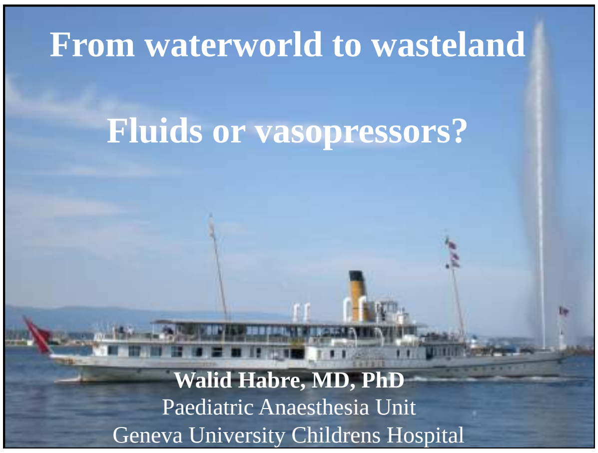


From waterworld to wasteland

Fluids or vasopressors?

Walid Habre, MD, PhD
Paediatric Anaesthesia Unit
Geneva University Childrens Hospital

Is it a controversial issue or an evidence-based consideration ?

→ **Goal-oriented approach**

Hôpitaux Universitaires Genève

UNIVERSITÉ DE GENÈVE
FACULTÉ DE MÉDECINE

Objectives :

1. Define the Goal-Oriented approach
2. Limitation of the classical approach based primarily on fluids
3. Methods that can help us deciding what kind of **intervention** and which **children** should benefit?
4. Provide some recommendations and strategies for peroperative management in children

---

Goal-Oriented approach

↓

Meet the requirements and effectiveness of individual treatment

Intravascular volume

Cardiac output

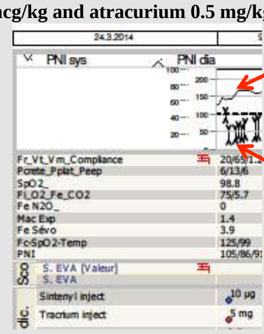
Blood Pressure

Manipulating haemodynamics to optimize oxygen transport

- Child (African American) 22 months, 10 kgs scheduled for difficult hypospadias repair.

(potential buccal mucosal graft)

Inhalation induction with sevoflurane, iv access and administration of fentanyl 1 mcg/kg and atracurium 0.5 mg/kg



HR increased to 170/min

Pressure dropped from 105/70 to 65/30

Classical : lowest acceptable SBP:
2 x age in yrs + 70

Age	Lowest acceptable SBP
Term neonates < 28 days	60
Infants 1 – 12 months	70
Children 1-10 yrs	2 x age (yrs) + 70
Children > 10 yrs	90

Current values for hypotension are not evidence-based and may need to be adjusted for patient height and for clinical condition.

SBP (5th percentile at 50th height percentile) =
2 x age in years + 65

MAP (5th percentile at 50th height percentile) =
1.5 x age in years + 40

MAP (50th percentile at 50th height percentile) =
1.5 x age in years + 55: in sick children

Hacque IU et al. Pediatr Crit Care Med. 2007; 8:138-44.

Should we consider the threshold that leads to a decrease in rSO_2

(- 37% variation in MAP)

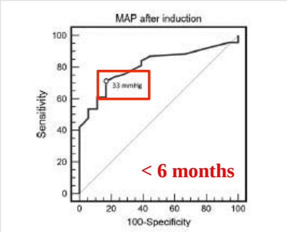


Figure 5 ROC curve. Threshold value of MAP during anesthesia associated with a rSO_2c variation ≤0%, in children younger than 6 months (AUC: 0.80; $P < 0.001$).

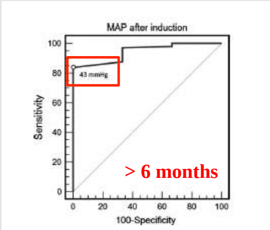
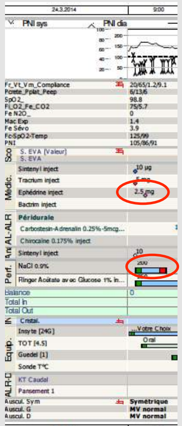


Figure 4 ROC curve. Threshold value of MAP during anesthesia associated with a rSO_2c variation ≤0%, in children older than 6 months (AUC: 0.94; $P < 0.001$).

Rhondali O. et al. Ped Anesth 2014; 24: 734-740



200 ml NS
and 2.5 mg ephedrine

Ultimate goal of Goal-Oriented approach

Combination of intravenous fluids & inotropes

↓

Goal directed therapy

↗ oxygen delivery index

↓

Improve outcome
in high risk patients

Classical approach:

➔Fluids to target the following:
- Preoperative fluid deficit **?**
- Maintenance fluid: 4-2-1 rule
- Crystalloid fluids replacement
- Third space fluid loss: 5ml/kg/hr **?**

	Crystalloids	**Colloids**
Estimated blood loss:	x 3	x 1

Goal-Oriented approach

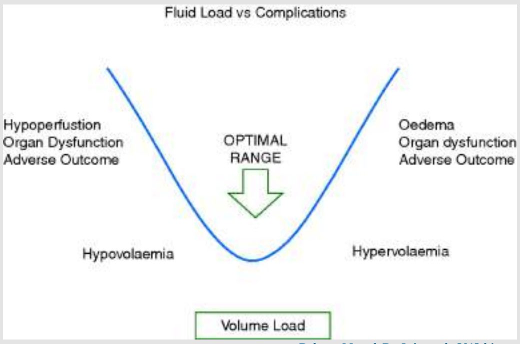
Match the increased <u>oxygen demand</u> by flow-based haemodynamic **<u>monitoring</u>** and **<u>therapeutic</u>** interventions to achieve a predetermined **<u>haemodynamic endpoint</u>**.

<u>New approach</u>:

➔Fluids and **<u>vasopressors</u>** to target the following:

- Preoperative fluid deficit: **<u>clear fluids 2h before</u>**
- Maintenance fluid: 4-2-1 rule
- Crystalloid or Colloids fluids replacement: **<u>1 to 1</u>**
- Third space fluid loss: **<u>not replaced</u>**
- **<u>Inotropes/vasopressors</u>**

Aim of intraoperative fluids: avoidance of both hypo- and hypervolaemia to **prevent adverse outcomes**



Doherty M et al. Br. J. Anaesth. 2012;bja.aes171

Effects of fluid overload

<u>Pros</u>

- Increase peripheral perfusion/ oxygen supply
- Increase intraoperative diuresis and avoid postoperative renal failure
- Fluid homeostasis decreases PONV

<u>Cons</u>

- Decrease in pulmonary function with risk for hypoxaemia and respiratory complications
- Promote extravascular fluid extravasation with oedema
- May impair oxygen diffusion and decrease tissue oxygen tension
- May have negative implications for wound healing

Effect of fluid load on lung function

Promote lung interstitial fluid accumulation

Impair gas exchange — Decrease compliance

Hypoxaemia

➚ intravenous fluid administration ➔ ➚ postop complications

Crystalloids and Colloids impair Respiratory compliance

Effect of fluid load on the renal function

Surgery-Stress

ACTH → **Cortisol**

ADH → **➚ water absorption**

Renin → **Aldosterone**

➘Diuresis
➘Na excretion

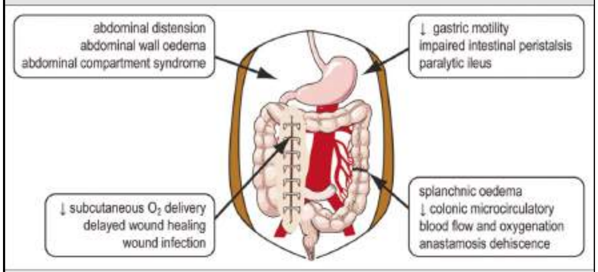
➘ GFR

Fluid load

➚Extracellular Fluid volume

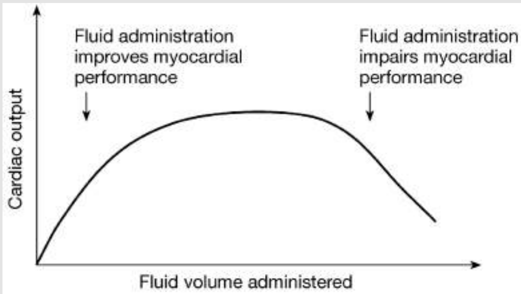
➚ GFR

Effect of fluid load on gastrointestinal function



Crystalloids seem to predispose to higher incidence of intestinal oedema than colloids

Effects of perioperative fluid therapy on the Starling myocardial performance curve



Holte K et al. Br. J. Anaesth. 2002;89:622-632

Aim of fluid challenge

↓

↗ **stroke volume (SV)**

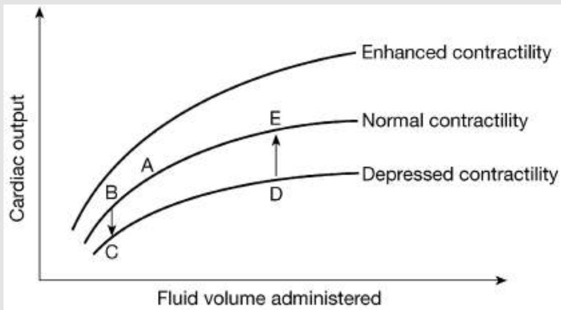
↓

↗ **cardiac output (CO)**

↓

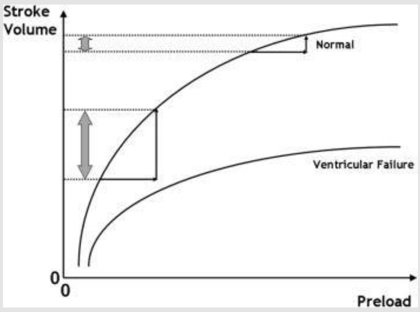
↗ **oxygen delivery**

Relationship between cardiac output and fluid administration.



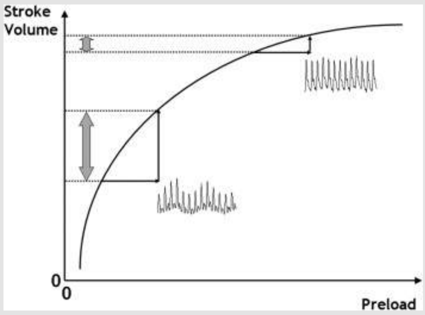
Holte K et al. Br. J. Anaesth. 2002;89:622-632

Frank-Starling relationship between ventricular preload and ventricular stroke volume



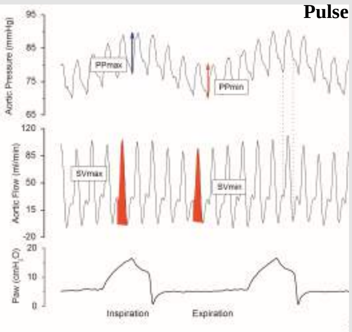
Cannesson M. J CardioThoracic Vasc Anesth 2010; 24: 487-497

Frank-Starling relationship with associated respiratory variations in the arterial pressure waveform signal



Cannesson M. J CardioThoracic Vasc Anesth 2010; 24: 487-497

The use of heart-lung interactions during mechanical ventilation to assess fluid responsiveness



Systolic pressure variation (SPV)
Pulse pressure variation (PPV)

↓

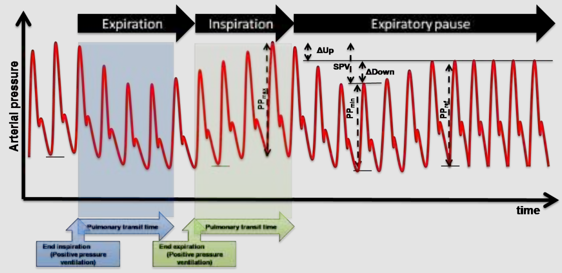
derived from analysis of arterial waveform

Stroke volume variation (SVV)

↓

derived from pulse contour analysis

Arterial pressure variation during positive pressure ventilation without spontaneous effort.



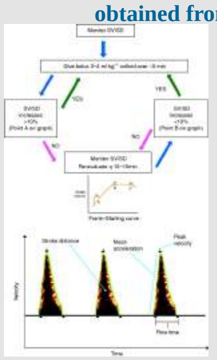
PPV % = 100 x (PPmax –PPmin) / ((PPmax + PPmin) / 2)

RCT's with SVV or PPV demonstrating improve outcome

Study	Surgical population	Hemodynamic goal	Clinical benefit
Benes and colleagues, 2010 [4]	Major abdominal	SVV <10 %	Decrease in complications and hospital length of stay
Goepfert and colleagues, 2013 [5]	Cardiac	SVV <10 %	Decrease in complications and ICU length of stay
Lopes and colleagues, 2007 [6]	Major abdominal	PPV <10 %	Decrease in complications and ICU and hospital length of stay
Mayer and colleagues, 2010 [7]	Major abdominal	SVV <12 %	Decrease in complications and hospital length of stay
Ramsingh and colleagues, 2013 [8]	Major abdominal	SVV <12 %	Faster return of gastrointestinal function and decrease in hospital length of stay
Salzwedel and colleagues, 2013 [9]	Major abdominal	PPV <10 %	Decrease in complications
Scheeren and colleagues, 2013 [10]	Major abdominal	SVV <10 %	Decrease in surgical site infections
Zhang and colleagues, 2012 [11]	Major abdominal	PPV <11 %	Faster return of gastrointestinal function and decrease in hospital length of stay
Zhang and colleagues, 2013 [12]	Thoracic	SVV < 10 %	Decrease in complications and intubation time
Zheng and colleagues, 2013 [13]	Major abdominal	SVV <12 %	Faster return of gastrointestinal function and decrease in ICU and hospital length of stay

Michard F. Crit Care. 2014; 18: 413

Typical algorithm for oesophageal Doppler-guided fluid management with characteristic velocity waveform obtained from the descending aorta



The haemodynamic profile integrates ABF, mean arterial pressure (MAP), heart rate (HR), and calculates a stroke volume in the descending aorta:
SVa (ml) = ABF/HR

Doherty M et al. J Br. J. Anaesth. 2012;bja.aes171

Predicting fluid responsiveness in children: is it realistic ?

- The Starling curve: does it exist in neonates?
- Dynamic variables derived form heart-lung interaction: are they good predictors?
- Are classical static variables reliable?

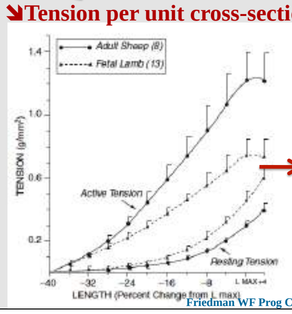
Less organized and efficient myofibrils

Extracellular matrix

Undeveloped Mitochondria

Composition of Sarcolemna

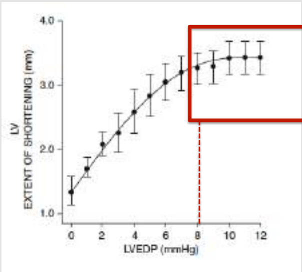
↘Tension per unit cross-sectional area



→ ↘ Compliance

Friedman WF Prog Cardiovasc Dis 15:87-111

The Frank-Starling curve exists in the neonatal heart but is shifted



Increase preload within physiological range (2-8 mmHg) ➔ Increase stroke volume

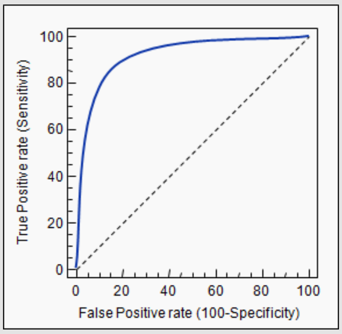
Thus, ➚ HR an important mechanism for ➚ CO

Kirkpatrick SE et al. Am J Physiol 1976; 231: 495-500

STATIC		
Clinical	Heart rate	HR
	Systolic arterial blood pressure	SAP
Preload pressure	Central venous pressure	CVP
	Pulmonary artery occlusion pressure	PAOP
Thermodilution	Global end diastolic volume index	GEDVI
Ultrasound dilution	Active circulation volume	ACV
	Central blood volume	CBV
	Total end diastolic volume	TEDV
	Total ejection fraction	TEF
Echocardiography and Doppler	Left ventricular end diastolic area	LVEDA
	Stroke volume index	SVI
	Corrected flow time	FTc
DYNAMIC		
Arterial pressure	Systolic blood pressure variation	SPV
	Pulse pressure variation	PPV
	Stroke volume variation	SVV
	Difference between minimal SAP and SAP at end-expiratory pause	ΔDown
	Difference between maximal SAP and SAP at end-expiratory pause	ΔUp
Plethysmography	Pulse oximeter plethysmograph amplitude variation	ΔPOP
	Plethysmograph variability index	PVI
Echocardiography and Doppler	Respiratory variation in aortic blood flow peak velocity	ΔV_{peak}
	Stroke distance variation	ΔVTI
	Inferior vena cava diameter variation	ΔIVCD
PASSIVE LEG RAISING (PLR)		
Echocardiography and Doppler	PLR-induced change in cardiac index	ΔCI_{PLR}
	PLR-induced change in stroke volume	ΔSV_{PLR}

Gan H et al. Anesth Analg 2013; 117: 1380-1392

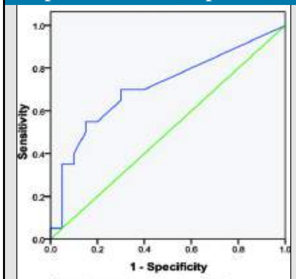
Accuracy is measured by the area under the ROC curve



An area of 1 represents a perfect predictor test

An area of .5 represents a worthless test

The role of passive leg raising to predict fluid responsiveness in pediatric intensive care unit patients

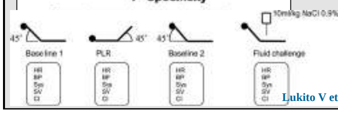


Receiver operating curves (ROCs) of cardiac index to discriminate responders and nonresponders to volume expansion.

↓

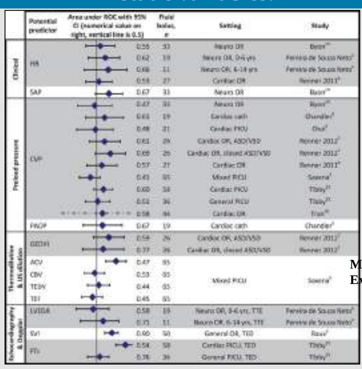
Area under the curve

0.71 ± 0.084 (95% CI 0.546-0.874)



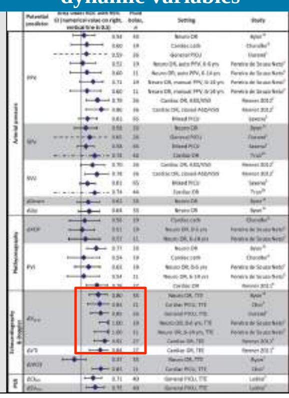
Lukito V et al. Ped Crit Care Med 2012; 13(3):e155-e160,

Comparison of the areas under the ROC curve for static variables:



More the ROC tend to 1
Excellent predictor

Comparison of the areas under the ROC curve for dynamic variables



Aortic Peak Flow Velocity

Low Predictability of 3 Different Noninvasive Methods to Determine Fluid Responsiveness in Critically Ill Children

	AUC	p	95% CI
Heart rate	0.417	0.43	0.21–0.60
Mean arterial pressure	0.502	0.98	0.29–0.71
Central venous pressure	0.490	0.92	0.25–0.70
Central venous oxygen saturation	0.596	0.36	0.39–0.81
CardioQ stroke volume index	0.494	0.95	0.28–0.71
CardioQ cardiac index	0.396	0.32	0.19–0.60
CardioQ flow time corrected[a]	0.538	0.72	0.33–0.75
CardioQ peak velocity[b]	0.717	0.046*	0.53–0.90
LiDCOrapid stroke volume index	0.371	0.22	0.16–0.58
LiDCOrapid cardiac index	0.371	0.22	0.17–0.57
LiDCOrapid stroke volume variation	0.513	0.91	0.30–0.72
LiDCOrapid systemic vascular resistance index	0.588	0.41	0.38–0.79
Inferior vena cava pulsations (dIVC%)[c]	0.502	0.98	0.29–0.71

AUC = area under the receiver operating characteristic curve, dIVC% = respiratory variations in vena cava inferior diameter distensibility index.
[a]Flow time corrected to a heart rate of 60 beats/min is inversely correlated with the systemic vascular resistance.
[b]Peak velocity is a marker of left ventricular contractility.
[c]Inferior vena cava diameter pulsations: ratio of $(D_{max} - D_{min}) / D_{max}$ = %, where D_{max} = maximal diameter of inferior vena cava at end-inspiration and D_{min} = minimal diameter of inferior vena cava at end-expiration.
Predictions are taken at baseline. Receiver operating characteristic curves, H_0 AUC = 0.5.

Hemodynamics of Responders (Stroke Volume Index [mL/m2] Increase > 10%) Versus Nonresponders with 10ml/kg fluid bolus

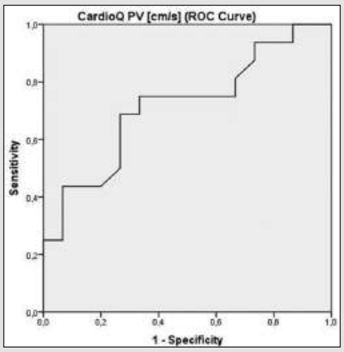
Weber T et al. Pediatr Crit Care Med 2015; 16:e89-e94,

Predictability of Fluid Responsiveness Defined as 10% Increase of Stroke Volume Index (mL/m2 Body Surface Area) Measured by Transthoracic Echocardiography Before Fluid Loading

	Responder (n = 16)			Nonresponder (n = 14)		
	Baseline	After Fluid Bolus	p	Baseline	After Fluid Bolus	p
Heart rate (beats/min)	125 ± 25	120 ± 26	0.020	133 ± 28	126 ± 26	0.027
Mean arterial pressure (mm Hg)	65 ± 19	75 ± 25	0.004	63 ± 16	71 ± 16	< 0.001
Central venous pressure (mm Hg)	10 ± 4	14 ± 5	< 0.001	10 ± 3	13 ± 4	0.001
$ScVo_2$ %	78 ± 8	80 ± 5	0.038	75 ± 7	76 ± 5	0.74
Blood lactate (mmol/L)	1.4 ± 0.6	1.3 ± 0.6	0.136	1.4 ± 0.7	1.4 ± 0.6	0.580
Echo SVI (mL/m²)	31.5 ± 10.8	39.7 ± 14.4	0.001	29.1 ± 10.4	29.1 ± 9.6	0.962
Echo CI (L/m²)	3.9 ± 1.1	4.6 ± 1.3	0.004	3.7 ± 1.4	3.5 ± 1.2	0.28
Echo velocity time integral (cm)	15.7 ± 4.0	18.2 ± 6.0	0.002	16.8 ± 4.2	16.9 ± 3.7	0.90
Echo fractional shortening %	40.9 ± 5.3	41.0 ± 4.1	0.97	39.9 ± 5.8	39.9 ± 5.7	0.97
CardioQ SVI (mL/m²)	29.7 ± 9.0	31.7 ± 10.5	0.001	29.3 ± 7.1	30.0 ± 6.8	0.40
CardioQ CI (L/m²)	3.5 ± 1.0	3.8 ± 1.0	0.012	3.8 ± 0.7	3.8 ± 0.8	0.60
CardioQ FTc (ms)	339 ± 51	366 ± 46	< 0.001	340 ± 37	360 ± 28	0.002
	123 ± 28	122 ± 29	0.86	147 ± 34	140 ± 33	0.031
LiDCOrapid SVI (mL/m²)	29.3 ± 14.2	32.9 ± 16.4	< 0.001	31.1 ± 10.8	33.0 ± 11.9	0.012
LiDCOrapid CI (L/m²)	3.7 ± 1.8	4.0 ± 2.2	0.018	4.0 ± 1.2	4.0 ± 1.3	0.62
LiDCOrapid stroke volume variation %	10.3 ± 4.3	7.4 ± 3.0	0.001	9.9 ± 3.1	7.0 ± 1.6	< 0.001
LiDCOrapid systemic vascular resistance index (dynes s/cm⁵/m²)	1,584 ± 473	1,623 ± 512	0.59	1,435 ± 410	1,460 ± 496	0.83
Inferior vena cava pulsations dIVC %	16.4 ± 7.5	11.1 ± 5.0	0.007	15.7 ± 4.2	10.1 ± 2.7	< 0.001

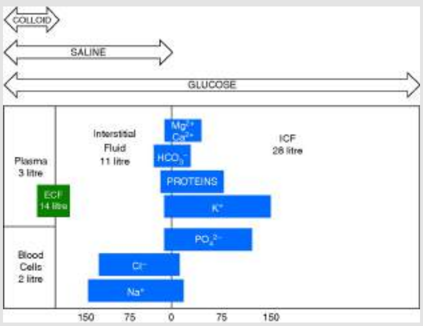
$ScVO_2$ = central venous oxygen saturation, SVI = stroke volume index, CI = cardiac index, FTc = flow time corrected to a heart rate of 60 beats/min, dIVC = respiratory variations in vena cava inferior diameter distensibility index.
Mean, SD, paired sample tests with two-tailed p values: baseline versus after fluid bolus.

ROC curve of CardioQ peak velocity to predict non-responders and responders



Which fluid to use in children ?

Body fluid compartments with main ion distribution



Doherty M , and Buggy D J Br. J. Anaesth. 2012;bja.aes171

Balanced crystalloids are closer to plasma content

Table 1. Types and Compositions of Resuscitation Fluids.*

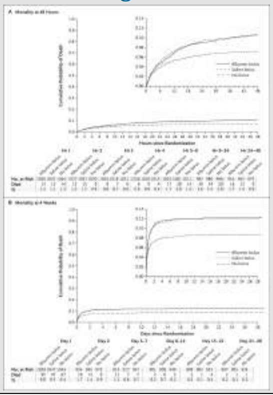
Variable	Human Plasma	Colloids									Crystalloids		
		4% Albumin	Hydroxyethyl Starch						4% Succinylated Modified Fluid Gelatin	3.5% Urea-Linked Gelatin	0.9% Saline	Compounded Sodium Lactate	Balanced Salt Solution
			10% (200/0.5)	6% (450/0.7)	6% (130/0.4)		6% (130/0.42)						
Trade name		Albumex	Hemohes	Hextend	Voluven	Volulyte	Venofundin	Tetraspan	Gelofusine	Haemaccel	Normal saline	Hartmann's or Ringer's lactate	PlasmaLyte
Colloid source		Human donor	Potato starch	Maize starch	Maize starch	Maize starch	Potato starch	Potato starch	Bovine gelatin	Bovine gelatin			
Osmolarity (mOsm/liter)	291	250	308	304	308	286	308	296	274	301	308	280.6	294
Sodium (mmol/liter)	135–145	148	154	143	154	137	154	140	154	145	154	131	140
Potassium (mmol/liter)	4.5–5.0			3.0		4.0		4.0		5.1		5.4	5.0
Calcium (mmol/liter)	2.2–2.6			5.0				2.5		6.25		2.0	
Magnesium (mmol/liter)	0.8–1.0			0.9		1.5		1.0					1.5
Chloride (mmol/liter)	94–111	128	154	124	154	110	154	118	120	145	154	111	98
Acetate (mmol/liter)						34		24					27
Lactate (mmol/liter)	1–2			28								29	
Malate (mmol/liter)								5					
Gluconate (mmol/liter)													23
Bicarbonate (mmol/liter)	23–27												
Octanoate (mmol/liter)		6.4											

* To convert the values for potassium to milligrams per deciliter, divide by 0.2558. To convert the values for calcium to milligrams per deciliter, divide by 0.250. To convert the values for magnesium to milligrams per deciliter, divide by 0.4114.

Myburgh JA et al. N Engl J Med 2013;369:1243-1251.

Children with severe febrile illness and impaired perfusion: 20 to 40 ml/kg of 5% albumin or 0.9% saline or no bolus

FEAST study



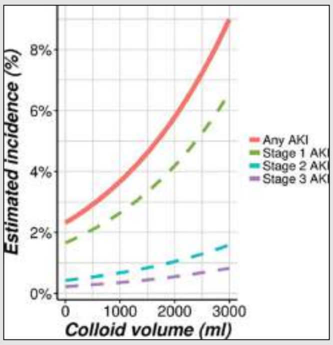
Principal cause of death:
cardiovascular collapse rather than fluid overload or neurologic causes

↓

Adverse interaction between bolus fluid resuscitation and compensatory neurohormonal responses ?

Maitland K et al. N Engl J Med 2011;364:2483-2495.

Relationship between hydroxyethyl starch volume and probability of acute kidney injury (AKI)



Kashy, Babak K et al. 2014; Anesthesiology 121(4):730-739

Which vasopressor to use in children ?

PALS algorithm: can we apply it in the perioperative period?

Push 20 ml/kg isotonic saline or colloid boluses (Up to 60ml/kg in sepsis)
Correct hypoglycemia and hypocalcemia

↓

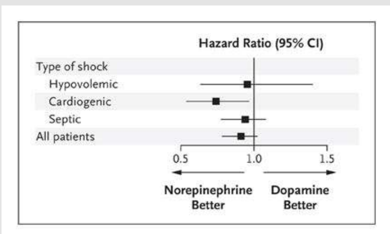
Begin Dopamine therapy

↓

Fluid refractory-dopamine resistant shock

Cold shock	Warm shock
↓	↓
Titrate Epinephrine	Titrate Norepinephrine

Dopamine or norepinephrine as first-line shock: SOAP-II trial



De Backer D et al. N Engl J Med 2010;362:779-789.

NON evidence-based recommendations ?

Peripheral line

↓

DOPAMINE
3 mcg/kg/min

β: ↗ HR & contractility: ↗ CO & SBP
δ_1: vasodilation of capillary beds increases renal perfusion

↓

Titrate up to 7 mcg/kg/min → **Get a central venous line and an arterial line**

Central line

↓

NOREPINEPHRINE
0.01 mcg/kg/min

α_1 : V-C and ↗ SVR
β_1 : some: ↗ inotropisme

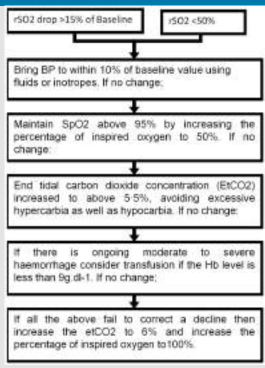
Other inotropes and/or vasopressors ?

To consider in case of cardiac failure

Adrenaline 0.01 mcg/kg/min		Dobutamine 2-10 mcg/kg/min	
β_1 & α_1		β_1 & β_2	
↗HR, SV, CO	↗ SVR	↗HR, CO	↘ SVR

Tachyarrhythmia and ↗ myocardial oxygen consumption

Optimisation of the depth of anaesthesia and interventions to rectify changes in cerebral oxygen desaturation



BIS between 40-60

Monitor rSO_2

Balard C. et al. PLoS One. 2012; 7(6): e37410.

Preoperatively:

- Watch up the NPO: clear fluids up to 2 hrs before
- If Vomiting or gastro-intestinal losses: give NaCl
- Post-induction hypotension: is not related to decrease volume and thus, very often responses to vasopressors

Intraoperatively:

- HR, BP, CVP, urine output, Cap filling: lack sensitivity
- Individualize goal-directed fluid therapy
- Use indices derived from Frank-Starling curve
- Use albumin for early resuscitation
- Use balanced fluids close to plasma content
- Avoid NaCl to decrease risk for Hyperchloremia

Postoperative period:

- Evaluate status : hypovolemia and/or tissue hypoperfusion
- Control unexpected blood or fluid loss
- Avoid hyperhydration (SIADH)
- Switch to oral intake rather than intravenous

Goal-Oriented approach

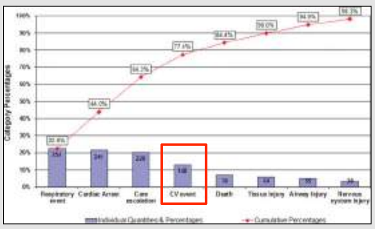
Intravascular volume → Cardiac output ← Blood Pressure

O_2 → ↗oxygen delivery index optimize oxygen transport ← Hb

↓

Improve outcome in high risk patients

1.4 Severe Adverse Events per 1000 anaesthetics



National Pediatric Anesthesia Safety Quality Improvement Program in the United States.

WAKE-UP SAFE

Tyler KC et al. Anesth Analg 2014: 119(1):112-121.