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Sommario/riassunto

Pediatric resuscitation medicine has witnessed significant advances with improved understanding of the pathophysiology of cardiac arrest and resuscitation. Multiple mechanisms of neurological injury have been identified, outlining potential avenues for neuroprotection following cardiac arrest. Resuscitation science exists at multiple levels of analysis, from biomechanics of chest compressions to implementation of best training procedures in real time, from epidemiology of cardiac arrest survival to molecular mechanisms of cellular injury due to ischemia and reperfusion. What next steps in research and in clinical practice will ensure the best possible neurologic outcome among children who survive cardiac arrest? How can we leverage novel technologies in neuroimaging, nanomaterials, drug delivery, biomarker-based risk stratification and next generation sequencing, among others, to resuscitate and to protect the Central Nervous System (CNS)? How can we improve clinical trial design and data analyses to maintain a robust clinical research infrastructure and to ensure validity and applicability? These are just some of the questions will addressed in this Research Topic. Using evidence-based algorithms and public health approaches to disseminate them, the last decade has seen a paradigm shift in pediatric resuscitation with significantly improved survival from pediatric cardiac arrests. However, neurologic outcome in survivors remains far from optimal. High quality CPR is increasingly recognized as a key factor for improving neurologic

outcomes. Advanced technologies allow monitoring the quality of CPR and just-in-time feedback to improve the quality of CPR. Further research is needed to evaluate impact of these technologies on neurologic outcome. The recent American Heart Association CPR guidelines emphasis on Circulation-Airway-Breathing (CAB) approach to CPR needs a careful evaluation in children, in whom timely airway and breathing support are as important as circulation. The growing controversy regarding use of epinephrine, and alternative routes of administration of epinephrine during CPR, warrants further evaluation in the setting of pediatric CPR. Improved outcome of hemodynamic goal-directed CPR over standard CPR in animal models of cardiac arrest has initiated interest in physiology-based CPR, especially in the in-hospital cardiac arrest. Basic and applied-science research have become relevant for specific subpopulations of pediatric cardiac arrest victims and circumstances (e.g., ventricular fibrillation, neonates, congenital heart disease, extracorporeal cardiopulmonary resuscitation). Just-in-time and just-in-place simulation training, which have evolved as training strategies to improve quality of CPR, are being evaluated for outcomes. The concept of just-in-time and just-in-place coaching of CPR providers on high quality CPR is a novel concept which has emerged recently and remains unstudied. Whilst there have been significant advances in newborn stabilization over the last decade many questions remain unanswered. These include the role of delayed cord clamping in preterm infants and term newborns requiring resuscitation, the role of sustained inflations as a method of respiratory support and the role of epinephrine and volume administration in neonatal resuscitation. Novel methods of assessment including the use of end tidal CO2 monitoring, respiratory function monitoring and near infrared spectroscopy warrant further evaluation. The use of transitioning animal models that accurately replicate the newborn circulation with patent fetal shunts are emerging but more assessments in these are required to better establish CPR strategies in newborn infants. Newborn resuscitation training programs have resulted in a reduction in neonatal mortality in the developing world, but key questions remain around the frequency of training, team training methods and the role of simulation training. Post resuscitation interventions, in particular therapeutic hypothermia, has resulted in significant improvements in long-term outcome and there is now a growing interest in adjunct therapies, such as use of melatonin, erythropoietin, or other neuroprotective molecules to improve therapeutic benefits of cooling. Therapeutic hypothermia did not provide any higher benefit than normothermia in children following out of hospital cardiac arrest, although three is considerable debate in the community whether 14% probability of observing a similar outcome if the study were repeated a 100 times applies to an individual child in the PICU. Exciting research is occurring in unraveling connection between inflammation, immune dysregulation and neuroinjury. This will further support research on the use of anti-inflammatory agents and immunomodulators for neuroprotection after cardiac arrest and birth asphyxia.