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FOCUS EDITORIAL

Focus on paediatrics: 2017

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Introduction

"It is a capital mistake to theorize before one has data. Insensibly, one begins to twist facts to suit theories, instead of theories to suit facts" observed Sir Arthur Conan Doyle. The scarcity of data available for Paediatric Intensivists means that, unlike Sherlock Holmes, we often have to act without evidence [1]. Here, we review the recent contributions to PICU evidence from *Intensive Care Medicine* (*ICM*).

Tight glycemic control

Following initial benefits of insulin to limit even mild hyperglycemia in critical illness, there was widespread uptake of tight glycemic control before the pendulum swung back towards more moderate glucose control in adults. Earlier this year, Agus and colleagues reported no difference in outcomes for critically ill children treated with tight versus mild glucose control [2]. Yamada et al. then published in *ICM* a network meta-analysis demonstrating that the totality of paediatric data demonstrates that mild glycemic control achieves similar outcomes as tight control, with less risk of hypoglycemia [3]

Sepsis

In 2017, the latest update to the American College of Critical Care Medicine (ACCM) Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock was published [4]. In the seven years elapsed since the last evidence-based review was completed, the taskforce noted that "the changes recommended were few" because most of the interim data focused on improving implementation of prior guidelines rather than new data. However, several recent studies in *ICM* have already begun to push the field of pediatric sepsis forward. First, paediatric investigators from Australia/New Zealand derived a pediatric sepsis score that predicted mortality with reasonable accuracy in the first hour of ICU admission [5]. Such early prediction is vital, as the authors showed that about half of sepsis-associated deaths occurred within 48 h of admission, a finding similarly reported in the UK and USA [6, 7]. Second, Schlapbach et al. reported superior utility of a derived pediatric version of the Sequential Organ Failure Assessment (SOFA) score over SIRS-based definitions of sepsis [8]. Together with a similar report from the US [9], these new data indicate potential to apply Sepsis-3 to update pediatric definitions of sepsis and septic shock.

But what cut-off points are most optimal to define pediatric hypotension, for septic and other types of shock? Ray et al. added to this discussion by comparing concurrently recorded invasive and non-invasive blood pressure measurements across 50,000 pairs. They found that non-invasive measurements gave systematically lower readings for mean and diastolic values [10]. How is one to determine which blood pressure targets are optimal in septic shock when it is not even clear how to best to measure? Finally, although not sepsis, James and colleagues studied use of nitric oxide (NO) during cardiopulmonary bypass—another systemic inflammatory insult—and found that patients randomized to NO had a lower incidence of cardiogenic shock and reduced length of stay, especially in neonates and complex heart disease [11]. Perhaps ameliorating reperfusion injury is as important as reperfusion itself.

Mechanical ventilation

In *ICM* in 2017, the Paediatric Mechanical Ventilation Consensus Conference (PEMVECC) developed and voted on 152 recommendations about paediatric mechanical ventilation [12]. However, data from randomised clinical trials were available for only three topic areas and most recommendations were either deferred

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Table 1 Summary of pediatric critical care trials published in 2017 Reference: http://picutrials.net

Topic	Number of trials	Cumulative enrollment	Population
Glycemic control	1	713	Shock or respiratory failure
Therapeutic hypothermia	1	329	In-hospital cardiac arrest
Transfusion	2	342	PICU/CICU
Infection prevention	1	150	PICU patients with bladder catheter
Respiratory	4	347	PICU patients pre-intubation, during intubation, and post-extubation
Nutrition/electrolytes	5	322	Sepsis, burns, CHD, DKA
Sepsis/shock	2	153	Septic shock
CHD/pulmonary hypertension	6	407	Post-surgical
Traumatic brain injury	1	14	Severe TBI with CSF drainage
Early mobilization	1	30	Expected PICU LOS > 48 h

CHD congenital heart disease, *PICU* pediatric intensive care unit, *CICU* cardiac intensive care unit, *DKA* diabetic ketoacidosis, *TBI* traumatic brain injury, *CSF* cerebrospinal fluid, *LOS* length of stay

or based on low-to-moderate evidence. But new data are emerging. The Oxy-PICU investigators described current practice of oxygenation targets in a PICU and showed, with high-fidelity SpO_2 data, that liberal oxygenation targets > 95% are the general rule irrespective of the FiO_2 or mean airway pressure used [13]. These data pave the way for a trial of oxygenation targets in critically ill children. The TRAMONTANE study randomized infants < 6 months with moderate/severe bronchiolitis to either high-flow nasal cannula (HFNC) or continuous positive airway pressure (CPAP) with cross-over allowed [14]. Overall, patients in both groups were rarely intubated, with similar rates of rescue using the alternative non-invasive modality, suggesting that clinician preference may be more important than the modality chosen even though initial randomization to HFNC was slightly less efficacious. Finally, a review by Moreira and Sapru in *ICM* discussed the potential for targeted use of epithelial, endothelial, coagulation, and inflammatory biomarkers to treat children with acute lung disease, further emphasizing the complexity in data-driven approaches to mechanical ventilation and other novel lung therapies [15].

Pain and sedation

A multidisciplinary taskforce published clinical recommendations for pain, sedation, withdrawal and delirium assessment in critically ill infants and children in *ICM* in 2016. Similar to mechanical ventilation, the authors noted a limited literature with most recommendations based on few data [16]. Addressing one aspect, Vet and colleagues compared protocolized sedation with versus without a daily sedation interruption and found no difference in ventilator-free days or length stay but a higher mortality in the interruption arm. Unfortunately, the study was terminated early for slow recruitment, hindering data quality [17].

Post-ICU survivor outcomes

In 2017, the long-awaited results of the therapeutic hypothermia after in-hospital cardiac arrest were published [18]. Similar to the previously reported out-of-hospital THAPCA trial, there was no benefit for moderate hypothermia compared to controlled normothermia on survival with a good neurobehavioral outcome. Of note, the investigators used the Vineland Adaptive Behavior Scale to measure their primary outcome with substantial caregiver reporting. However, van Zellem et al. showed that parents and teachers systematically reported different levels of function following survival from cardiac arrest [19]. Thus, even when outstanding attempts are made to collect longer-term morbidity outcomes, the most appropriate measures remain unclear. Finally, Verstraete and colleagues demonstrated that there may also be risk factors right under our noses that we fail to consider when they showed that environmental phthalate exposure leaching from indwelling medical devices was common in PICU patients, with higher levels associated with long-term attention deficits [20].

Conclusions

Sherlock Holmes' skill was to solve challenging cases by finding clarity despite seemingly limited data. Paediatric intensivists are arguably faced with similar challenges, but without necessarily the same genius. Holmes understood "there is nothing like first-hand evidence". The work carried out in 2017 (Table 1) may assist us non-sleuths to make better decisions.

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Compliance with ethical standards

Conflicts of interest
None of the authors report any conflicts of interest.

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