NEONATAL RENAL PHYSIOLOGY

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WORKSHOP ON NEONATAL FLUID AND ELECTROLYTE BALANCE

OCTOBER 20TH 2018

IPNA

GREAT CARE FOR LITTLE KIDNEYS, EVERYWHERE

Plan

- Definitions
- Anatomical development of the kidney
- Evolution of renal function in the neonate
- Summary

Basic terms

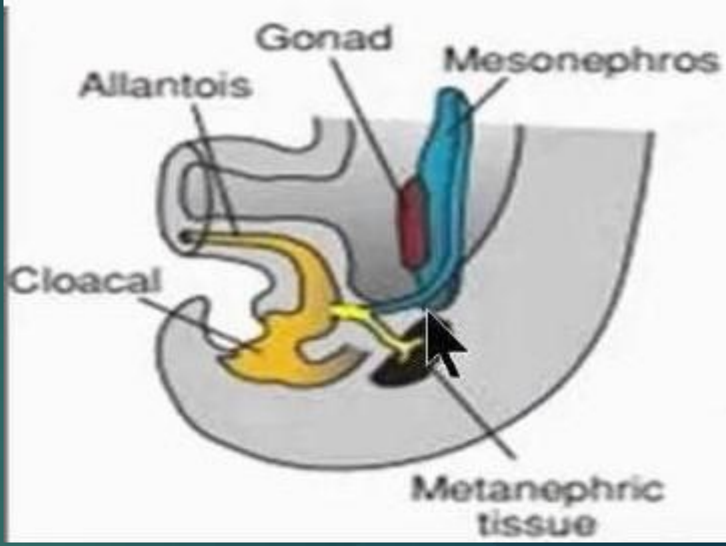
- Renal function assessment
  - Blood creatinine and urea
  - Biomarkers
    - Serum **Cystatin C**
    - **N Gal** (Neutrophil gelatinase-associated lipocalin (NGAL):
- GFR ml/min/1.73m2
  - Schwartz formula – $\frac{\text{Ht (cm) x k *}}{\text{pCr (umol/l or mg/dl)}}$
- Neonatal normal values differ from older children

Definitions

TERMINIOLOGY	GESTATIONAL AGE/ WT
TERM	$\geq$ 37/40
PRETERM	< 37/40
LATE PRE TERM	$32\text{-}36^{+6}/40$
VERY PRE TERM	$28\text{-} 31^{+6}/40$
EXTREME PRETERM	<28/40
VERY LOW BIRTH WEIGHT	<1500G
EXTREMELY LOW BIRTH WEIGHT	<1000G

ANATOMICAL DEVELOPMENT

Development



Intermediate mesoderm

Nephrotome

Pronephros

regresses

Mesonephros

5th week urine

11th -12th week involutes

Caudal tubules form part of male genital tract

Mesonephric duct outgrowth

Ureteric bud

Metanephros

Metanephric blastema

The kidney

Ureteric bud

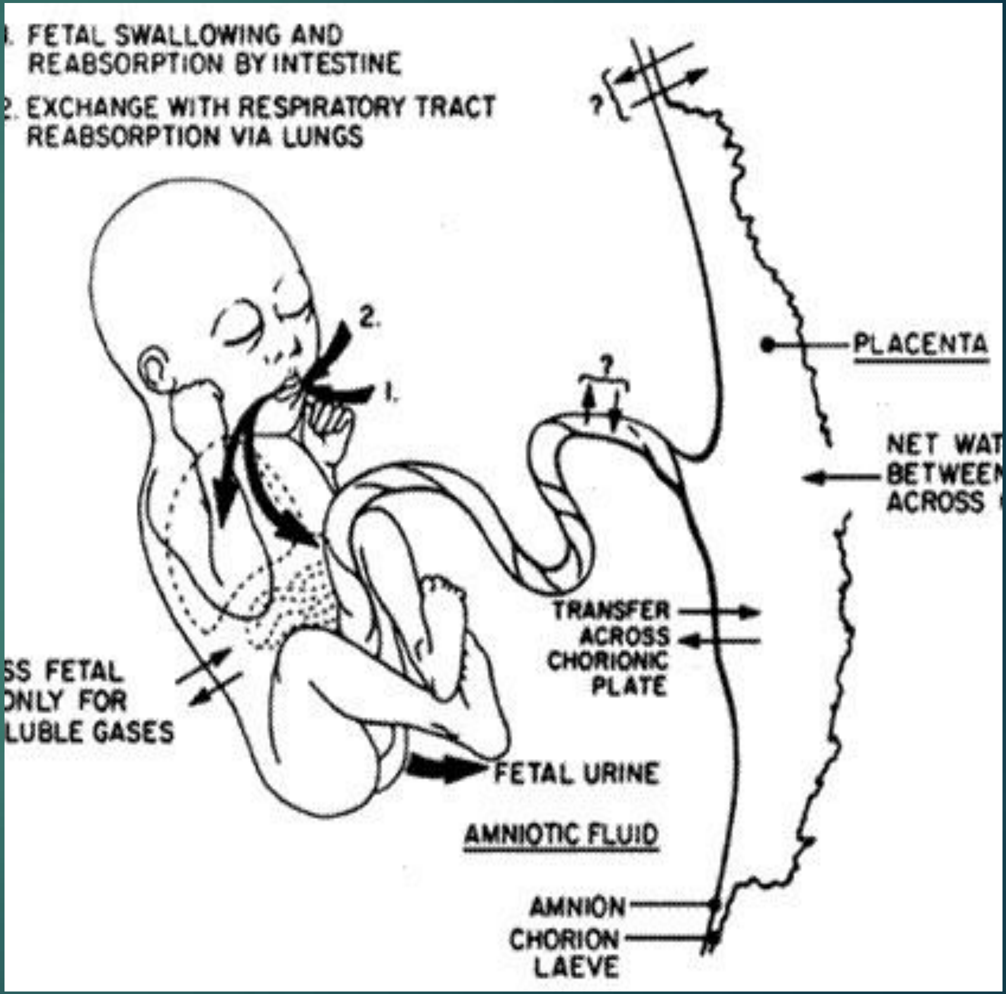
- Ureters
- Pelvis
- Collecting tubules
- Drainage system

Metanephric blastema

- Nephrons
  - Glomeruli
- Filters

The placental "dialysis" system

- Amniotic fluid - stage 1
  - diffusion of water and solute through placenta and fetal skin
  - dialysate of maternal and fetal plasma
- 25/40 – skin diffusion stops
- Amniotic fluid stage 2
  - fetal urine by 11 weeks



The kidney

- First glomeruli 9/40
- Urine production 11/40
- Nephrogenesis ends 34-35/40
- Preterm infants <35/40 **do not** have full nephron quota
- Most nephrons form in 3rd trimester
- Then…glomeruli – become larger and their functions mature
- Mature by 18-24 months post natal life

FUNCTIONAL DEVELOPMENT

Effective renal plasma flow

- Increases towards term and up to age 2 years
- Premature 20ml/min/1.73m^2
- Term 83ml/min/1.83m^2
- Age 2 years (adult value)

  650ml/min/1.73m^2

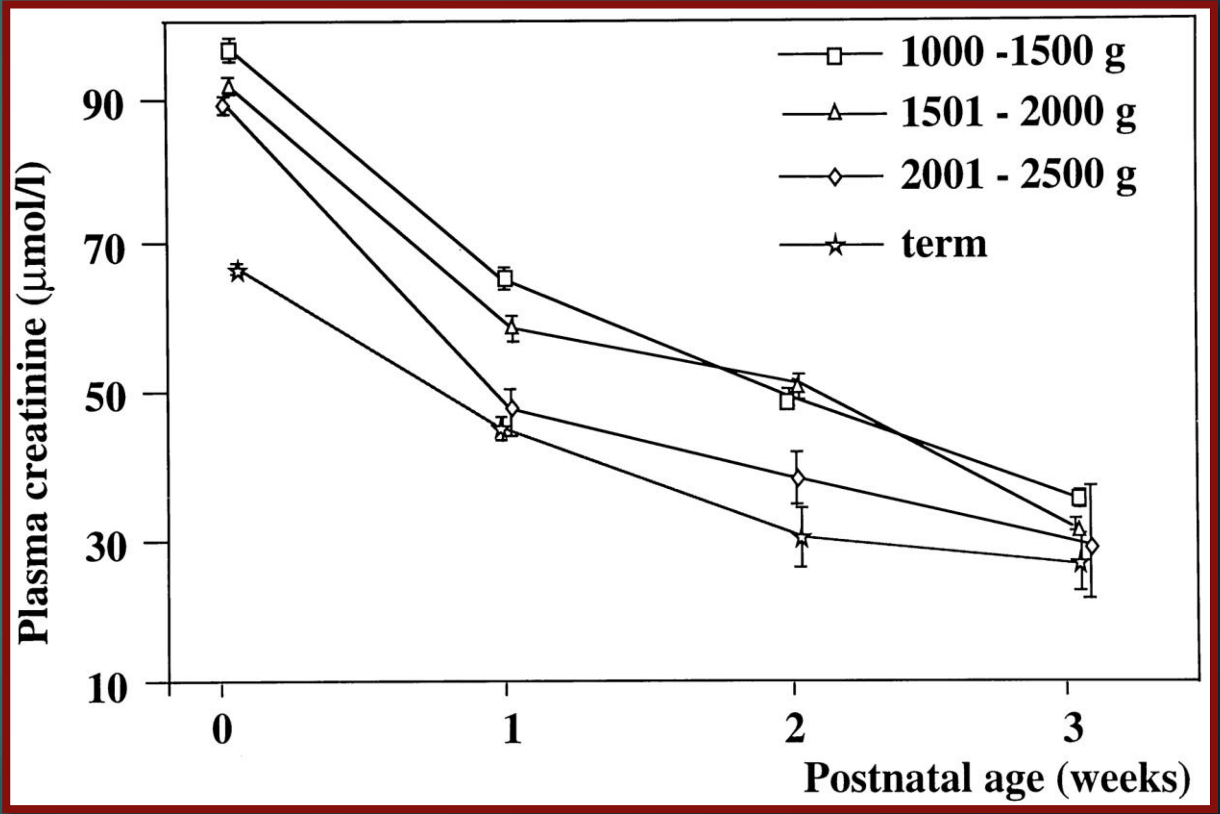
- Renal perfusion pressure increases
- Renal vascular resistance falls
- Autoregulation improves

GFR

- Intrauterine: placental filter
- At birth: active glomerular filtration
- GFR increases with age
  - Neonate: 40m/min/1.73m2
  - 2 years: 100-125 m/min/1.73m2 = adult levels
  - Premature infants:
    - Slower rise in GFR – normal values achieved later
    - VLBW – normal values at age 8 years
- Important for drug dosing / assessing renal function

Creatinine

- At birth s Cr = maternal values
  - Usually falls slowly to baseline
- But filtered creatinine is **absorbed** by neonatal tubules in the first few days of life
- Serum creatinine may actually rise briefly after birth



Creatinine

- The greater the prematurity the higher plasma creatinine will rise
- Serum creatinine in the first few days of life may not truly reflect infants renal function
- **Cystatin C** may be better measure of GFR
  - Freely filtered across capillaries and completely reabsorbed by proximal tubules

WATER BALANCE

Urinary concentrating ability

- Max urinary concentrating ability low in neonate
  - Term 700mOsm – low
  - 6-12 months – adult levels – 1400mOsm
- Immature tubules
- Relative tubular insensitivity to ADH, aldosterone

Fluid balance in the neonate

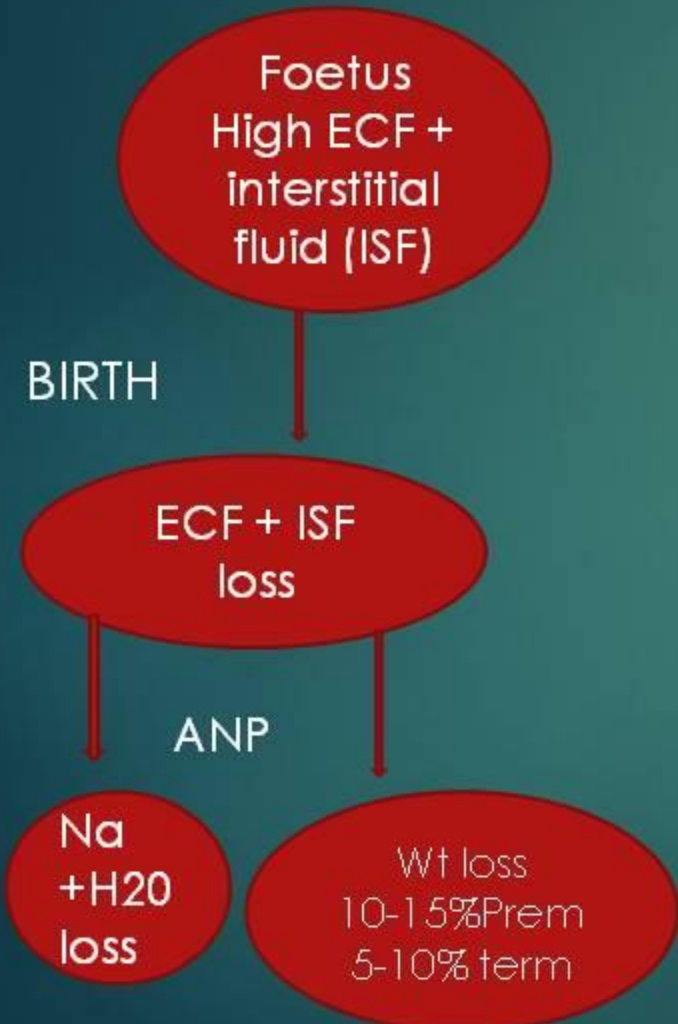
In foetus

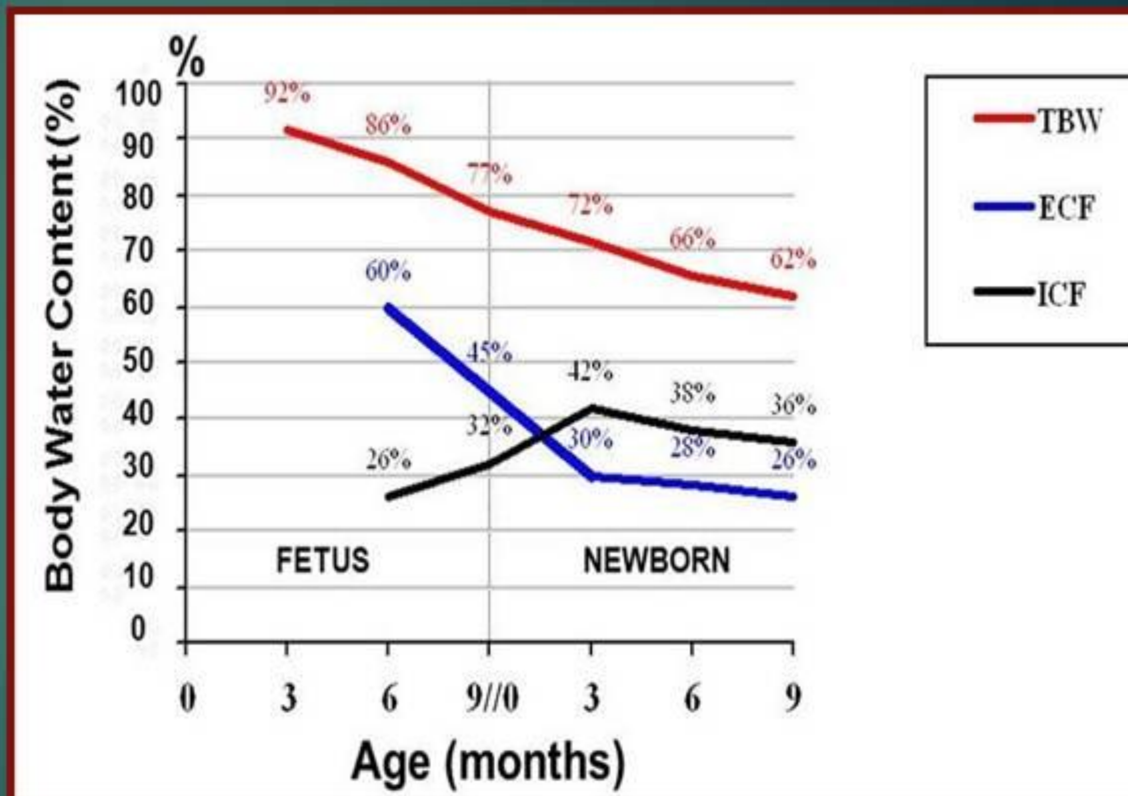
- fluid balance – amniotic fluid
- total body water (ICF + ECF) is 95% total body weight
- large interstitial volume

ECF = **interstitial fluid** + intravascular fluid

	Premature	Infant	Child	Adult
Total body water (TBW)	80%-90%	75%	65%-70%	55%-60%
Extracellular fluid (ECF)	50%-60%	40%	30%	20%
Intracellular fluid (ICF)	60%	35%	40%	40%

Water balance – Immediate post natal changes





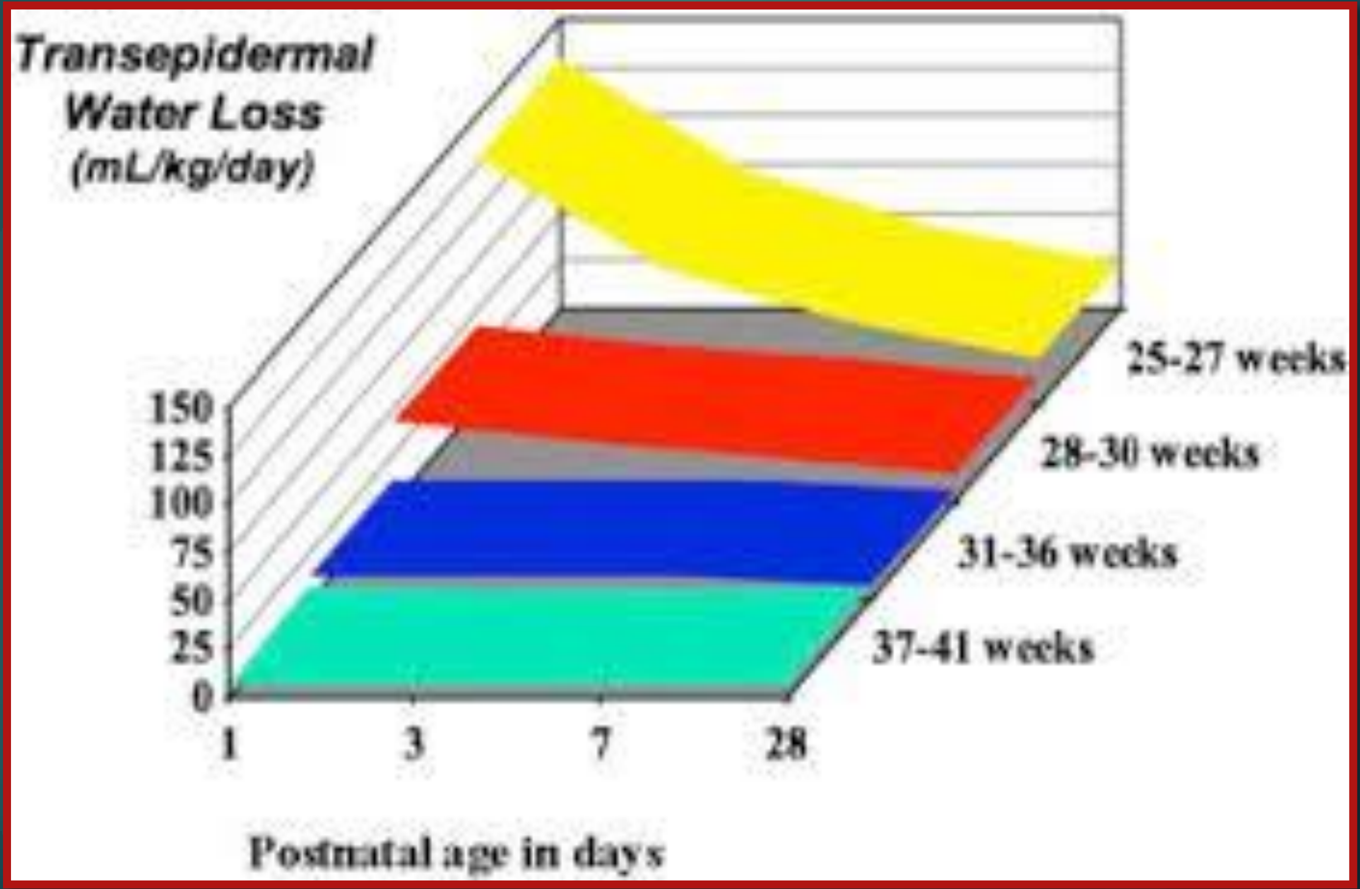
Implications of postnatal changes

- Weight gain in first week of life - Na retention
- Fluid management should allow isotonic ECF loss (less fluid intake initially then graduated increase)
- Avoid sodium intake until
  - postnatal diuresis / natriuresis end
  - Or till weight loss of 7% of birth weight
- Premature infants –
  - risk of initial hypernatraemia – as very dilute urine
  - Later hyponatremia – high urinary sodium losses

Fluid balance regulation

Immature urinary Na and water conservation

Risk of dehydration * High insensible losses



Urine production postnatally

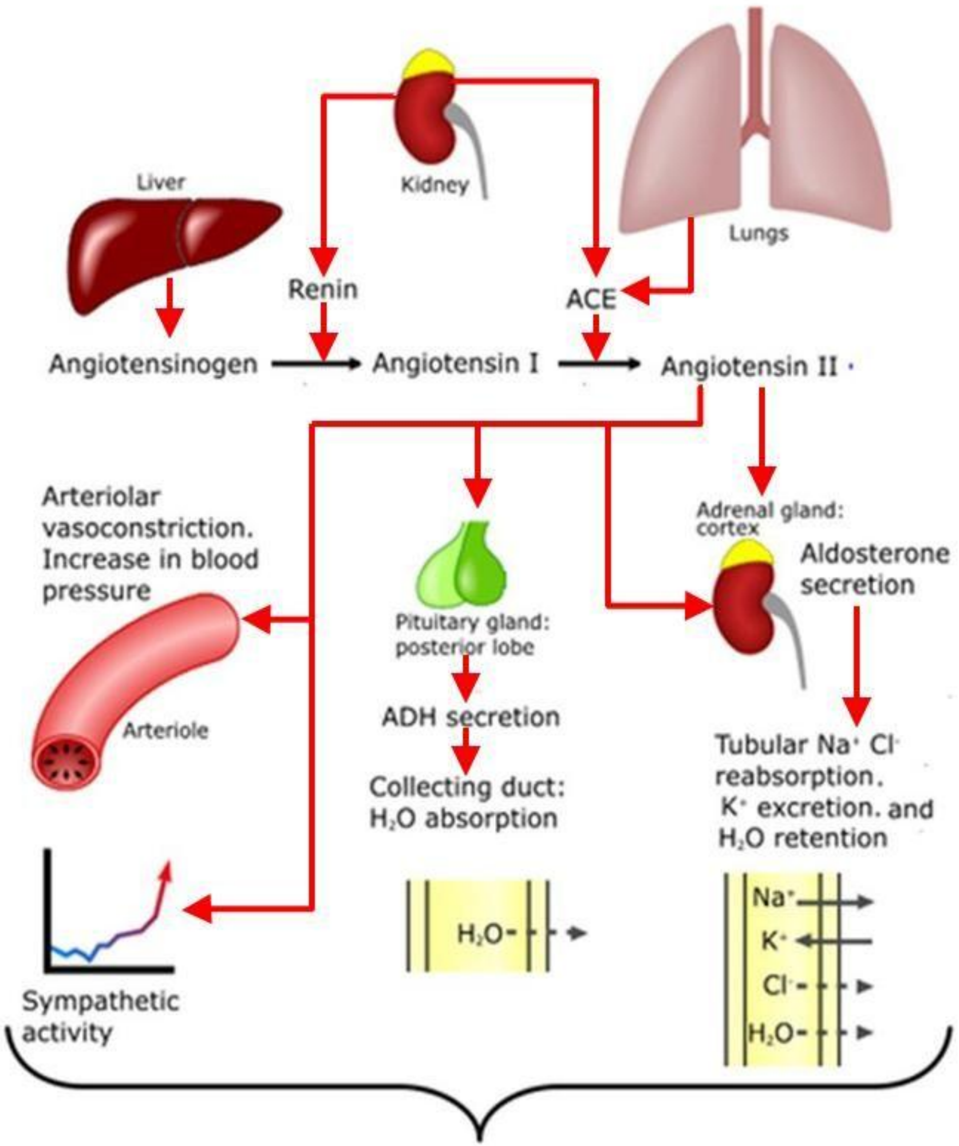
- 99% pass urine in the first day
- Day 1-2 urine output 13-30cc/kg/day
- Oliguria < 1cc/kg/ hr
- If postnatal weight loss is $> 10\%$ investigate

ELECTROLYTES

Renin **A**ngiotensin **A**ldosterone **S**ystem

- Blood pressure regulation
- Intrarenal blood flow
- Fluid and electrolyte balance

Renin-Angiotensin-Aldosterone System (RAAS)

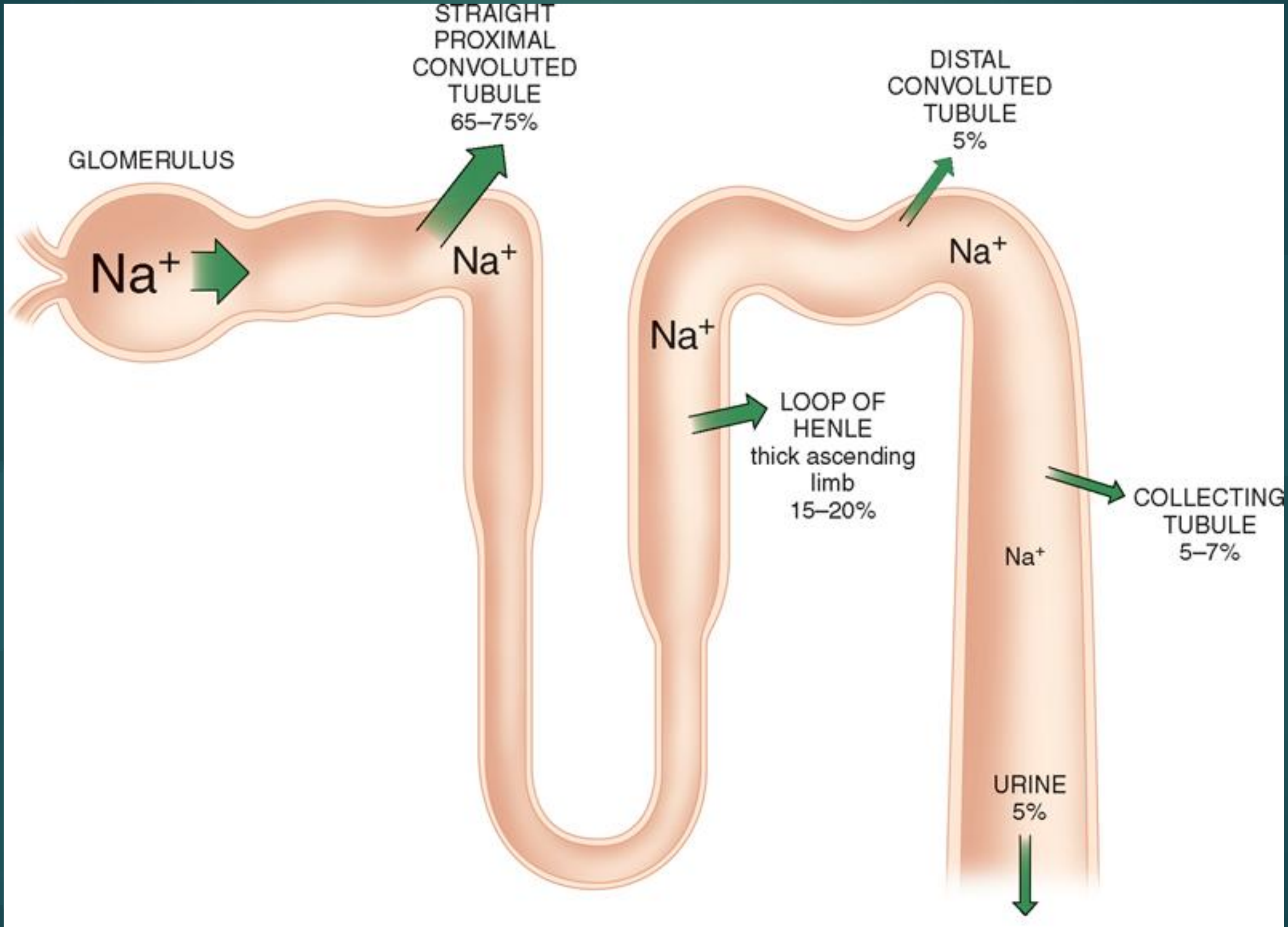


Water and Sodium retention.
Increased circulating volume. Increased renal perfusion.

RAAS

- Fetus
  - Relative insensitivity of adrenal to angiotensin >>
  - >> reduced aldosterone secretion
- In premature infant
  - Insensitivity and immaturity of nephron development >> negative Na and H20 balance

Sodium balance



Source: Butterworth JF, Mackey DC, Wasnick JD: *Morgan & Mikhail's Clinical Anesthesiology*, 5th Edition: www.accessmedicine.com

Sodium balance

- Distal tubule – site of most sodium exchange
- Premature infants have
  - Higher Na delivery to the tubules
  - Lower Na resorption in DCT and Intestine vs. term
  - Higher sodium losses

After initial post natal diuresis

- Thriving term infants have positive Na balance
- Preterm infants $< 35/40$ continue to have negative Na balance in first 3 weeks after birth

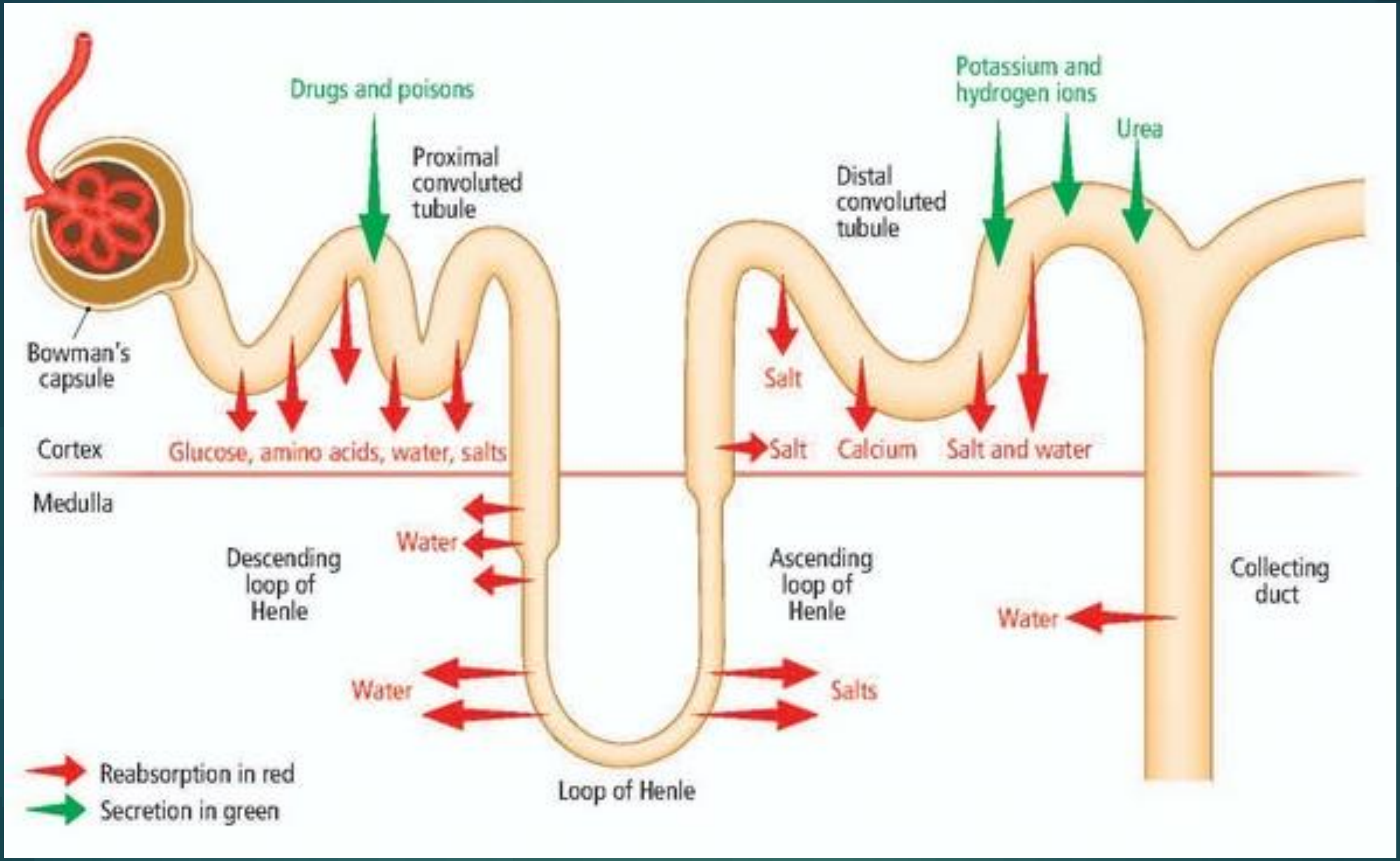
Sodium balance

- Prems
  - At risk for hyponatraemia
  - Age < 33/40 need 3-5mEq/kg/day for initial weeks after birth
- Excessive Na to term infants
  - Fluid retention, oedema, hypernatraemia
- FeNa – fractional excretion of Na
  - Highest in first 10 days of life
  - < 0.4% by age 1 month (adult values)

Sodium balance

- Na excretion increased by
  - Hypoxia, diuretics, jaundice, high fluid or salt intake, respiratory distress
- Modulators of Na excretion
  - RAS – **R**enin **A**ngiotensin **A**ldosterone **S**ystem
  - ANP – **A**trial **N**atriuretic **P**eptide
  - prostaglandins, catecholamines

Potassium



K filtered at glomerulus – reabsorbed in proximal tubules
– reabsorption in ascending loop (slight)
- Secreted in distal convoluted tubule

Potassium

- Neonatal hyperkalemia (especially prems)
  - Immaturity of distal tubules
  - Reduced sensitivity of cortical collecting duct to aldosterone
- In premature infants
  - immediately after birth, K shifts from intracellular to extracellular compartment
  - During the diuresis K is lost and serum K gradually returns to normal

Calcium

- Last trimester – calcium actively transported from mom to foetus
- Maternal PTH does not cross placenta
- After birth – calcium levels in newborn depend on
  - intrinsic PTH secretion
  - dietary calcium intake
  - renal calcium reabsorption, bone stores and Vit D status

Calcium

- Active and passive reabsorption throughout nephron
- Ionized Ca is the active portion – PTH regulated
- Ca levels stabilize and reach adult levels by first week of life

Early neonatal hypocalcaemia

- Normally after birth calcium levels fall (faster in the premature)
- Hypocalcaemia
  - In first 3 days of life
- Ca < 2mmol/l (8mg/dl) (term)
- Ca <1.75 mmol/l (7mg/dl) (premature)
- Term, prems, low and N bwt
- Rarely symptomatic

Early neonatal hypocalcaemia

Causes:

- Hypo-parathyroidism –
  - fall in PTH levels in firs 48 hrs
  - end organ unresponsiveness to PTH
- Hypercalciuria
- Hyperphosphataemia
- Excessive Na intake >> hypercalciuria

Phosphate

- Phosphate levels higher in the newborn and young children
- Causes:
  - Lower GFR – less PO4 secretion
  - Relative tubular unresponsiveness – to PTH less phosphaturia

Albumin

- Albumin levels are low in neonates especially premature infants
- Albumin levels rise throughout gestation
    - Some albumin from placenta
    - Increased hepatic albumin production
    - Mean serum albumin 19g/l <30/40
    - Rises to mean of 31g/l at term
  - Post natal rise at term ? related to ECF volume contraction postnatally

ACID BASE BALANCE

Acid base balance - antenatally

- Foetal carbonic and organic acids – neutralized by blood buffers bicarbonate and Hb
- Organic acids, uric acid, lactate, keto-acids lactate
  - Eliminated via placenta and maternal kidneys

Acid base balance postnatally

- Respiratory / buffer / renal
- Buffers – first line
  - bicarbonate /carbonic acid
  - Hb oxy Hb
  - Protein
  - Phosphate buffer
- Respiratory – respiratory acidosis limiting compensation
- Renal – tubular immaturity

Acid base

- Premature infants often acidotic
  - BUT usually **do not** need bicarbonate
  - Reduced bicarbonate reabsorption
  - Reduced H+ secretion
- Regulation of acid / base balance improves with advancing gestational age

Normal Acid – Base Values

	pH	HCO_3 (mmol/L)	$PaCO_2$ (mmHg)	Base excess (mmol/L)
Birth	7.24 (7.14–7.34)	20 (14–26)	49 (29–69)	–14 to –4
Newborn	7.37 (7.18–7.50)	20 (17–24)	34 (27–40)	–10 to –2
Infant	7.39 (7.20–7.50)	22 (19–24)	35 (27–41)	–7 to –1
Toddler	7.40 (7.27–7.49)	22 (19–24)	36 (29–41)	–5 to 0
Child	7.40 (7.34–7.46)	23 (18–25)	37 (32–48)	–4 to +2
Adolescent	7.38 (7.32–7.44)	24 (20–26)	41 (35–47)	–3 to +2
Adult	7.39 (7.37–7.41)	25 (20–28)	41 (37–45)	–3 to +3

SUMMARY

Summary
Neonatal renal physiology

- Progressive maturation of glomerular and tubular function with age
- Immaturity of glomerular filtration
  - Implications for drug elimination
- Immaturity of salt, water and acid base balance
  - Risk of dehydration
  - Electrolyte disturbance
  - Acid base disorders
- Be aware of neonatal normal values

Caution

Handle with care