Role of Fluid Resuscitation in AKI Management in Children

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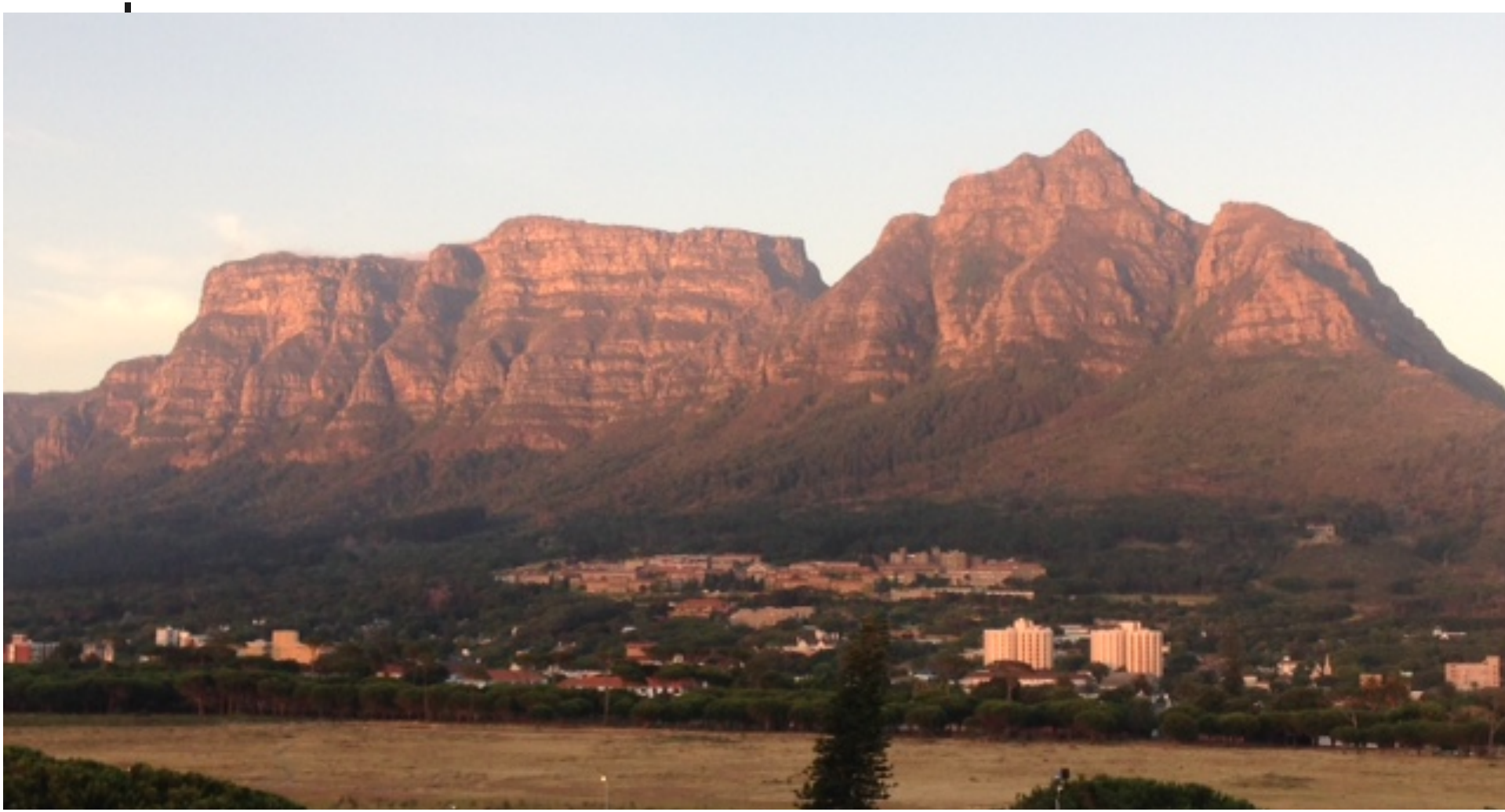

Clinical Patients

- 9 month old boy
- Diarrhoea and vomiting
- Assessed as shocked
- No assisted ventilation or inotropic support available
- Management?

- 12 year old boy
- Meningococcal Sepsis
- Assessed as shocked
- Needing inotropic support initially
- Poor urine output x 12hrs
- What next?

What if fluid was considered as an IVI drug?

- Or…What fluid would you like to be resuscitated with…

Resuscitation Fluids

Myburgh JA, Mythen MG NEJM 2013;369:1243-51

- No ideal fluid exists
- Clinical practice determined by
  - Clinician preference
  - Regional variation
- Type and dose may affect patient centred outcomes
- All resuscitation fluids used excessively contributes to interstitial oedema under inflammatory conditions

Different Solutions

- Colloid solutions no substantive advantages over crystalloid solutions haemodynamically
- Albumin cost limitations and concerns in certain patient groups – traumatic brain injuries
- Hydroxyethyl starch(HES) solutions increased rates of RRT & adverse events in ICU
- Semisynthetic colloid solutions – no evidence for recommendation

Hazardous journeys

Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials

Cite this as: BMJ 2003;327:1459

Parachutes reduce the risk of injury after gravitational challenge, but their **effectiveness has not been proved with randomised controlled trials**

Historically

Finfer SR, Vincent JL NEJM Sept 2013,369;13:1243-1251

- *1832*: *Robert Lewins* – ivi administration alkalinized salt solution in cholera

  'Quantity necessary to be injected depend on quantity of serum lost; place patient in his ordinary state as to quantity of blood circulating in vessels'
- *1885*: *Sidney Ringer* physiologic salt solution for rehydration of children with gastroenteritis
- *Alexis Hartmann* modified this fluid
- *1941*: Blood fractionation to produce human albumin – large quantities of burns Pearl Harbour

Ideal Resuscitation fluid

Myburgh JA, Mythen MG NEJM 2013;369:1243-51

- Predictable and sustained increase in intravascular volume
- Chemical composition close to extracellular fluid
- Metabolised & completely excreted without accumulation in tissues
- Does not produce metabolic or systemic adverse effects
- ***Cost effective***

Saline

- Isotonic sodium chloride(0.9%) – commonest ivi fluid in world
  - USA > 200million litres sold annually
- 1882 Hartog Hamburger – Dutch physiologist – concentration of salt in human blood 0.9% actually 0.6%(Awad et al Clin Nutri2008;27:88)
- Strong ion difference of 0.9% Saline is zero
  - Large volumes of saline results in hyperchloraemic metabolic acidosis

0.9% Saline vs Ringers Lactate in Normal Human Volunteers

Williams EL et al Anesth Analg 1999;88:999-1003

- 18 Healthy volunteers 20 – 48yrs
- 50ml/kg over 1 hour of RL and 0.9% Saline separately
- Venous samples
  - T1 Baseline
  - T2 End of infusion
  - T3 1 hour after T2
- Time to first urination

0.9% Saline vs Ringers Lactate in Normal Human Volunteers

- Outcomes studied
  - Serum osmolality – transient reduction RL
  - pH changes – persistent acidosis NS
  - Mental changes – subjective mental changes NS including lassitude & perceived difficulty in abstract thinking
    - Mental arithmetic
    - Reading medical journals & replying to anesthesiology board questions
  - Abdominal pain – discomfort more common in NS

Saline – the bad – hyperchloraemic acidosis

- Animal studies
  - Immune dysfunction
  - Decreased renal blood flow
- Human studies
  - Acidosis
  - Reduced renal cortical blood flow
  - Decreased and delayed urine output/AKI
  - Gastrointestinal dysfunction
  - Increased infectious complications
  - Large volume infusions of saline lead to coagulopathy

Saline vs Plasma-Lyte

- Adult Trauma patients requiring blood transfusion, intubation or surgery within 60 minutes or arrival
  - Young J et al *Ann Surg* 2014;259:255-262
  - Improved acid base status
  - Less hyperchloraemia @ 24hrs post-injury
  - Chloride-restrictive IVI fluid strategy critically ill adults – less AKI
    - *Yunos NM JAMA 2012;308:1566-72*

Saline vs Plasma-Lyte

Shaw AD et al *Ann Surg* 2012;255:821-9

- Adults undergoing major abdominal surgery
  - retrospective study 500 000 patient records
- Hospital mortality 5.6% saline group vs 2.9% balanced($P < 0.001$)
- Postoperative infection ($P = 0.006$)
- Renal failure requiring dialysis ($P < 0.001$)
- Blood transfusion ($P < 0.001$)
- Electrolyte disturbance ($P = 0.046$)
- Acidosis investigation ($P < 0.001$) were all more frequent in patients receiving 0.9% saline

Ringers Lactate in Medical Emergency Unit and PICU

Red Cross Children's Hospital(RXH) University of Cape Town Experience

Hot off the Press – A Argent

- 2015 – Admissions 1349 to PICU
  - Acute medical cases 520
  - Surgical 159
  - Cardiac surgical 219
  - Trauma + Orthop 56
  - Neurosurgical 48
  - Burns 46
  - Other Rest
- Mortality 6.83%
- Dialysis 2.7%


PILOT

Less than 1km down the road…

RCT or Gut Feeling

- Clinicians' gut feeling about serious infection: observational study
  - To investigate the basis and added value of clinicians 'gut feeling' that infections in children are more suggested by clinical assessments
  - *Van der Bruel BMJ Sep 25, 2012*

International Evidence for Paediatric Fluid Resuscitation Guideline

Guidelines based on 2 retrospective analyses from one hospital (Pittsburgh; 3^{O} referral ICU)

Patient population : Survivors to ICU admission: ventilated & inotrope

- **First study:**

5 year review: **34 children** with septic shock ~ 7 children/yr

>=40mls/kg initial fluid resuscitation **(9 children)** associated with better outcome (Carcillo et al, JAMA 1991)

Recommended as the standard of care following publication.

- **Second study:**

10 year review of Septic shock (**91 children**) ~ 9 children/yr

>60mls/kg over 15 mins (**34 children**): early reversal of shock improves outcome; (Han Y et al, Pediatrics 2003)

Now recommended as the standard of care

✓ ***Surviving Sepsis 2012 guideline graded 2C level of evidence***

= ***Weak recommendation based on very poor evidence***

Goal directed therapy

The New England Journal of Medicine

EARLY GOAL-DIRECTED THERAPY IN THE TREATMENT OF SEVERE SEPSIS AND SEPTIC SHOCK

EMANUEL RIVERS, M.D., M.P.H., BRYANT NGUYEN, M.D., SUZANNE HAVSTAD, M.A., JULIE RESSLER, B.S., ALEXANDRIA MUZZIN, B.S., BERNHARD KNOBLICH, M.D., EDWARD PETERSON, PH.D., AND MICHAEL TOMLANOVICH, M.D., FOR THE EARLY GOAL-DIRECTED THERAPY COLLABORATIVE GROUP*

1368 · N Engl J Med, Vol. 345, No. 19 · November 8, 2001 · www.nejm.org

Study of Emergency Department Management

Intensive Care Med
DOI 10.1007/s00134-008-1085-9

PEDIATRIC ORIGINAL

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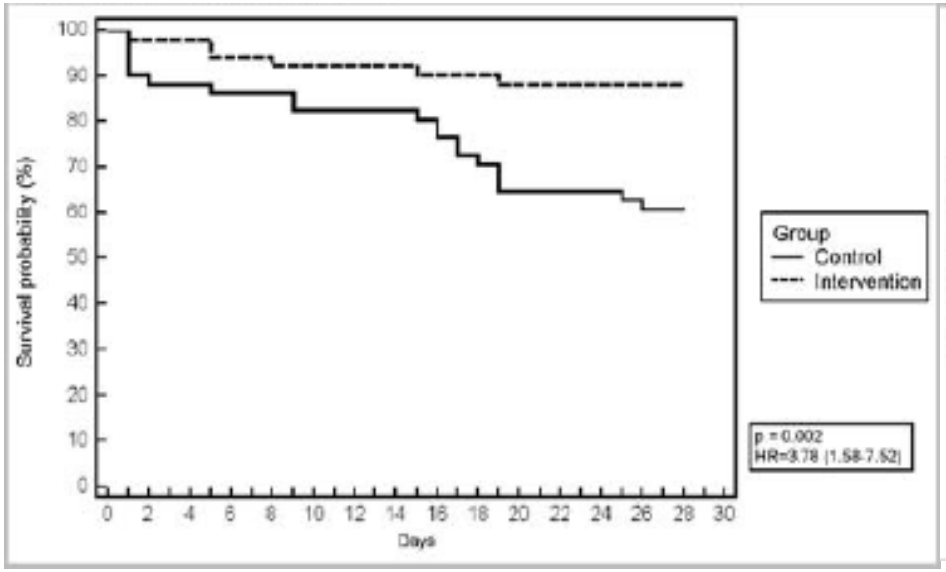
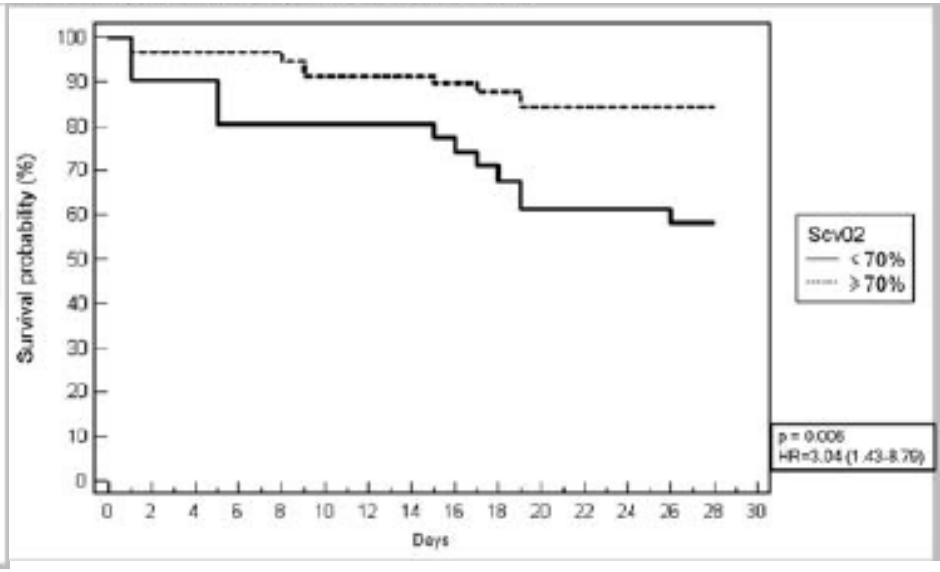
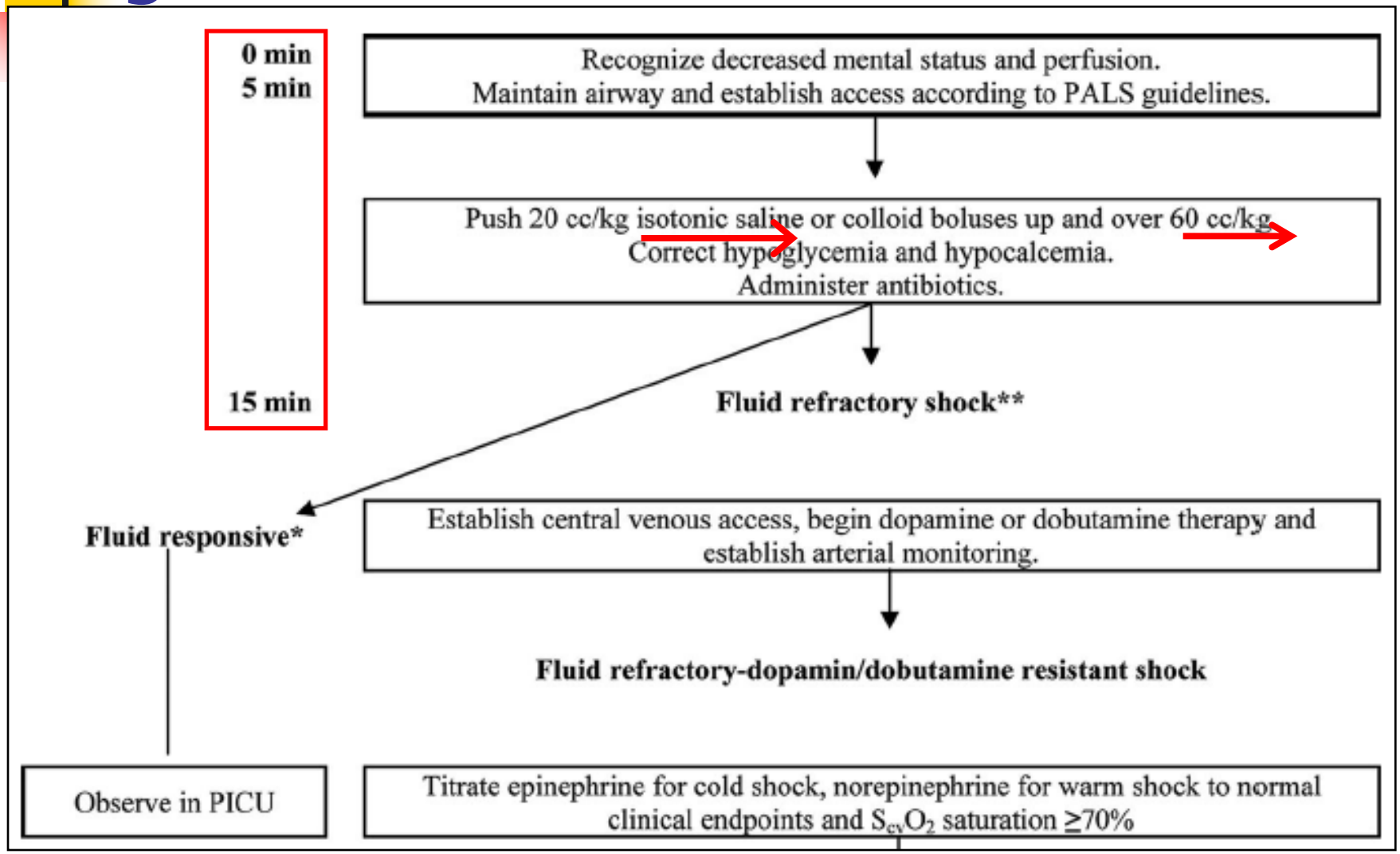
ACCM/PALS haemodynamic support guidelines for paediatric septic shock: an outcomes comparison with and without monitoring central venous oxygen saturation





Severe sepsis and septic shock guidelines 2012 *Dellinger Surviving Sepsis 2012*



FEAST Trial ?

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Mortality after Fluid Bolus in African Children with Severe Infection

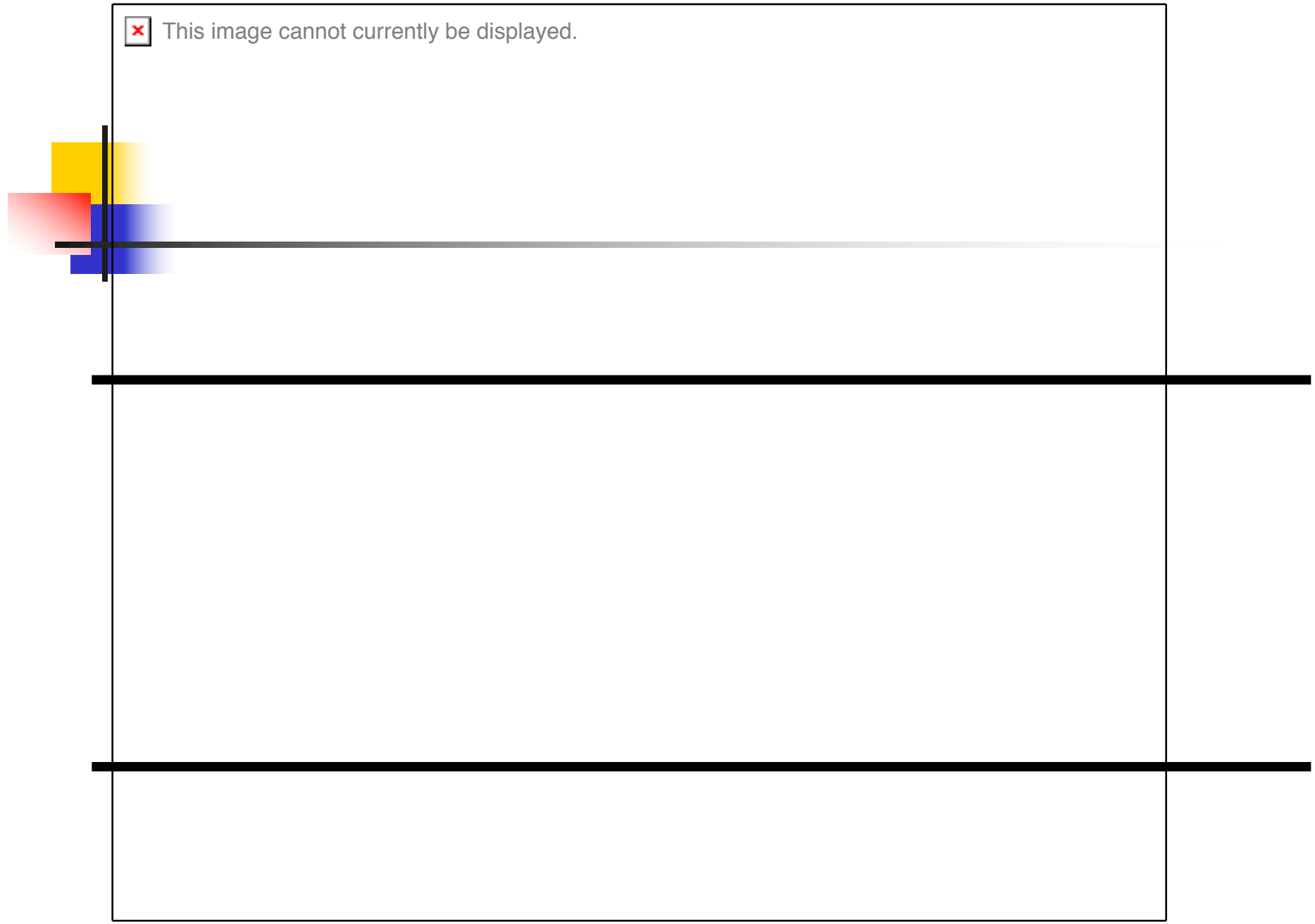
Kathryn Maitland, M.B., B.S., Ph.D., Sarah Kiguli, M.B., Ch.B., M.Med., Robert O. Opoka, M.B., Ch.B., M.Med., Charles Engoru, M.B., Ch.B., M.Med., Peter Olupot-Olupot, M.B., Ch.B., Samuel O. Akech, M.B., Ch.B., Richard Nyeko, M.B., Ch.B., M.Med., George Mtove, M.D., Hugh Reyburn, M.B., B.S., Trudie Lang, Ph.D., Bernadette Brent, M.B., B.S., Jennifer A. Evans, M.B., B.S., James K. Tibenderana, M.B., Ch.B., Ph.D., Jane Crawley, M.B., B.S., M.D., Elizabeth C. Russell, M.Sc., Michael Levin, F.Med.Sci., Ph.D., Abdel G. Babiker, Ph.D., and Diana M. Gibb, M.B., Ch.B., M.D., for the FEAST Trial Group*

CONCLUSIONS

Fluid boluses significantly increased 48-hour mortality in critically ill children with impaired perfusion in these resource-limited settings in Africa. (Funded by the Medical Research Council, United Kingdom; FEAST Current Controlled Trials number, ISRCTN69856593.)

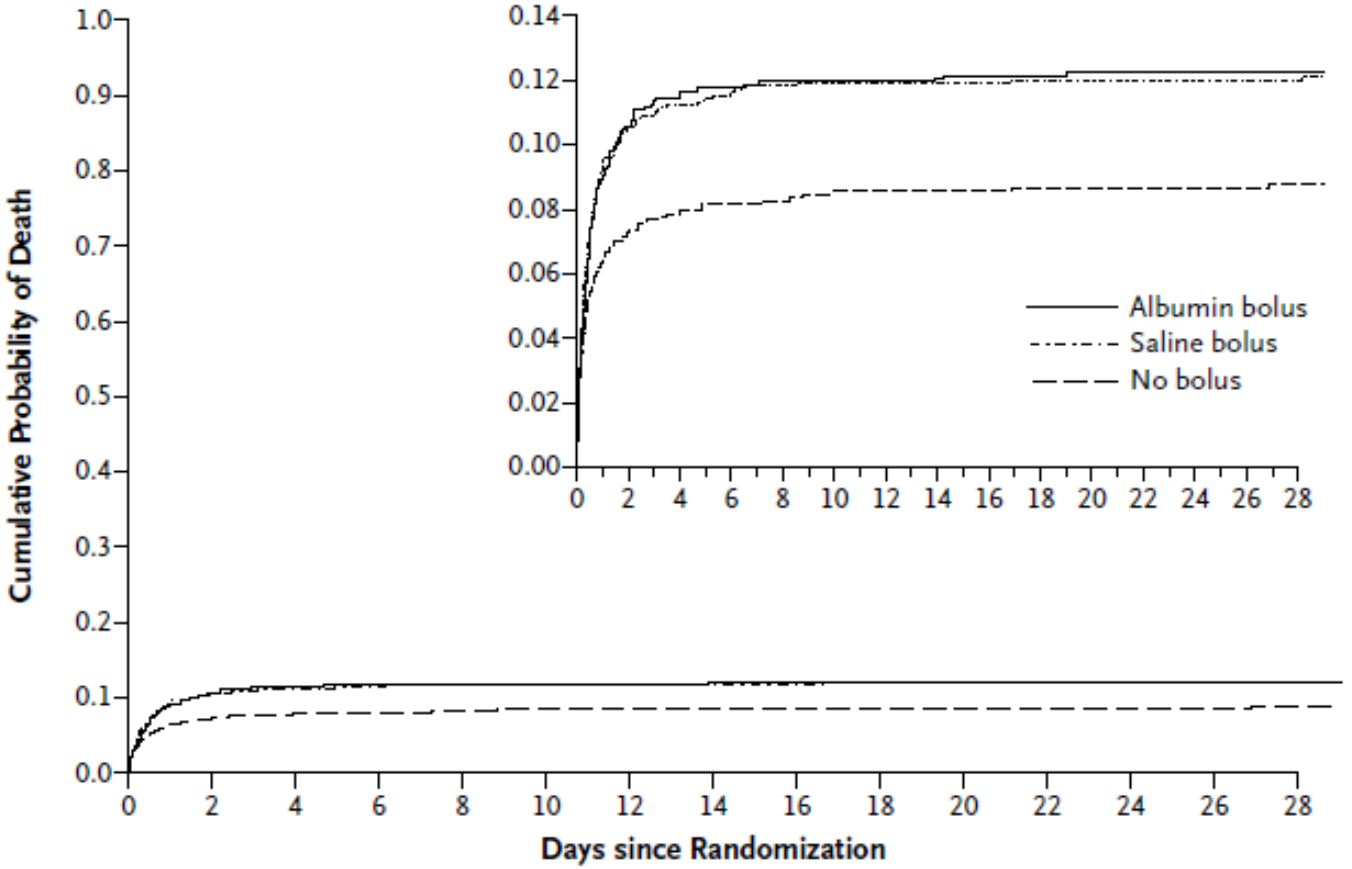
FEAST Study
(Fluid Expansion as Supportive Therapy)
NEJM June 30, 2011 Maitland et al

- Severe febrile illness & impaired perfusion randomised to:
  - Bolus 5% Albumin 20-40ml
  - **Bolus 0,9% Saline**
  - No bolus
- Halt recruitment **3141**/3600
  - 48hour mortality
  - 10.6% bolus vs 7.3% non-bolus(p=0.003)



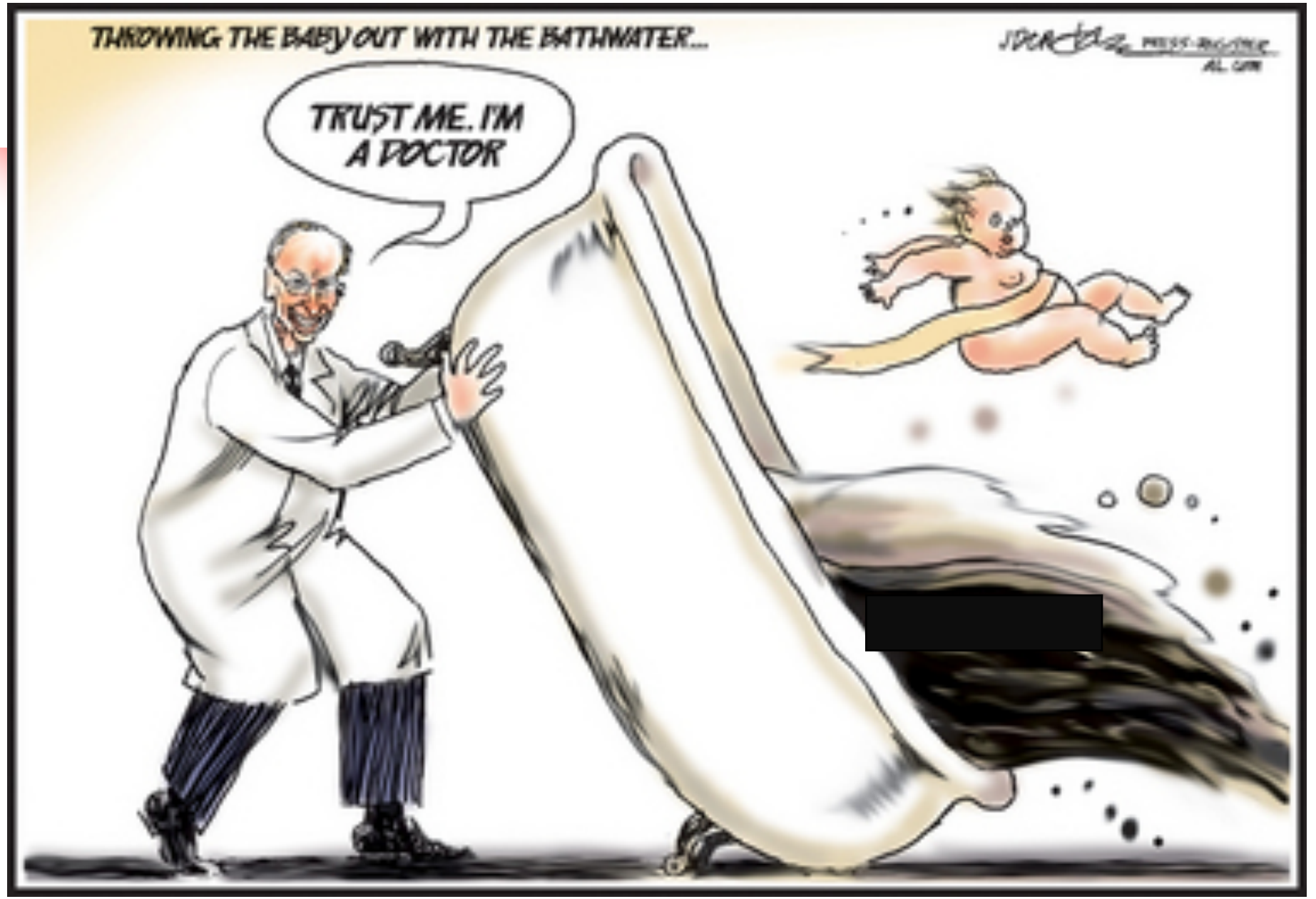
Maitland et al, N Engl J Med, 2011

B Mortality at 4 Weeks



	Day 1			Day 2			Day 3–7			Day 8–14			Day 15–21			Day 21–28		
	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus	Albumin bolus	Saline bolus	No bolus
No. at Risk	1050	1047	1044	954	945	975	914	917	947	901	909	940	899	902	933	897	901	934
Died	95	97	67	16	13	9	11	7	7	2	6	2	2	1	4	2	1	1
%	9.0	9.3	6.4	1.7	1.4	0.9	1.2	0.8	0.7	0.2	0.7	0.2	0.2	0.1	0.4	0.2	0.1	0.2

Maitland et al, N Engl J Med, 2011


THROWING THE BABY OUT WITH THE BATHWATER...
TRUST ME. I'M A DOCTOR

Surviving Sepsis Campaign

- Fluid bolus using CVP as 1st & critical end-point
  - CVP unable to predict haemodynamic response to fluid challenge *Marik PE Critic Care med 2013;14:1774-8*
- Vasopressin in Septic Shock trial *Boyd JH Critic Care Med 2011*
  - CVP >12 higher mortality
  - 67% fluid overloaded at 24hrs
  - 48% fluid overloaded at 72hrs
  - Fluid overload independently associated with increased hospital mortality

Meta-analysis *Chen C Critic Care Med 2013;18:481*

- 18 Observational trials of EGDT
  - Significant increase in odds of surviving with bundled care compared to controls p=0.0001
  - Uncontrolled retrospective studies
- *Edusepsis Study Spain*
  - Mortality decr 44 to 39% but 6hr resus bundle *including fluid bolus* compliance only 10%
    Ferrer R JAMA 2008; 299:2294-303

ProCESS and ARISE

NEJM 2014;370;1683-93; NEJM 2014;371:1496-506

- *ProCESS* USA Trial 1341 adult patients
  - *NEJM* 2014 May
- *ARISE* Australian sepsis 1600 adult patients
  - *NEJM* 2014 Oct

ProCESS and ARISE

NEJM 2014;370;1683-93; NEJM 2014;371:1496-506

- ScvO2 >70%
  - **EGDT does not improve outcome of patients with severe sepsis and septic shock**
  - Titrating therapeutic interventions to increase the ScvO2>70% does not improve the outcome of patients with severe sepsis and septic shock
  - Titrating fluid to a CVP>8mmHg is likely to lead to a more positive fluid balance
  - ***Fluid balance at 12hours strongly correlated with CVP and independently predictive of mortality***

New Areas for Research

Norepinephrine (Noradrenaline)

Bai X Crit Care 2014;18:532

- Early use of norepinephrine was associated with a lower cummulative fluid balance

Other targets

- Lactate – tissue hypoxia
- Oxygen consumption and energy expenditure
- Microcirculation
- Children different to Adults
  - Low Cardiac Index/Low SCVo2 shock

    Oliveira & Carcillo Ped Critic Care Med 2014;15(4) 380-2

Fluid resuscitation guidelines

Hilton and Bellomo *Critical Care* 2012, 16:302
http://ccforum.com/content/16/1/302

VIEWPOINT

A critique of fluid bolus resuscitation in severe sepsis

Andrew K Hilton[1] and Rinaldo Bellomo[2]*

The Demise of Early Goal-directed Therapy for Severe Sepsis and Septic shock

Marik PE. *Acta Anaesthesiologica Scandinavica 59(2015) 561-567.*

New papers from Emergency Medicine and Anaesthetic Domains

- ARISE, and Cast off the Shackles of EGDT
  - *Emergency Medicine Literature of note Radecki Oct 3, 2014* response to NEJM
  - EGDT receives credit for awareness of impact of early identification and intervention on mortality
  - **Leave EGDT behind and identify new resus targets and sensible strategies for identifying them.**

Bigger picture

- Fluid therapy only 1 component of complex haemodynamic resus strategy
- Primary target:
  - Restore intravascular volume
- Adjunctive therapies
  - Catecholamines – augment cardiac contraction and venous return
  - Changes to microcirculation
  - End-organ function


10
9
8
7
6
5
3
Fisher & Paykel
HEALTHCARE
Bubble CPAP
Generator


RED ZONE


NEWLIFE elite
AIRSEP

Role of Fluid after admission

- FO >20% @ time of CRRT initiation

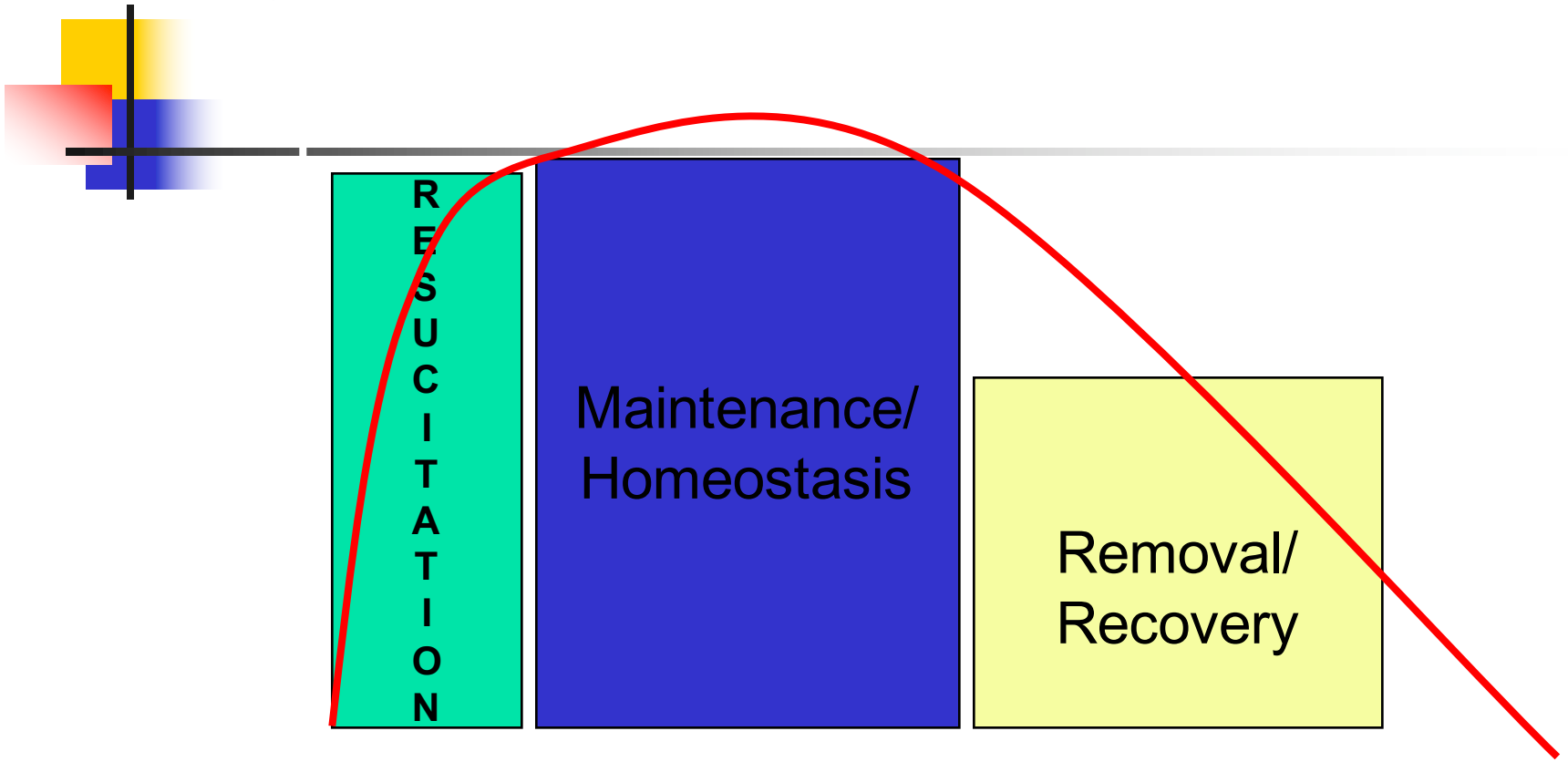
$$\%FO = \frac{(\text{Fluid In} - \text{Fluid Out})}{(\text{PICU Admission weight})} \times 100\%$$

Goldstein et al(2005). KI 67:653-658

- But what happens before?

Fluid Management in Acute Kidney Injury

Stuart L. Goldstein, MD[1]



Journal of Intensive Care Medicine
2014, Vol. 29(4) 183-189

Controversies

- What fluid to give?
  - Saline vs Ringer's vs Plasmalyte B
- How much?
  - 5 or 10 or 20-40 or >60ml/kg
- How fast?
- What causative organism?
- What support is needed?
- Where geographically?

Next step…in rest of the World

Need Large randomized controlled trials of

- Fluid Resuscitation or not?
- What fluid
  - Balanced crystalloids vs 0.9% Sodium chloride
- Earl Goal Directed Therapy or not
- Components of EGDT
- In Children compared to Adults with low CI/SCVo2

To design the ideal fluid

- Balanced electrolyte solution
- Well tolerated to administer peripherally
- Interstitial expansion unavoidable but
  - Minimal acid-base & tonicity disturbances
- Isotonic
- 'In-vivo' SID 24mEq/l
- pH unlikely to cause haemolysis or endothelial damage

Role of Fluid Resuscitation in AKI Management in Children

- AKI due to diarrhoeal disease or fluid loss
  - Give fluid
- AKI due to sepsis or NON-fluid loss
  - Be cautious with fluid – give carefully

"To prevent a heart attack, take one aspirin every day. Take it out for a run, then take it to the gym, then take it for a bike ride..."