Fluid Dynamics in the Fetus and Foal

The Goldilocks Principle

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Fluid Physiology

Fluid Physiology Fetus/Neonate

- Unique characteristics of Fetus/ Neonate
  - Interstitium
  - Lymph flow
  - Capillary endothelial permeability

Fluid Physiology Fetus/Neonate

- Interstitium
  - Heterogeneous space
  - Dynamically controls its fluid content
  - Compliance 10X adult (fetal lamb)

Fluid Physiology Fetus/Neonate

- Lymph flow
  - Thoracic duct lymph flow
    - Fetal lamb - 0.25 mL/minute/kg
    - 5x the adult rate
  - Lymph flow - subcutaneous
    - Puppies 2X adult dogs (per kg)
  - Pulmonary lymph flow
    - Newborn lambs and puppies > adults
  - Neonate – local/ whole body lymph flow > adult
    - Increased interstitial volume
    - Higher capillary permeability

Fluid Physiology Fetus/Neonate

- Capillary endothelial permeability
  - Filtration rate in fetal lambs vs adults
    - Fluid 5x
    - Proteins 15x
  - Why?
    - Poor precapillary tone
    - Higher capillary hydrostatic pressure
    - Higher filtration
    - The role of the glycocalyx?
  - Filtration related to hydrostatic pressure
    - Precapillary tone lambs – develops during 1st week
    - Doesn’t develop in a uniform manner

Fluid Physiology At Birth

- Arterial blood pressure increases
  - Studied in lambs
  - Last weeks – increases 20%
  - During labor – increases another 18%
  - At birth – increases another 12%
- Transmitted to capillaries
- Increased transcapillary filtration
  - Poor precapillary tone

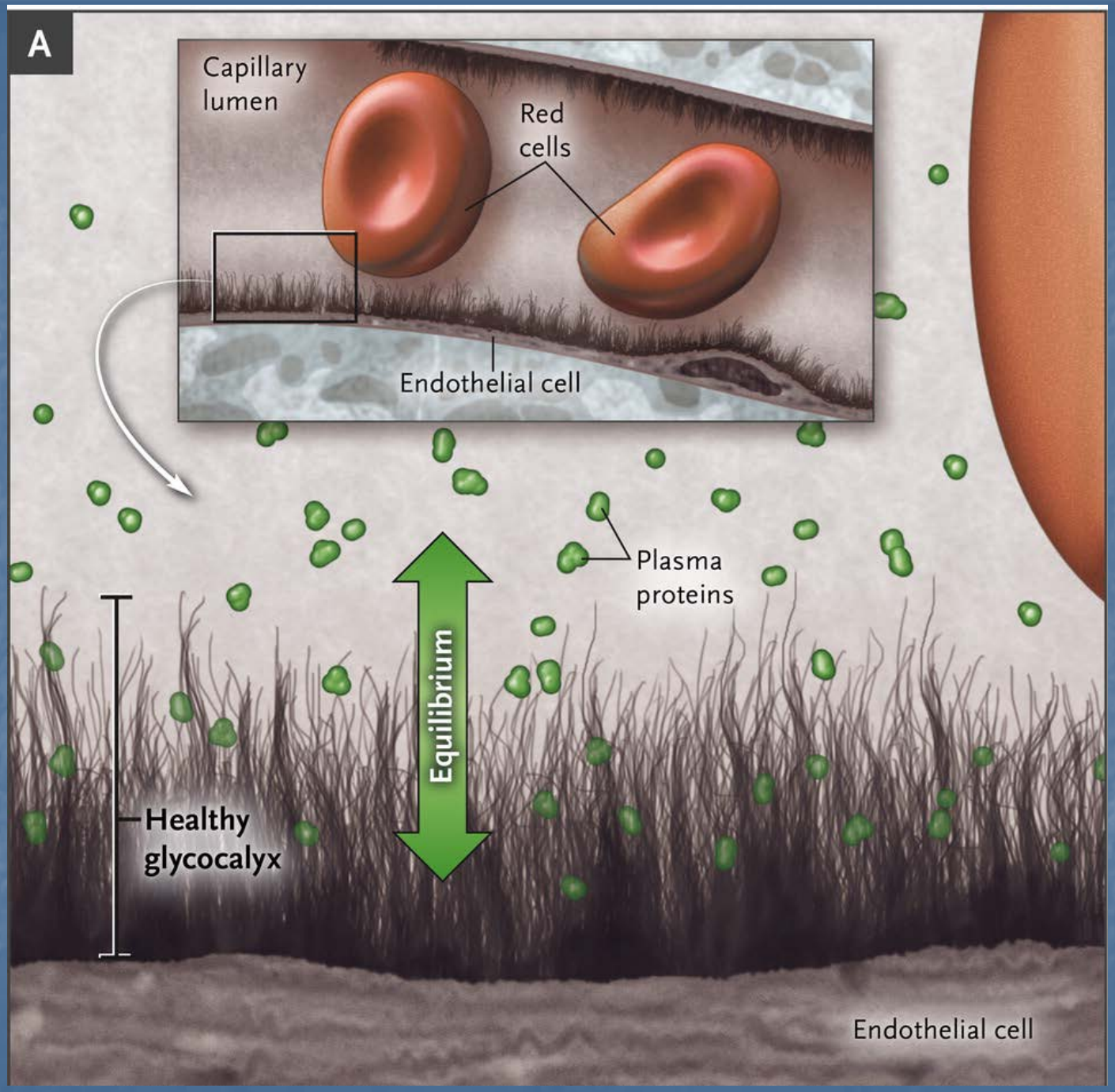
Fluid Physiology At Birth

- Other reasons for fluid shifts
  - Direct compression of the fetus
    - Increased venous pressure
  - Vasoactive hormones
    - Arginine vasopressin
    - Norepinephrine
    - Cortisol
    - Atrial natriuretic factor

Fluid Physiology
Neonates are Born Fluid Overloaded

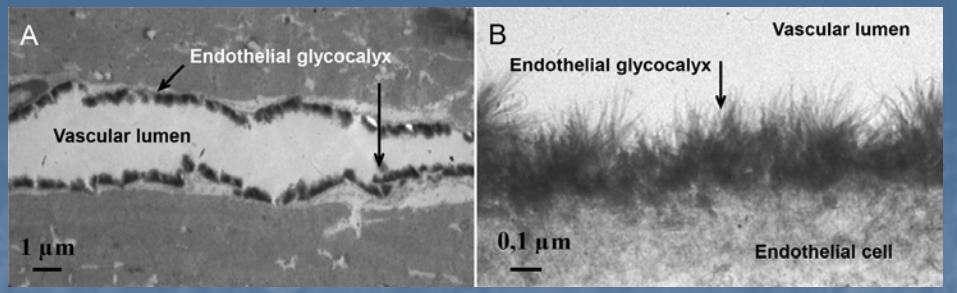
- Fluid shifts
  - From fetal fluids / maternal circulation
  - Accumulating in the fetal interstitium
- ***All Neonates Are Born Fluid Overloaded***
- Rate of loss of this fluid - species variation
  - Foal – weeks
  - Other species
    - 10-15% body weight rapidly after birth
  - Important not to replace fluid loss
    - Poor outcomes with persistent fluid overload

Why?



Myburgh JA, Mythen MG. Resuscitation Fluids. **N Engl J Med 2013;369:1243-51**

EGL barrier

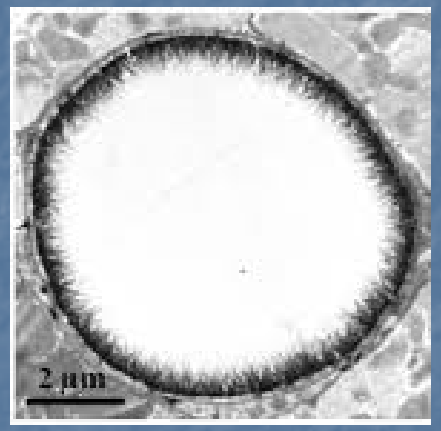


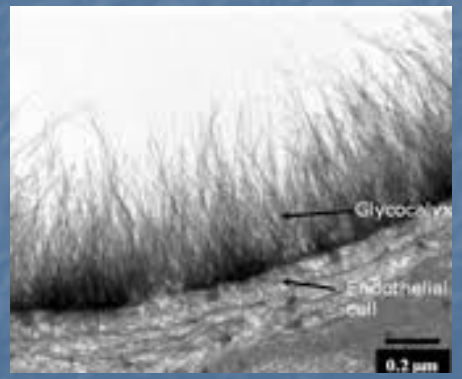
Best Practice & Research Clinical Anaesthesiology 28 (2014) 227-234.

- Endothelial glycocalyx
  - Carbohydrate-rich layer
  - Proteoglycans and glycoproteins
  - Bound plasma proteins, mainly albumin
- Hydrostatically forced fluid
  - Forces albumin and other osm particles into web
  - Forms a gradient with more caught outside
  - Any protein making it through washed into interstitium
  - Layer of fluid on luminal side of endothelium – protein free
  - Forms oncotic gradient
  - Not effected by interstitial protein content

Fluid Type and the EGL

- Transvascular fluid filtration
  - Depends on endothelial glycocalyx
    - If intact with normal capillary pressures
      - Crystalloids freely pass
      - Colloids are held back
    - If damaged neither are held back
- Intravascular hypovolemia
  - Low capillary pressures
  - No filtration crystalloids or colloids
- Damage EGL – loss of filtering ability
  - Hypervolemia
  - Rapid fluid administration
  - Sepsis (inflammatory mediators, TNF)
  - Ischemia/Reperfusion

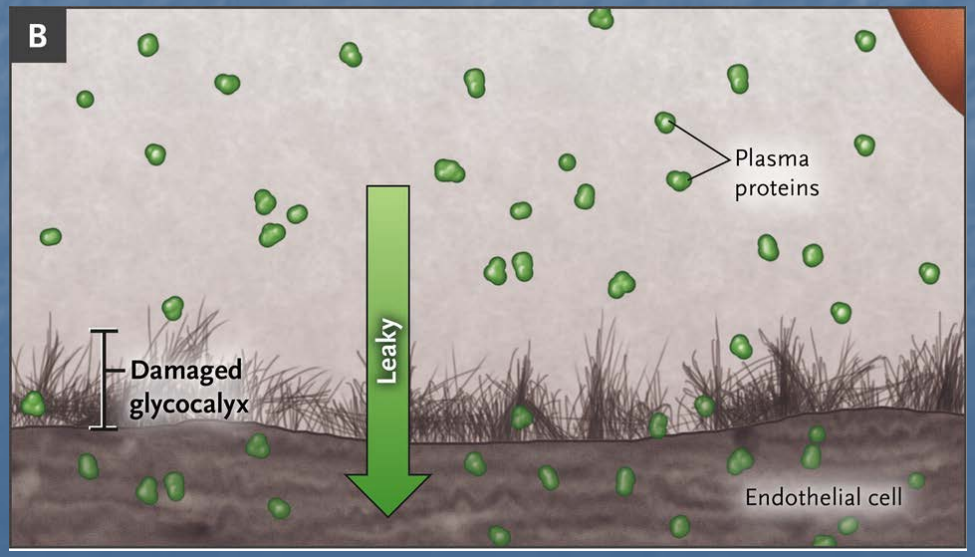




From: http://www.hubrecht.eu

EGL – Damage by Hypervolemia

- Theory
  - Volume sensed by atria
  - Release natriuretic peptides (ANP)
  - Which activates metalloproteinases



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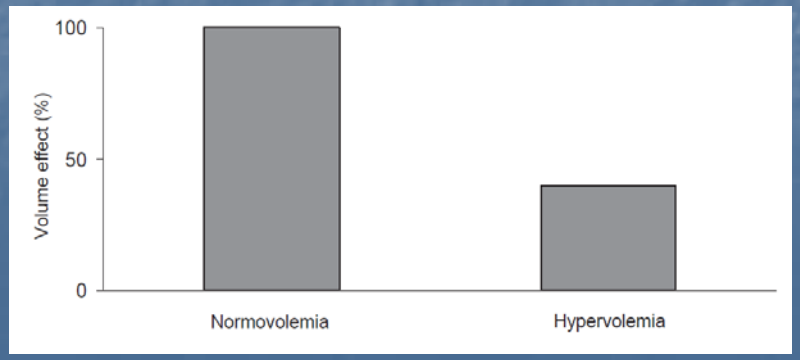
EGL – Damage by Hypervolemia

- Studies
  - Acute blood loss
    - Add HES or albumin to maintain normovolemia
    - Almost 100% retained
  - Hypervolemia – HES or albumin
    - Infuse same volume without loss
    - 60% colloid escapes into interstitium
    - Glycocalyx is decreased
- Fetus/Neonate?

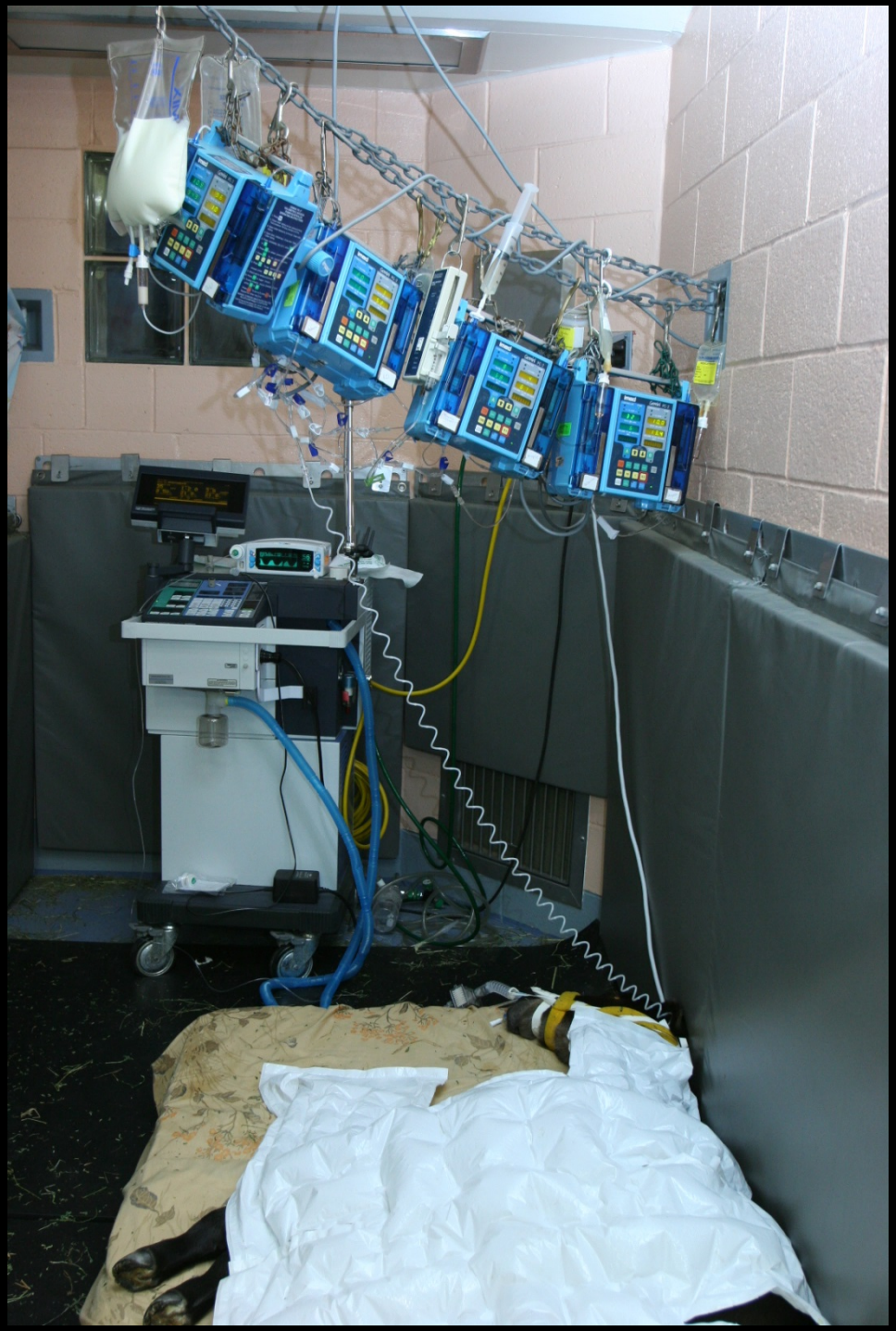


Fluid Type
Crystalloids vs Colliods

- Depend on state of endothelial glycocalyx
- Colloid increases intravascular volume
  - Resuscitation from hemorrhage
- No difference intravascular volume
  - Sepsis
  - Inflammatory states
  - Trauma
  - Hypervolemia
- Crystalloids or colloids will have the same effect

Endothelial Glycocalyx "Capillary Leak"

- Normovolemia
  - Endothelial glycocalyx healthy
  - Colloids remain intravascular
  - Crystalloids leak
- Hypervolemia (fluid therapy, fetal fluid shifts)
  - Endothelial glycocalyx damaged
  - Colloids and crystalloids leak
- Hypovolemia
  - Colloids and crystalloids remain intravascular
- Sepsis
  - Endothelial glycocalyx damaged
  - Colloids and crystalloids leak with fluid therapy

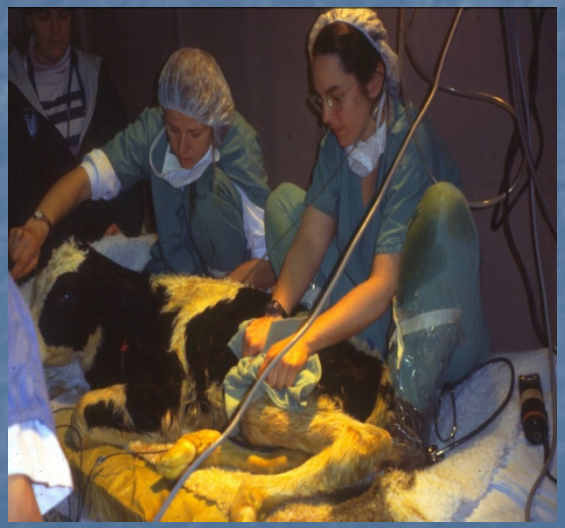


Fluid Dynamics Consequences

- Response to Hemorrhage
- Response to Volume Loading
- Response to Hypoxia

Fluid Dynamics
Response to Hemorrhage

- Perinatal blood loss
  - Premature placental separation
  - Rupture of umbilical vessels
  - Long bone fractures
  - Gastrocnemius rupture
  - Necrotizing enterocolitis



Fluid Dynamics
Response to Hemorrhage

- 30% loss of blood
  - Adult horses, dogs, cats, and sheep
    - With out fluid therapy - 24 to 48 hours
  - Fetus or neonate is shorter
    - Fetal sheep blood volume
      - 2x adults within 30 minutes
      - 100% within 3 to 4 hours

Fluid Dynamics Response to Hemorrhage

- Neonatal kittens and rabbits
  - Greater blood loss /kg before BP decrease
    - Translocation fluid and protein
    - From the interstitial space
  - Tolerate blood loss better than adults

Fluid Dynamics
Response to Volume Loading

- Rapid intravascular infusions crystalloids
  - Fetal lambs - 6 to 7% retained at 30-60 min
  - Adults – 20% to 50% retained at 30-60 min
- Rapid transfer into the interstitial space
  - High interstitial compliance
  - High capillary filtration coefficient
    - Suppression of the endothelial glycocalyx?

Fluid Dynamics
Response to Volume Loading

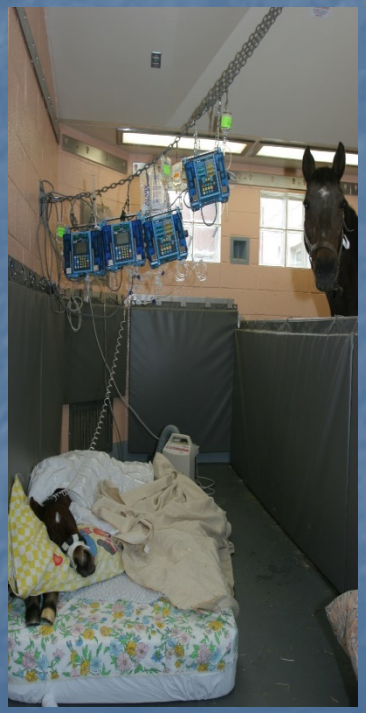
- Fluid Overload – lack of intravascular retention
  - Adults (dogs, sheep)
    - The adult clears the fluid load hours
    - Renin
    - Vasopressin
    - Atrial natriuretic factor

Fluid Dynamics
Response to Volume Loading

- Fluid Overload – lack of intravascular retention
  - Neonates (puppies, lambs)
    - 24 to 36 hr to clear fluid load
    - Volume load escapes vasculature space quickly
    - Escape volume sensors detection
    - No diuretic response
    - Urine flow rapidly returns to normal
      - Before clearing volume load

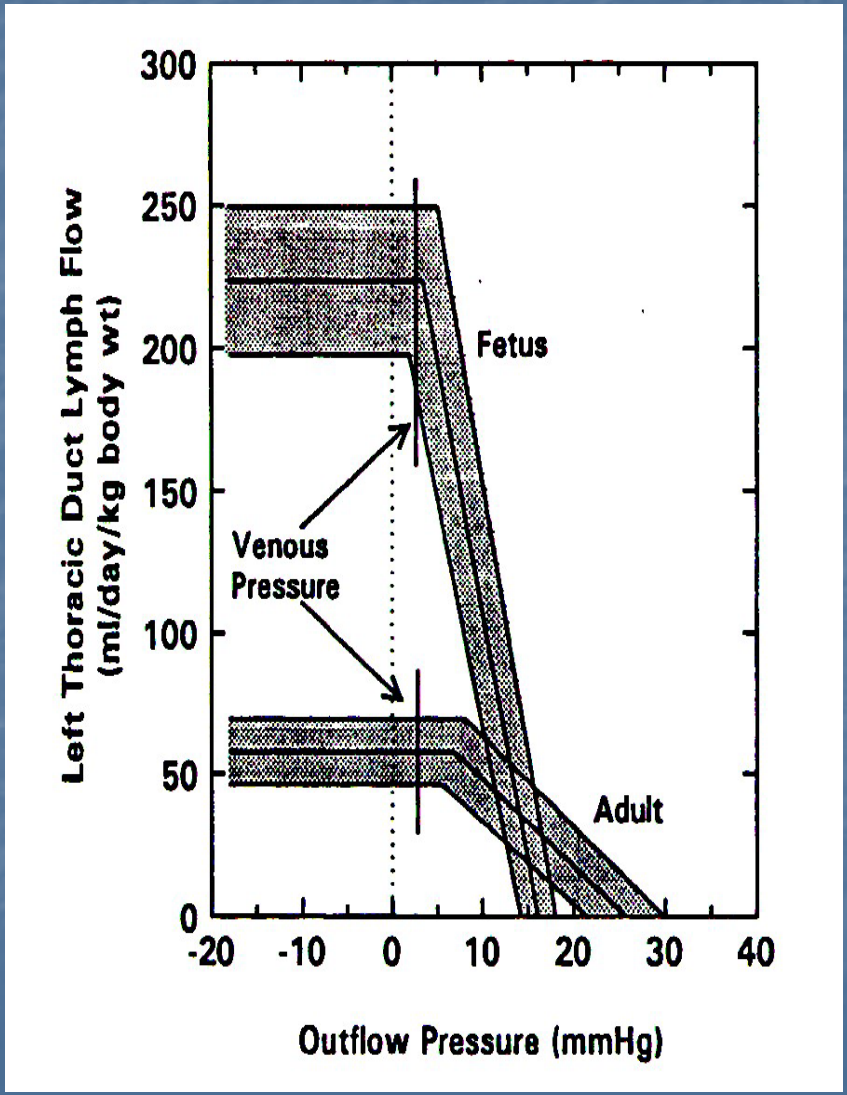
Fluid Dynamics
Response to Volume Loading

- After fluid loading (fetal lambs, neonatal lambs)
  - Increase thoracic duct lymph flow
    - Increase by 3.5 times (max flow rate)
    - Angiotensin II augments lymph flow
  - Fluid therapy – rapid infusion
    - Increases CVP
    - Dramatic decrease in lymphatic flow
    - Result in edema



Thoracic Lymph Flow

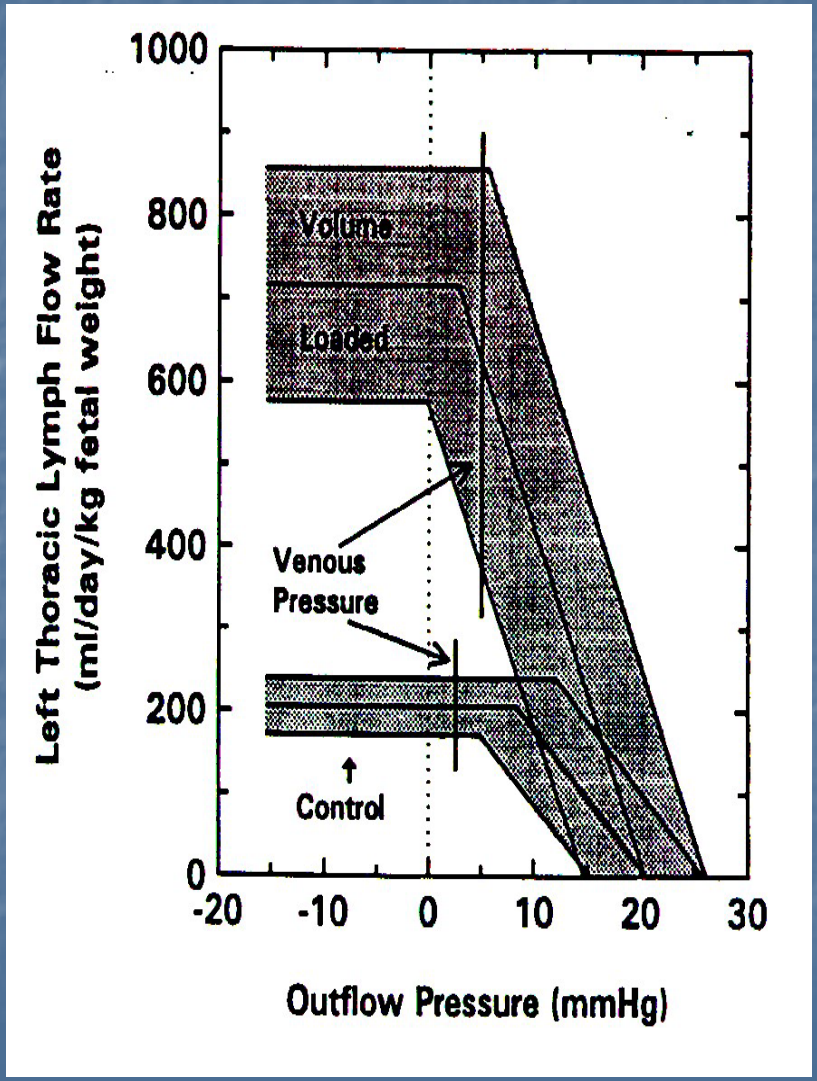
- Fetal lamb
- Adult sheep



From: Brace RA et.al.

Thoracic Lymph Flow

- Fetal lamb
- With large volume intravenous infusion
  - ↑↑ Lymph flow as much as 340%
  - Limited by CVP



From: Brace RA et.al.

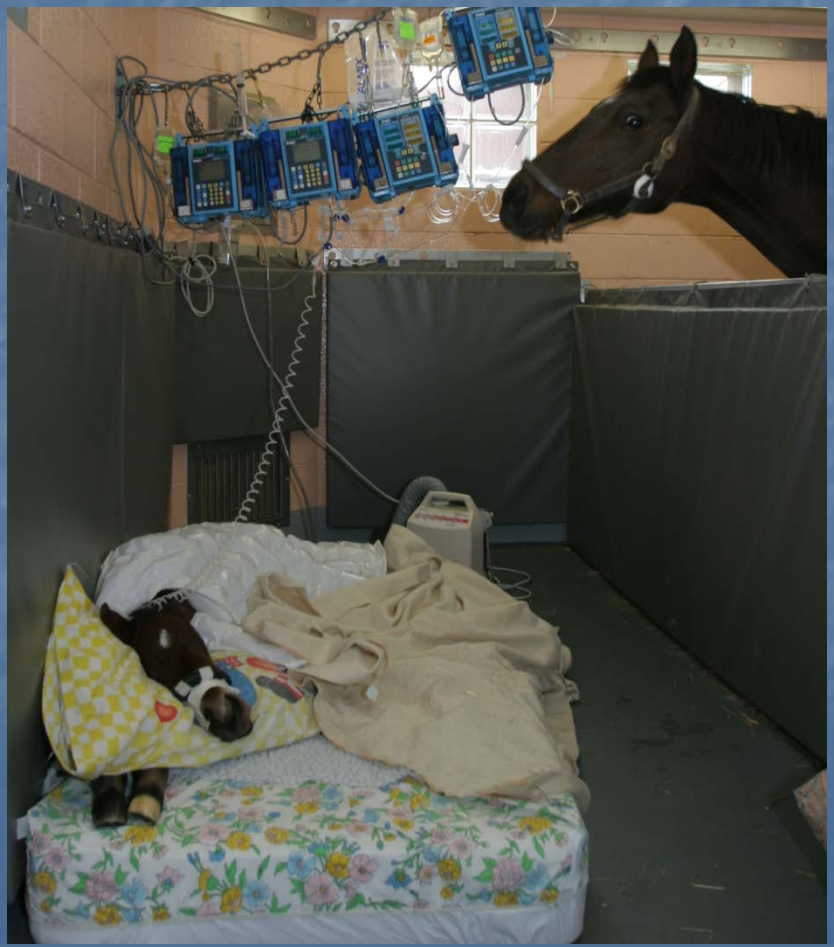
Fluid Dynamics Response to Hypoxia

- Moderate/severe hypoxemia (fetal lambs)
  - Increases arterial and venous pressures
  - Poor precapillary tone
    - Increase capillary pressure
  - Greater fluid shift interstitial space
  - Leading to excessive fluid overload

Fluid Dynamics Response to Hypoxia

- All neonates
  - Fluid overloaded at birth
- With hypoxia/asphyxia (and with fluid therapy)
  - Greater degree of fluid overload
- ***Hypovolemic with concurrent fluid overload***

Are our patients getting better because of our therapy or despite our therapy???



FEAST Study
Fluid Expansion As Supportive Therapy

- Attempt to justify modernizing hospitals
- Attempt to deliver fluids expediently
- Children with poor perfusion
  - But not severe sepsis
- Bolus vs slow drip
- Backfired
  - Bolus fluids increased the risk of death
  - No subgroup fluid resuscitation beneficial

Fluid-Bolus Resuscitation

- Patients with compensated shock
  - Harmful? Mechanisms?
  - Interruption catecholamine responses
    - Rapid increase in plasma volume
    - Reperfusion injury?
  - Transient hypervolemia/hyperosmolality
    - Exacerbate capillary leak
    - Harmful edema
- Bolus-fluid resuscitation in compensated shock
  - If no clinical fluid deficit
  - Practice with caution

Septic Shock
Volume Resuscitation

- Immediate positive effect
  - Increased perfusion
  - Patient “looks better” but ...
- Rapid infusion – adverse effects
  - Fluid responder
    - CO increases
    - Vasodilatation
    - BP unchanged (perfusion?)
  - Increased shear stress
    - Increases NO

Septic Shock
Volume Resuscitation

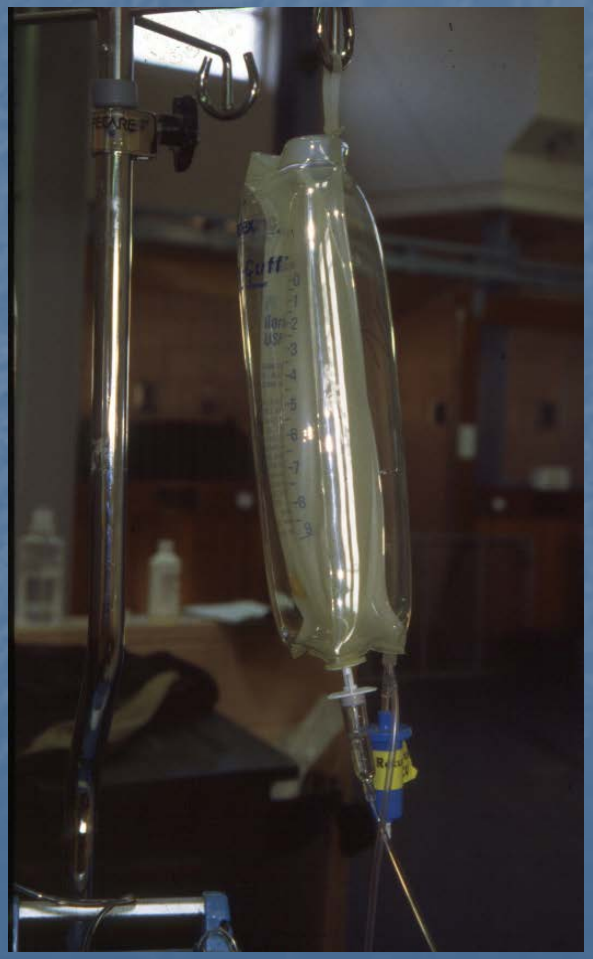
- Increased cardiac filling pressure
  - Increased right atrial pressure
  - Increase natriuretic peptide
    - cGMP-mediated vasodilatation
    - Cleaves endothelial glycocalyx
    - Endothelial barrier injury
- Capillary leak
  - At 3 hr. < 5% crystalloid intravascular
  - Increased tissue edema
  - Myocardial dysfunction

Once Shock Reversed

- Positive fluid balance = increased mortality
  - Acute load
  - Rapid unload – diuresis
- Patients who rapidly unload live
  - Less severe disease?
  - Can we influence outcome?
- Dilemma
  - Initially fluids are helpful in shock
  - But once reversed – harmful
- Restrictive fluid strategy
  - Early use inopressors
  - Reverse severe vasodilatory shock

Are Fluid Boluses Needed?

- Clinical guess
  - Clinicians can't guess correctly
    - Clinical examination
    - Hemodynamic indices (e.g. CVP)
  - 50% improve outcome
  - 50% cause harm



Fluid Therapy
Critical Patients

- Past focus on short-term goals
  - Rapid correction of hypovolemia
  - Emergency resuscitation
  - Clinically immediately rewarding but ...
- Potential longer-term consequences
  - Contribution to organ failure
  - Long term mortality/morbidity

Fluid Therapy
Things I Try to Do

- Bolus fluids but not too much
  - No good stall side guide
- Stop high rates fluids early
  - Before legs warm
  - Give IV nutrition
    - In as small a volume as practical
  - Na restriction in neonates
  - Cl restriction

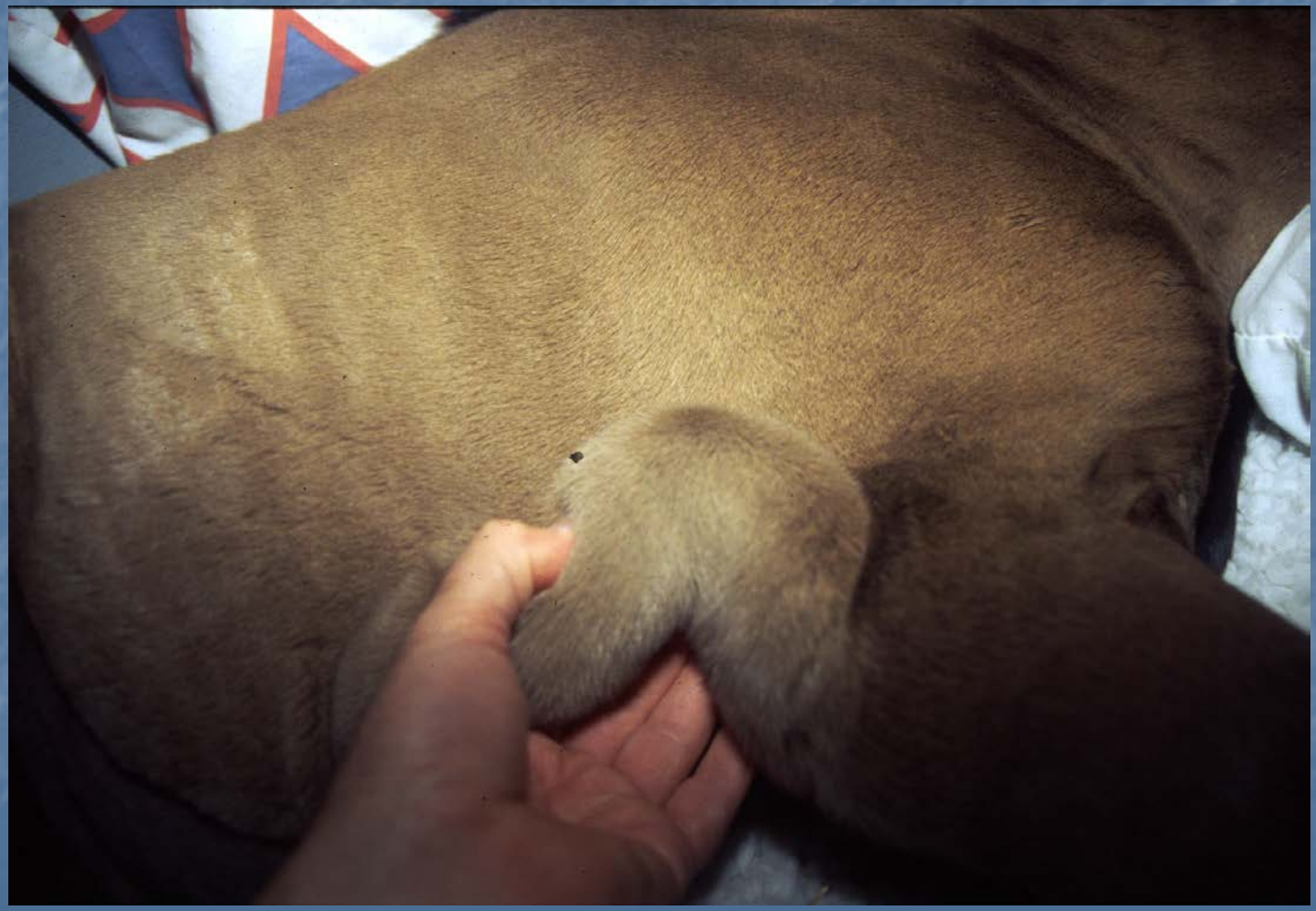
Fluid Therapy
Things I Try to Do

- Watch weight increases as gauge?
  - Confounding factors
- Fluid restriction
  - If good perfusion
  - Signs fluid overload
    - Edema
    - Weight gains
- No good clinical guides
  - Too much vs too little
  - Be well aware of possible harm
- Type of fluid
  - Sodium restriction (3-4 mEq/kg/day)
  - Chloride restricion

Goldilocks Principle

Getting it “Just Right”

No Jelly Belly



Fluid Dynamics in the Fetus and Foal

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In the past decade attitudes about fluid therapy have changed greatly. We have come a long way from the "more is better and get them in as fast as we can" philosophy of the 90s. We now realize that fluids are drugs and just like all other drugs we are in danger of overdosing or under dosing, both of which are equally harmful. We have also realized that one size does not fit all. To do the most good and least harm we need to carefully tailor our fluid therapy to the individual. This is especially true in the neonate whose physiology is in transition from the fetal state.

FLUID PHYSIOLOGY

Fluid dynamics in the fetus and neonate is much different than that of the adult and these differences have significant implications in responses to fluid therapy. These differences are due to unique characteristics of the interstitium, lymph flow and endothelial permeability. The interstitium is a heterogeneous space which dynamically controls its fluid content much like the vascular space but by poorly understood mechanisms. The interstitial space of the fetus and neonate is easily expanded relative to that of the adult with compliance in the ovine fetus roughly 10 times that observed in the adult. The volume of fluid within the lymphatic system is surprisingly small and averages only 1 mL/kg body weight in adult dogs and may be similar in the fetus and neonate. In fetal sheep, thoracic duct lymph flow averages 0.25 mL/minute/kg which is substantially higher (about 5x) than those in the adult. As with most physiologic phenomena the neonate appears to fall between these 2 extremes. The lymph flow from subcutaneous tissue in anesthetized puppies is approximately twice that observed in adult dogs per kg body weight Furthermore, lymph flow from the lungs is higher in anesthetized newborn lambs and puppies than in adults. Local as well as whole body lymph flow rates are significantly greater in the neonatal period than later in life. The increased lymphatic flow during the neonatal period is probably indicative of the elevated interstitial volume in the neonate in relation to the adult and the higher capillary permeability. The capillary filtration rate of fluid in fetal lambs is approximately 5 times that of the adult and the filtration rate for proteins about 15 times higher. This increased filtration rate has been thought to be primarily due to poor precapillary tone resulting in higher capillary hydrostatic pressure. The role of the glycocalyx, the major endothelial barrier, has not been investigated. The neonate, depending on the maturity at birth, may have very similar endothelial filtration characteristics in many vascular beds.

During the last few days of gestation fetal blood pressure increases significantly (by 20% in fetal lambs) although fetal blood pressures are still much lower than adult blood pressure. Part of this increase in blood pressure is thought to be transmitted to the capillaries because of poor precapillary tone resulting in increased transcapillary filtration of fluid and protein. Further increases in blood pressure during labor and birth is thought to result in a decrease in plasma and blood volume (18% and 12% respectively in fetal sheep) resulting in an increased hematocrit secondary to these fluid shifts. Other reasons for the fluid shift include direct compression or transformational change of the fetus leading to increased venous pressure and increases in vasoactive hormones including arginine vasopressin, norepinephrine, cortisol, and atrial natriuretic factor.

As the result of these fluid shifts drawing from the fetal fluids or maternal circulation and accumulating in the fetal interstitium all neonates are born fluid overloaded to one degree or another. In the normal neonate the rate of loss of this fluid varies. Foals hold on to this extra fluid and slowly lose it over weeks. Many other species may lose 10-15% of their body weight in the first days after birth. It is important to recognize this fluid loss for what it is and not try to replace it with more fluid as persistent fluid overload is now recognized as a major contributor to poor outcomes.

The Endothelial Barrier

The function of the endothelial glycocalyx barrier is the major determinant of fluid movement out of the capillaries and into the interstitium. This barrier that lines the inner surface of vascular endothelial cells consists of a very fine network of web-like fibers made up of proteoglycans and glycoproteins. This fine structure binds plasma proteins, mainly albumin, as well as other osmotically active particles as they are carried by hydrostatically forced fluid into the web. This forms a gradient with more particles caught outside. Any protein making it through the web is

washed into interstitium so the layer of fluid on luminal side of endothelium is virtually protein free. This forms an oncotic gradient which is not affected by interstitial protein content.

The amount of transvascular fluid filtration depends on the health of the endothelial glycocalyx. If it is intact and capillary pressures are normal, crystalloids freely pass and colloids are held back just as Starling promised. But if the glycocalyx layer is damaged neither are held back. On the other hand, if there is intravascular hypovolemia leading to low capillary pressures neither crystalloids or colloids will be filtered. This is independent of colloid osmotic pressure. When does damage to the endothelial glycocalyx layer occur resulting in loss of filtering ability? Clearly this occurs with sepsis (mediated by inflammatory mediators, especially TNF) and ischemia/reperfusion injury. But, surprisingly it also occurs with hypervolemia, especially with rapid fluid administration. If the endothelial glycocalyx is present in the fetus then hypervolemia that occurs leading up to birth also would, in theory, result in the disruption of the barrier.

How is the endothelial glycocalyx layer damaged by hypervolemia? The most popular theory goes something like this: The hypervolemia is sensed by the atria which results in release of natriuretic peptides (ANP) which in turn activates metalloproteinases which destroy the glycocalyx. These ideas are reflected in studies done where acute blood loss is induced and either albumin or colloid is used to maintain blood volume. In this case almost 100% of the fluid given is retained in the vascular. But if no blood loss occurs and the same volume of albumin or colloid is given (resulting in hypervolemia), 60% colloid escapes into the interstitium and the glycocalyx layer is decreased. Obviously we should stop the practice of preloading patients in anticipation of impending hypovolemia. Rather we should treat hypovolemia as it occurs. In the fetus/neonate I think it is equally likely that with the absence of precapillary tone, the transmission higher pressure to the capillary is also responsible for a lack of epithelia glycocalyx in neonates although this has not been studied.

Thus when fluid therapy is used in any neonate, whether normal or when treating sepsis, inflammatory states the fluids are not likely to be retained in the vasculature and will rapidly escape into the interstitium. And, as colloids will escape just as fast as crystalloids there will be no difference in increasing intravascular volume between equal volumes of colloid or crystalloid when treating sepsis, inflammatory states, trauma or indeed in hypervolemia. But colloids (with the exception of plasma) will have other negative effects and we now realize that the plasma COP, which has a central role in Starlings ideas of fluid movement, has no role in maintaining volemia.

Consequences of Neonatal Fluid Physiology

Response to Hemorrhage: Perinatal blood loss of the fetus or neonate can occur during premature placental separation, after rupture of umbilical vessels, or by internal bleeding, for example, long bone fractures, gastrocnemius rupture or intestinal hemorrhage e.g. secondary to necrotizing enterocolitis. In adult horses, dogs, cats, and sheep, 24 to 48 hours is required for blood volume to return to normal after a 30% loss of blood, if no fluids are given. This restoration of volume occurs as plasma volume returns to or rises above normal, whereas RBC volume remains reduced. The time required for full volume restoration after hemorrhage in the fetus or neonate is shorter than in the adult. Fetal sheep restore twice the volume than adults within 30 minutes after rapid hemorrhage. The ovine fetus restores its blood volume to normal within 3 to 4 hours after a 30% hemorrhage which is in one tenth the time required in the adult. This rapid restoration is mediated by a translocation of fluid and protein from the interstitial space into the vascular space. Neonatal kittens and rabbits are also better able to tolerate blood loss than adults, as more blood per kg must be removed before arterial pressure decrease. This was attributed to a more rapid mobilization of interstitial fluid in the young animals in the first week of life. Neonatal lambs also rapidly restore their blood volume to normal after hemorrhage.

Responses to Volume Loading: Rapid intravascular infusions of isotonic solutions expand plasma volume of fetal lambs by only 6 to 7% of the infused volume after 30 to 60 minutes because of rapid transfer of the infused fluid into the interstitial spaces. When adults receive IV fluids average intravascular retention is 20% to 50% of the infused volumes after 30 to 60 minutes. The poor intravascular retention of crystalloid during fetal life and the early neonatal period is due to the high interstitial compliance and the high capillary filtration coefficient (suppression of the endothelial glycocalyx?) which permits very rapid fluid shifts.[1,3]

Once fluid overloaded the neonate retains the fluid much longer than the adult which is thought to be largely because of the reduced intravascular retention of fluid in the neonate. After volume loading, normal adults (dogs, sheep) will excrete the entire volume load through their kidneys over a period of several hours as plasma renin activity and plasma concentrations of arginine vasopressin and atrial natriuretic factor all change in a direction appropriate for elevating urine flow. Puppies and lambs and likely other neonates will retain the same fluid load for 24 to 36 hours probably because the volume load escapes the intravascular space before plasma volume sensors can recruit these

hormones to exert their diuretic response. Thus the neonatal urine flow quickly returns to normal after rapid vascular volume expansion.

Both fetal and newborn sheep undergo an increase in left thoracic duct lymph flow up to 3.5 times normal after vascular volume expansion augmented by angiotensin II. Because of the dynamics of this increased lymph flow even small increases in central venous pressure as will occur in response to rapid administration of intravenous fluids will result in a dramatic decrease in the lymphatic flow rate making the neonate receiving intravenous fluid therapy particularly susceptible to the development of edema.

Responses to Hypoxia: Hypoxia in the fetal lamb results in elevation of capillary pressure within the fetal body. There are no changes in fetal arterial or venous pressure if the hypoxia is mild because of vasodilation in selected organs but if the hypoxia is moderate to severe there will be an increases in arterial and venous pressures. This change in capillary pressure due to hypoxia will result in a greater transfer of fluids into the interstitial space leading to increased fluid overload. So although all neonates at birth and just after are fluid overloaded, the fetus or neonate suffering from hypoxia/asphyxia has a greater degree of fluid overload often resulting in the somewhat unique situation of having a hypovolemic individual who is fluid overloaded.

FLUID THERAPY IN NEONATES

How do these fluid dynamics related to fluid therapy in neonates? One hallmark study in human pediatrics which is still surrounded by much controversy was the FEAST study (Fluid Expansion As Supportive Therapy) published 5 years ago. It was a study undertaken in an attempt to justify modernizing hospitals in poorer areas of Africa where children requiring fluid resuscitation were placed in wards where there was no attempt to deliver fluids expediently. The study backfired as it seemed to show that modern volume resuscitation was unhelpful or even harmful to the hypovolemic children. There was no evidence supporting a benefit from bolus fluid infusion. In fact, bolus fluids increased the absolute risk of death at 48 hours by 3.3%. They could not identify any subgroup in which fluid resuscitation was beneficial despite moderate hypotension and severe metabolic acidosis. In fact, excess mortality with fluid resuscitation was consistent across all subgroups irrespective of physiological derangement or underlying microbial pathogen.

Why did this happen? Perhaps the vasoconstrictor response in shock confers protection by reducing perfusion to nonvital tissues and that rapid reversal with fluid resuscitation is deleterious. Perhaps interruption of catecholamine-mediated host defense responses by the rapid increase in plasma volume might result in a reperfusion injury. Or perhaps transient hypervolemia or hyperosmolality might exacerbate capillary leak in patients, as seems to be part of the normal physiologic response in neonates. Whatever the case the entrenched practice of fluid-bolus resuscitation in patients with compensated shock has become questionable. Bolus-fluid resuscitation in compensated shock with no clinical fluid deficit must be practiced with caution and may do more harm than good.

Abnormalities commonly seen in septic shock include myocardial depression, endothelial injury and venodilation causing increase in the unstressed blood volume, decrease in the mean systemic pressure and decreasing cardiac preload. When this is corrected by rapid infusion of a fluid volume there is an increase in cardiac index which results in vasodilation (via NO release), the endothelial glycocalyx is cleaved resulting in endothelial barrier injury and capillary leak. At 3 hours less than 5% of delivered crystalloids remain intravascular resulting in increased tissue edema and myocardial dysfunction. Although in the short run fluids may restore volemia in the long run there is a clear association of positive fluid balance and increased mortality in man. This has lead to a move to follow a restrictive fluid strategy and the early use of inopressors when reversing severe vasodilatory shock in human adults.

When giving bolus fluid therapy timing is important as there can both be positive and negative effects. Clearly when used for resuscitation of shock the fluids must be given both in a timely manner and in adequate volumes. The problem is deciding when it is needed and how much. There is no easy answer. In several studies in man it appears that once the shock has been reversed restrictive fluid therapy will improve outcome. That is fluid-overloading (hypervolemia) is harmful. In man, those patients who have a negative fluid balance at 5 days after onset clearly have a better outcome. But is this the effect of late restriction of fluids or do these patients simply just have a less severe illness?

How good are we at guessing if another bolus of fluids would be beneficial? Basically, using clinical examination and simple monitoring aids (CVP, etc.) it becomes just that…"a guess." About 50% of the time the clinical decision to give or withhold a bolus is helpful and about 50% of the time it is harmful. We as clinicians do not appear to be particularly good at determining whether a patient will benefit from the administration of a fluid bolus, especially when basing this decision on clinical examination.

The role of neonatal renal function and dysfunction in the fluid dynamics is beyond the scope of this talk. Needless to say, its role is pivotal.

The clinical challenge is to give the appropriate dose of fluids knowing that you can do harm if you give an inadequate dose and harm if you give an excessive dose. You need to achieve physiological targets when there is no clinical way to monitor how close you are to the targets or if indeed you have overshot them. It is dangerous to uncritically attempt to achieve these targets. The timing of intervention is crucial. Early positive fluid balance may be needed to achieve perfusion but late negative balance is critical to survival.

Here are the ideas I currently use in guiding my fluid therapy in neonates. I give fluid boluses to foals in clinical shock but I am constantly asking myself if I have given enough and may stop before the legs become warm. Unfortunately there is no good stall-side guide to tell you when you have reached your goal. I stop high infusion rates of fluids early; often before complete warming of the legs but as pulses return. I also give IV nutrition in as small a volume as practical regularly using 20% dextrose solutions or making an early transition to TPN. I also think it is important to practice Na restriction in neonates (3-4 mEq/kg/day) and also practice Cl restriction. I think it is important to estimate urine output and also watch weight increases as a gauge of fluid overload despite the confounding factors this entails. I am not afraid to fluid restrict sick neonates with adequate perfusion. I currently feel that waiting until edema is evident to decide that fluid overload is a problem is too late. It requires rather massive fluid overload before edema is evident in many neonates. Unfortunately there are no good clinical guides to decide if you have given too much vs. too little fluids. But above all it is important to be aware of the possible harm of fluid overload.

Further Reading:

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