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Strategic Planning for Research in Pediatric Critical Care

Robert F. Tamburro, MD, MSc¹, Tammara L. Jenkins, MSN, RN, PCNS-BC¹, and Patrick M. Kochanek, MD, MCCM²

¹Pediatric Trauma and Critical Illness Branch, Eunice Kennedy Shriver National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland ²Safar Center for Resuscitation Research, Departments of Critical Care Medicine, Anesthesiology, Pediatrics, Bioengineering, and Clinical and Translational Science, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

Abstract

Objective—To summarize the scientific priorities and potential future research directions for pediatric critical care research discussed by a panel of experts at the inaugural Strategic Planning Conference of the Pediatric Trauma and Critical Illness Branch of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development.

Data Sources—Expert opinion expressed during the Strategic Planning Conference.

Study Selection—Not applicable

Data Extraction—Chaired by an experienced expert from the field, issues relevant to the conduct of pediatric critical care research were discussed and debated by the invited participants.

Data Synthesis—Common themes and suggested priorities were identified and coalesced.

Conclusions—Of the many pathophysiological conditions discussed, the multiple organ dysfunction syndrome emerged as a topic in need of more study that is most relevant to the field. Additionally, the experts offered that the inter-relationship and impact of critical illness on child development and family functioning are important research priorities. Consequently, long-term outcomes research was encouraged. The expert group also suggested that multidisciplinary conferences are needed to help identify key knowledge gaps to advance and direct research in the field. The Pediatric Critical Care and Trauma Scientist Development National K12 Program and the Collaborative Pediatric Critical Care Research Network were recognized as successful and important programs supported by the branch. The development of core data resources including biorepositories with robust phenotypic data using common data elements was also suggested to foster data sharing among investigators and to enhance disease diagnosis and discovery. Multicenter clinical trials and innovative study designs to address understudied and poorly understood conditions were considered important for field advancement. Finally, the growth of the pediatric critical care research workforce was offered as a priority that could be spawned in many

Corresponding Author: Robert Tamburro, MD, MSc, Medical Officer, Pediatric Trauma and Critical Illness Branch, *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD), 6100 Executive Blvd Room 8B07K, Rockville, MD 20852, Phone: 301-480-2619, robert.tamburro@nih.gov.

ways including by expanded transdisciplinary and multiprofessional collaboration and diversity representation.

Keywords

Pediatric Critical Care Medicine; Pediatrics; Research; Study Design; Mortality; Multiple Organ Dysfunction Syndrome

Introduction

The provision of pediatric critical care is a rapidly expanding and evolving area of medicine that encompasses a wide variety of multidisciplinary disease processes and therapeutic interventions. First recognized as a subspecialty by the American Board of Pediatrics in 1985, there are currently over 300 pediatric intensive care units (PICU) and 67 approved Fellowship Programs in the United States and Puerto Rico (1,2,3). To help address the needs of critically ill and injured children and their families, the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) created the Pediatric Trauma and Critical Illness Branch (PTCIB) in April of 2012. The NICHD has long supported research in the fields of pediatric trauma and critical illness, and the branch was formed to coordinate this varied research and to provide direction for future research efforts. To help inform the direction of this new branch, experts in the fields of pediatric trauma, injury prevention and critical illness were convened from across the country to share insight and expertise at an inaugural Strategic Planning Conference. The purpose of this manuscript is to describe priorities and future directions for pediatric critical care research as discussed and debated by participants of that conference.

Methods

The inaugural Strategic Planning Conference of the PTCIB of the NICHD was conducted during a single, two day meeting in April of 2014 at the National Institutes of Health (NIH) main campus in Bethesda, Maryland. Experts were selected by the branch leadership based on publication and NIH funding records as well as leadership roles in their respective professional societies. After introductory presentations including a historical overview of the PTCIB, the experts were divided into three groups (Trauma and Emergency Care, Injury and Violence, and Critical Care) based on their area of expertise. These three groups conducted individual break-out sessions over the course of the two days where priorities and future directions for their respective fields were discussed and debated. In the end, each group chair summarized their deliberations and conclusions, and presented them to the entire conference constituency. There was no formal voting process. This manuscript is limited to only the deliberations of the Pediatric Critical Care group.

Scientific Priorities

Given the vast heterogeneity of disease processes and treatment options in the field of pediatric critical care, one of the foremost challenges is identifying focused priorities for future investigation. The expert panel suggested that pathophysiology-based topics including, but not limited to, multiple organ dysfunction syndrome (MODS), respiratory

failure, sepsis, and brain injury all merit significant attention as they constitute much of the morbidity and mortality associated with critical illness in children. Of these various topics, the need for further study of MODS emerged as the most consistent theme expressed during the conference. MODS is triggered by a host of disease processes, most notably sepsis, and is the final common pathway of morbidity and mortality for many of these conditions (4,5). However, much remains to be learned regarding MODS in children beginning with its fundamental pathophysiology and extending out to more global issues such as its epidemiology and long-term outcomes. An enhanced understanding of the similarities and differences of the various precipitants of MODS may ultimately result in the development of specific therapies to halt and ameliorate this life-threatening condition. Such understanding and therapeutic intervention may result in improved outcomes for children. Given the cross cutting nature of this condition, the PTCIB could serve to facilitate coordination of this field of study for children among the relevant scientific branches at the NICHD and other National Institutes of Health (NIH) Institutes and Centers, as well as other federal agencies and organizations with mutual interests and priorities.

In addition to specific pathophysiological processes, the panel of experts suggested a need for focused study of the impact of age and developmental status on critical illness and injury. Although other Institutes are invested in studying many of the disease processes common to critical care, it is likely that the investigation of the effect of age and developmental status on these conditions is most consistent with the mission of the NICHD. The expert panel contended that such study may be important to the field. For example, data suggest that MODS is much more common in neonates and infants than in older children (6,7); study delineating the reasons for such differences may help inform a better understanding of the condition, and ultimately result in improved outcomes.

Conversely, the need to assess the impact of critical illness on growth and development must also be evaluated. The experts offered that long-term outcomes of critical illness need to be a priority for the field. As the practice of pediatric critical care has advanced, mortality has decreased significantly. Data from the NICHD Collaborative Pediatric Critical Care Research Network suggest a collective 2.7% mortality rate among all non-moribund admissions to the PICUs of eight large quaternary care children's hospitals (8); comparable results have been reported by others using multicenter data (6,9). Although the primary goal of pediatric critical care research will always be to enhance the understanding and management of acute pathophysiology in the PICU to maximally and optimally affect outcomes, these encouraging data suggest that mortality should no longer be considered the sole outcome variable for research in the field. These data support the contention that other long-term outcomes of critical illness need to be a priority. These long-term outcome assessments must not only include data pertaining to physical outcomes, but also indices of cognitive function and quality of life. Currently, the branch is funding a large multicenter study assessing the impact of sepsis and organ failure on long-term health-related quality of life (HRQL) indices and functional status in children. Similarly, the branch is supporting an ancillary study of the recently published Randomized Evaluation of Sedation Titration for Respiratory Failure (RESTORE) trial to determine the relationships between sedative exposure during pediatric critical illness and long-term neurocognitive outcomes (10).

In considering outcomes beyond survival, the expert panel asserted that the effect of critical illness on the family unit is an important and understudied area, and therefore, should be considered a priority for the field. Such an approach would appear to dovetail well with the call for an emphasis on long-term outcome analysis. The ability to support and maintain a well-functioning family despite critical illness in a child is not only a laudable goal, but vital to the health and welfare of the family members.

Other issues relevant to the field offered by the group of experts included the care of the chronically ill/technology-dependent child with critical illness, the development of therapeutics, technologies, and devices to improve care in the PICU, and patient safety concerns as related to critical illness. The incorporation of pediatric critical care into disaster medicine was also recognized as an ever-growing priority. Similar to many other topics, these issues are relevant to a number of other NIH Institutes, federal agencies and organizations, and thus, the branch is likely to work closely and in conjunction with these other groups in addressing these topics.

Future directions

In terms of future research directions, investigator-initiated projects addressing many of the priority areas identified by the expert panel will be important in advancing the mission of the branch. Although definitive, large scale, multicenter trials are clearly needed to advance the field, the application of innovative study designs may be necessary to address the relatively small and heterogeneous PICU patient population. In addition, there would also appear to be a need for exploratory, hypothesis-generating projects. These smaller scale studies are required to develop and inform the foundation upon which large scale studies can be based. Such exploratory work can help elucidate the pathophysiological processes driving critical illness and suggest targets for therapeutic intervention. However, it is important that “pilot” randomized, controlled trials result in further, more definitive study as this has been a challenge for the pediatric critical care community (11). Additionally, secondary analyses of existing datasets and biorepository specimens represent another attractive, cost-effective method of analysis (12). Moreover, given the multidisciplinary nature of pediatric critical care, collaboration will remain essential in advancing the science and transforming the field. Such collaboration should include efforts with a variety of clinical subspecialties and disciplines, basic scientists, NIH Institutes and Centers, federal agencies, small businesses and other private sector entities.

Plans for the future must also include a strong and continued commitment to the development, mentoring and support of new and early stage investigators to assure a continuous pipeline of successful pediatric critical care researchers from a range of disciplines. Maintaining a robust workforce of researchers in the field must be a high priority. In 2014, less than a quarter of the individuals taking the Pediatric Critical Care Medicine certification exam for the first time responded that research would be a major part of their career; only 13% of their time was currently devoted to any research (13). As discussed at the Strategic Planning Conference, there appears to be a need for more effective mentors, more opportunities for research collaborations, and improved and expanded research education and training for new and early stage investigators in pediatric critical

care. Currently, the branch supports a number of Institutional Training and Career Developments Awards. Among these, the Pediatric Critical Care and Trauma Scientist Development Program (PCCTSDP), a national K12 Program, is particularly noteworthy (<http://www.pccsd.org/>). Since its inception in 2005, this Program has trained 34 junior faculty members from across the United States. As of November 2014, nearly 60% of these individuals have subsequently been awarded additional federal funding consisting of a total of 24 awards and three R01s. In addition, participants at the Strategic Planning Conference asserted that the PCCTSDP K12 Program is invaluable and noted that in addition to the awards, the Program has created a community of young scholars who network effectively. Moreover, to further secure and augment the workforce in pediatric critical care research, the branch recognizes the expressed need to expand both multiprofessional training opportunities and diversity in the field with greater inclusion of trainees who are minority, disadvantaged, or have a disability.

The branch also supports the sites and data coordinating center of the Collaborative Pediatric Critical Care Research Network (CPCCRN). It was noted by the expert panel that the CPCCRN is a core function of the branch and that it is key to generating Level I and II evidence for the field. Since its inception in 2004, the Network has published over 40 manuscripts and played an integral role in the recently published Therapeutic Hypothermia After Pediatric Cardiac Arrest (THAPCA) trial (14). The Network has also developed several detailed public use datasets that are available to the field at large (15). As described above, secondary analyses of these data represent a cost effective manner to advance the field and should be encouraged.

In addition to public use datasets, the development of other core resources such as biorepositories, prototype devices, and drug development registries is also important to advancing the science of pediatric critical illness and injury. The collection and safe storage of data and specimens now will foster and facilitate future study. The need to phenotype individual diseases and to standardize phenotypic descriptions using common data elements is paramount to the development of such resources. It was offered by the experts that the utilization of the electronic medical record and bioinformatics may facilitate such study.

In addition to developing core resources, the field must build upon its tradition and recent success of sponsoring conferences that advance the field (16). The branch can use its “power to convene” to facilitate this process and provide investigators the opportunity to meet to clarify the needs of the field, to identify knowledge gaps, and to propose future study. In response to insight expressed at the Strategic Planning Conference, the branch recently sponsored a multidisciplinary conference on Pediatric MODS. Participants included early career and senior scholars from a range of disciplines whose collective expertise helped inform the branch on the state of the science and identified key research priorities for the future. Meetings such as this offer the opportunity to promote the importance of pediatric critical care research outside of the field and help to build working relationships among important constituencies. This is paramount to the success of the field given the breadth of pathophysiology and disease processes encountered in the PICU, and the limited available resources to address such understudied and poorly understood conditions. Additionally, collaboration among the many invested, established and successful groups focused on

enhancing the care of critically ill children such as the Society of Critical Care Medicine, the American Academy of Pediatrics, the Pediatric Acute Lung Injury and Sepsis Investigators (PALISI Network), the World Federation of Pediatric Intensive and Critical Care Societies as well as the many other groups in the United States and across the world should be fostered. The effective use of conferences may represent one method to nurture such collaborations.

Conclusions

In summary, the provision of pediatric critical care is an ever-expanding and evolving science. To meet the challenges of this important practice, the NICHD has created a new Pediatric Trauma and Critical Illness Branch. As one of its initial actions, the branch sponsored a conference to convene experts in the fields of pediatric trauma, injury prevention and critical illness to discuss and describe key knowledge gaps and areas for further study in these fields. The field of pediatric critical care is most broad and filled with much heterogeneity, and thus, developing an exhaustive list of key knowledge gaps is an endless task. For example, important issues such as the genetic basis of critical illness, the use of point prevalence trials, and surrogate short-term outcomes for mortality were not discussed in any meaningful way at the meeting. However, it is hoped that the priorities and potential future directions for pediatric critical care research as discussed by the participants at this conference will provide useful insight for the field.

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