Challenges of Fluid Therapy in Critical Patients

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Goals

- Hydration Status
- Why to give fluids in CC
- 4 D's of fluid therapy
- Fluid Endpoints
- Fluid resuscitation strategies
- Fluid in Sepsis

Which one is dehydrated?

Clinical Signs of Dehydration

Estimated Percentage Dehydration	Physical Examination Findings
<5	History of fluid loss but no findings on physical examination
5	Dry oral mucous membranes but no panting or pathological tachycardia
7	Mild to moderate decreased skin turgor, dry oral mucous membranes, slight tachycardia, and normal pulse pressure.
10	Moderate to marked degree of decreased skin turgor, dry oral mucous membranes, tachycardia, and decreased pulse pressure.
12	Marked loss of skin turgor, dry oral mucous membranes, and significant signs of **shock**

How good are we?

- GI disease
- Sepsis
- Kidney disease
- Diabetis

Clinical signs of dehydration in children

Mackenzie A, Shann F, Barnes G. Lancet. 1989 Dec 23-30;2(8678-8679):1529-30.

False positive	False positive: signs present/ <4% dehydrated (%)	True positive: signs present/ >4% dehydrate d(%)	p
Urea>6.5 mmol/l	17/58 (29)	29/41 (71)	< 0.01
Deep acidotic breathing	15/58 (26)	21/42 (50)	0.023
Ph< 7.35	11/56 (20)	18/42 (43)	0.024
CRFT	8/58 (14)	15 /43 (35)	0.054
Skin turgor	26/58 (44)	28/45 (65)	0.056
RR	17/55 (31)	21/41 (51)	0.072
Tachy MM	42/59 (71)	35/43 (85)	0.154
Sunken eyes	43/59 (73)	35/43 (81)	0.447
HR > 130/min	30/59 (51)	24/43 (56)	0.768

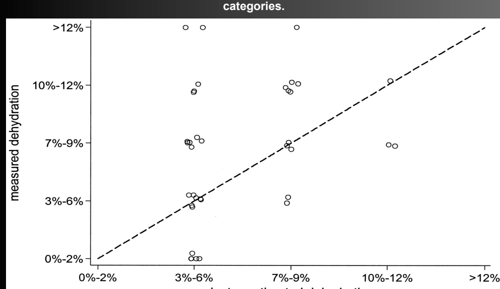
Ability to predict dehydration > 4 %

- We are not really good at it!!
- Between 4% and 9% we overestimate
- in specific diseases the signs will change

The Accuracy of Clinical Assessment of Dehydration During Diabetic Ketoacidosis in Childhood

Koves I H et al. Diab Care 2004;27:2485-2487

The relationship between estimated (by doctor 1) and measured dehydration, grouped into five categories.



Koves I H et al. Dia Care 2004;27:2485-2487

Results

- Patients were between 5 and 10% dehydrated at presentation median of 8.7% dehydration

Results

- There was a good level of agreement between the primary and secondary assessor ($\kappa = 0.5$).
- There was no agreement between assessed and measured dehydration ($\kappa = 0.05$)

Results

- In patients who were <6% dehydrated (measured), the trend was to overestimate dehydration.
- Whereas in patients >6% dehydrated (measured), the trend was to underestimate dehydration.

Results

- Seventy percent of the patients had their hydration status incorrectly assessed:
  - 24% overestimated
  - 46% underestimated

Comparing the accuracy of the three popular clinical dehydration scales in children with diarrhea

Pringle et al. International Journal of Emergency Medicine 2011, 4:58

WHO Scale

Table 1
WHO Scale for dehydration for children 1 month-5 years old

	A	B	C
Look at condition	Well, alert	Restless, irritable	Lethargic or unconscious
Eyes	Normal	Sunken	Sunken
Thirst	Drinks normally, not thirsty	Thirsty, drinks eagerly	Drinks poorly or not able to drink
Feel: Skin pinch	Goes back quickly	Goes back slowly	Goes back very slowly

Scoring: Fewer than two signs from column B and C: no signs of dehydration < 5%, ≥2 signs in column B: Moderate dehydration 5-10%, ≥2 signs in column C: > 10% severe dehydration

Gorelick Scale

Table 2

The 10- and 4-point Gorelick Scale for dehydration: for children 1 month-5 years; 4-point scale physical exam signs highlighted in italic font

Characteristic	No or minimal dehydration	Moderate to severe dehydration
General appearance	*Alert*	*Restless, lethargic, unconscious*
Capillary refill	*Normal*	*Prolonged or minimal*
Tears	*Present*	*Absent*
Mucous membranes	*Moist*	*Dry, very dry*
Eyes	Normal	Sunken; deeply sunken
Breathing	Present	Deep; deep and rapid
Quality of pulses	Normal	Thready; weak or impalpable
Skin elasticity	Instant recoil	Recoil slowly; recoil > 2 s
Heart rate	Normal	Tachycardia

CDC Scale

Table 3

CDS scale clinical features for prediction dehydration in children 1-36 months

Characteristic	0	1	2
General appearance	Normal	Thirsty, restless, or lethargic, but irritable when touched	Drowsy, limp, cold, sweaty, and/or comatose
Eyes	Normal	Slightly sunken	Very sunken
Mucous membranes	Moist	"Sticky"	Dry
Tears	Tears	Decreased tears	Absent tears

Scoring: 0: no dehydration < 3%, 1-4: some dehydration ≤3 × < 6%, 5-8: moderate dehydration ≥6%

Results

	Sensitivity	Specificity	Sensitivity	Specificity
	Moderate (5-10% dehydr.)		Severe >10% dehydration)	
WHO Scale	50 %	61 %	79%	43%
Gorelick Scale 4 point	64 %	69 %	21%	82%
Gorelick Scale 10point	21 %	82%	68%	82%
CDC Scale	68 %	45 %	70 %	40 %

Conclusions

Clinical scoring system used did not reduce the variability of assessment of dehydration compared to doctors' conventional methods.

Lets face it!

We kind of suck in predicting dehydration!!!

But…

Why to give fluids?

In hope that our patient is fluid responsive

Fluid Resuscitation

3 main goals to achieve:

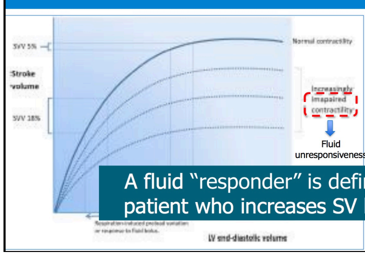
- ✓ Restoration of adequate oxygen delivery
- ✓ Resolution of existing oxygen debt
- ✓ Elimination of anaerobic metabolites

Fluid Responsiveness in Critical Care

Dario Maestrini
1909

The Starling Law

Ernest Henry Starling
1915



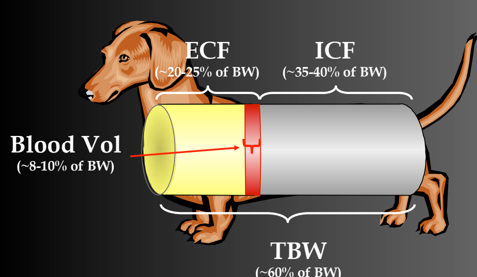
The higher EDV the higher SV

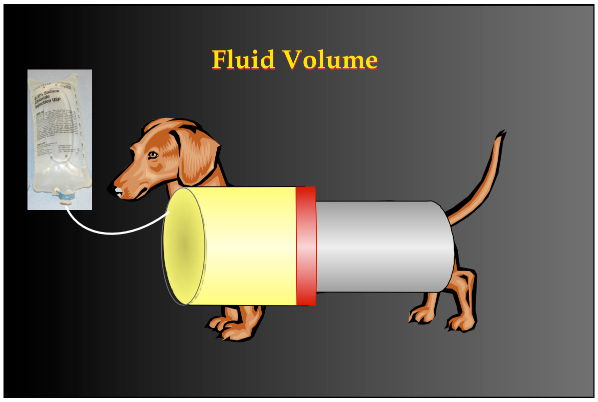
Fluid responsiveness

A fluid "responder" is defined as a patient who increases SV by 15%.

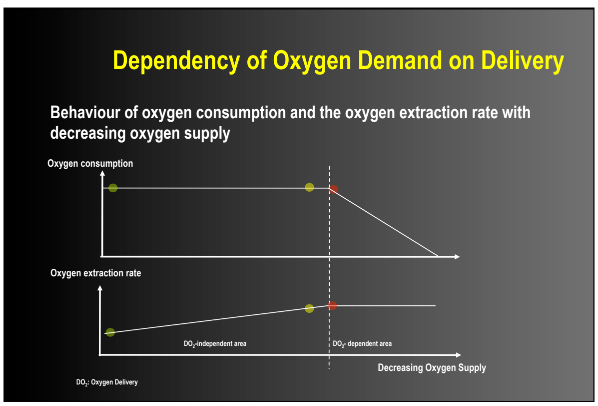
Miller et al, 2016

Fluid Volume

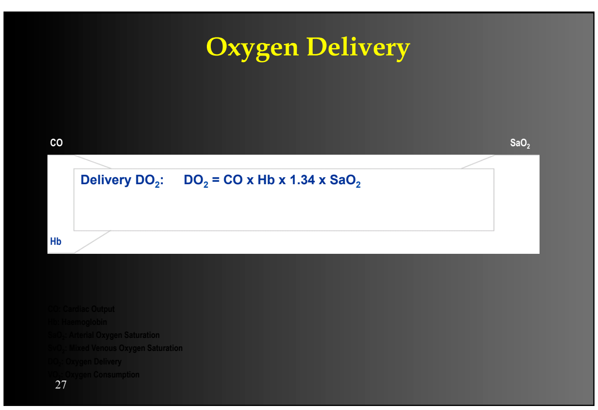




Fluid Volume



Dependency of Oxygen Demand on Delivery
Behaviour of oxygen consumption and the oxygen extraction rate with decreasing oxygen supply
Oxygen consumption
Oxygen extraction rate
DO_2-independent area
DO_2- dependent area
Decreasing Oxygen Supply
DO_2: Oxygen Delivery



Oxygen Delivery
CO
SaO_2
Delivery DO_2: DO_2 = CO x Hb x 1.34 x SaO_2
Hb
CO: Cardiac Output
Hb: Haemoglobin
SaO_2: Arterial Oxygen Saturation
SvO_2: Mixed Venous Oxygen Saturation
DO_2: Oxygen Delivery
VO_2: Oxygen Consumption
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Determinants of Oxygen Delivery and Consumption

Central role of mixed central venous oxygen saturation

CO

SaO_2

Delivery DO_2: $DO_2 = CO \times Hb \times 1.34 \times SaO_2$

Consumption VO_2: $VO_2 = CO \times Hb \times 1.34 \times (SaO_2 - SvO_2)$

Hb

SvO_2

Mixed Venous Saturation SvO_2

CO: Cardiac Output
Hb: Haemoglobin
SaO_2: Arterial Oxygen Saturation
SvO_2: Mixed Venous Oxygen Saturation
DO_2: Oxygen Delivery
VO_2: Oxygen Consumption

Organ specific differences in oxygen extraction

$DO_2 = CaO_2 \times CO = Hb \times 1.34 \times SaO_2 \times CO$

Transfusion

- Transfusion

CO: Cardiac Output
Hb: Haemoglobin
SaO_2: Arterial Oxygen Saturation
CaO_2: Arterial Oxygen Content

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Organ specific differences in oxygen extraction

$DO_2 = CaO_2 \times CO = Hb \times 1.34 \times SaO_2 \times CO$

Ventilation

- Transfusion
- Ventilation

CO: Cardiac Output
Hb: Haemoglobin
SaO_2: Arterial Oxygen Saturation
CaO_2: Arterial Oxygen Content

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Organ specific differences in oxygen extraction

$DO_2 = CaO_2 \times CO = Hb \times 1.34 \times SaO_2 \times CO$

Volume
Catecholamines

- Transfusion
- Ventilation
- Volume
- Catecholamines

CO: Cardiac Output
Hb: Haemoglobin
SaO_2: Arterial Oxygen Saturation
CaO_2: Arterial Oxygen Content

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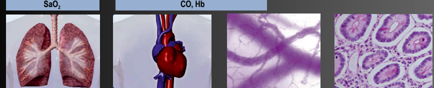
Supply

$DO_2 = CO \times Hb \times 1.34 \times SaO_2$

SaO_2 | CO, Hb



Oxygen Absorption — Lungs
Oxygen Transport — Blood
Oxygen Delivery — Tissues
Oxygen Utilization — Cells / Mitochondria

CO: Cardiac Output; Hb: Hemoglobin; SaO_2: Arterial Oxygen Saturation

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The 4 D's of Fluid Therapy

1. Treat Fluids as Drugs
   - (contra) indications
   - Adverse effecs
2. Fluid Dose
   - ✓ Timing, initial dose, speed, cumulative dose
3. Duration
   - ✓ Stop when no longer fluid responsive
   - ✓ Use dynamic indices when possible
4. De-escalation
   - ✓ Deresuscitation if fluid overload (FO)
   - Fluid overload causes increased morbidity and mortality

Endpoints of Fluid Resuscitation

3 main goals to achieve
- ✓ Restoration of adequate oxygen delivery
- ✓ Resolution of existing oxygen debt
- ✓ Elimination of anaerobic metabolites

Traditional endpoints
- ✓ HR, BP, mental status, urine output

Global endpoints
- ✓ Lactate , base deficit , ScVO2

What we all learned in Veterinary School:

Shock:
90 mls /kg (dog)
40 mls /kg (cat)

And why it doesn't always work that way!!!

Which one? How much?

Severe Polytrauma

6 YO F Springer Sp.
Weighing 18 kg
HBC 30 min earlier
Initially:

- ✓ Unconscious, anisocoria
- ✓ HR 220, pale mucous membranes, T 97.4F, poor femoral pulse quality
- ✓ Tachypnea, RR 85/min
- ✓ BP 50 systolic

Initial treatment

Place IV catheter

- ✓ PCV/TS 36/6.2
- ✓ Lactate 7.6mmol/L

1500 ml LRS IV over 30 minutes
Improves pulse quality and heart rate
Recheck bloodwork

- ✓ PCV 32/TS 5.0
- ✓ Lactate 0.8

Did we fix her?

20 minutes after bolus ends…

Neurological Status:
- Dilated pupils, unresponsive to light

Cardiovascular Status:
- Bradycardic HR 44 bpm, femoral pulses fair-good

Respiratory Status:
- Severe dyspnea, cyanosis

Why did we give a bolus of fluids?

Pros

Cons

Alternatives?

What happened?

Severe head trauma (MGCS:5)
- Must maintain cerebral blood flow
- But large volumes of isotonic crystalloids may exacerbate cerebral edema

Pulmonary contusions
- Will be worsened by excessive fluid therapy

The Guide to Fluid Therapy

1. Resuscitation Endpoints
2. Resuscitation Strategies

Choosing an Endpoint

Parameters must be reliable, easy to obtain and with timely results in all critically ill patients

Endpoints must accurately reflect physiologic state of the patient

Algorithm-based approach to decrease patient morbidity/mortality

Traditional Endpoints

Heart rate

Respiratory rate

Mucus membrane color

Capillary refill time

Urine output

Systolic BP

Lactate

Other Endpoints

Central venous pressure (CVP)

Mean arterial pressure (MAP)

Hematocrit (HCT)

Cardiac output, SVR

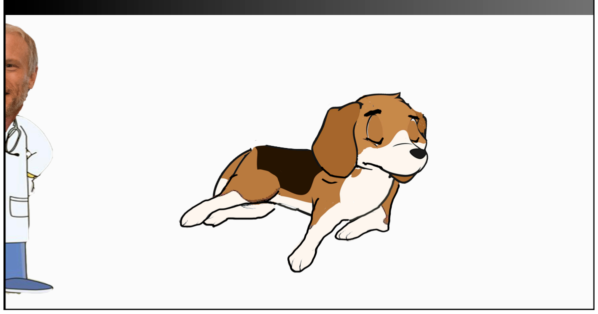
Central venous oxygen saturation ($ScvO_2$)

Static versus Dynamic Markers

Dynamic Markers (provoking the circulation by inducing changes of loading conditions):

- Heart- Lung interactions
- Postural changes

Fluid Responsiveness



Fluid Responsiveness

Dario Maestrini
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The Starling Law

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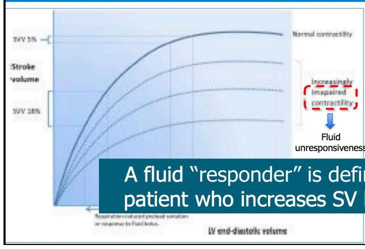


The higher EDV the higher SV

Fluid responsiveness

A fluid "responder" is defined as a patient who increases SV by 15%.

Miller et al, 2016

Venous Return

LV Preload (Venous Return, VR)

Effect of sympathetic nervous system on the splachnic venous district

The higher VR the higher EDV

$$VR = \frac{MBP - RAP}{SVR}$$

MBP = Mean Blood Pressure
RAP = Right atrial pressure
SVR = Systemic vascular resistance

Epub 2020 Oct 16.

Caudal vena cava collapsibility index as a tool to predict fluid responsiveness in dogs

Pablo A Donati [1], Juan M Guevara [1], Victoria Ardiles [2], Eliana C Guillemi [1], Leonel Londoño [3], Arnaldo Dubin [4]

Affiliations + expand

PMID: 33063922 DOI: 10.1111/vec.13009

Abstract

Objective: To evaluate the use of the caudal vena cava collapsibility index (CVCCI) as a predictor of fluid responsiveness in hospitalized, critically ill dogs with hemodynamic or tissue perfusion abnormalities.

Design: Retrospective observational study.

Setting: Private referral center.

Animals: Twenty-seven critically ill, spontaneously breathing dogs with compromised hemodynamics or tissue hypoperfusion.

Interventions: None.

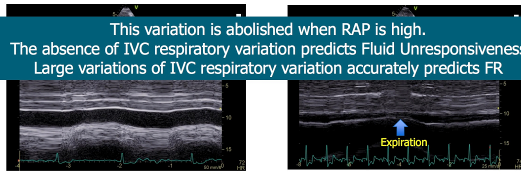
Measurements and main results: The electronic medical records were searched for dogs admitted for any cause, from August 2016 to December 2017. We included dogs with ultrasound measurements of: CVCCI, performed at baseline; and velocity time integral (VTI) of the subaortic blood flow, carried out before and after a fluid load. CVCCI was estimated as: (maximum diameter-minimum diameter/maximum diameter) × 100. Dogs in which VTI increased ≥15% were considered fluid responders. The CVCCI accurately predicted fluid responsiveness with an area under the receiver operating characteristic curve of 0.96 (95% CI, 0.88 to 1.00). The optimal cut-off of CVCCI that better discriminated between fluid responders and nonresponders was 27%, with 100.0% sensitivity and 83.3% specificity. At baseline, fluid responders had lower VTI (5.48 [4.26 to 7.40] vs 10.61 [7.38 to 13.23] cm, $P = 0.004$) than nonresponders. The basal maximum diameter of the caudal vena cava adjusted to body weight was not different between responders and nonresponders (0.050 [0.030 to 0.100] vs 0.079 [0.067 to 0.140] cm/kg, $P = 0.339$). The increase in VTI was related to basal CVCCI ($R = 0.60$, $P = 0.001$). Bland-Altman analysis showed narrow 95% limits of agreement between measurements of CVCCI and VTI performed by different observers or by the same observer.

Conclusions: The results of this small cohort study suggest that CVCCI can accurately predict fluid responsiveness in critically ill dogs with perfusion abnormalities. Further research is necessary to extrapolate these results to larger populations of hospitalized dogs.

Great Veins Variation (over the respiratory cycle)

Caudal Vena Cava Collapsibilty Index

In controlled ventilation, the IVC expands in inspiration and reduces in expiration



This variation is abolished when RAP is high.
The absence of IVC respiratory variation predicts Fluid Unresponsiveness
Large variations of IVC respiratory variation accurately predicts FR

Caudal Vena Cava Collapsibility Index

Great Veins Variation (over the respiratory cycle)

Caudal Vena Cava Collapsibilty Index

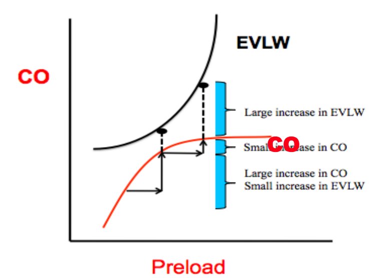
First Formula

IVC Diameter Variability (DV)

$$DV_{IVC} = 100 \times \frac{(D_{max} - D_{min})}{D_{mean}}$$

Cut-off of CVCCI between fluid responders and nonresponders was 27%, with 100.0% sensitivity and 83.3% specificity.

The Frank-Starling & Marik-Phillips Curves



Resuscitation Strategies

- Standard resuscitation
- Damage Control Resuscitation
- Hypertonic resuscitation
- Permissive hypotensive resuscitation
- Supra-physiologic resuscitation

Standard Resuscitation

- Uses traditional endpoints to maintain tissue perfusion and oxygen delivery
- Administration of crystalloids, colloids, blood products, vasopressors and/or ionotropes
- Patient population
  - ✓ Most commonly practiced approach to resuscitation regardless of etiology for CV instability
- Lack of standard algorithm approach

Brendon

Brendon, 3 year old, MC, Great Dane

Sudden onset of panting
Distended abdomen
HR: 220/min
Blood gas:

- Metabolic Acidosis
- Lactate 7 mmol/l
- MAP 45 mmHg

Which strategy would you have used?

Standard resuscitation

Damage control resuscitation

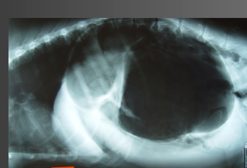
Permissive hypotensive resuscitation

Supra-physiologic resuscitation

Early goal-directed therapy

Brendon, 3 year old, MC, Great Dane

What do you want to do?



Brendon, 3 year old, MC, Great Dane

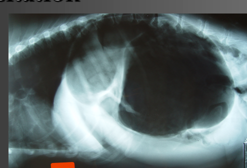
Endpoints?

- ✓ HR
- ✓ Lactate
- ✓ Blood Pressure

Brendon, 3 year old, MC, Great Dane

Strategy:

- ✓ Standard resuscitation



Hypertonic Resuscitation

Similar endpoints as standard resuscitation

Use of hypertonic agents as main resuscitative fluid

Proposed benefits

- ✓ Lower volumes required to attain intravascular volume expansion
- ✓ Reduce endothelial and tissue edema
- ✓ Improve microcirculation
- ✓ Immunomodulatory effects

Head Trauma

Key is normovolemia

- "Just enough" resuscitation
- Consider hypertonic fluids
- Avoid Colloids and Albumin

Head Trauma

Hypertonic fluids:

- Will decrease intracranial edema
- Will decrease inflammatory cascade
- Prevent fluid overload

Head Trauma

Goal is to reach:

- MAP: 65-70 mm HG
- Improvement of neurological signs (modified Glascow Coma Score)
- Not to volume overload your patient

Thoracic Trauma

Avoid Volume overload:

Use low volume resuscitation and permissive hypotension strategy

Excessive volume of fluids will leak into lungs and worsen the interstitial edema

Permissive Hypotensive Resuscitation

Hypotensive resuscitation
- Administration of small volume resuscitation to achieve lower than normal end-points.
  - Uncontrolled, closed body cavity hemorrhage
  - Pulmonary contusions
  - Noncardiogenic pulmonary edema
- Attempt to minimize further bleeding due to fluid administration in preparation for surgery
- Endpoint: MAP (60-65mmHg)

Hypotensive resuscitation

Definition: deliberate tolerance of lower MAP in face of uncontrolled hemorrhage

Goal: maximize body's homeostasis
- ✓ Arteriolar vasconstriction
- ✓ Increased blood viscosity
- ✓ Thrombus formation

Controversial
Optimal BP debatable

Decreased blood loss and lower mortality in animal models (Burris 1999)

Slight increase in survival (70% vs. 62%) humans with torso trauma (Bickell, 1999)

Permissive Hypotensive Resuscitation

Hypotensive resuscitation

- Balance of maintaining adequate perfusion, but preventing exsanguination until surgical bleeding can be controlled
- Administration of small volume resuscitation to achieve lower than normal end-points
  - Uncontrolled, closed body cavity hemorrhage
  - Pulmonary contusions
  - Non-cardiogenic pulmonary edema
- Attempt to minimize further bleeding due to fluid administration in preparation for surgery
- Endpoint: MAP (65mmHg)
  - If MAP is <65, then resuscitate with IVF or blood products
  - If MAP >65, the check perfusion
    - If Perfusions seems good>> no further fluids
    - If perfusion is poor >>> check pain control and consider opiodes

Supra-physiologic Resuscitation

Cardiac output is main endpoint
- ✓ Maximize cardiac output to predefined target

Patient population
- ✓ Septic shock

Proposed benefits
- ✓ Maximize oxygen delivery to the tissues
- ✓ Avoid hypoxic related organ injury

Septic Shock

Animals in septic shock secondary to trauma may need significant fluid therapy

Endpoints for fluid resuscitation are :
- ✓ MAP 65 mmHg
- ✓ Normal Lactate
- ✓ Oxygen Delivery

Supra-physiologic Resuscitation

Cardiac output is main endpoint
- ✓ Maximize cardiac output to predefined target

Patient population
- ✓ Septic shock

Proposed benefits
- ✓ Maximize oxygen delivery to the tissues
- ✓ Avoid hypoxic related organ injury

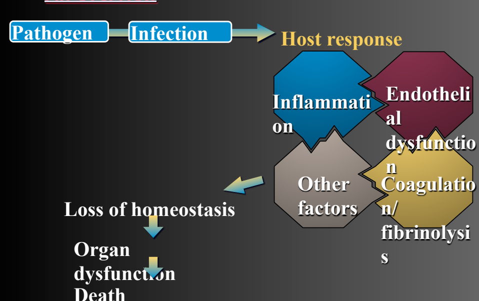
Definition of sepsis

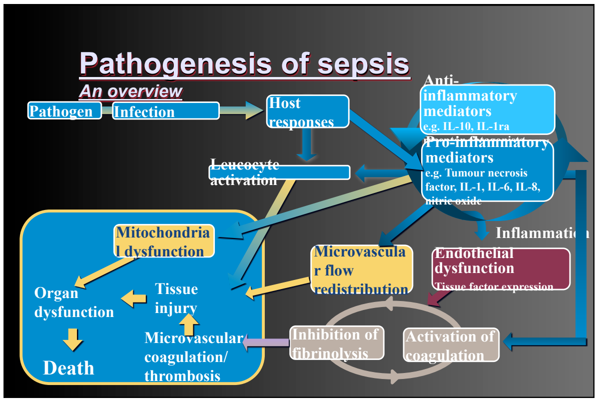
'Sepsis is a life-threatening condition that arises when the ***body's response to an infection injures its own tissues and organs***.

The 'Merinoff Definition', September 2010

Pathogenesis of sepsis

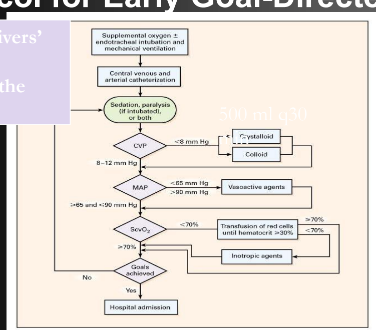
An overview





Protocol for Early Goal-Directed

Back to Rivers' paper…
Here was the algorithm



Systemic circulation in sepsis

Early sepsis:

- Low systemic vascular resistance (SVR) and normal to decreased CO
- Heart is already compromised by poor contractility
- Stroke volume is maintained but there is an increase in left ventricular end-systolic volume (LVESV) and left ventricular end-diastolic volume (LVEDV) and decrease in ejection fraction

Systemic circulation in sepsis

Early sepsis:

- There is also a diastolic dysfunction due to decreased left ventricular compliance and subsequent increased left ventricular end-diastolic pressure (LVEDP)

- **Severe Sepsis:**
  - During severe sepsis, there is a decrease in LVEDV and LVESP. There is hypotension.

Peripheral circulation in sepsis

Vasodilation:

NO serves as a vasodilator

- ✓ **Released in response to high blood flow rate and signaling molecules (Ach and bradykinin)**
- ✓ **Highly localized and effects are brief**
- ✓ **If NO synthesis is inhibited, blood pressure skyrockets**
- ✓ **NO aids in gas exchange between hemoglobin and cells**
- ✓ **Hemoglobin is a vasoconstrictor, Fe scavenges NO**
- ✓ **NO is protected by cysteine group when O2 binds to hemoglobin**
- ✓ **During O2 delivery, NO locally dilates blood vessels to aid in gas exchange**
- ✓ **Excess NO is picked up by HGB with CO2**

Peripheral circulation in sepsis

Vasodilation:

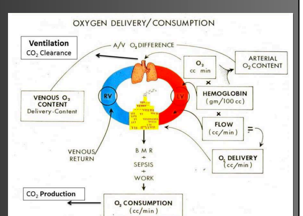
- **In a physiologic stage NO , diffuses into vascular smooth muscle cells and activates guanylyl cyclase, which decreases intracellular calcium concentration and activates potassium channels causing smooth muscle relaxation**

- **During sepsis NO is produced in an excess amount by iNOS**
  - Increased NO leads to hyper polarization of potassium channels and persistent relaxation of the smooth muscle cells

So how can sepsis outcomes be improved?

Treatment strategy for septic cardiomyopathy

- Strategy is to achieve a balanced DO2/VO2 by increasing cardiac index to improve DO2
- VO2 can be decreased by sedation, mechanical ventilation, antipyretics



Fluid Management

- 2012 Surviving Sepsis Campaign recommends specific physiologic goals for fluid resuscitation:
  - MAP > 65 mmHg
  - CVP 8-12 mmHg (or 12-15 during mechanical vent)
  - Central venous O_2 sat > 65% or Mixed venous > 70%
  - Urine output > 0.5 ml/kg/h
  - Normalization of lactate
- It is important to note that these goals are for the <u>first 6 hours</u> of sepsis therapy
- We are going to dive deeper into fluids and central venous O_2 saturation ($ScvO_2$) in a few slides

Fluid Management

- 2018 Surviving Sepsis Campaign recommends specific physiologic goals for fluid resuscitation:
  - 30 mls/kg over first 3 hours

Fluid Management

- Increasing preload with increase stroke volume based on Frank–Starling relationships
- Cardiomyopathy will shift the Frank–Starling curve and over-aggressive fluid management can lead to worsening organ failure
- SOAP trial showed that a positive fluid balance is a poor prognostic factor in sepsis

Vasopressors

- Norepinephrine:
  - has stronger alpha adrenergic profile (rather then beta-1)
  - increases mainly afterload

Vasopressors

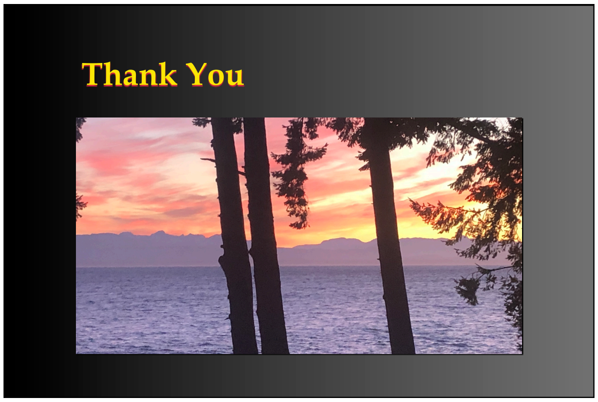
- First-line: Norepinephrine (dose: 0.01 - 1 µg/kg/min)
  - Increases MAP mainly by vasoconstriction, but also is a mild inotrope which is important for sepsis-mediated cardiac stunning
  - Low doses improve cardiac output, and cerebral, renal, and splanchnic blood flow
  - Compared to dopamine: Less tachycardia, fewer arrhythmias, lower RR of death (0.91; 0.83–0.99)

Vasopressors

- Second-line: Vasopressin (dose: 0.01 – 0.04 units/min)
  - Goal is to decrease dose of NE
  - Reasonable to start when NE dose gets to 0.2 µg/kg/min
  - Quality of evidence is moderate

Vasopressors

- Third-line: Epinephrine (dose: 0.01 - 1 µg/kg/min)
  - Same dosing regimen as norepinephrine
- Can use Phenylephrine infusion in certain situations, e.g. avoidance of beta-adrenergic activation if patient has rapid Afib


Thank You


Questions?