Steroids In CaRdiac Surgery) and the DECS (DEexamethasone for Cardiac Surgery) trials. Full details of the SIRS and DECS trials are available at www.clinicaltrials.gov. These trials together have a target enrollment of at least 14 000 patients and are powered to assess clinically meaningful endpoints. A review of these two landmark trials will be provided during the panel discussions. The findings of these well-designed randomized trials will likely determine the future indications for steroid prophylaxis in adult cardiac surgery.

(C) The Evidence for Steroids in Pediatric Cardiac Surgery

Recent meta-analysis demonstrated weak evidence that steroid therapy reduced duration of mechanical ventilation and length of stay in pediatric cardiac surgery. Two recent multicenter observational trials (cumulative N = 49910) failed to detect any outcome benefit due to steroid therapy in pediatric cardiac surgery. In fact, these two large observational trials suggested that steroid therapy may increase perioperative morbidity. Although there are small single-center steroid trials in progress, the cumulative evidence to date suggests that it is time for large adequately powered trials in pediatric heart surgery to evaluate whether steroid therapy affects mortality and major morbidity in neonates, infants and children undergoing cardiac surgery with CPB. A recent interrogation of clinical trial registries failed to detect any definitive trials matching these criteria. This evidence gap represents a major clinical research opportunity for the cardiac anesthesia community.
References


