MATERNAL CHANGES

▪ *Fluids*

• blood volume increases by ~ 30%,

a. increase in plasma ~ 50% ∝ aldosterone & oestrogen

b. increase in RBC mass ~ 30%

→ decreased [Hb] & haematocrit

• plasma Na^+, K^+ and Cl^- fall slightly

• albumin, globulins & total protein increase, but plasma []n's decrease
• the albumin/globulin ratio of 1.6:1 → ~ 1:1 at term

• a hypercoagulable state exists due to,

a. an increase in clotting factors I, VII, VIII, IX, X, and fibrinogen

b. a decrease in antithrombin III

• plasma cholinesterase decreases ~ 30% and continues to fall for several weeks postpartum

▪ *Cardiovascular*

• cardiac output increases up to 40%, reaching a plateau at ~ 30/52
• this is due to;

a. an increase in SV & HR

b. decreased TPR - uterine AV shunt
- decreased viscosity

NB: net change → slight decrease in BP

• CVP changes little, except during labor and due to the effects of aortocaval compression → decreased renal & placental function
• oxygen flux increases despite the slight decrease in [Hb] and O_2 content, due to the marked increase in CO

• 2,3-DPG increases at term which improves unloading of O_2 to the foetus
• cardiac work is increased, which may → LVF when there is poor cardiac reserve
• increased blood flow to the epidural venous plexuses decreases spinal CSF volume
• this decreases the volume of LA required for epidural anaesthesia
• the valsalva maneuver during delivery may increase CSF turbulence and cephalad spread of anaesthetic ??

Uterine Circulation

• in the nonpregnant state, blood flow parallels the metabolic activity of the myometrium and endometrium, undergoing cyclic variations with the menstrual cycle
• during pregnancy, blood flow increases rapidly with the increasing uterus and foetus, producing up to ~ 20 fold increase
• early in pregnancy the O_2 extraction of the uterus is low
• therefore, some factor increases blood flow in excess of needs (? oestrogen)
• as the size, and requirements of the foetus increase >> than blood flow during pregnancy, the O_2 extraction ratio increases progressively with pregnancy
• early studies showed that just prior to parturition uterine blood flow decreased markedly
• this has now been shown to be due to aortocaval compression, and if this is avoided there is actually no change
• average blood loss during delivery;

a. vaginal delivery ~ 200 ml
b. episiotomy ~ 150 ml
c. LSCS + GA ~ 1000 ml
d. LSCS + epidural ~ 600 ml

■ ***Respiratory***

** overall ~ 50% loss of respiratory reserve

i. increased BMR
ii. increased O_2 consumption
iii. decreased FRC
iv. decreased CVS reserve
v. airway changes

• thus, on induction mothers become hypoxic quickly
• capillary engorgement $\rightarrow$ hoarse voice + greater nasal and upper airways obstruction
• therefore nasal intubation is generally avoided
• due to increased abdominal contents, the diaphragm is elevated and its maximal excursion decreased
• lung volumes decrease from about 5/52 and changes are exaccerbated by the supine position,

i. FRC decreases up to 25%
ii. RV decreases up to 25%
iii. ERV decreases up to 25%
iv. TV increases up to 25%
v. VC unchanged
vi. IRV decreases up to 25%

- the overall V/Q ratio decreases $\rightarrow$ increased P_{AO2}
- however, there is little change in P_{aO2} as the $P_{A\text{-}aO2}$ gradient increases
- increased levels of progesterone $\rightarrow$ bronchodilation and decreased airways resistance
- lung compliance is unaltered, though, chest wall compliance is increased
- minute volume is increased, increase in TV > RR

NB: P_{AO2} = 105 mmHg
P_{ACO2} = 32 mmHg

- ratio of V_D/V_T is unaltered

** importance for anaesthesia;

a. intubation - bleeding, hypoxia, difficult
b. decreased respiratory reserve - low P_{aO2} & FRC, high BMR
c. induction - rapid due to lowered MAC, low FRC, high MV

▪ ***Hepatic Function***

- LFT's show a general increase due to enzyme induction
- liver blood flow is not altered significantly

▪ ***GIT***

- tone of the lower oesophageal sphincter decreases
- in addition, tone decreases with,

a. narcotics
b. anti-ACh agents
c. diazepam

- this, together with increases in,

a. gastric emptying - decreased by pain, drugs
b. intragastric pressure - uterus, lithotomy
c. gastric acidity

NB: greatly increased risk of aspiration (Mendelson's Synd)

Endocrine

- earliest changes are increased levels of,
    a. oestrogen
    b. progesterone
    c. βhCG

- there are increases in the size of,
    a. thyroid - remain euthyroid
    b. parathyroid - PTH rises → increased Vit.D_3
    increased Ca^{++} absorption
    decreased Ca^{++} excretion
    - plasma [Ca^{++}] remains normal, the increase supplying foetus
    c. anterior pituitary → ACTH & PRL
    d. adrenals → cortisol & aldosterone

Metabolism

- increases in BMR & O_2 consumption by ~ 25% at term
- O_2 consumption increases by 100% at delivery

Acid-Base Balance

- there are small decreases in plasma levels of Na^+, Cl^-, Mg^{++}, & Ca^{++}
- plasma HCO_3^- decreases to ~ 21 mmol/l to compensate for increased ventilation
- therefore, mother has less buffer reserve

Renal

- there is a progressive increase in GFR starting early in the first trimester
- urine volume increases due to the need to excrete a greater mass of waste products, mother + foetus
- both BUN and [Cr]pl decrease due to an increased creatinine clearance
- during the 3rd trimester there may be alterations of renal function due to aortocaval compression
- generally tone decreases and volume increases in the collecting system

NB: predisposing to UTI's

FOETAL PHYSIOLOGY

Placental Circulation		
Normal Values	(* average at maturity)	Adult Comparison
Weight	500 g	
Lobules	200, each multiple villi	
Diffusion Distance	3.5 µm	c.f. 0.5 µm in lung
Surface Area	3-4 m^2	c.f. 70 m^2 in lung
P_{ma}	30 mmHg	
$Blood\ Flow_m$	600 ml/min	
$Blood\ Volume_m$	150 ml intervillous spaces	
RBC Transit Time	15 secs	
PmO_2	50 mmHg	
P_f	?	
$Blood\ Flow_f$	300 ml/min	(~ 50% of CO)
PfO_2	30 mmHg	

- the placenta is effectively the "foetal lung"
- the maternal portion is a large blood sinus, or lake, into which project the foetal placental villi
- these contain the small branches of the umbilical arteries and vein (see Ganong, fig. 32-17)
- O_2, CO_2 and nutrient exchange occur across the cellular layers covering the villi
- these are thicker and less permeable than those for the lung and exchange is considerably less efficient

▪ *Foetal Circulation (See Ganong, Fig. 32-19)*

- ~ 55% of the foetal CO supplies the placenta via the umbilical arteries, where S_{uaO2} ~ 60%
- umbilical vein S_{uvO2} ~ 80% c.f. 98% of maternal arterial blood
- of this, the majority passes through the liver, a small fraction passing directly into the IVC via the ductus venosus
- the portal and systemic venous blood of the foetus → S_{svO2} ~ 26%
- the mixed venous blood in the IVC → S_{vO2} ~ 67%
- most of the blood entering the RA from the IVC passes directly to the LA via the patent foramen ovale
- most of the blood entering the RA from the SVC passes into the pulmonary artery, then via the ductus arteriosus into the descending aorta

NB: the net effect being the head receives the better oxygenated blood

▪ ***Foetal Respiration***

• the tissues of foetal and newborn mammals have high resistance to hypoxia
• three factors aid in foetal transfer of O_2,

a. [HbF] ~ 50% greater than [HbA] → greater [O_2] ml
b. HbF binds 2,3-DPG less effectively → left shift
c. "double" Bohr effect, → HbF-CO_2 → HbA-CO_2

NB: HbF-O_2 dissociation curve lies above and to the left,

HbF-P_{50} = 19 mmHg vs. HbA-P_{50} = 26 mmHg

• the total diffusing capacity of,

a. the placenta at birth ~ 1.2 ml/O_2/min/mmHg
b. normal lung ~ 20 ml/O_2/min/mmHg

• the gamma chains of HbF have the neutral amino acid valine at 143 & 146 position
• the replacement of histidine in beta chains is the basis for the decreased binding affinity for DPG
• maternal 2,3-DPG increases near term, improving unloading of O_2 to the foetus
• HbA begins to appear around the 20th week of foetal life and at birth constitutes ~ 20% of the circulating Hb
• no HbF is formed after birth and by 4 months > 90% is HbA

• as CO_2 is 20x more diffusable and []n gradient is high, diffusion does not present a problem
• maternal P_{CO2} is reduced by hyperventilation of pregnancy

Normal Values	**Maternal**	**Foetal**
Hb concentration	12 g/100ml	18 g/100ml
Blood flow	600 ml/min	300 ml/min
Uterine/Umbilical aa.		
• P_{aO2}	95 mmHg	15 mmHg
• SaO_2	97%	58%
• P_{aCO2}	35 mmHg	48 mmHg
Uterine/Umbilical vv.		
• P_{O2}	33 mmHg	30 mmHg
• SvO_2	50%	80%
• thus the maternal capillary blood P_{50} = 33 mmHg		

- ***Double Bohr Effect***

  a. HbF loses CO_2 shifting its dissociation curve to the left

  b. HbA gains CO_2 shifting its dissociation curve to the right

  → increases the gradient for oxygen diffusion

- ***Foetal Oxygen Extraction***

  Q_{fO2} ~ (80-60)/100 . (18g x 1.37) . (300/100 ml/min)
  ~ 15 ml.O_2/min

- ***Placental Oxygen Extraction***

  Q_{pO2} ~ (97-50)/100 . (12g x 1.37) . (600/100 ml/min)
  ~ 46 ml.O_2/min

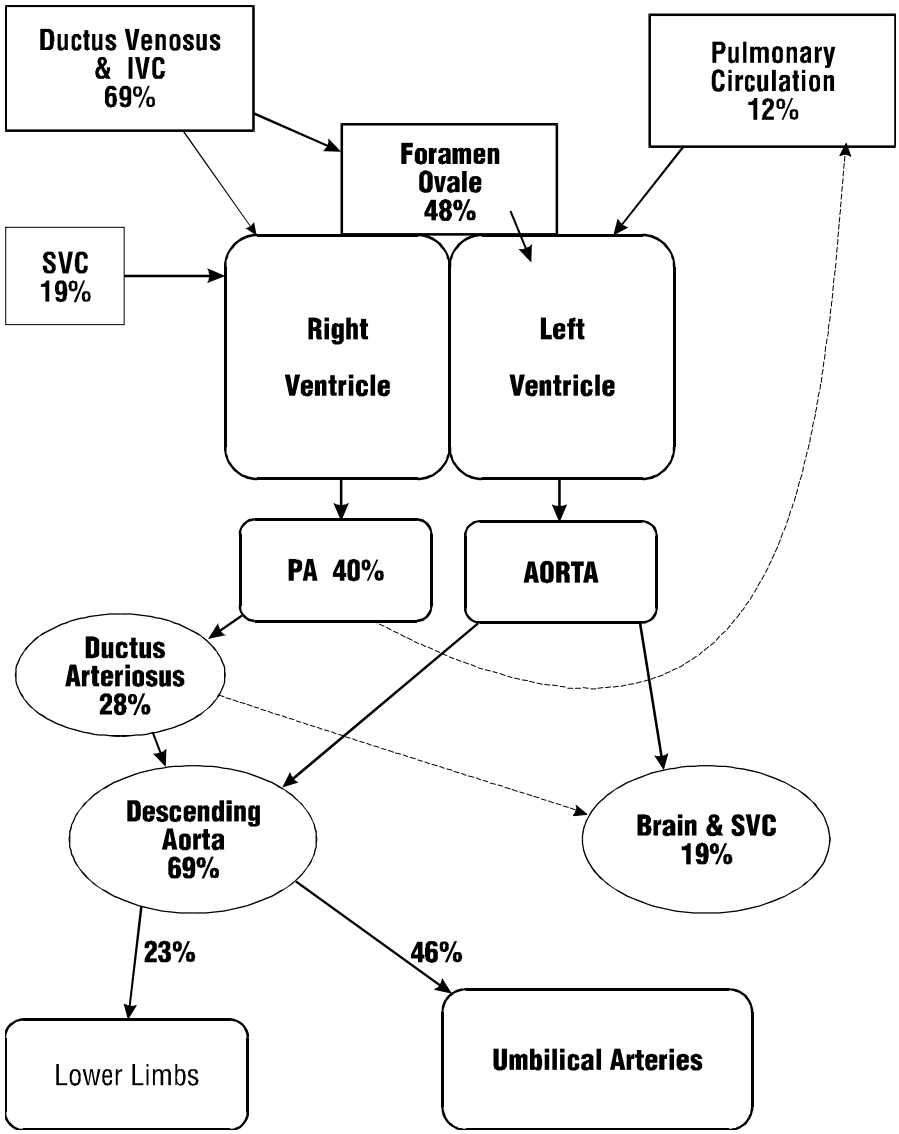
  NB: the foetus uses only ~ 1/3 of the placental MRO_2

- ***Other Placental Functions***

a.	active nutrient absorption	- where $[x]_F > [x]_M$ - amino acids, Cr, PO_4
b.	metabolism	- various drugs by MFO's and Plasma-ChE
c.	metabolic functions	- stores Pr., Fe, Ca^{++} - acts ~ liver early until foetal liver est.
d.	hormone synthesis	- βhCG - oestrogen - progesterone - hPL

NEONATAL PHYSIOLOGY

- ***Distribution of the Foetal Cardiac Output***



Circulatory Changes at Birth

• umbilical vessels have thick, muscular walls that are extremely reactive to trauma, tension, catecholamines, bradykinin, angiotensin and changes in P_{O2}
• closure of these vessels → increase in foetal TPR and BP
• when flow through the umbilical vein ceases, the ductus venosus closes by an unknown mechanism
• asphyxia from the cessation of placental circulation and cooling of the body

→ activation of the respiratory centre of the newborn

• with inflation of the lungs, pulmonary vascular resistance falls to about $1/10^{th}$ of its intrauterine value
• this is not caused by the presence of O_2, as inflation with N_2 produces the same decrease in resistance
• the LA pressure rises above that of the RA and IVC due to;

a. decrease in pulmonary resistance → increased LA filling
b. decreased RA filling due to occlusion of the umbilical vein
c. increased LV afterload due to closure of the umbilical arteries

→ abrupt closure of the foramen ovale & fusion in several days

• pulmonary arterial pressure falls to 1/2 of its intrauterine value → 35 mmHg
• this change, plus the increase in aortic pressure, reverses flow through the ductus arteriosus
• however, within minutes the ductus begins to close producing turbulent flow

→ "murmur of the newborn"

• closure of the ductus is usually complete 1-2 days after birth, and appears to be initiated by the raised $_{PaO2}$
• possible mediators being prostaglandins, bradykinin, or adenosine
• at birth, the two ventricles are about the same weight, having been pumping in parallel in the foetal circuit
• the arterioles of the pulmonary circuit are thick and muscular, maintaining the high pulmonary vascular resistance during foetal life
• after birth, the RV fails to grow to the same extent as the LV, the later becoming predominant and the muscular layer of the pulmonary vessels is lost
• these changes take several weeks

Respiratory Changes at Birth				
Normal Values	At Birth		Adult	
Respiratory Rate	**30-40**[1] **bpm**		15	bpm
Tidal Volume, TV	7.0	ml/kg (~ 20 ml)	same	(~ 500 ml)
Minute Volume, V_M	**230**	**ml/kg/min**	70	ml/kg/min
Vital Capacity, VC	40	ml/kg	50-60	ml/kg
FRC	27-30	ml/kg	30	ml/kg
Physiological V_D/V_T	0.3-0.5		0.3	
Physiological Q_S/Q_T	**0.1**	(10%)	0.01-0.03 (1-3%)	
Lung Compliance, Specific	0.067 67	l/cmH_2O/l ml/cmH_2O/l	same	
Lung Compliance, Absolute	**0.005** **5**	**l/cmH_2O** **ml/cmH_2O** ~ 1/20th adult	0.100 100	l/cmH_2O ml/cmH_2O
Compliance, chest wall	**0.26** **260**	**l/cmH_2O/l** **ml/cmH_2O/l** ~ 5x adult	0.06 60	l/cmH_2O/l ml/cmH_2O/l
Total Pulmonary Resistance	**30-50**	**cmH_2O/l/s** ~ 10x adult	4-5	cmH_2O/l/s
Mean Time Constant (tau)	0.12 s		0.5 s	
PaO_2 (NB: Q_S/Q_T)	65-80	mmHg	98	mmHg
$PaCO_2$	34	mmHg	40	mmHg
O_2 consumption	**7.0** (thermoneutral)	**ml/kg/min**	3.5	ml/kg/min
Airways Resistance:	• high, proportional to $1/r^4$ • obligate nose breather			
Compliance:	• similar in infants/adults → ***increased work of breathing***			

[1] the increased RR acts to decrease the work of breathing, increased due to
a. lower compliance of chest wall
b. the higher oxygen consumption

Respiratory Changes At Birth

Element	Appearance	Maturation
bronchi	16/52	~ 23/52
alveoli	17/52	post-partum
surfactant	24/52*	~ 36/52

* composition is different and production is unstable until 36/52
L/S ratio increases to 2:1 at term
production is ***decreased*** with stress, hypoxia, acidosis, etc.

- production is decreased with stress, hypoxia, acidosis, etc.
- stimulus to first breath includes circulatory changes, (raised TPR), and physical stimuli such as cold, pain, voices, etc.
- with the first gasps against the low compliance, lung PIP reaches -60 cmH_2O
- however this rapidly decreases as the lung expands and compliance increases

Intubation

- poor tone of the neck muscles and the large head $\rightarrow$ "floppy"
- high position of the larynx
- "V-shaped", highly mobile epiglottis
- the cricoid area is narrow, therefore use uncuffed tubes
- the trachea only 4 cm long, therefore tube easily dislodged, or positioned in right main bronchus
- relatively large nose $\rightarrow$ nasal and oropharyngeal airways ~ the same diameter

- ***Renal Changes***

Normal Values	**Neonate**	**Adult**
GFR • ***premature*** • at birth • at 1 month	10-20 ml/min/m^2 0.7-0.8 ml/min/m^2 1-2 ml/min/m^2 50 ml/min/m^2	60-80 ml/min/m^2 (70kg → 1.7m^2)
Maximum Urine Concentration	450-600 mosmol/l	1400 mosmol/l
Plasma Creatinine	• maternal at birth[1] • infant ~ 18-35 µmol/l • child ~ 30-60 µmol/l • youth ~ 45-90 µmol/l	• male ~ 55-120 µmol/l • female ~ 45-95 µmol/l • pregnant ~ 30-80 µmol/l
pH	7.35	7.4
[HCO_3^-]	20 mmol/l	25 mmol/l

[1] decreases due to low muscle mass and high rate of anabolism

• the renal cortex is relatively underdeveloped at birth
• this reaches maturity by 12-18 months
• urea excretion is always low due to protein anabolism
• there is limited excretion/conservation capability of the kidney for salt, water and acid-base alterations
• renal drug excretion is decreased, eg. tubular secretion of penicillin is low due to underdeveloped active tubular transport systems

- ***Fluid Requirements***

Body Compartment Volumes			
Normal Values	Premature	Term	Adult
Total Body Water	80%	75%	55-60%
ECF ICF	45% 35%	40% 35%	20% 40%
Blood Volume	90-100 ml/kg	85 ml/kg	~ 70 ml/kg
H_2O/day - at 1 day - at 1 week[1]		50 ml/kg/d 150 ml/kg/d	

[1] increases until 6/52, then decreases to adult values

- ***Daily Calculation Of Fluid Requirements***

Weight	Water Requirement[1]	Cumulative Total
0 to 10 kg	100 ml/kg	1000 ml
10 to 20 kg	50 ml/kg	500 ml
20 & over	20 ml/kg	??[2]

[1] daily kcal can be substituted in the same formula

[2] → 2500 ml for a 70 kg male

Temperature Regulation

- ***Deficits In Regulation:***

a. minimal hypothalamic control of - cutaneous vasomotor tone
- sweating

b. high SA/weight ratio ~ 2x adult

c. high evaporative losses - high RR & MV

d. inability to take evasive action

- ***Gains In Regulation:***

= posses "brown fat" → heat production by the uncoupling of oxidative phosphorylation in increased number of mitochondria

- this is present in the neck, back, axillae, inguinal regions and around the kidneys
- activity is mediated by the action of NA on β-receptors
- this requires an increased O_2 consumption ~ 60%
- neither neonates, nor adults, can temperature regulate via white fat

NB: → neonates must be kept in ***thermoneutral zone***

~ 32-35 °C naked, or
~ 24 °C clothed