UPDATES ON SHOCK

Can we use the new evidences from adults?

SAMUEL NEGASH, MD
PEDIATRIC SURGERY RESIDENT
ADDIS ABABA UNIVERSITY

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OBJECTIVES

- To highlight new concepts in the management of shock in adults
- To discuss application to pediatric patients

OUTLINE

- **Part 1 – Traumatic shock**
  - Background
  - Coagulopathy & tranexamic acid
  - Damage control resuscitation
  - Massive transfusion
  - Summary
- **Part 2 – Septic Shock**
  - Background
  - Recommendations in adults & 2018 update
  - Latest Pediatric guideline & New evidences
  - Summary
- **Conclusion**
- **References**

TRAUMATIC SHOCK: NEW CONCEPTS

- COAGULOPATHY & TRANEXAMIC ACID
- DAMAGE CONTROL RESUSCITATION
- MASSIVE TRANSFUSION PROTOCOL

BACKGROUND

- Trauma is the leading cause of death in pediatrics
- Advanced trauma life support guidelines
  - 1980 (1st edition), 1982, 1984, 1993, 1997, 2004, 2008, 2012 (9th edition) >> 2018 (10th edition)
- In adults there are recent advancements
  - Understanding of pathophysiology of traumatic shock
    - Systemic response (proinflammatory activation & multiorgan failure)
  - New medications and protocols to improve survival
- Lack of evidence to reduce mortality in pediatric trauma

PATHOPHYSIOLOGY OF ADULT TRAUMA

- Hemorrhage is the 1st cause of death after arrival to hospital
- Acute coagulopathy of trauma (25%) exacerbates situation
  - Acute traumatic coagulopathy (ATC)
    - Hyperfibrinolysis (TEG, ROTEM)
    - Anticoagulation, consumption, platelet dysf.
  - Iatrogenic coagulopathy (IC)
    - acidosis & hypothermia (vicious cycle)
    - hemodilution (overly aggressive crystalloid)
    - Transfusion PRBC without other component

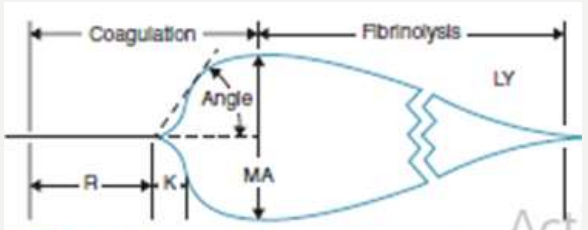


Figure 4-6. Illustration of a thromboelastogram (TEG) tracing.

COAGULOPATHY IN PEDIATRIC TRAUMA

- Hemorrhage 2nd leading cause of death (after TBI)
- Coagulant maturity lags behind anticoagulant
- Coagulopathy prevalent in pediatric trauma, but role of hyperfibrinolysis not well established

Coagulopathy and shock on admission is associated with mortality for children with traumatic injuries at combat support hospitals.

Jason T Patregnani, Matthew A. Borgman, Marc G. Maegele, Charles E. Wade, Lorne H. Blackbourne, Philip Charles Spinella

Published 2012 in Pediatric critical care medicine : a journal of...

CONCLUSIONS

In children with traumatic injuries treated at combat support hospitals, coagulopathy and shock on admission are common and independently associated with a high incidence of inhospital mortality. Future studies are needed to determine whether more rapid and accurate methods of measuring coagulopathy and shock as well as if early goal-directed treatment of these states can improve outcomes in children. (Less)

EARLY USE OF TRANEXAMIC ACID IN ADULT TRAUMA

- Antifibrinolytic (stabilize clot)
- Cheap (~11 Canadian dollars)
- Reduced mortality in both military and civilian trials (saves 1 in 67 lives)

**Available in TASH in anesthesia & ortho departments

- **CRASH-2** (RCT)
  - Adult (≥16 yr)
  - Suspected trauma hemorrhage
  - Mortality benefit in 1st 3hr
  - 1g over 10 min then 1g over 8hr
  - Thrombotic comp. very rare

CAN WE USE TXA IN PEDIATRIC TRAUMA?

- Use in non traumatic perioperative setting reduces transfusion requirement
- Denying injured children TXA due to the lack of pediatric trauma trial evidence ?

Immediate need for transfusion, with any one of the following indicating severe shock[a]
• Systolic blood pressure low (<80 mmHg <5 years and <90 mmHg ≥5 years)
• Poor blood pressure response to crystalloid 20–40 ml/kg
• Obvious significant bleeding

Age	Loading dose (administer within 3 hours)	Subsequent dose
≥12 years:adult protocol	1 g intravenously over 10 minutes	1 g intravenous infusion over 8 hours
<12 years	15 mg/kg intravenously over 10 minutes (maximum dose 1 g)	2 mg/kg/hr intravenous infusion over 8 hours or until bleeding stops

The Hospital for Sick Children Massive Hemorrhage Protocol for the use of tranexamic acid in pediatric trauma. April 2014. Adapted from Royal College of Paediatrics and Child Health: Evidence statement - Major trauma and the use of tranexamic acid in children [39].

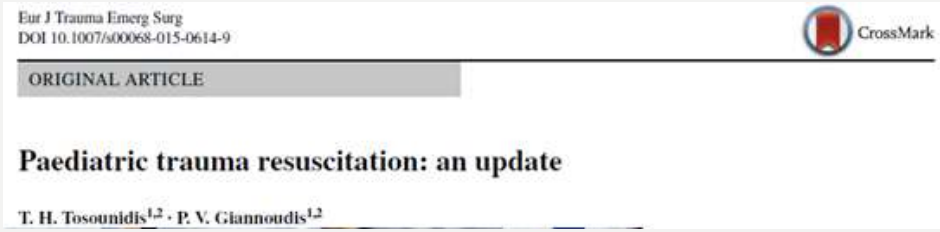
RESUSCITATION IN ADULT HEMORRHAGE

Damage control resuscitation

1. **Controlled resuscitation / Permissive hypotension**
   (avoid disruption of thrombus)
2. **Limit crystalloids** (avoid hemodilution)
3. **More blood products**
4. **Rapid surgical control** of bleeding
5. **Prevent acidosis, hypothermia, coagulopathy**
   (lethal triad)

EVIDENCE IN PEDIATRIC TRAUMA

- No appropriate physiologic triggers of resuscitation strategies based on age
- Children decompensate very quickly
- Principles may be applied to children but ?permissive hypotension



Eur J Trauma Emerg Surg
DOI 10.1007/s00068-015-0614-9

CrossMark

ORIGINAL ARTICLE

Paediatric trauma resuscitation: an update

T. H. Tosounidis[1,2] · P. V. Giannoudis[1,2]

Permissive or low volume resuscitation is a concept that has evolved over the last years in the management of adult trauma patient and has gained considerable attention both in clinical setting and the related basic research [16–19]. This practice has not gained wide acceptance in the management of paediatric patients and some authors advocate extreme vigilance, questioning the non-validated theoretical benefits of such an approach in children [20].

MASSIVE TRANSFUSION PROTOCOL IN ADULT TRAUMA

- How much is massive?
  - use of > 10 U of PRBC in 24hr or >4-6 units in 4-6hr
  - loss of one blood volume in 24 hours or 50% in 3 hours
  - ongoing loss of 150 mL/h.
- In which patients should we anticipate MT?
  - Patients who are unstable or
  - Do not respond after 1–2 RBCs
- How do we transfuse after initiating MT protocol?
  - Fixed ratio component therapy (PRBC:FFP:platlet = 1:1:1)

    *benefits of fresh whole blood in military population
  - 6 units should be available (may add cryoprecipitate after)
  - Obtain labs (CBC, INR, fibrinogen, PH, TEG)
  - Terminate when patient active bleeding stops

PROTOCOLS FOR PEDIATRIC TRAUMA

- Guidelines are vague or nonexistent
  - time to transition from crystalloid to blood?
  - what blood products should be given?

Seminars in Pediatric Surgery (2010) 19, 286-291

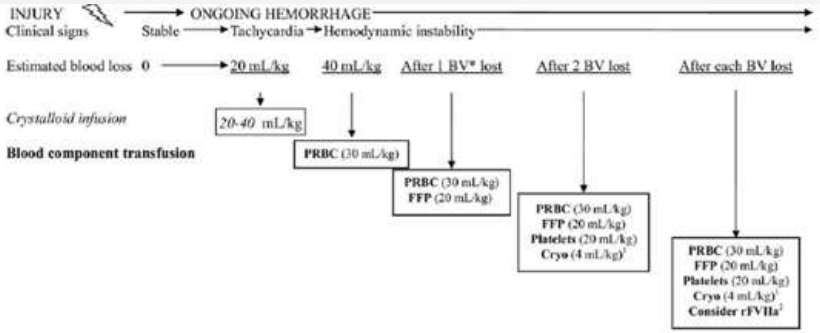
ELSEVIER

SEMINARS IN PEDIATRIC SURGERY

Massive transfusion and blood product use in the pediatric trauma patient

Jeffrey J. Dehmer, MD,[a] William T. Adamson, MD[a,b]

1. Initiation of MT protocol in traumatic hemorrhagic shock with persistent hemodynamic instability or ongoing bleeding after 40 mL/kg of crystalloid infusion
2. Blood components delivered to larger pediatric patients (>30 kg) at a ratio of 1:1:1 units of PRBCs/FFP/platelets with cryoprecipitate given for low fibrinogen levels (<1-1.5 g/L) or ongoing bleeding after the administration of 1 round of all 3 blood components. For pediatric trauma patients less than 30 kg, a weight-based protocol at a ratio of 30:20:20, such as seen in Figure 1,[63] would be initiated.



SUMMARY: PEDIATRIC TRAUMA

- Too vigorous fluid might be harmful for children
- Permissive resuscitation is not well accepted in pediatric population
- MTP is gaining popularity in severe shock
- Trauma-related coagulopathy in children constitutes a major factor contributing to mortality
- TXA use is not supported by robust evidence but expert opinion suggests its use

SEPTIC SHOCK: NEW CONCEPTS

- DEFINITION OF SEPSIS
- ASSESSMENT OF ORGAN DYSFUNCTION
- TREATMENT GUIDELINE
  - Fluid management
  - Monitoring
  - Antimicrobials
  - ionotropic/vasoactive agents
  - Corticosteroids
  - Other aspects

BACKGROUND

- Sepsis is among one of the leading cause of mortality among children
- It is a medical emergency (early identification and management improves outcomes)
- Morality seems to be gradually declining for the past decade with the implementation of SCC guidelines
  - 2004 (1st guideline) >> 2008 (1st revision) >> 2012 (2nd revision) >> 2016 (3rd)
- Unlike previous versions, the pediatric considerations are not included in the latest guideline

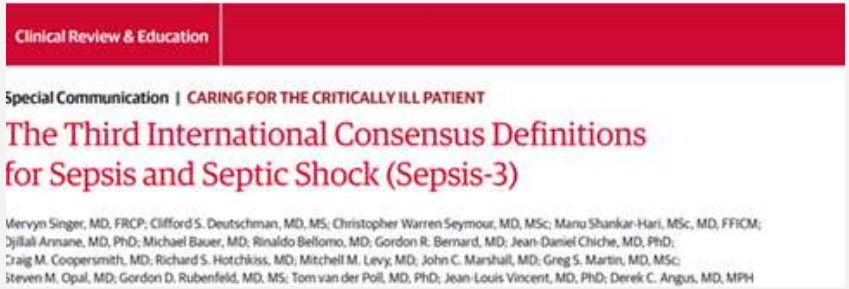
NEW DEFINITION OF SEPSIS & SEPTIC SHOCK

Sepsis (definition)

- life-threatening organ dysfunction caused by a dysregulated host response to infection (formerly severe sepsis)

Septic shock (definition)

- Subset of sepsis profound circulatory, cellular, and metabolic abnormalities are associated with a greater risk of mortality than with sepsis alone (formerly sepsis induced hypotension persisting despite adequate resuscitation)


Clinical Review & Education

Special Communication | CARING FOR THE CRITICALLY ILL PATIENT

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

Mervyn Singer, MD, FRCP; Clifford S. Deutschman, MD, MS; Christopher Warren Seymour, MD, MSc; Manu Shankar-Hari, MSc, MD, FFICM; Djillali Annane, MD, PhD; Michael Bauer, MD; Rinaldo Bellomo, MD; Gordon R. Bernard, MD; Jean-Daniel Chiche, MD, PhD; Craig M. Coopersmith, MD; Richard S. Hotchkiss, MD; Mitchell M. Levy, MD; John C. Marshall, MD; Greg S. Martin, MD, MSc; Steven M. Opal, MD; Gordon D. Rubenfeld, MD, MS; Tom van der Poll, MD, PhD; Jean-Louis Vincent, MD, PhD; Derek C. Angus, MD, MPH

NEW ASSESSMENT OF SEPSIS & SEPTIC SHOCK

Assessment of organ dysfunction

- Increase in SOFA (sequential organ failure assessment) score by 2 points (formerly SIRS)
- *qSOFA (quick SOFA) for screening

Assessment of septic shock

- Vasopressor requirement to maintain MAP >65
- Serum lactate >2 in absence of hypovolemia

(formerly hypotension persisting after infusion of 30ml/kg fluid)

NEW TREATMENT GUIDELINE

3hr bundle (to be completed in 3 hours)

1. Measure lactate
2. Obtain blood culture (aerobic & anerobic) before antimicrobial
3. Administer antimicrobials (at least 2 IV broad spectrum antibiotics)
4. Administer 30ml/kg crystalloid (for hypotension or lactate>4mmol/L)
(formerly 4 target Goals in first 6 hrs)

* Add albumin if require substantial amount of crystalloids (weak recom.)

6h bundle (to be completed in 6 hours)

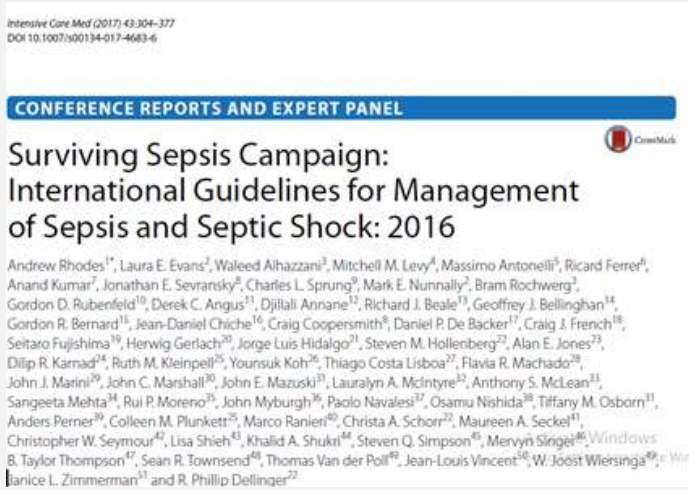
5. Apply vasopressor (for fluid unresponsive shock)

*NE is first line but may add vasopressin & epi. to achieve target MAP of ≥65

6. Remeasure lactate (if initial elevated)

?Corticosteroids

- Low dose hydrocortisone for vasopressor unresponsive (weak recom.)



Intensive Care Med (2017) 43:304–377
DOI 10.1007/s00134-017-4683-6

CONFERENCE REPORTS AND EXPERT PANEL

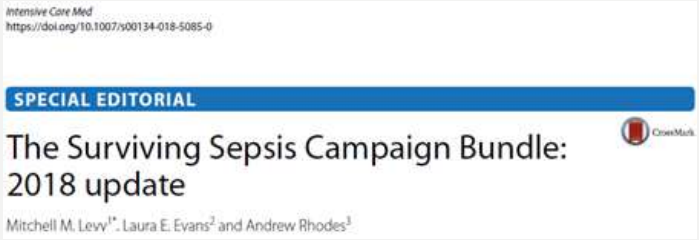
Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016

Andrew Rhodes[1*], Laura E. Evans[2], Waleed Alhazzani[3], Mitchell M. Levy[4], Massimo Antonelli[5], Ricard Ferrer[6], Anand Kumar[7], Jonathan E. Sevransky[8], Charles L. Sprung[9], Mark E. Nunnally[2], Bram Rochwerg[3], Gordon D. Rubenfeld[10], Derek C. Angus[11], Djillali Annane[12], Richard J. Beale[13], Geoffrey J. Bellinghan[14], Gordon R. Bernard[15], Jean-Daniel Chiche[16], Craig Coopersmith[8], Daniel P. De Backer[17], Craig J. French[18], Seitaro Fujishima[19], Herwig Gerlach[20], Jorge Luis Hidalgo[21], Steven M. Hollenberg[22], Alan E. Jones[23], Dilip R. Karnad[24], Ruth M. Kleinpell[25], Younsuk Koh[26], Thiago Costa Lisboa[27], Flavia R. Machado[28], John J. Marini[29], John C. Marshall[30], John E. Mazuski[31], Lauralyn A. McIntyre[32], Anthony S. McLean[33], Sangeeta Mehta[34], Rui P. Moreno[35], John Myburgh[36], Paolo Navalesi[37], Osamu Nishida[38], Tiffany M. Osborn[31], Anders Perner[39], Colleen M. Plunkett[25], Marco Ranieri[40], Christa A. Schorr[22], Maureen A. Seckel[41], Christopher W. Seymour[42], Lisa Shieh[43], Khalid A. Shukri[44], Steven Q. Simpson[45], Mervyn Singer[46], B. Taylor Thompson[47], Sean R. Townsend[48], Thomas Van der Poll[49], Jean-Louis Vincent[50], W. Joost Wiersinga[49], Janice L. Zimmerman[51] and R. Phillip Dellinger[22]

UPDATES TO THE NEW GUIDELINE

Hour-1 bundle (to be completed in 1 hour)

- 3-h and 6-h bundles have been combined to a single bundle


Intensive Care Med
https://doi.org/10.1007/s00134-018-5085-0

SPECIAL EDITORIAL

The Surviving Sepsis Campaign Bundle: 2018 update

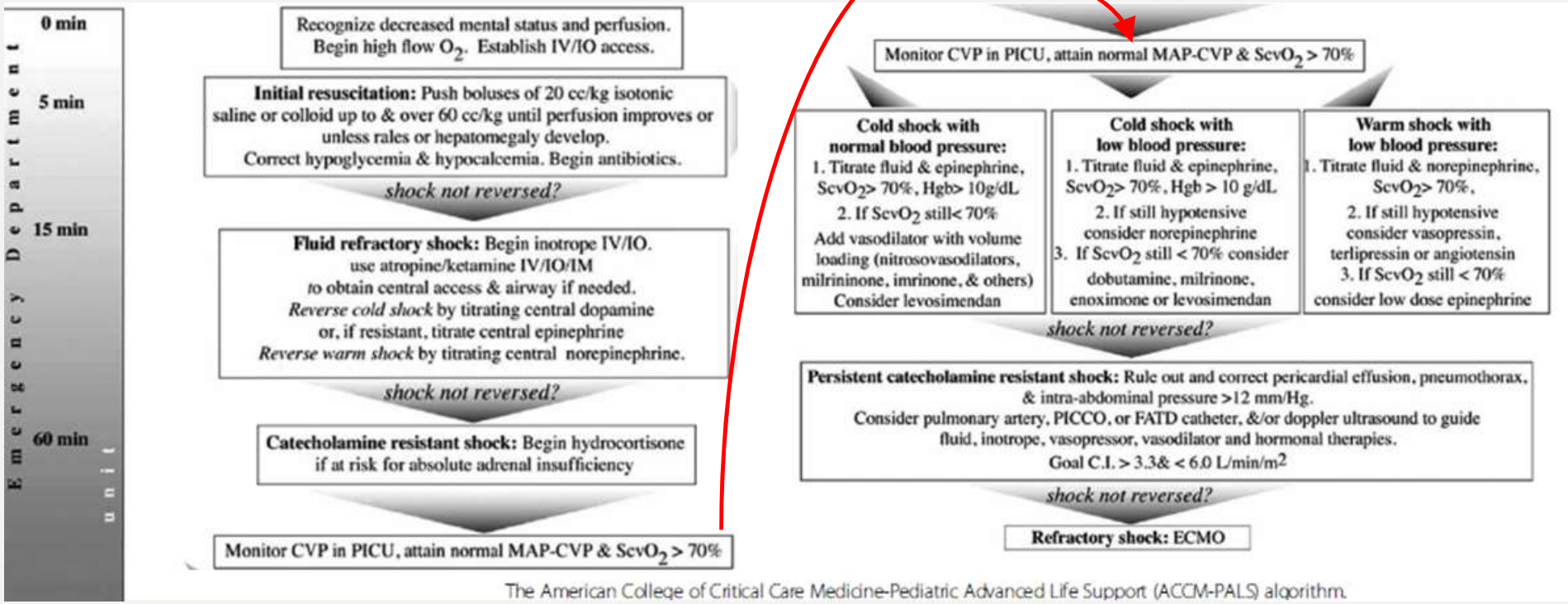
Mitchell M. Levy[1*], Laura E. Evans[2] and Andrew Rhodes[3]

Table 1 Bundle elements with strength of recommendations and under-pinning quality of evidence [12, 13]

Bundle element	Grade of recommendation and level of evidence
Measure lactate level. Re-measure if initial lactate is > 2 mmol/L	Weak recommendation, low quality of evidence
Obtain blood cultures prior to administration of antibiotics	Best practice statement
Administer broad-spectrum antibiotics	Strong recommendation, moderate quality of evidence
Rapidly administer 30 ml/kg crystalloid for hypotension or lactate ≥ 4 mmol/L	Strong recommendation, low quality of evidence
Apply vasopressors if patient is hypotensive during or after fluid resuscitation to maintain MAP ≥ 65 mm Hg	Strong recommendation, moderate quality of evidence

Surviving Sepsis Campaign

Recommendations: Special Considerations in Pediatrics*



The American College of Critical Care Medicine-Pediatric Advanced Life Support (ACCM-PALS) algorithm.

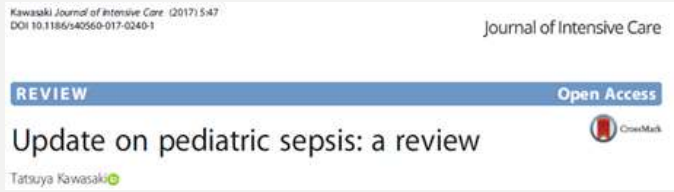
DO WE NEED A NEW DEFINITION IN PEDIATRICS?

Sepsis (definition)

- Face same problem with SIRS as adults (doesn't identify clinically hazardous patients)

Assessment of organ dysfunction

- The standardized criteria for organ dysfunction & SIRS thresholds are not based on evidence related to clinical outcome



NEW EVIDENCES ON TREATMENT OF SEPSIS IN PEDIATRICS

Initial resuscitation & monitoring

- Considering recent trends in adults, an original form of early goal directed therapy will not be applied to pediatric sepsis
- - Patients given bolus fluid as initial intervention had a higher 48-h mortality rate (FEAST trial, 2011)
- - Albumin use is a significant risk factor of PICU mortality (SPROUT study, 2015)
- - *if lactate was normalized (<2 mmol/L) within 2–4 h of initial measurement, patients had a significantly lower risk of persistent organ dysfunction over 48 h (Scott et al,2016)

Antimicrobial

- 3-h delay of antibiotic was associated with a significant increase in PICU mortality (Weiss et al, 2014)

TREATMENT OF SEPSIS IN PEDIATRICS

Vasopressor

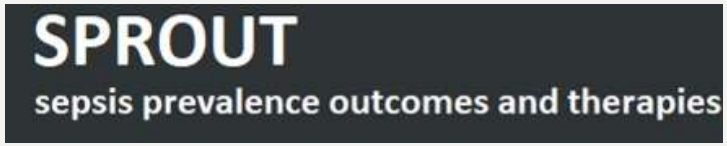
- - Comparative studies are lacking to recommend first line agent
- - Comparison b/n dopamine & adrenalin revealed 28-day mortality lower in the adrenaline group (ventura et al, 2015) and higher rate of shock resolution in 1st hr (Narayanan et al, 2015)

Corticosteroid

- Use of corticosteroids was significantly associated with mortality (SPROUT study, 2015)

Other

- ? ECMO (for refractory with resp failure)
- ? diuretics & dialysis (for fluid overload),
- ?plasma exchange



SUMMARY: PEDIATRIC SEPSIS

- Definition of sepsis should be reconsidered on the basis of organ dysfunction scoring in accordance with adult Sepsis-3
- Optimal dose & type of fluid is very difficult to recommend b/c negative finding in children are in contrast to adults
- Early antibiotic (within 3hours) is essential in the initial management
- Lactate clearance might be a non inferior method of monitoring reversal of tissue hypoxia in septic children
- Vasopressin/terlipressin use for children with fluid-refractory septic shock should be more cautious
- Adrenaline would be more preferable to dopamine for the first line catecholamine in children with fluid-refractory septic shock
- Corticosteroid use should be more “conservative” than ever

CONCLUSION

- There is emerging evidence but high quality studies in pediatrics are still sparse
- Some guiding principles may be applied to children according to best possible recommendation from adults and best available evidence in pediatrics
- If these protocols/therapeutics are implemented, dedicated multicenter research will be needed to evaluate outcomes

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THANK YOU!