To describe the foetal circulation.

Overview of the foetal circulation:
- RV (pulmonary circulation) and LV (systemic circulation) work in “parallel” due to shunts (foramen ovale and ductus arteriosus)
- LV and RV are of equal size and wall thickness
- Foetal C.O. is dependent on HR (120-140 bpm) → thus, foetal distress (esp during labour) is indicated by HR < 100 bpm (“bradycardia” → foetal hypoxaemia) or > 180 bpm (“tachycardia” → foetal skull pressure)

Blood flow and blood oxygenation within foetal circulation:

- Oxygenated blood (PO$_2$ 30 mmHg; SpO$_2$ 80%) returns from placenta via 1x Umbilical vein → passes into L branch of Hepatic portal vein:
  - 60% of blood is shunted away from portal venous circulation into the IVC via “Ductus venosus”
  - 40% of blood mixes with the portal venous circulation of the GIT/liver
- Oxygenated blood shunted via the “ductus venosus” mixes with blood draining from the portal circulation within the IVC → IVC blood remains well oxygenated (SpO$_2$ 67%)
- IVC blood then enters the RA:
  - 60% of this blood is directed across “Foramen ovale” to the LA by the “Crista terminalis” (muscular ridge in RA) → then passes into LV (PO$_2$ 25 mmHg/SpO$_2$ 65%) → then into the ascending aorta to supply the coronary arteries and brain with well oxygenated blood
  - 40% of this blood mixes with poorly oxygenated blood draining from the head/neck via the SVC (SpO$_2$ 30%) → then passes into RV (SpO$_2$ 50%) → then into pulmonary artery where:
    - 10% of blood enters the lungs (due to ↑ PVR 2° collapsed lungs)
    - 90% of blood is shunted across the “Ductus arteriosus” (wide muscular arterial channel b/t pulmonary artery and aorta) into the descending aorta → perfuses lower body (PO$_2$ 20 mmHg/SpO$_2$ 60%) and returns to placenta via 2x Umbilical arteries

Note – Venous return to the heart – 70% via IVC, 20% via SVC, 10% via lungs/coronary sinus

Note:
- LV afterload → high resistance cerebral circulation and upper body circulation
- RV afterload → low resistance ductus arteriosus and placenta, and high resistance pulmonary vasculature and lower body circulation
To describe the circulatory and respiratory changes that occur at birth.

(I) Circulatory changes at birth:

Overview of circulatory changes at birth:
- At birth, the circulatory system changes from a foetal system where the LV and RV function in “parallel” to an adult system where they function in “series” → this is initiated by Δs in resistances throughout the neonatal circulation, which produce haemodynamic changes that cause shunt closure

Key circulatory changes at birth:
- (1) Loss of low-resistance placental circulation
  o Due to clamping/closure of umbilical vessels
  o Causes – (i) ↑ SVR → ↑ LVEDP and ↑ LAP, and (ii) ↓ VR via IVC → ↓ RAP
- (2) Significant ↓ in resistance of pulmonary circulation
  o Due to (i) expansion of lung parenchyma initially (opens up extra-alveolar vessels), then (ii) removal of pulmonary HPV by ↑ PAO2 later
  o Causes – (i) Significant ↓ PVR → ↓ PAP → ↓ RVEDP and ↓ RAP, (ii) Significant ↑ pulmonary blood flow 2° ↓ PVR, (iii) ↑ LAP 2° ↑ pulmonary BF
- (3) Closure of ductus venosus
  o Occurs few hrs post-delivery (?mechanism).
  o Causes ↓ VR via IVC → ↓ RAP
- (4) Shunt closures → reversion to adult circulation where LV/RV function in “series”
  o (a) Closure of foramen ovale → occurs when LAP > RAP. Permanently closes by fusion of septum secundum (4-6/52)
  o (b) Closure of ductus arteriosus → occurs within 10-15 hrs post-delivery
    (constricts in response to ↑ PaO2 after the 1st breath, and ↓ [ ] of local/circulating PGE1/E2). Permanently closes by thrombosis/fibrosis (2-3/52)

(II) Respiratory changes at birth:

Overview of respiratory changes at birth:
- (1) Loss of placental gas exchange → due to clamping/closure of umbilical vessels
- (2) Initiation of ventilation of newborn’s lungs with the 1st few breaths → leading to (i) commencement of pulmonary gas exchange, and (ii) rapid establishment of FRC

Key respiratory changes at birth:
- (1) Foetal thorax is compressed during vaginal delivery (as the chest wall is very compliant due to a soft rib cage) → causes 35 mL of lung fluid to be squeezed out and reabsorbed into pulmonary circulation
- (2) Loss of placental gas exchange due to clamping/closure of umbilical vessels → causes hypoxaemia (PaO2 ↓ from 30 to 15 mmHg), hypercapnoea (PaCO2 ↑ to 60 mmHg) and acidemia in newborn
- (3) Initiation of ventilation of newborn’s lungs:
  o First few breaths are stimulated by various factors:
    - (i) Environmental sensory stimuli at birth (Eg. sound, touch, temperature, gravity) → afferent signals stimulate the reticular system → ↑ sensitivity of medullary respiratory centres
    - (ii) ↑ responsiveness and control over respiration of central and peripheral chemoreceptor (due to ↑ blood flow through them)
    - (iii) Central and peripheral chemoreceptors are stimulated by hypoxaemia, hypercapnoea and acidemia caused by loss of placental circulation
  o First few breaths results in:
(i) 1st breath requires a ↑ -ve P_{INSPIRATORY} 70-100 cmH_{2}O → but magnitude of -ve P_{INSPIRATORY} for subsequent breaths progressively ↓ ↓ ↓ due to (a) establishment of an air-liquid interface and (b) presence of surfactant (which ↓ ST at this interface)

(ii) Rapid establishment of FRC → FRC ↑ to 20 mL/kg after a few minutes, then to 30 mL/kg (= adult FRC) within 1 hr

(iii) Start of pulmonary gas exchange as lung is inflated
- Newborn breathes with a TV 5 mL/kg (≈ 20 mL) and RR 30 breaths/min → MV 150 mL/kg/min
- Rapid ↑ PaO_{2}, ↓ PaCO_{2} and ↑ pH
- Physiological DS ≈ 1.5-2 mL/kg

(iv) Significant ↓ in resistance of pulmonary circulation (↓ PVR)
- Due to (a) expansion of lung parenchyma initially (opens up extra-alveolar vessels), then (b) removal of pulmonary HPV by ↑ PAO_{2}
- Causes → ↓ PAP/RVEDP/RAP, ↑ pulmonary BF and ↑ LAP → creates haemodynamics that favour closure of foramen ovale

(v) Closure of ductus arteriosus (within 10-15 hrs post-birth) → due to VSMC contraction 2° PaO_{2} a/w 1st breaths and ↓ [PGE1/2]

- (4) Foetal lung has 20 mL/kg of fluid at term → absorbed into pulmonary circulation:
  o During vaginal delivery → 35 mL absorbed 2° to thoracic compression
  o Post-delivery → remaining fluid is absorbed 2° to ↑ PBF a/w initiation of ventilation

Aside – Foetal respiratory system:
- Bronchial tree of foetal lung fully developed at 16/40
- Type II pneumocytes present in alveolar epithelium and produces surfactant at 24/40 (Nb. ↑ surfactant with (i) ↑ cortisol or thyroxine in mother (Ie. steroids), and (ii) ↑ lecithin in amniotic fluid)
- Preacinar pattern of foetal airway, and arteries/veins formed with capillaries in alveolar wall at 28/40
- Foetal breathing movements present → irregular initially, then later regular and rapid (60 breaths/min)
To explain temperature regulation in the neonate and how this differs from the adult.

Thermoneutral zone (TNZ) of neonate:

Recall – TNZ is defined as the range of ambient temperatures in which core body temperature is maintained without an increase in metabolic rate and O₂ consumption (i.e., body heat production) above a resting level → within this zone, thermoregulation is performed only by mild changes in skin blood flow

TNZ of neonate vs adult:

- (i) Range of neonatal TNZ is higher and narrower cf. adult (see below) → this is b/c they have ↑ evaporative heat losses requiring higher ambient temperatures to maintain core body temperatures without a significant ↑ in metabolic rate
  
  | Pre-term neonate: | 35-36 °C |
  | Full-term neonate: | 32-34 °C (24-30 °C clothed) |
  | Adult: | 25-30 °C (20-22 °C clothed) |

- (ii) “Critical temperature limits” of neonatal TNZ ↓ with ↑ maturity and body side (i.e., lower limit is 35 °C if preterm, 33°C at term, 32 °C after 2/52)

Neonatal thermoregulation:

The ability to maintain a stable core body temperature with Δs in ambient temperatures depends on the ability to balance heat production and heat loss → this balance is difficult for a neonate (due to the reasons below), resulting in ↑ risk of heat/cold stress with Δ in ambient temperatures:

- (1) Large SA:volume ratio (2-3x cf. adult) → ↑ environmental heat gain and losses
- (2) Thin subcutaneous tissues (50% cf. adult) → ↓ insulating capacity and ↑ evaporative losses (esp when skin is wet) → ↑ environmental heat gain and losses
- (3) Higher TNZ (32-34 °C) → neonates have high evaporative heat losses and thus require a higher ambient temperature to maintain core body temperature without a significant rise in metabolic rate → this means they have ↑ environmental heat losses at lower ambient temperatures
- (4) Higher BMR (2x cf. adults) → significant heat loss is required to maintain thermal equilibrium (so TNZ is < body temperature) → so ↑ susceptible to heat stress (i.e., keeping a baby at 37 °C is a form of heat stress)
- (5) Limited sweating capacity (↑ susceptibility to heat stress), shivering response (↑ susceptibility to cold stress), and ability to exert direct control on environment

Mechanisms of neonatal thermoregulation:

- Within TNZ → temperature is maintained by changes in skin blood flow only → requires little ↑ in metabolic rate (or O₂ consumption)
- Cold stress → responses include:
- (i) Behavioural changes (esp crying to signal attention)
- (ii) Skin vasoconstriction
- (iii) Non-shivering thermogenesis (involving brown fat)
- (iv) ↑ muscular activity and shivering → these are NOT well developed cf. adults, and thus play a minor role

- Heat stress → responses include:
  - (i) Behavioural changes (Ie. crying, removing coverings)
  - (ii) Skin vasodilation
  - (iii) Sweating → limited role in neonates (33% effectiveness cf. adults), BUT sweating results in significant evaporative heat loss (↑ heat loss by 2x)

Aside – Non-shivering thermogenesis → SNS-mediated (β3 receptor) uncoupling of oxidative phosphorylation in brown fat and skeletal muscle → ↑ metabolic heat production without production of ATP or mechanical work

Brown fat:
- Found in newborns only (base of neck, interscapular areas, perinephric fat, around large abdominal vessels) → 2-6 % of total body weight of neonate
- Metabolically active fat tissue → contains many fat globules and mitochondria, highly vascular, and SNS-controlled (via β3 receptor) → responsible for metabolic heat production in neonates during cold stress (can ↑ metabolic rate by 2x)
- Mechanism – Uncouples mitochondrial oxidative phosphorylation so more heat is generated for a given amount of metabolism of metabolic fuels (esp FA oxidation):
  - (i) Metabolism of metabolic fuels → generates a H+ gradient across the inner mitochondrial membrane → this leads to production of heat
  - (ii) Brown fat uncouples oxidative phosphorylation by inserting channels into this membrane → dissipates the H+ gradient so no ATP is produced

Dangers of hypothermia in neonate are similar as in adults – but in neonates there is especially:
- (1) ↑ hypoxaemia due to (i) ↑ MRO₂/metabolism and (ii) ↑ respiratory distress 2° to ↓ surfactant synthesis
- (2) ↑ CVS instability (↓ C.O., BP and HR)
- (3) ↑ hypoglycaemia risk due to ↑ metabolism
- (4) ↑ delayed recovery from anaesthesia
- (5) ↑ coagulopathy
- (6) Significant alteration in PK of drugs

Dangers of hyperthermia in neonate:
- (1) ↑ evaporative water loss (due to ↑ SA:vol ratio) → ↑ dehydration
- (2) ↑ apnoeic attacks
(d) *To compare the physiological differences in organ function between neonate and adult.*

(e) *To explain the control of body fluids in the neonate and how the control and composition differ from the adult.*

Overview of physiological differences in organ function between neonates and adults:
- Before birth → foetus relies on mother for O₂, nutrition, excretion, temperature regulation and homeostasis (via the placenta)
- After birth → placental functions are taken over by the neonate’s organs → but these organs are not completely mature at birth → thus, they require continuous physiological adaptations such that they become “mature” at the end of the neonatal period

Important to note → “Neonatal period” (first 28 days of life) vs “Infancy” (1-12 months post-birth)

Organ-specific physiological differences:

(1) Cardiovascular system:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Description</th>
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| C.O.      | - C.O. very high at birth (280-430 mL/min/kg) → later ↓ to 150 mL/min/kg at 8/52 (cf. 70 mL/min/kg in adults)  
  - ↑ distribution to VRG (Ie. heart, brain, liver, kidney; 50% vs 25% in adults) → to cope with ↑ MRO₂ of metabolically active organs  
  - C.O. is dependent on HR → b/c SV is “fixed” due to a poorly compliant LV (which is a result of a ↑ % of non-contractile myocardial cells in the LV) |
| HR        | ↑ HR → 120-160 bpm at birth → gradually decreases to 100 bpm by 1 yr |
| BP        | ↓ BP → 70-90/40 mmHg at birth → ↑ gradually to 100/60-70 mmHg by 1 yr |

  - SNS system is immature → results in ↑ hypotension and bradycardia with hypoxia, and ↓ efficient response to Δ in postural BP  
  - Aortic chemoreceptors play a more vital role → prevents hypoxaemia-induced changes in haemodynamics (Ie. ↓ BP, vasoconstriction, and variable HR Δs) that is not properly compensated for by an immature SNS system  
  - Circulation remains very labile → easily reverts back to foetal circulation if there is pulmonary vasoconstriction (triggered by hypoxaemia, hypercapnoea, acidemia) causing ↑ PAP  

Others ↑ physiological shunting (20% cf. 7% in adult)

(2) Respiratory system:

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<tr>
<th>Anatomy</th>
<th>Upper AW</th>
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|         | - Large tongue and mandible angle (140° cf. 120° in adults)  
  - Narrow nasal passages (accounts for 50% of AWR)  
  - Obligate nasal breathing (cf. mouth breathing) → due to large tongue and mandible angle, and cephalad larynx → so nasal obstruction can precipitate respiratory distress! |

  - Larynx |
  - Epiglottis is stiff, long, U-shaped and angled back 45° → so straight laryngoscope blade used for intubation  
  - Glottis is situated at C3/C4 level (cf. C6 in adults) and is angulated anteriorly → so backward pressure on larynx assists intubation  
  - Cricoid ring is the narrowest part of larynx → it enlarges during puberty so vocal cord in the narrowest part in adults |

<table>
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<tr>
<th>Anatomy</th>
<th>Lower AW</th>
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|         | - Trachea is shorter (3-7 cm length) and smaller (6 mm diameter)  
  - Bronchi branch angle is similar to adults (30° R; 45° L) → risk of R endobronchial intubation remains |
- Small peripheral AWs (< 2 mm diameter) → account for remaining 50% of AWR (cf. 20% in adults)
- ↓↓↓ bronchial muscle → so bronchospasms uncommon and bronchodilator drugs have minimal response

**Chest wall**
- Ribs more horizontal → limited AP expansion (lose pump handle mechanism) and transverse expansion (lose bucket handle mechanism) → thus, minimal thoracic component to ventilation and ↑ reliance on diaphragmatic breathing
- ↓ % type I muscle fibres (highly oxidative/slow contraction) in diaphragm (25% in neonate vs 55% in adults) and IC muscles (45% vs 65%) → ↑ risk of muscle fatigue

**Lung volumes**
- FRC (30 mL/kg) → same as adult (as FRC remains 40% of TLC) BUT ↓ stable and ↑ risk of atelectasis due to following reasons:
  - (i) Significant ↓ in outward recoil of CW (as rib is cartilaginous and contains very little respiratory muscles)
  - (ii) Mild ↓ inward recoil
- TLC (75-80 mL/kg) → same as adult
- VC (45 mL/kg) → lower cf. adult (60 mL/kg)
- TV same as adult (7 mL/kg)
- ↑ CC due to low elastic recoil of lungs → in fact, CC > FRC such that there is small AW closure during tidal ventilation → results in gas trapping and hypoxaemia

**Minute ventilation**
- MV = 140 mL/kg/min (2x adult) → required to cope with ↑ MRO₂
- ↑ MV generated by ↑↑ RR (30-40/min – cf. 12-15/min in adults) rather than ↑ TV (7 mL/kg – same as adult) → this minimises “work of breathing”

**Lung mechanics**
- Compliance
  - Lung – ↑ from 1.5 to 6 mL/cmH₂O within 24 hrs post-birth. Specific compliance similar as in adult (0.05/cmH₂O)
  - Chest wall – Very compliant due to soft rib cage (allows thorax compression to assist vaginal delivery) → BUT ↑ risk of respiratory failure due to sternal retraction and restricted diaphragm movement caused by AW obstruction
- Airway resistance:
  - AWR ↓ from 90 cmH₂O/L/sec to 25 cmH₂O/L/min after 24 hrs post-birth
  - Resistance of nasal passages = 50% AWR
- End-expiratory P_{INTRAPLEURAL} ~ 0 (cf. →ve pressure in adults)
- I:E ratio ~ 1 (cf. 1.5 in adults)

**V/Q matching**
- Significant V/Q mismatch (V/Q = 0.4) due to shunting caused by small AW closure/gas trapping during tidal ventilation → thus, neonate normally has a ↓ PaO₂ 50-60 mmHg with A-a gradient of 30 mmHg
- Dead space same as in adults (2.2 mL/kg), including physiological DS (V_D/V_T = 0.3)

**Control of ventilation**
- Respiratory control less developed (cf. adults)
- Peripheral and central chemoreceptors are responsive:
  - CO₂ ventilatory response curve is shifted left cf. adult → so ventilation occurs at a ↓ level of PaCO₂
  - O₂ ventilatory response → hypoxaemia causes a transient ↑ MV (2 mins only) post-birth → sustained ↑ MV response after 1 week
  - Nb. O₂/CO₂ ventilatory responses are depressed by hypothermia
- Any ↑ in MV is achieved by ↑ TV (as RR is already ↑)
- “Hering-Breuer reflex” (transient apnoea lasting 5 secs evoked by gradual lung inflation) and “Head’s paradoxical inflation reflex” (↑ inspiratory
effort evoked by partial inflation of lungs) are prominent.
- “Periodic respiration” is common and normal (pauses lasting 5-10 sec (up to 6 x per hr during sleep) → BUT “Apnoeic spells” are abnormal (pauses > 20 secs a/w bradycardia).

O₂ flux to tissues  
- ↑ O₂ flux to tissues due to:
  - (i) ↑ O₂ carrying capacity of blood cf. adult (by 1.25x) → due to:
    - ↑ [Hb] → 170-180 g/L
    - HbF (α2γ2) → left shift in Hb O₂ dissoc’n curve 2° inability to bind 2,3-DPG (lacks β subunits) → ↑ O₂ affinity (P₅₀ = 19 mmHg)
  - (ii) ↑ C.O. (esp ↑ % to VRG)
- MRO₂  
  - ↑ resting MRO₂ (6-8 mL/kg/min → 2x adult resting MRO₂) due to ↑ metabolic rate → matched by ↑ O₂ flux to tissues
  - MRO₂ varies with ambient temperature → MRO₂ is lowest within “thermoneutral zone” → it ↑ 2x for every ↓ 2 °C
- ABG  
  - Umbilical cord blood → combined respiratory and metabolic acidosis (pH 7.26, pO₂ 20 mmHg, pCO₂ 55 mmHg)
  - After birth → pH ↑ to 7.35 (within 2/52) then later to 7.40, pCO₂ ↓ to 32-36 mmHg initially then later ↑ to 40 mmHg, pO₂ ↑ to 50-60 mmHg

(3) Haematological system:
- Haemopoiesis – Starts in utero at (i) yolk sac (from 14 days gestation), then (ii) liver (from 14 days gestation until 1 week post-birth) and (iii) BM (from 5 months gestation)
- Red cell survival – 30-40 days in utero → ↑ to 60-70 days at term
- [Hb] – Foetal and neonatal Hb is 170-180 g/L at term → ↑ further 10-20 g/L in 1st few days post-birth (due to ECF excretion) but normalises after 1 week → ↓ steadily to 110-120 g/L by 1-2/12 post-birth (due to ↓ red cell mass) and remains low until puberty where it ↑ to adult levels
- Hb type – In utero, HbF accounts for 90% of total Hb → this ↓ to 75% at birth → then ↓ gradually until it is replaced by HbA at 6/12 post-birth
- Platelets  
  - Same levels as adults, but transient and mild defect in function (due to ↓ 5-HT and adenine levels)
- Coagulation  
  - Vitamin K CF deficiency due to (i) ↓ liver synthesis (5-20% adult levels) and (ii) ↓ vitamin K stores

(4) Renal system:
- Renal blood flow  
  - ↓ RBF (5% C.O. after birth → ↑ to 10% C.O. after 1/52) due to incomplete glomerular development and renal arteriolar vasoconstriction.
  - ↑ % RBF perfuses medulla → ↑ cortical blood flow when cortical nephrons develop
- Glomerular function  
  - Neonate has incomplete glomerular development → GFR is ↓ at birth → gradually rises such that it reaches adult values at 2 yrs
- Tubular function  
  - Marrates at different rates (distal tubules mature early → then proximal tubules → then loop of Henle) → this means in neonates have:
    - Impaired ability to secrete substances from proximal tubules
    - Impaired urine concentration ability (Ie. cannot concentrate urine > 600 mosm/L in 1st week post-birth)
  - Lack of diuretic response to H₂O load (esp in 1st 48 hrs post-birth) → functional at end of 1st week (Ie. can make dilute urine)
- Body fluid compartments  
  - Neonate has a TBWV 75% of body weight, ECFV 40% of body weight, ICFV 35% of body weight (↑ cf. adults due to ↑ ECFV)
  - Few days post-birth, excess ECF is excreted → continues until 4-6/12
where ICFV = ECFV → then ICFV and ECFV continue to ↑ and ↓, respectively, until adult volumes achieved

(5) Hepatic system:
- Many liver functions are poorly developed (esp CHO metabolism and detoxification):
  o ↓ glycogen reserves (4 g/kg in neonate)
  o ↓ ability to conjugate drugs or bilirubin with glucuronide due to ↓ activity of hepatic UDP-glucuronyl transferase → enzyme activity reaches adult levels by 2/12
  o Immature liver enzyme systems → mature rapidly after birth such that they function at adult level by 3/12
  o ↓ albumin levels → synthesis starts in utero (at 12-16/40) and ↑ towards term

(6) Metabolic function:

| Foetus | - Glucose is the main metabolic substrate → essential for foetal growth |
|        |   - Mainly transferred from mother across placenta via “facilitated diffusion” (small amounts produced from a.a./fats in foetal liver) |
|        |   - Foetal BGL ~ 70% of maternal BGL |
|        | - In 3rd TM → glycogen stores and fat stores are laid down (Ie. liver and skeletal muscle glycogen stores ↑ from 9 g at 33/40 → 34 g at term) |
|        |   - MRO₂ = 4-5 mL/kg/min |

| Neonatal | - Immediate ↑ MR after birth: |
|          |   - ↑ resting MRO₂ (6-8 mL/kg/min → 2x adult resting MRO₂) → matched by ↑ O₂ flux to tissues |
|          |   - MRO₂ varies with ambient temperature → MRO₂ is lowest within “thermoneutral zone” → it ↑ 2x for every ↓ 2 °C |
|          | - Energy source is 1°ly from glucose (BGL 2.7-3.3 mmol/L at term) → can also metabolise fat/proteins |
|          | - Energy stores: |
|          |   - ↓ glycogen stores cf adult (esp if pre-term) → easily exhausted within 3-4 hrs of starvation (cf. 12 hrs in adults) → thus, ↑ risk of hypoglycaemia (a/w apnoea, seizures and cerebral injury) |
|          |   - Fat stores are important → need to mobilise them earlier during starvation cf. adults due to rapid depletion of glycogen |

(7) Nervous and neuromuscular systems:

| Brain | - Brain is large at term (10% total body weight) → weight ↑ 3x by 1 yr due to myelination and growth of dendrite processes |
|       |   - H₂O content ↓ by 1 yr (90 to 80%) |
|       |   - BBB is immature (this permits ↑ passage of drugs into brain) |
|       |   - ↑ levels of β-endorphins |

| NMJ | - End of 1° TM → peripheral muscles are innervated by motor nerves |
|     | - From 28/40 → motor nerve endings differentiate to form MEPs, BUT there are lower [ ] of ACh within NMJ (this means delayed recovery from NMBD) |