Fluid and Electrolyte Therapy

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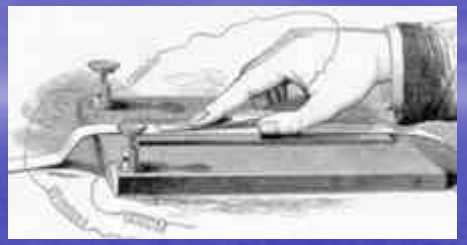
Fluid and Electrolyte Therapy

- Physiologic Approach to Neonatal Fluid Therapy
- Understanding Strong Ion Difference
- Metabolic Acid/Base Abnormalities
- Electrolyte Abnormalities in Neonates
- Practical Approach to Fluid Therapy in Neonates
- When Fluids are Not Enough: Inopressor Therapy

History of IV Fluid Therapy

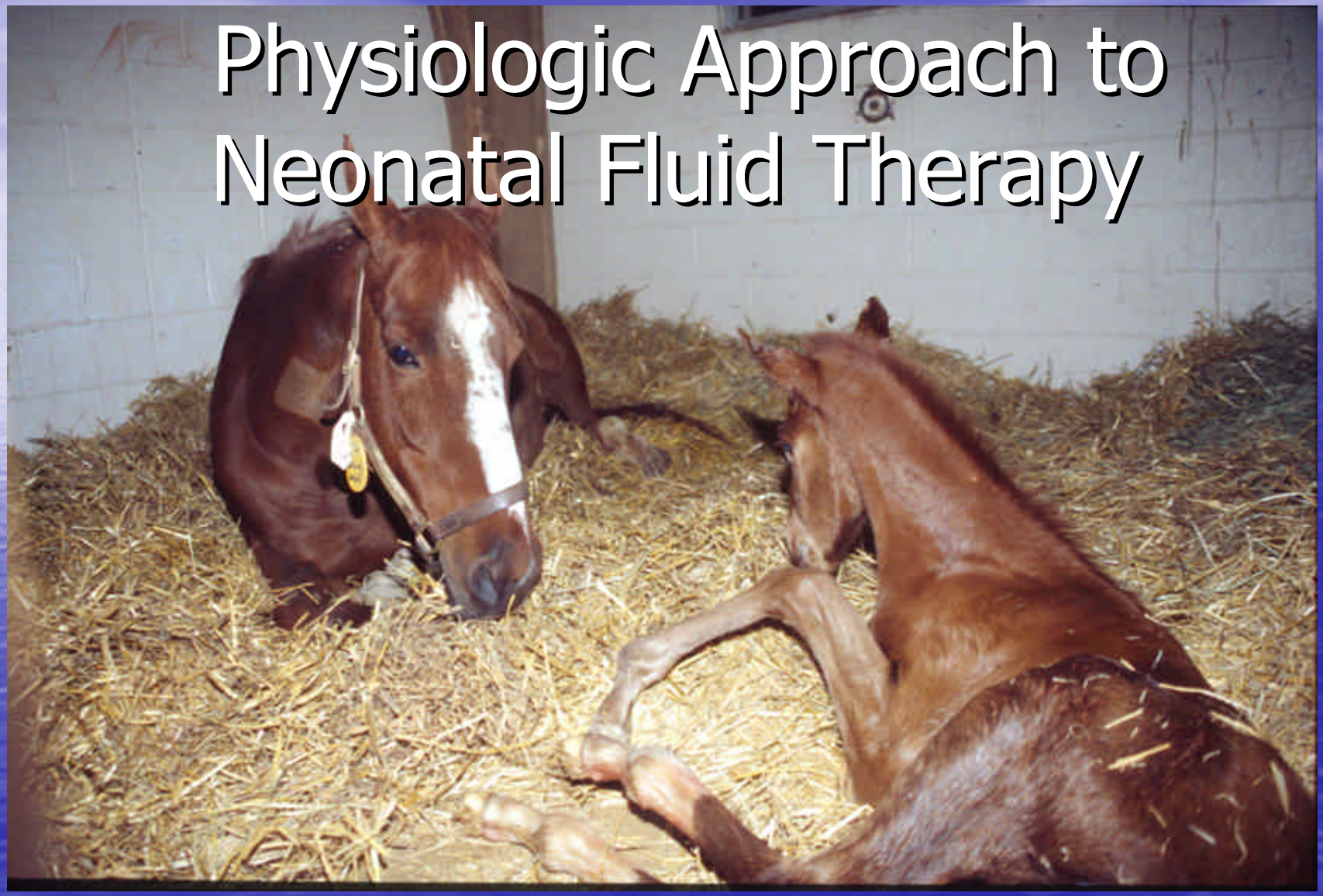


- Cholera pandemic 1831
- Dr. William O'Shaughnessy
  Proposed fluid resuscitation of hypovolemic shock
  - Lancet
  - Victim's blood - "lost a large portion of its water"
  - suggested treatment
    return blood to its "natural specific gravity"
    "replacing its deficient saline"
    Na 178 mEq/l Cl 144 mEq/l, HCO3 34 mEq/l
- Dr. Thomas Latta
  June 1832
  Recovery of women in septic shock
- Criticism from the acknowledged medical leaders

History of IV Fluid Therapy

- Modern era of fluid resuscitation
  - Began in the 1960s
  - IV therapy replaced subcutaneous therapy
- 1960 metal intravenous catheters
  - Decreased infant deaths from diarrhea
    - 60%
  - Clean drinking water
- Plastic intravenous catheters
  - Establishment of intensive care medicine
  - Decreased infant deaths from diarrhea
    - An additional 90%

Physiologic Approach to Neonatal Fluid Therapy

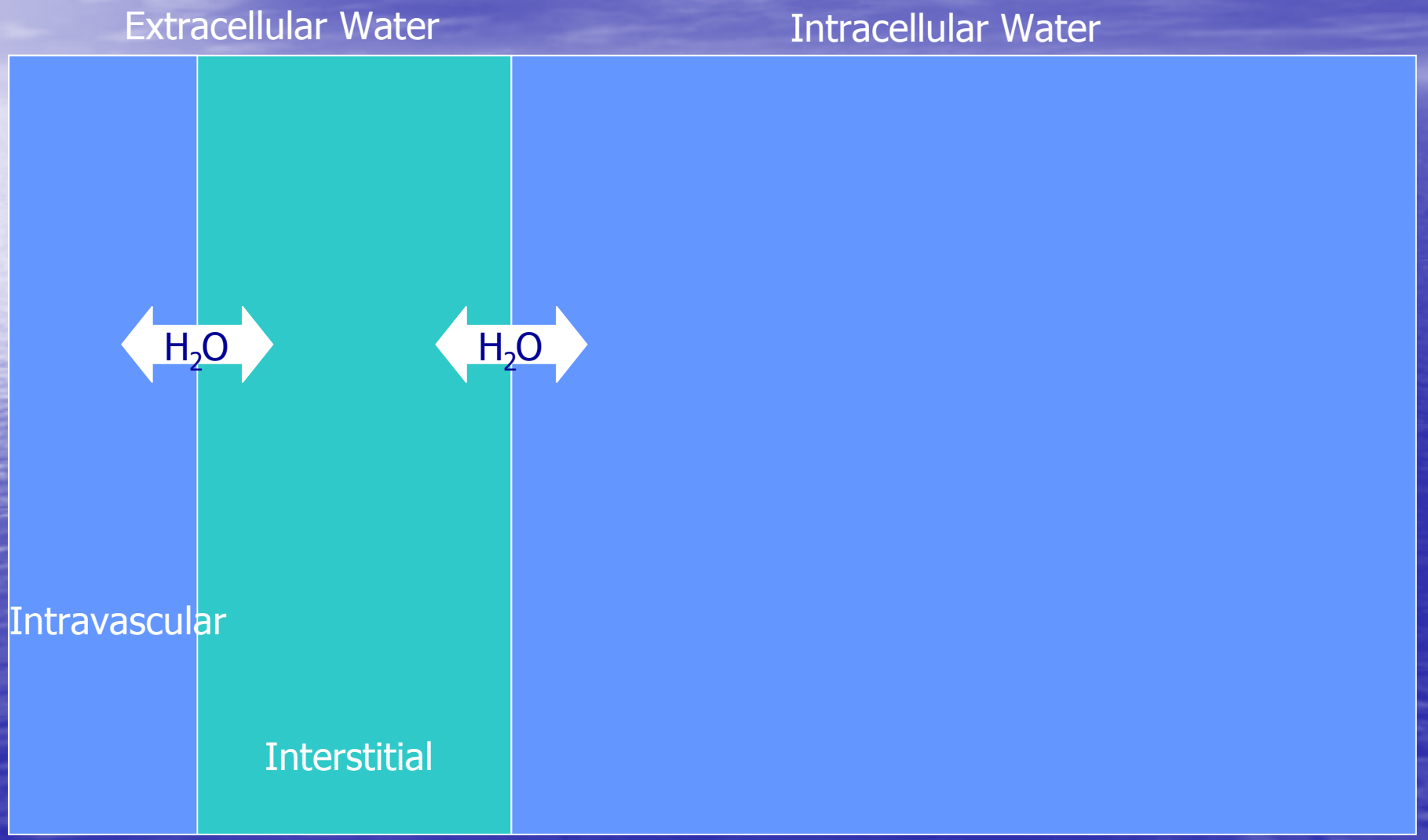


Physiologic Approach to Neonatal Fluid Therapy

- General principles of fluid balance
- Fetal physiology of fluid balance
- Neonatal physiology of fluid balance

  Transition period
- Implications for therapeutic interventions

Total Body Water - adult



Interstitial Fluid

- Normal cell function requires
  - Water
  - Osmolarity
  - H^+ concentration
- Interstitial fluid acts as
  - Water reservoir for cells
  - Osmotic damper
  - Buffer reservoir
  - Water reservoir for vascular volume

Interstitial Fluid

- Critical illness
  - Interstitial fluid volume decreased
  - Decrease water reserves
  - Decreases osmotic damper function
  - Decreases fluid reserves for cells
  - Decreases fluid reserves for vascular space
- Fluid therapy
  - Replenish interstitial reservoir
  - Protect cell from osmolar shifts
  - Insure volemia
  - Buffer acidemia

Osmolarity

- Hypovolemia = loss of intravascular fluid
- Dehydration = ↓ cellular water
- Infusion of sodium containing fluids

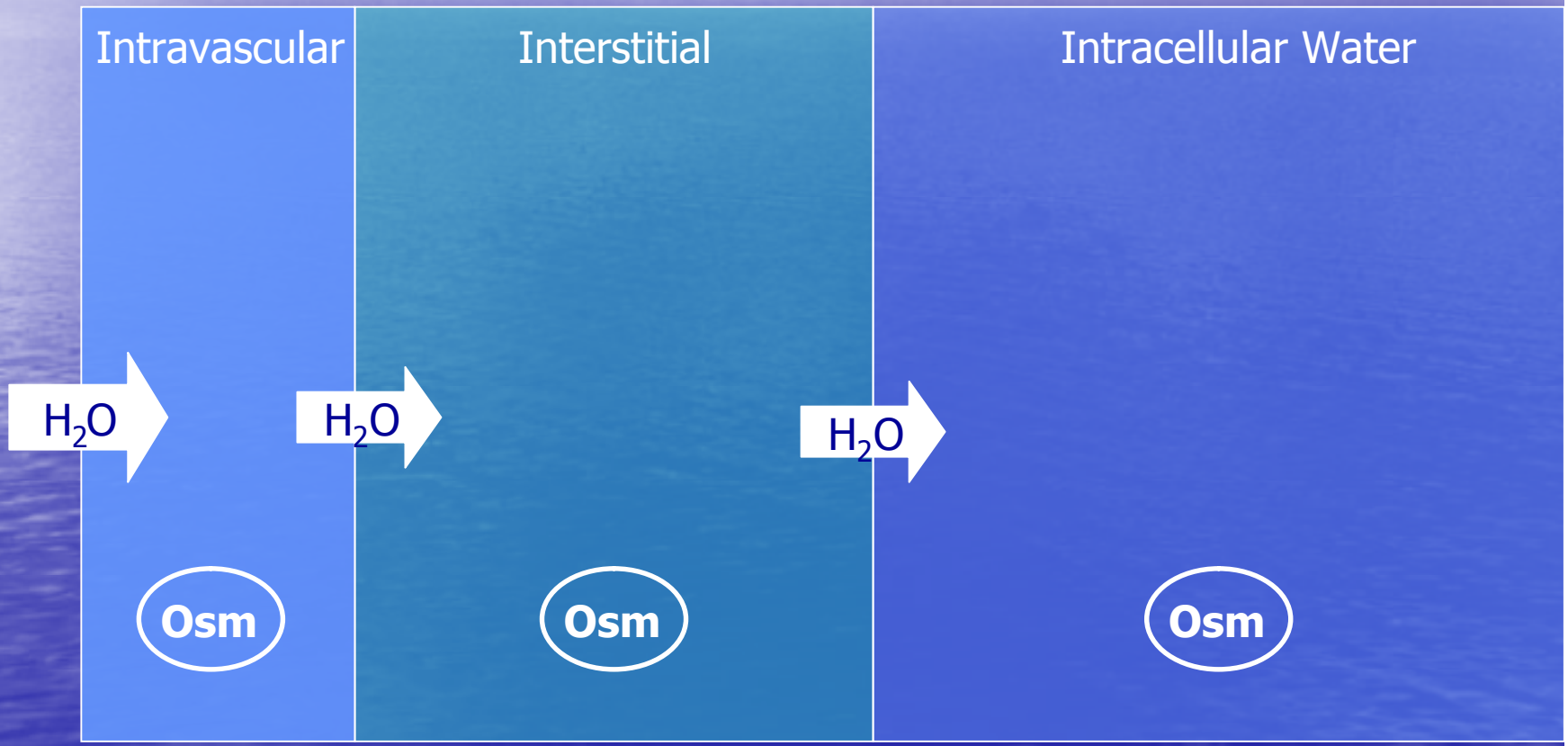
  Alter extracellular volume without changing intracellular volume

  - Primary extracellular electrolyte
  - Not the primary intracellular electrolyte
- Infusion of water (dextrose in water)

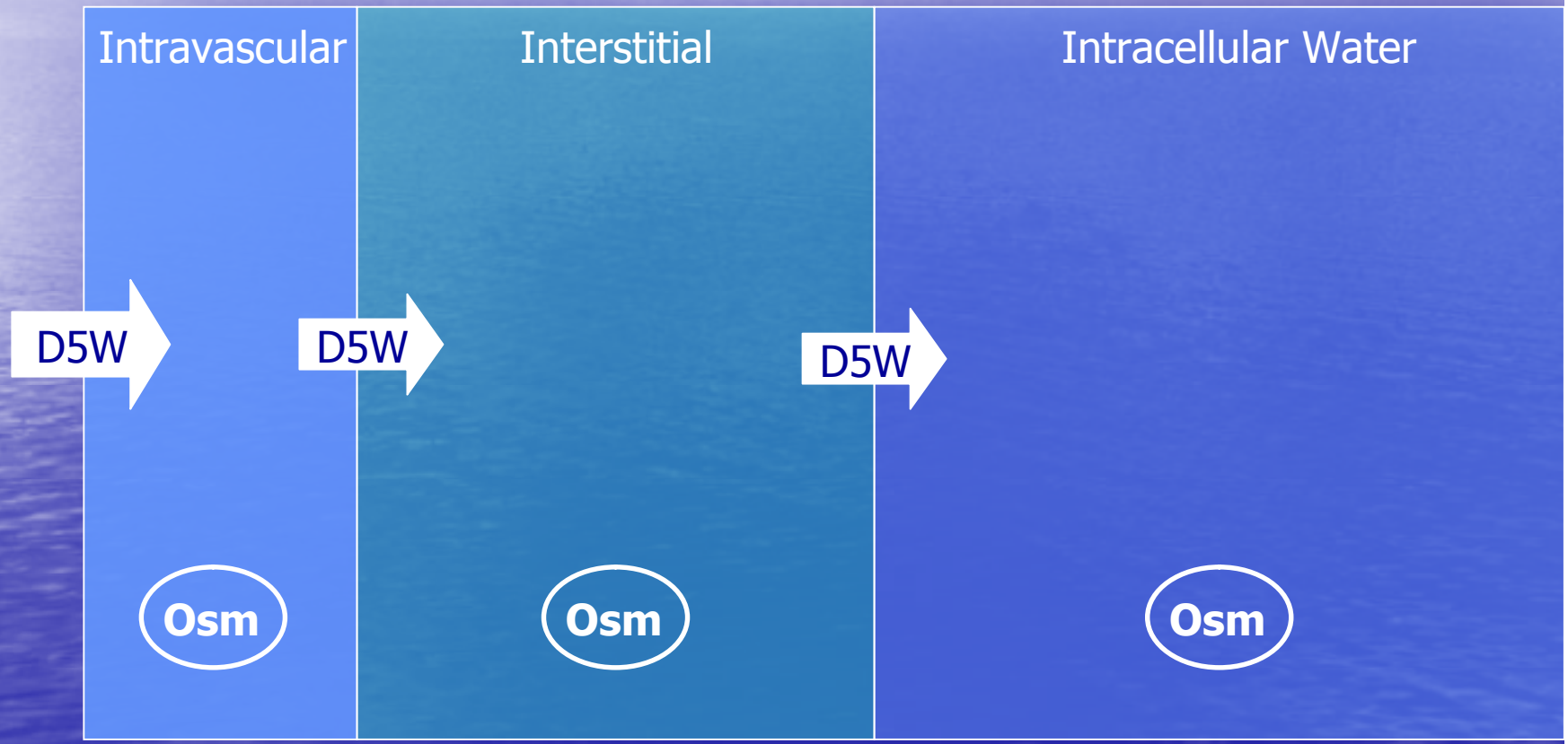
  Affects osmolarity of all compartments equally

  Not change intracellular/extracellular water distribution

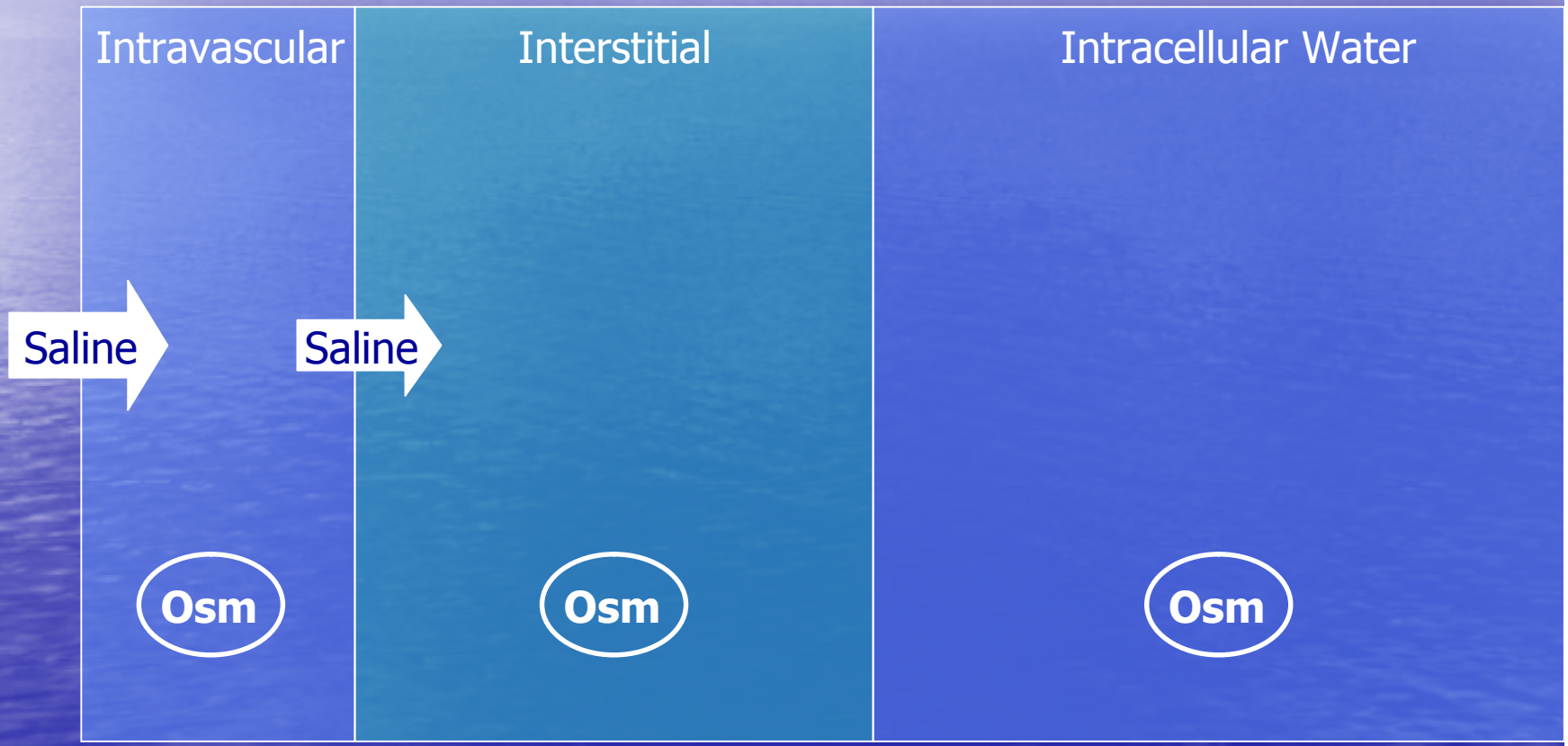
Fluid Therapy
Water



Fluid Therapy
D5W

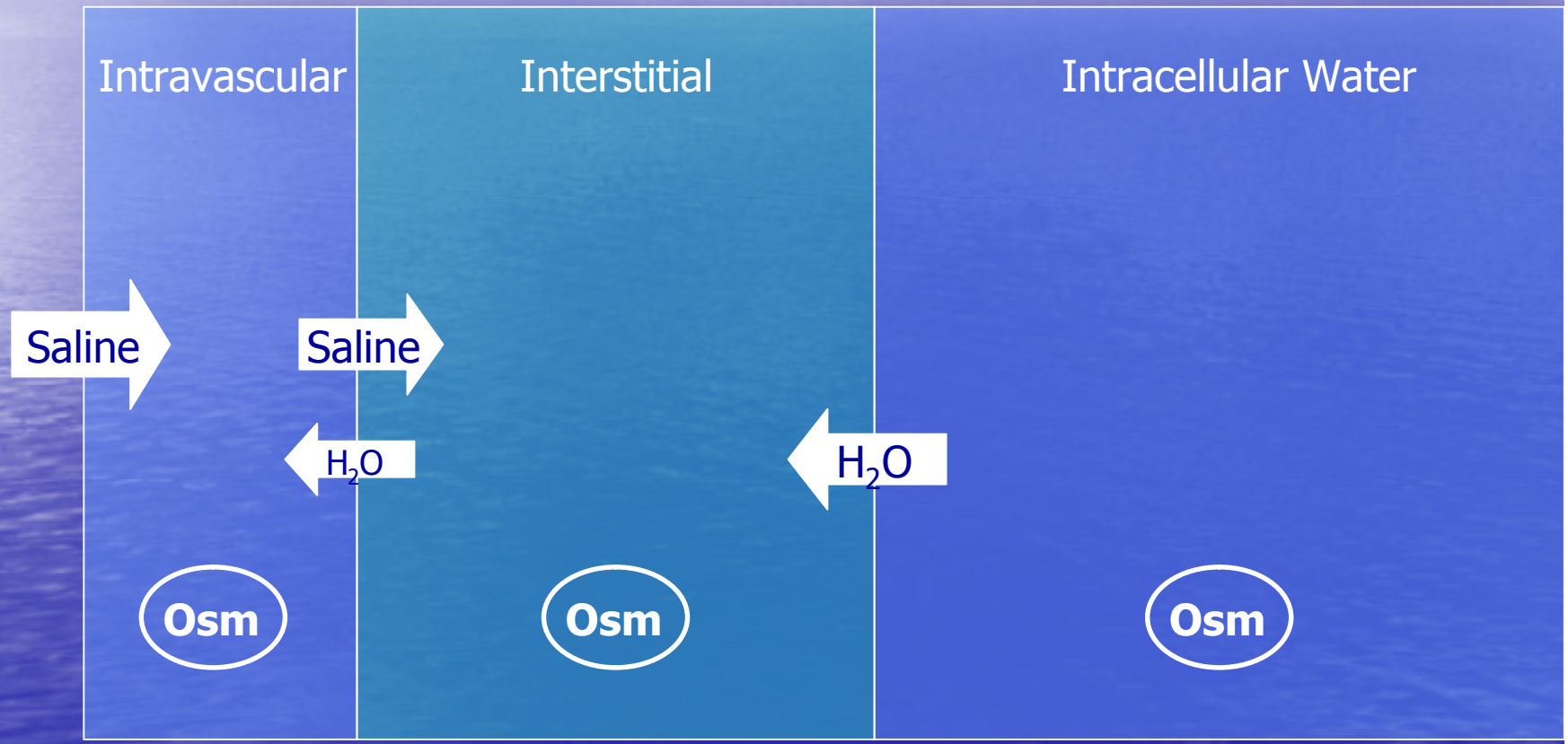


Fluid Therapy
0.9% Saline (any isotonic crystalloids)

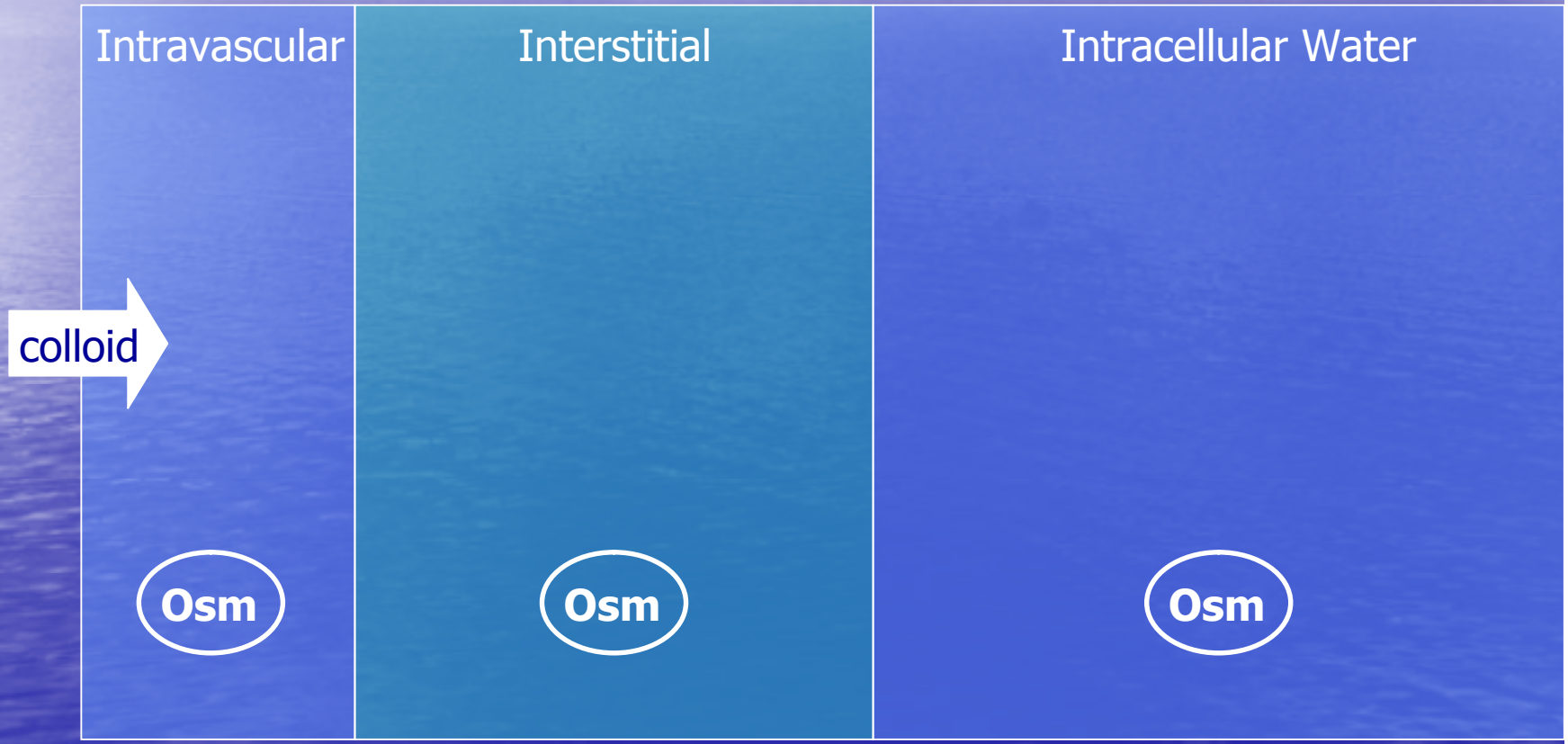


Varies with hypovolemia

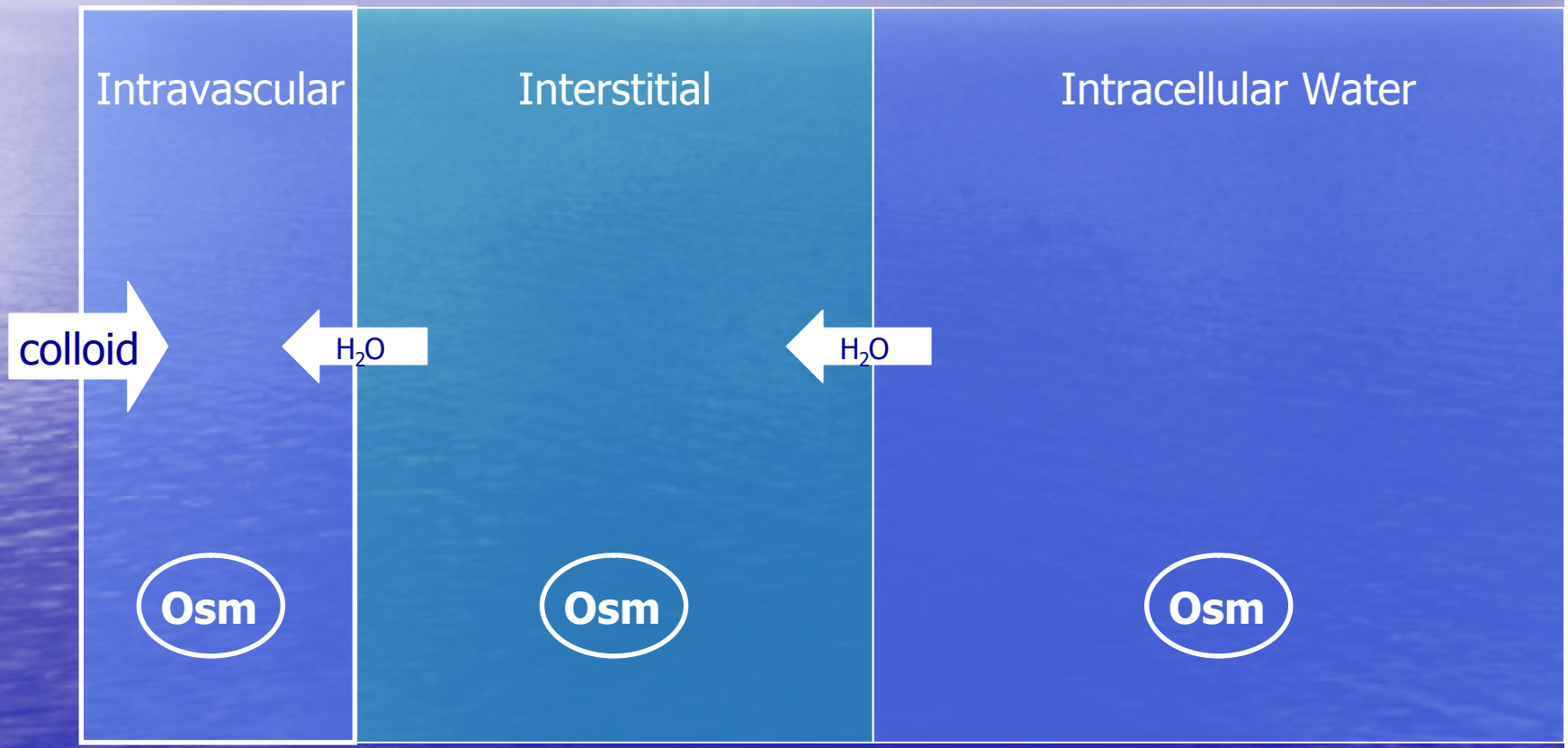
Fluid Therapy
Hypertonic Saline



Fluid Therapy
Isoncotic Colloid



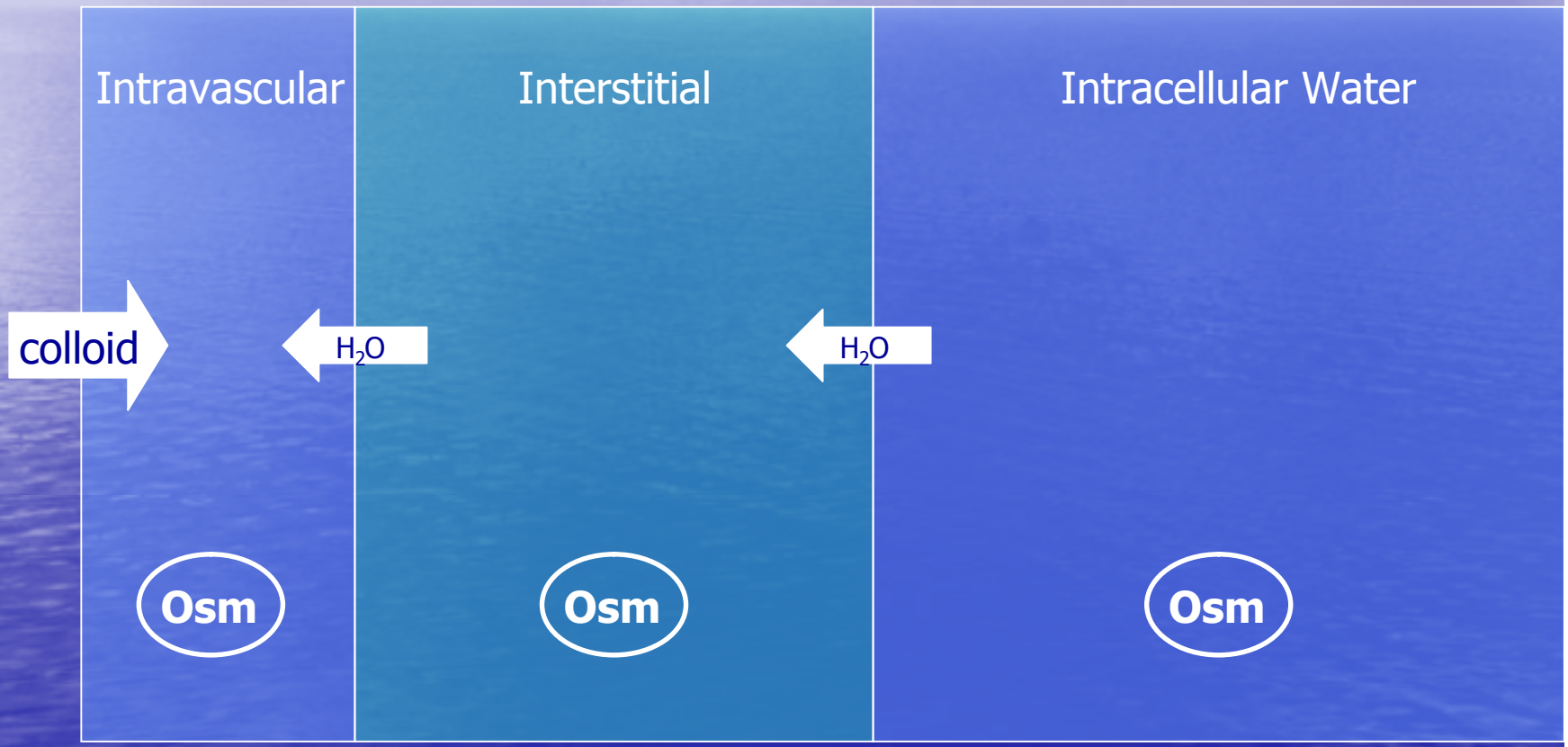
Fluid Therapy
Hyperoncotic Colloid



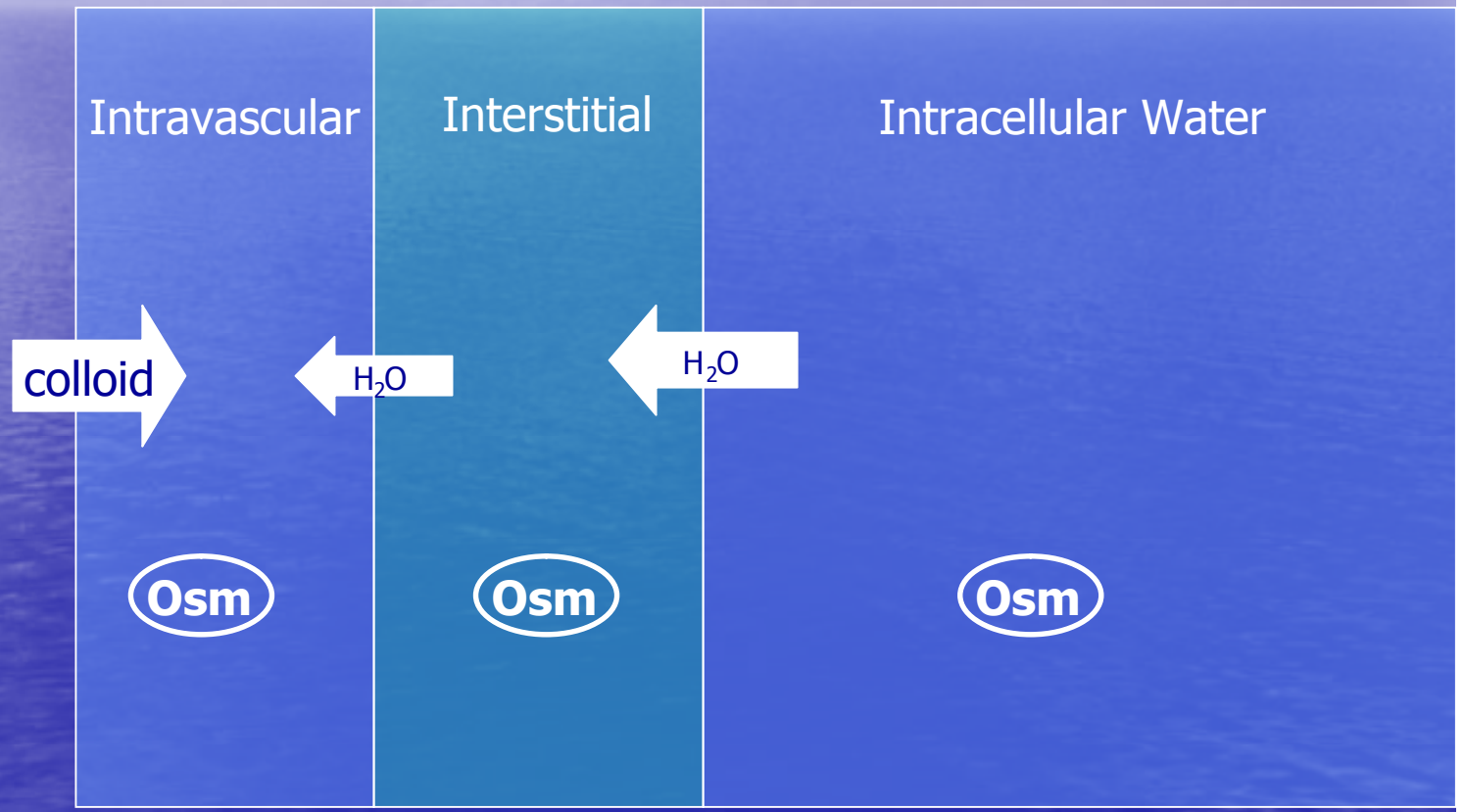
But ...

- Critical patients – hypoproteinemia
- Decreased interstitial volume
- Capillary epithelial cell barrier decreased

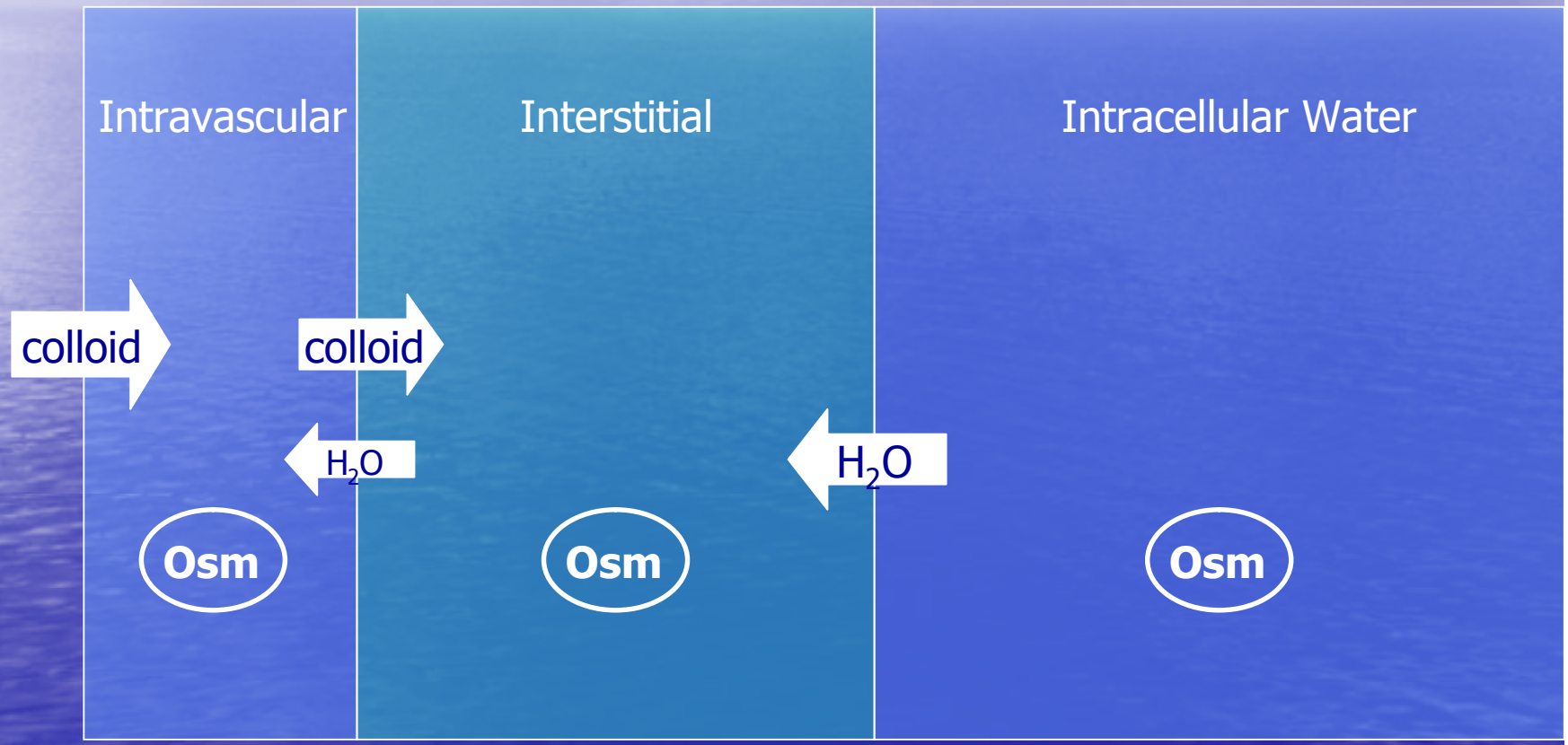
Fluid Therapy
Isoncotic Colloid with hypoproteinemia



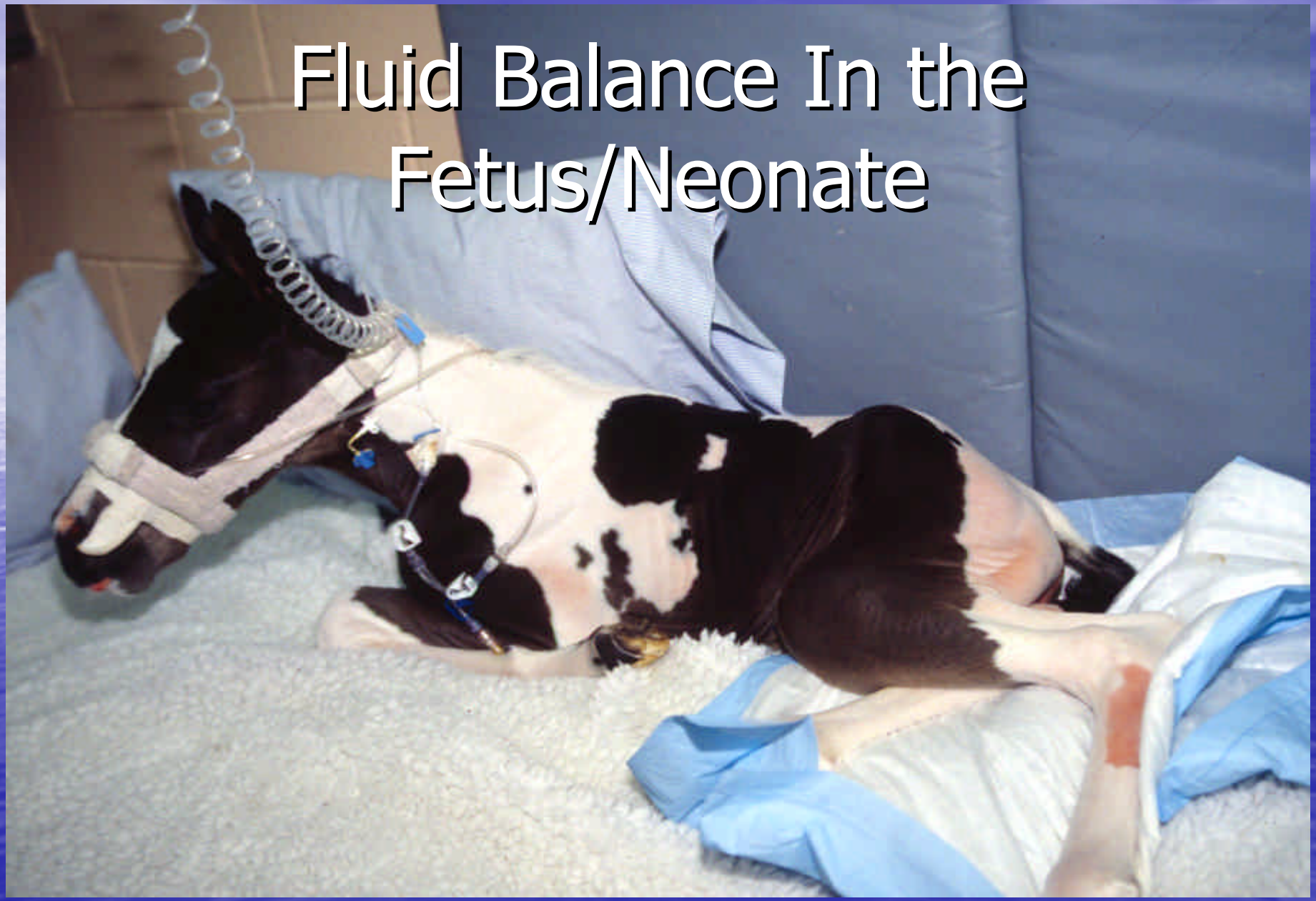
Fluid Therapy
Hyperonomic Colloid with ↓ Interstitial space



Fluid Therapy
Colloids with ↓ Epithelial Cell Integrity



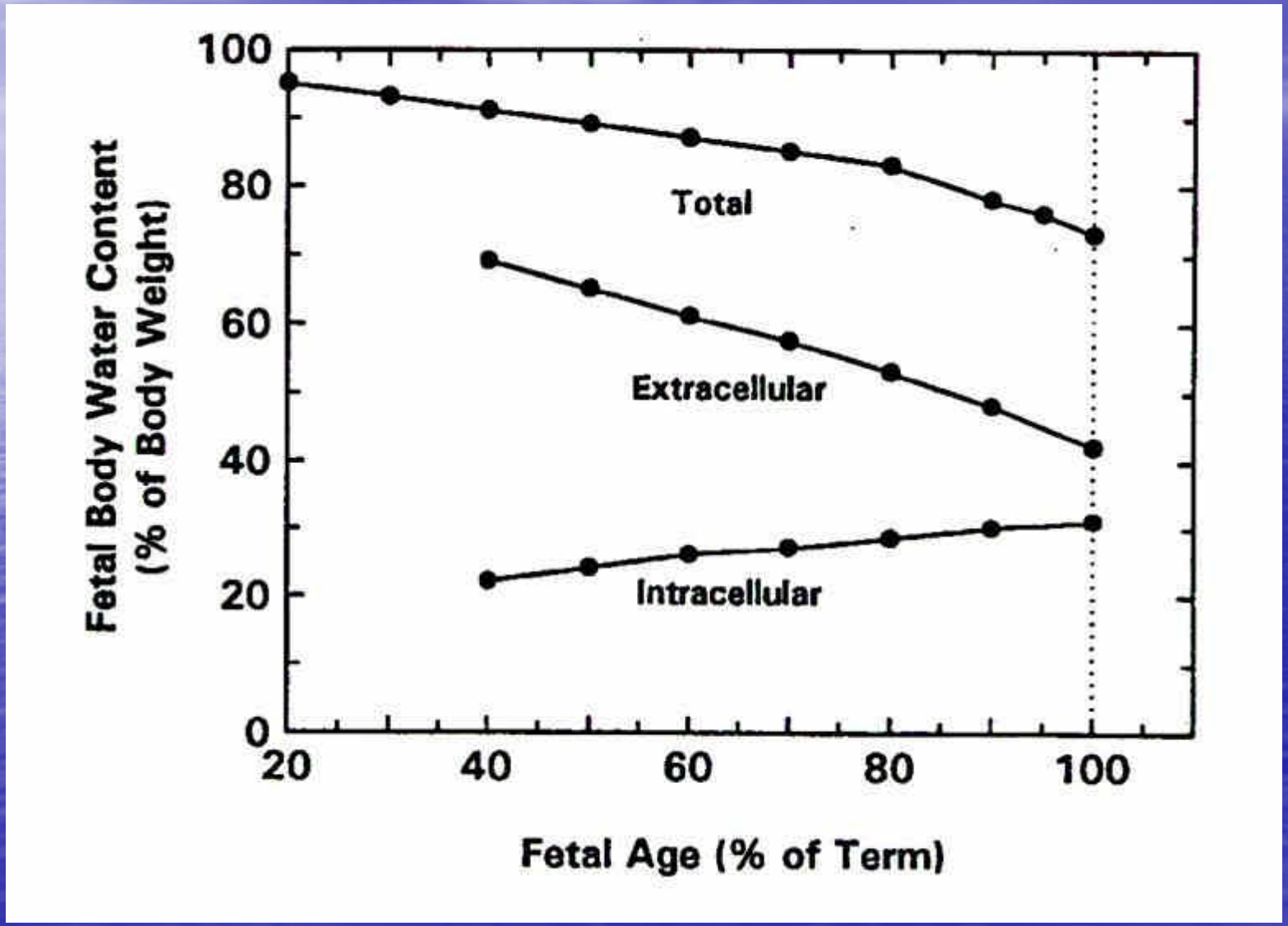
Fluid Balance In the Fetus/Neonate



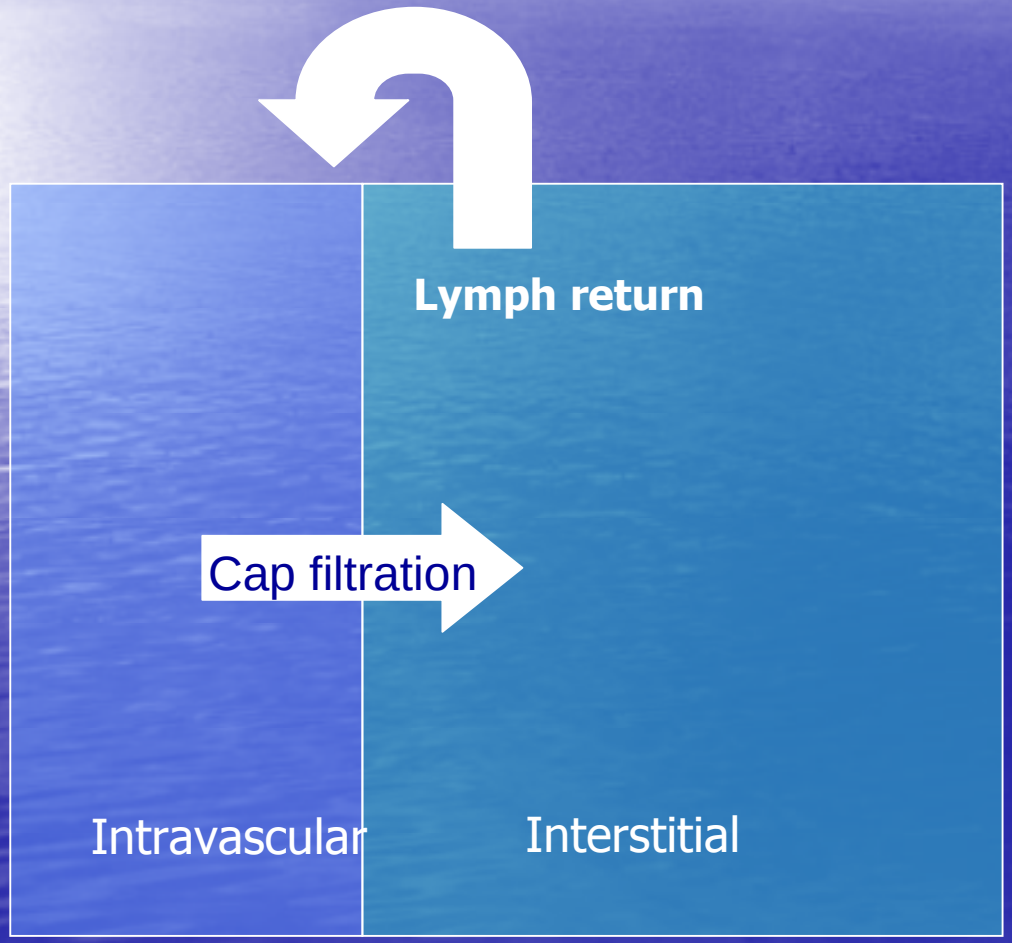
Fetal Fluid Balance Differences from Adult

- Total body water
- Rates of fluid movement greater
- Fetus surrounded by fluid
- Self-contained system

Fetal Fluid Balance



Determinants of ECF distribution
Intravascular : Interstitial



Capillary filtration

Lymph flow rates

Starling Forces

- Protein levels/leak
- Blood pressure

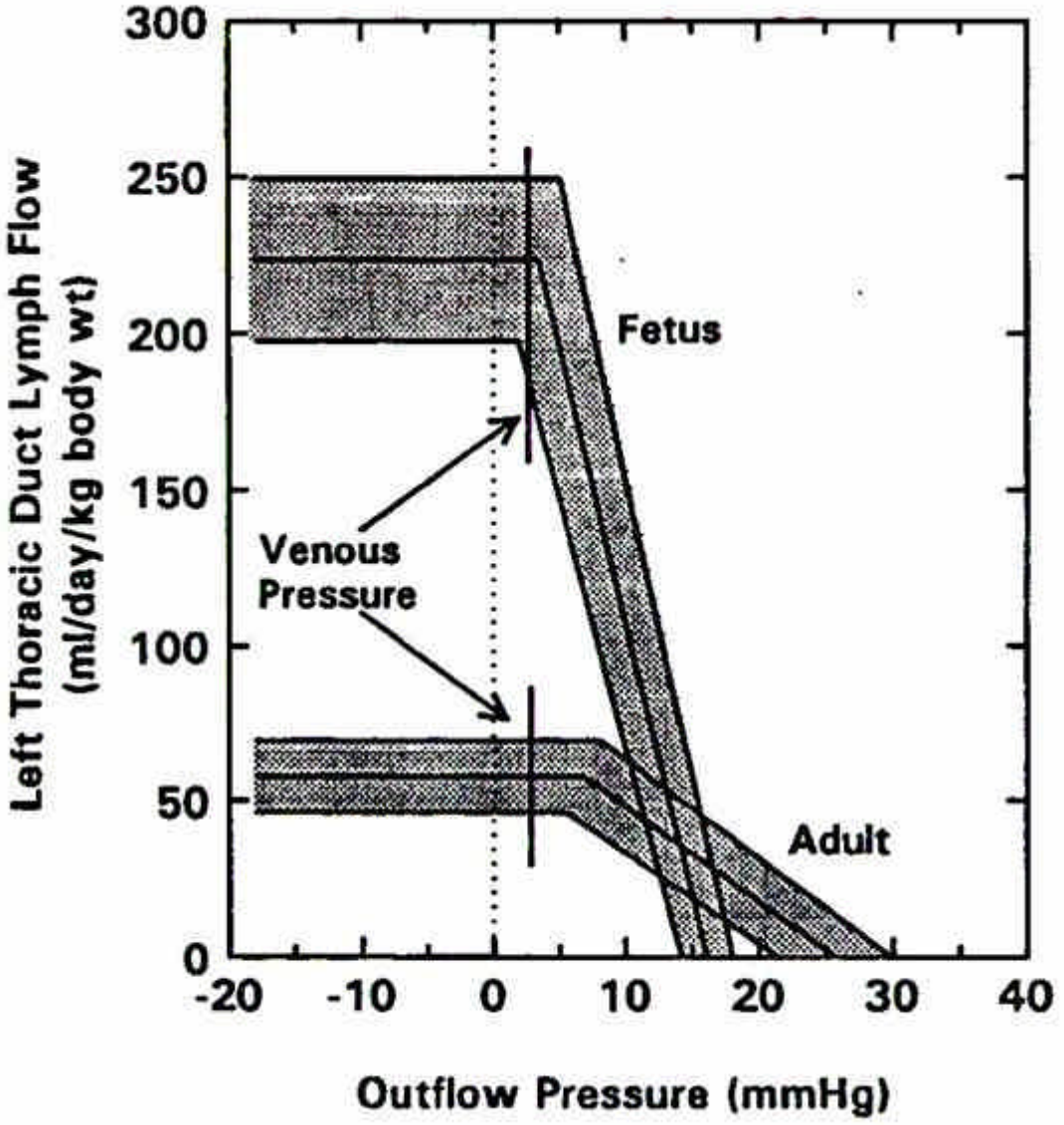
Fetal Fluid Balance
Plasma and Interstitial Compartments

- Circulating blood volume/kg
  - Constant throughout gestation
- ↑ extracellular fluid = ↑ interstitial fluid
- Fetus interstitium
  - Contains more ground substance
  - Holds large amounts of fluid
  - No free fluid (edema)

Fetal Fluid Balance
Basal lymphatic function

- Sheep
  - Only measured in fetal sheep
  - Adult sheep
    - 0.03-0.04 ml/kg/min
  - Fetus 5X adult
    - 0.15-0.20 ml/kg/min
- Lymph flow from the lungs fetus > adult
  - Puppies 2.5X > adult
  - Lambs 3.4X > adult

Fetal Fluid Balance
Lymph Flow



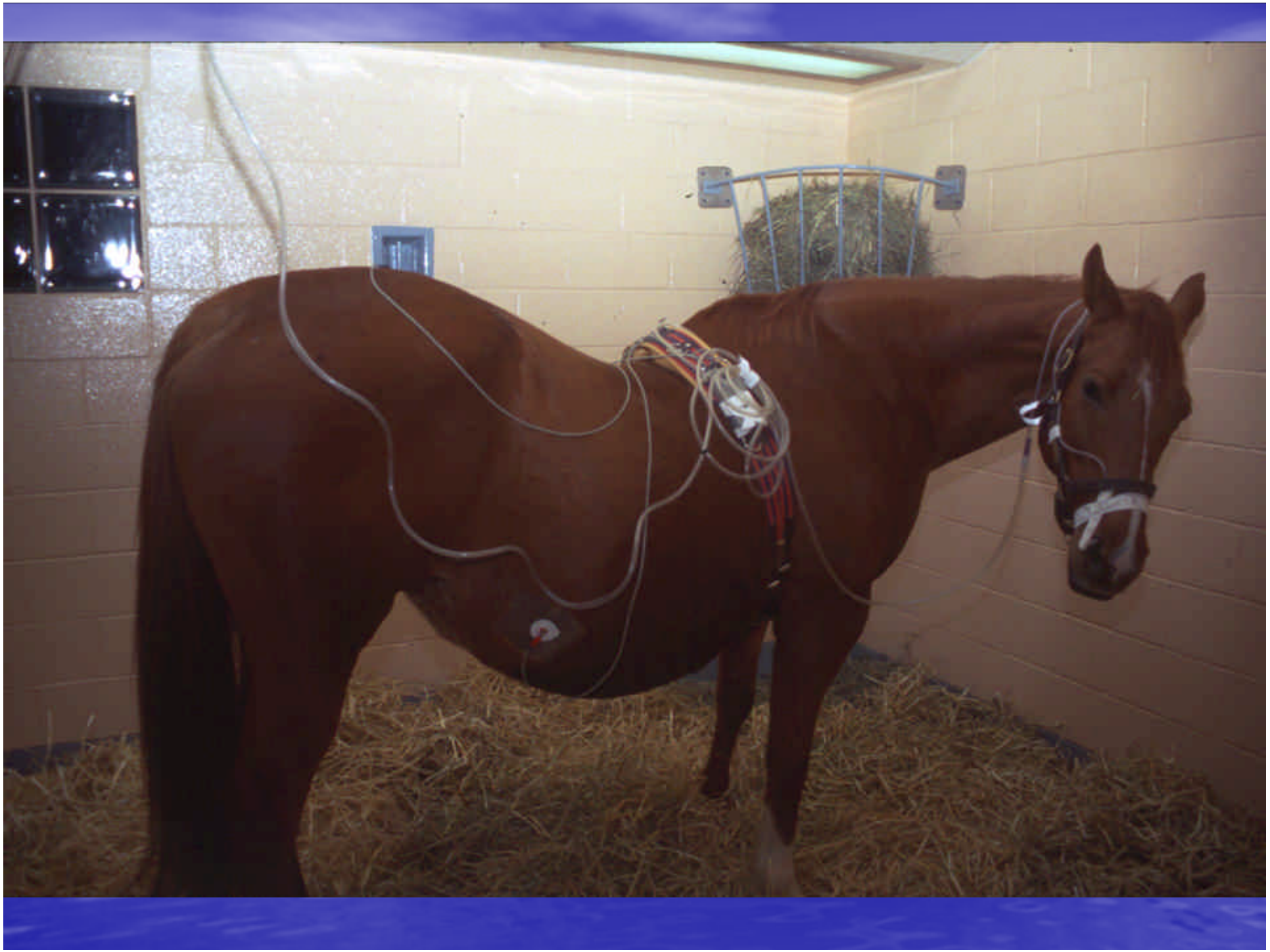
Fetal Fluid Balance
Transcapillary Fluid Shifts

- Filtration coefficient body capillaries 5X adult

  Filtration of plasma proteins 15X adult
- Interstitial compliance 10X adult
- Filtration coefficient fetal body 100X placenta
- Body transcapillary fluid movements

  Dominant on short-term

  Transplacental shifts more important long-term



Fetal Fluid Balance
Transcapillary Shifts - Blood Loss

Acute hemorrhage (5-25% over 5 min)

- 50-60% loss volume replaced in 30 min
- 2X to 3X volume replaced by adult
- Primarily fluid across capillary of wall
- Also plasma protein across capillary wall

Fetal Fluid Balance
Transcapillary Shifts - Blood Loss

30% blood volume over 2 hrs

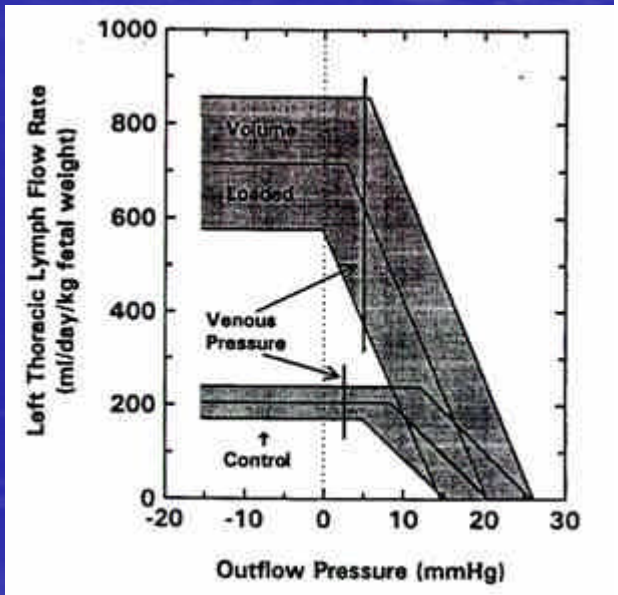
- Blood volume returns to normal
  - Fetus - within 3-4 hrs of the end of the bleed
  - Adult requires 24-48 hours
- Translocation fluid and protein
  - From fetal interstitial space
  - Not osmotic shifts across placenta

Fetal Fluid Balance
Transcapillary Shifts - Blood Loss

- Interstitial fluid
  - Acts as a reserve volume (fluid and protein)
  - Maintain volemia
- Rapid volume restoration
  - Fluid and protein across capillary
    - From interstitial space to capillary
  - Normal high rate lymphatic return
    - Via thoracic duct
- Slower volume restoration
  - Increased rate lymphatic return
    - Via thoracic duct
  - Fluid and protein across capillary
    - Less movement into interstitial space
- Acute – replenish across capillary
- Slower – replenish via lymphatics

Fetal Fluid Balance
Lymph Fluid Shifts

- Lymph flow – maintains interstitial volume
- Lymph flow several times greater than adult
  Interstitial fluid mobilized more rapidly
- Lymph flow ↑ with rapid infusion fluid 2%
  Lymph flow = 5% of infuse volume in 30 min
- With large volume intravenous infusion
  ↑↑ Lymph flow as much as 340%
  ↑↑ Lymph flow limited by venous pressure
- ↑ Interstitial Fluid ↑ Lymph flow



Fetal Vascular Volume Loading Transcapillary Shifts

- Rapid saline infusion
  - 2% body weight
  - 6-7% intravascular retention 30 min
    - Adult 20-40% retention
  - Most fluid moves transcapillary
    - Epithelium is "leaky"
    - Interstitium highly compliant
    - Maintains vascular volume
    - % filtration of fluid
      - Depends on the state of volemia

Fetal Vascular Volume Loading Transcapillary Shifts

- Hours to days infusion large volume

  4-7 liter in fetal lamb

  Fetal blood volume only increases 2-4%

  Interstitium volume only increase if over a few hours

  - Most as infusion transferred via placenta to mother
  - Placental filtration capacity ↑ 100X

- Transcapillary movement

  dominates over minutes to hours

- Transplacental fluid movement

  dominates over hours to days

Regulation Fetal Fluids and Lymphatic Function

- Acute change maternal osmolarity
  - Rapid placental transfer of fluids
  - Change fetal osmolarity
  - Secondary change fetal plasma volume/red cell volume
- Short-term
  - After hypertonic infusion in mother
  - Fetal blood volume returns normal 1-2 hours
- Long-term
  - Maternal water deprivation over several days
  - Not alter normal ↑ fetal blood volume with growth

Regulation Fetal Fluids

Transcapillary Shifts and Lymphatic Function

- *All fluid movements of the fetus are regulated in order to maintain blood volume*
- Fetal circulating blood volume/kg is constant throughout gestation
- Will protect against acute hemorrhage
- Will protect against maternal crisis
  - Acute change maternal osmolarity
  - Free water overload, hyperosmotic states
  - Therapeutic interventions


Fetus, birth, neonate
Fluid Balance Changes

Important Points

- Fetal/neonate capillary epithelium
  - Dynamic barrier – immature??
- Plasma volume
  - Negatively correlated with BP
  - Increased capillary pressure
    - Increases epithelial leak
  - Both fluid and "colloid" leak
  - PCV rises with decreasing plasma volume

Perinatal Fluid Shifts

- Fetus undergoes significant changes
  Last days, hours and minutes before birth
- Days before
  Decrease fluid production from lungs
    - Poorly understood
    - Changes in catecholamine, vasopressin or cortisol

  Decrease urine flow (equine)
    - Urine osmolarity high in foals at birth

  Fetal fluid reserves shifted to fetus?
  Increase in blood pressure by 20%
    - Transmitted to the capillary beds
    - Cause significant intravascuar fluid/protein shifts

Perinatal Fluid Shifts
Plasma Loss During Labor

- Uterine contractions

  Prelabor
  - Mild fetal compression
  - Increase fetal vascular pressure
  - Decrease in blood volume 2-4%

  During labor
  - Cause more blood volume loss

  Increase capillary leak

Perinatal Fluid Shifts
Plasma Loss - Increase BP

- Days before delivery (fetal sheep)
  - Increased arterial pressure
  - Results in increase capillary pressure
  - Decreased plasma volume
- During labor
  - Increased vasoactive hormones
    - Vasopressin, norepinephrine, cortisol, ANF
  - Decrease plasma volume

Perinatal Fluid Shifts
Hypoxia Associated Plasma Loss

- Mild hypoxia

  Loss of plasma volume into interstitial

- Severe hypoxia

  Greater decrease in plasma volume

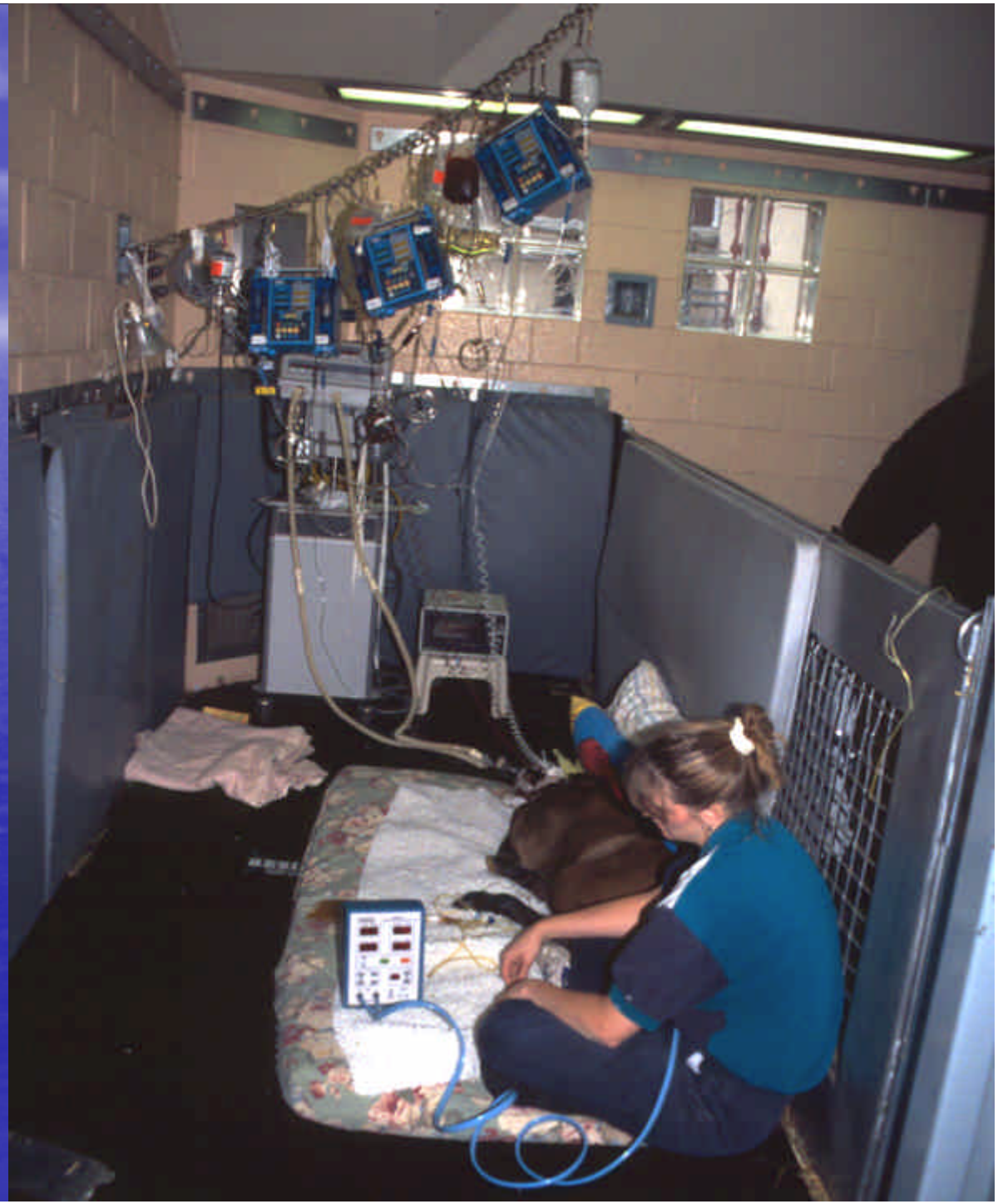
  Associated with ↑ arterial/venous pressure

  - Causes increased epithelial leak

Perinatal Fluid Shifts
Adaptive Advantages

- Rapid recovery from acute hemorrhage
- More blood loss is required before BP↓
  - Rapid mobilization of interstitial fluid
- Blood volume restored
  - 1/10 the time of adult
- Protect against neonatal hemorrhage
- Persist for the first week of life
- Same mechanism protects against hypovolemia

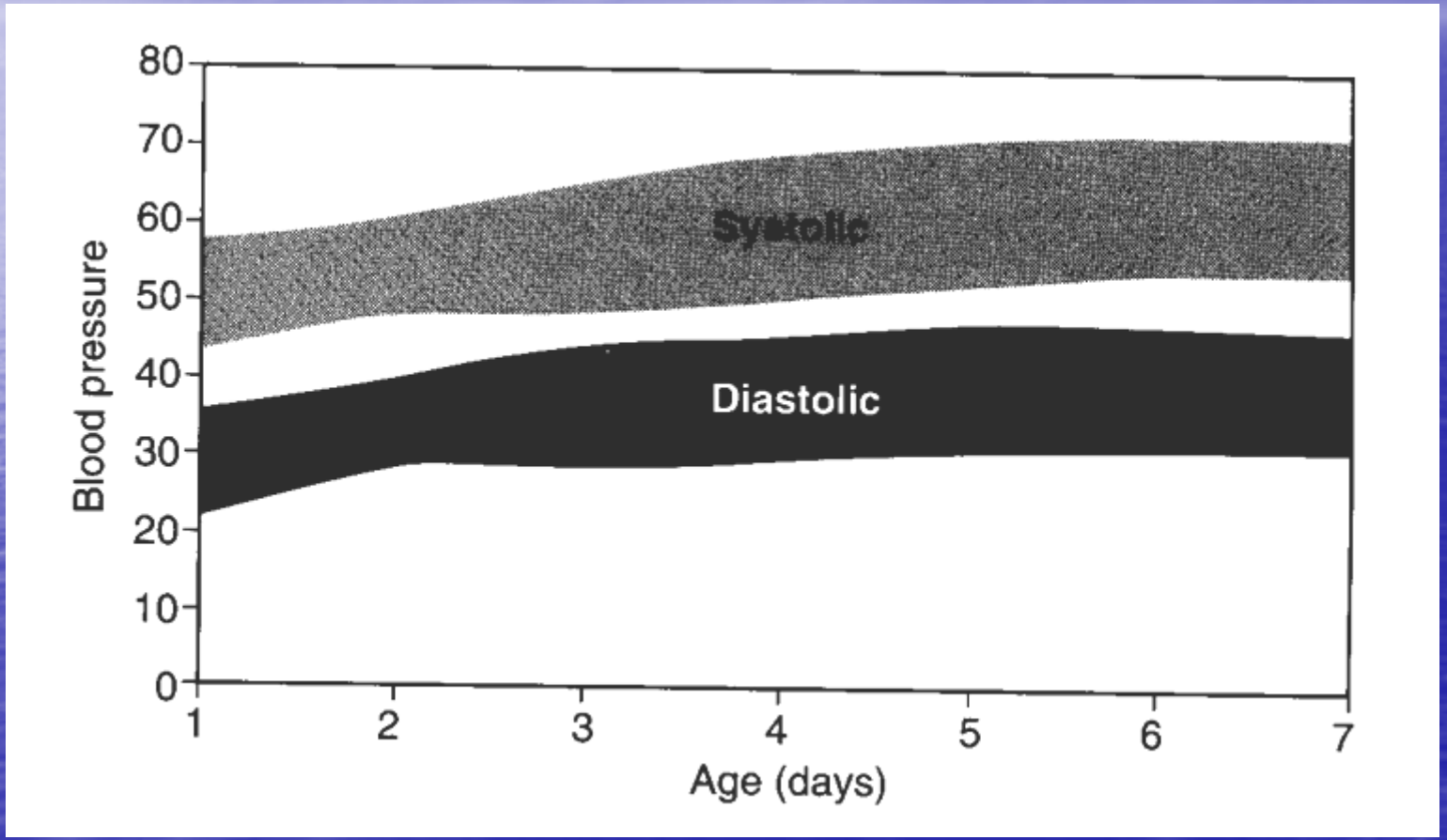
Therapeutic Implications of Neonatal Physiology



Therapeutic Implications Fluid Therapy

- Isotonic crystalloids
  - Poor intravascular retention in the fetus
    - High capillary filtration coefficient
    - High interstitial:vascular compliance ratio
    - Highly dependent on state of volemia
  - 30-60 min after infusion
    - Adult retains 20-50% intravascular
    - Fetus only 6-7% intravascular
    - Newborn in between
    - Dependent on state of volemia
- Colloids
  - Not retained intravascular
  - Epithelial filtration
    - Fetus 15X adult for plasma proteins
    - Neonate – transition state
- Retention related to volemia

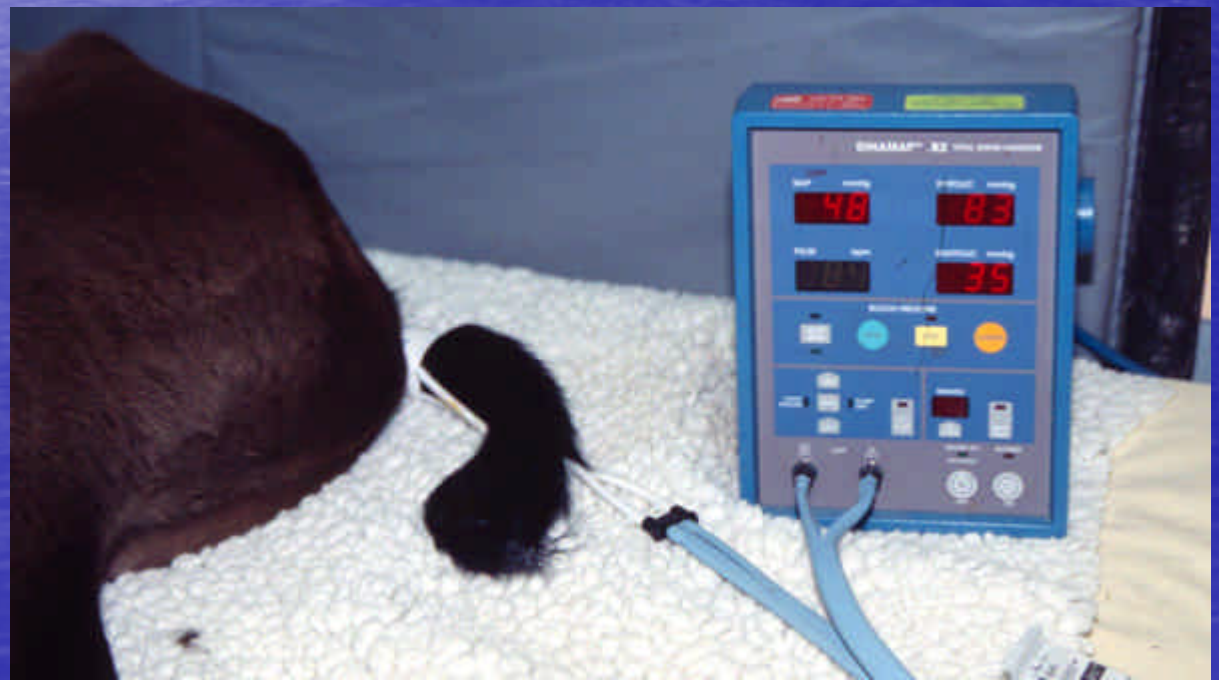
Therapeutic Implications
Blood Pressure



Human Neonate – sleeping

Implications for Intervention

- Fetal existence depends on low systemic ABP
- Neonate
  - Also has a low pressure vascular system
  - Important in maintaining plasma volume



Implications for Intervention

- Neonate is in a transitional state for BP
  - Precapillary tone may be the key
    - Development not simultaneous in all tissues
  - Once established
    - Systemic BP not transmitted to capillary
- Attempts to increase pressure
  - Before the transition
  - May decrease intravascular fluid volume
    - Cause protein leak
  - Interfere with return of volemia

Implications for Intervention

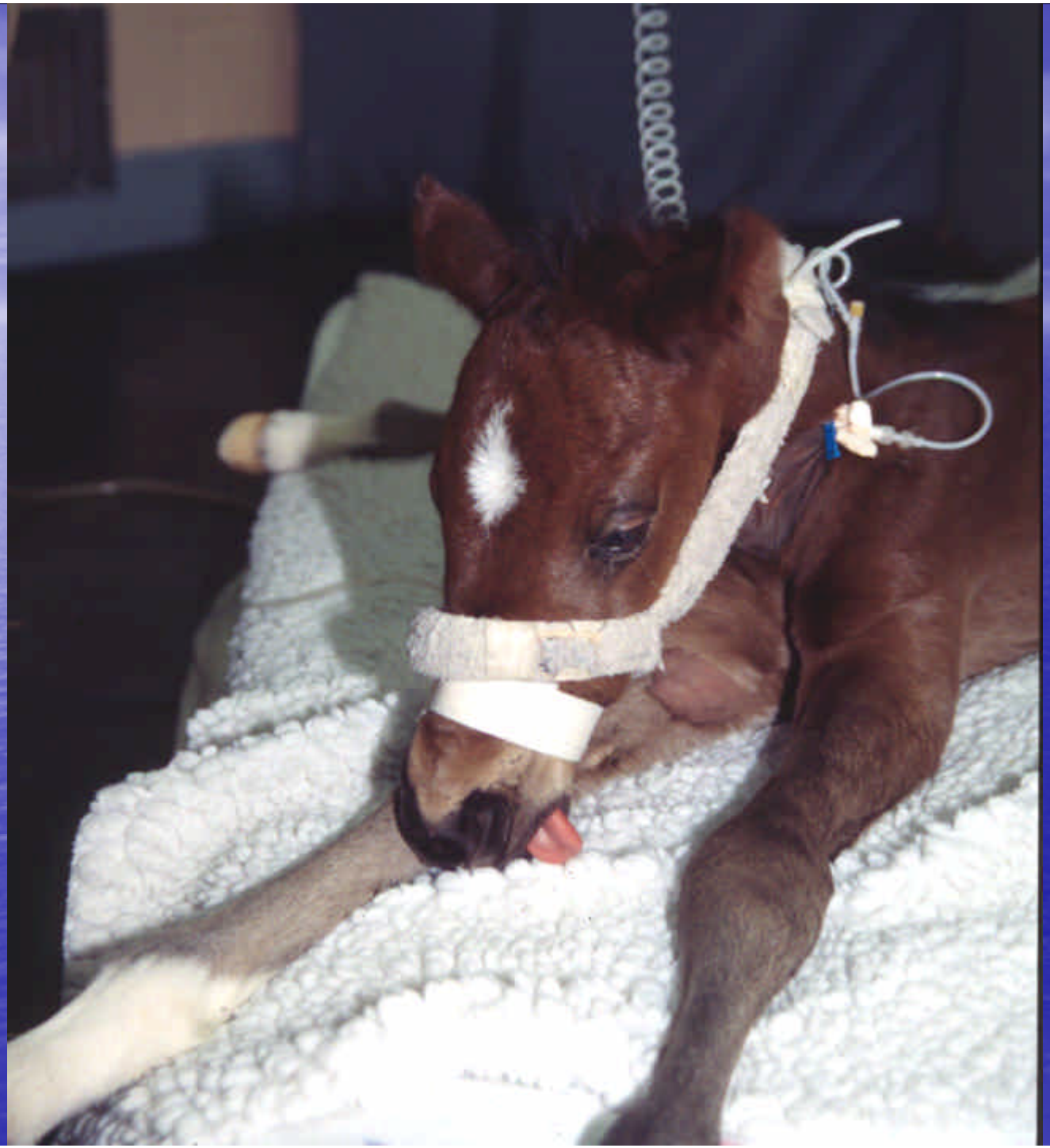
- Method used to raise BP may be important
  - Fluid loading transmitted to the capillaries
  - Adrenergics ?
    - May depend on drug
    - Neonate's receptor maturation
    - Complex physiologic responses
- Lymph Flow
  - Slowed by increased central venous pressure
    - May occur with high fluid infusion rates
    - Advantage of periodic boluses

Therapeutic Implications Volume Loading

- Adult
  - Volume load excreted via kidneys within hours
- Fetus and neonate
  - Low intravascular retention
  - Little change in vasopressin or rennin levels
  - Atrial natriuretic factor only transient increase
  - Urine flow only very transiently increases
  - Retained fluid load long term
  - Not handle fluid loads well
- Once fluid overloaded
  - Prolonged retention
  - Giving colloids may exacerbate retention

Implications for Intervention

- Neonate is changing
  - Response will depend on state of
    - Maturation of capillary membrane
    - Precapillary tone and transfer of pressure to capillary
    - Presence of epithelial damage
    - Pathologic states may alter maturation
  - Failure to make transition
- Neonate may be able to respond rapidly
  - Ready for fluid challenges
  - Better able to respond than adult – more tolerant
  - Able to mobilize interstitial reserves rapidly
    - Maintain volemia
- Corollary:
  - Once we detect distress in neonate they are in real trouble



Physiologic Approach to Neonatal Fluid Therapy

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As in all aspects of medicine, when formulating a rational fluid therapy plan, a basic understanding of physiology is essential. It is important to remember that the neonatal period is a dynamic transition state between the fetus and the pediatric period. Thus to understand fluid balance in the neonate, an understanding of the fluid physiology of the fetus and the dynamic changes that occur during the neonatal period are essential.

Water moves freely across cell membranes driven by the number of discrete particles on each side. Water molecules move from areas with lower concentration of dissolve particles to regions with more dissolve particles until the concentration of particles in water are equal on both sides. This movement determines the distribution of water between the intracellular and extracellular spaces and in the extracellular space between the intravascular and interstitial compartments. This results in an osmolality (mOsm/kg of water) which is approximately the same in the interstitial and intracellular spaces. It is slightly higher in the intravascular space because of its higher protein content (producing the colloid oncotic pressure). Oncotic pressure is the osmotic pressure produced by nondiffusible molecules. In plasma, albumin accounts for 85% of the oncotic pressure because of its abundance. But the difference in osmotic pressure caused by the plasma proteins is small because the actual number of molecules is not large. The intravascular osmotic pressure is approximately 2 mOsm per liter greater than the interstitial osmotic pressure. Plasma osmolarity (mOsm/l of water) can easily be measured, but when measurement is unavailable, a clinical estimate can be made using the following formula: Plasma osmolarity = 2 X Na (mEq/l) + urea (mg/dl)/2.8 + glucose (mg/dl)/18. As normally urea and glucose are constant, Na is the major determinant of extracellular volume as it is the major extracellular ion (particle).

As osmolality is fundamental to normal cell function, it is tightly regulated. In fact, without this regulation, a 20% increase in extra cellular water will result in a decrease in plasma Na concentration to a dangerous level of 116 mmol/l resulting in a decrease in interstitial osmolality and a dangerous increase in intracellular water. However, doubling the total body sodium will be matched by retention of water which will result in edema but no change in plasma sodium concentration or osmolality or change in intracellular water content. Frequently water loss is secondary to Na loss, leading to decrease in extracellular volume which is termed hypovolemia. But when water loss is in excess to Na loss, interstitial osmolality increases drawing water out of cells leading to dehydration (inadequate cellular fluid). Hypovolemia is loss of extracellular fluid including intravascular fluid by loss of sodium and water together. Dehydration is loss of water with relative excess of sodium (increase extracellular osmolality) resulting in a loss of intracellular water. Changes in sodium alters extracellular volume without changing intracellular volume because it is the primary extracellular electrolyte and plays no role intracellularly. On the other hand, infusion of dextrose containing fluids devoid of sodium results in a change in osmolarity of all compartments resulting in even distribution of the fluid in both intracellular as well as extracellular compartments.

Infusion of hypertonic saline will be distributed throughout the intravascular and interstitial space. The increase in osmolarity will result in movement of intracellular water into the extracellular space. The consequence of this cellular dehydration on cellular health depends on the state of hydration at the onset. Infusion of isotonic colloid into the intravascular space will result in fluid expansion of that space without changing the fluid distribution in the other spaces. Infusion of hypertonic colloid into the intravascular space will result in an increase in the intravascular fluid compartment at the expense of the interstitial and intracellular fluid spaces.

All of the preceding effects are based on beginning with the patient with normal physiologic parameters. However the intensive care patient rarely begins as a normal starting point. Rather, generally they are hypoproteinemia, have a contracted interstitial volume and lack of capillary epithelial integrity. Critical care patients, especially neonates, generally have low albumin levels resulting in low oncotic pressure. In such a situation, infusion of isotonic fluids actually act similar to hypertonic fluids to a variable effect. In turn, the effect of infusion of hypertonic fluids depends on the volume of the interstitial space. If the interstitial space is contracted, as may be the case in hypovolemia, infusion of mOsm will have a greater effect on the osmolarity of this fluid. This amplifies the effect of the fluids on intracellular dehydration. This dehydration will have an escalating effect as the cells are compromised. Finally, loss of capillary epithelial cell integrity can have the major effect on fluid distribution. With leaky epithelial cells, the colloid will not stay intravascular but will leak into the interstitial space. The plasma expansion component contributed by the colloid will be lost. In such cases, giving colloid will increase the oncotic pressure of the interstitium and contribute to peripheral edema as well as cellular dehydration.

When applying fluid therapy principles to the neonate, an understanding of the differences between neonatal and adult physiology must be appreciated. The most important differences involved the dynamic nature of the fetal/neonatal capillary epithelial barrier and the degree that the plasma volume is negatively correlated to blood pressure because of increased capillary leak induced as blood pressure increases resulting in fluid and colloid leak (plasma volume contraction).

The fetus undergoes significant changes during the last days, hours and minutes before birth. Beginning days before birth there is a decrease in fluid production from the lungs probably brought about by changes in catecholamine, vasopressin and cortisol levels. Concurrently there is an increase in blood pressure by 20% which is transmitted to the capillaries resulting in significant intravascular fluid/protein shifts. During labor there is a further loss of plasma volume. Prelabor uterine contractions result in mild fetal compression resulting in an increase in fetal vascular pressure decreasing blood volume by 2-4%. During labor, even more fluid shifts occur. Both of these are caused by an increase in capillary leak associated with increased capillary pressure. In addition to physical pressure on the fetus, during labor there is an increase in vasoactive hormones such as vasopressin, norepinephrine and cortisol. This results in an additional decrease in plasma volume.

If hypoxia is an important component, it will amplify the loss of plasma volume into the interstitium. Mild hypoxia will result in increased capillary permeability. Severe hypoxia is associated with increased arterial/venous pressures which are likely to be felt in the capillary beds. There may also be significant translocation of fetal blood from the placenta to the fetal body

causing a further increase in capillary pressure. The increased capillary pressure will increase trends capillary filtration and further decrease plasma volume.

Both the physiologic and pathophysiologic response results in an increase in interstitial fluid volume. This has important adaptive consequences. Take for instance the response to hemorrhage in the fetus or neonate. Neonates are at high risk of hemorrhage from umbilical structures. The expanded interstitial space serves as a reservoir for both fluid and protein in response to acute hemorrhage. After acute hemorrhage in adults, 24 to 48 hours is required for full return of plasma volume when not treated. The response is much more rapid in the neonate. First of all, a higher proportion of blood must be lost before there is a significant decrease in blood pressure because of the very rapid mobilization of interstitial fluid. Second, the return to normal plasma volume is much more rapid. After the loss of 30% of the plasma volume over 2 hours, the neonate will have restored two times the amount which would occur in an adult within 30 minutes and the total blood volume will be normal within 3-4 hours (about 1/10 the time required for the adult). This is mediated by translocation of fluid protein from the interstitial reserves. This response is present in the fetus and neonate during the first week, at least in lambs.

Differences can also be seen in the response of the fetus and neonate to isotonic fluid loading. In adults between 20-50% (dependent in part on state of hypovolemia and dehydration) of an isotonic fluid load is retained in the intravascular space 30-60 minutes after infusion. In the fetus only 6-7% will be retained. The neonate, in the transition state between fetus and adult, has intravascular fluid retention in between these two extremes but approaching the adult value. The poor intravascular retention has to do with capillary filtration coefficient and high interstitial to vascular compliance ratio. High capillary filtration coefficient results in rapid fluid movement across a capillary. The interstitial to vascular compliance ratio allows more extensive fluid movements without resistance. So, vascular fluid expansion by crystalloid infusion results in a transient increase in capillary pressure, which in turn, allows for rapid redistribution of the fluid.

This same phenomenon has important implications in the neonate's inability to compensate for increased fluid loads. In the normal adult, when a crystalloid fluid load is administered, it is rapidly excreted via the kidneys. This does not occur in the neonate. The rapid redistribution of fluids with low intravascular retention allows little stimulus for changes in vasopressin or rennin levels. Atrial natriuretic factor only transiently increases. As a result increased urine flow is very transient and most of the fluid load is retained long-term. Neonates, especially ill neonates, retained fluid loads a long time and thus do not handle large fluid loads well.

These physiologic differences have therapeutic implications. The neonate is in the state of constant change. Any individual’s response will depend on the state of maturation of the capillary membrane. Because of the interstitial reserve built into the neonate, the neonate can respond more rapidly and completely than the adult to hypovolemic challenges by rapid mobilization of these reserves. They are better able to maintain volemia. However the corollary is that once distress is detected in the neonate they are in real trouble. The neonates have a low-pressure vascular system. The low systemic blood pressures may be important in maintaining plasma volume. Any increase in arterial pressure, if transmitted to the capillary, will decrease fluid volume and cause increased protein leak. The presence of this response depends on the state of maturation but probably is

present at least for the first five to seven days of life. During this period, attempts to increase blood pressure may actually decrease volemia. Giving large volumes of crystalloids will result in little retention in the intravascular space. Giving colloids may not help since they will also leak into the interstitial space. When giving parenteral fluids, the neonate will tend to become fluid overloaded because of its inability to handle fluid loads, because of the low intravascular to interstitial compliance and because of the limitations of renal function. Once fluid overloaded, prolonged retention should be expected. Colloids may exacerbate the retention of fluids by holding fluid in the interstitial space. All of these responses depend on the state of maturation of the epithelial cells and the presence of epithelial damage which may occur with hypoxic insults or sepsis. Such pathologic states may alter maturation and result in the failure of the neonate to make the transition to a more mature fluid handling ability.