MATERNAL PHYSIOLOGY

(a) ***To explain the cardiovascular and respiratory changes during pregnancy, their causes, and their consequences.***

(b) ***To explain the consequences of the supine posture during pregnancy.***

(c) ***To outline the functions of the placenta.***

(d) ***To describe the transfer of gases between mother and foetus including the double Bohr and Haldane effects.***

(e) ***To describe the endocrine changes that occur during pregnancy and their consequences.***

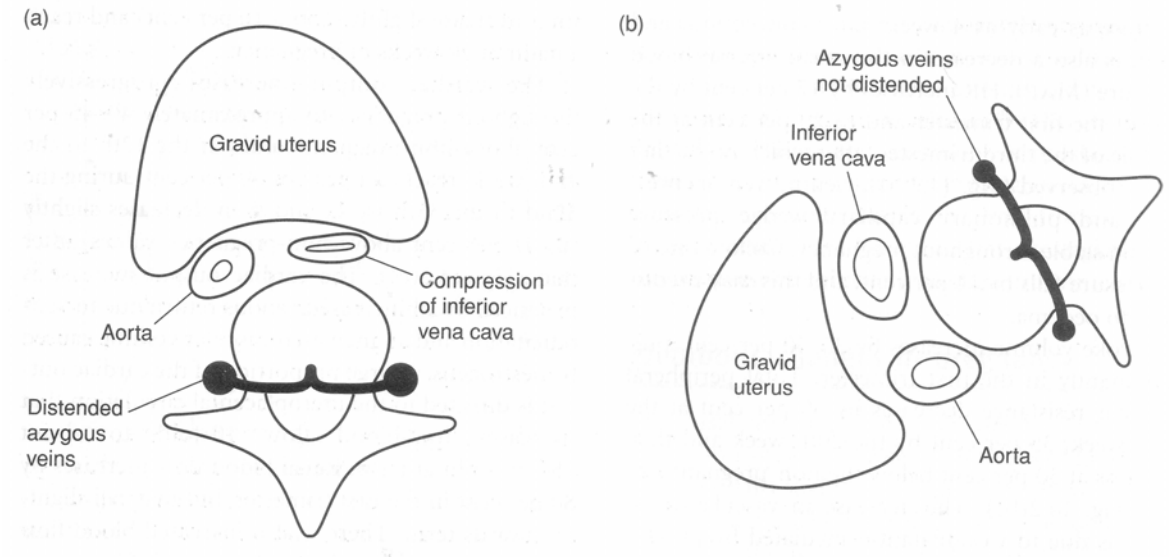
(f) ***To describe the haematological changes with pregnancy.***

(I) **<u>Maternal Physiological Changes During Pregnancy</u>**:

> Important to note → Physiological changes occur in pregnancy due to 4 key factors:
> - (1) Hormonal changes (Eg. progesterone, oestrogen, HPL, hCG)
> - (2) Mechanical effects of enlarging uterus
> - (3) ↑ metabolic demands (Eg. MRO_2 ↑ by 20% at term)
> - (4) Placental circulation acting as low pressure AV shunt

<u>CVS changes during pregnancy</u>:

- (1) ↑ HR (by 15% at end of 1st TM → then by 25% by mid 3rd TM)
- (2) ↑ SV (by 20-30% from 8/40 to 32/40) → due to ↑ BV (40%)
- (3) ↑ C.O. (by 30% from 8/40 to 32/40) → due to ↑ HR, ↑ SV (a/w ↑ BV), ↓ TPR (a/w ↑ VR), and ↑ MRO2
- (4) ↓ SVR (by 20-30% by end of 1st TM) → due to (i) placental circulation (10% of C.O.) acting as a low resistance AV shunt, and (ii) progesterone and PG-mediated peripheral vasodilation (esp renal, splanchnic, heart, breasts, skin circulation)
- (5) ↓ PVR (by 35% by end of 1st TM) → due to progesterone/prostaglandins
- (6) ↑ tissue blood flow (esp to uterus/placenta, heart, kidneys, GIT, breasts, skin) → due to (i) ↑ C.O. and (ii) hormone-mediated regional vasodilation – Nb. CBF is NOT affected!!!
- (7) ↓ BP (↓ MAP, ↓ DBP > ↓ SBP) by 10% (esp at 20/40) due to ↓ SVR → BUT this normalizes towards term
- (8) CVP and PCWP unchanged
- (9) Aortocaval compression
    - Abdominal aorta and IVC may be occluded by effects of gravid uterus as early as 2nd TM (max. effect at 36-38/40), especially when supine → characterised by:
        - (i) Complete compression of IVC:
            - 85% of ♀– Compensatory vasoconstriction, tachycardia and collateral blood flow (venous return diverted via paravertebral and epidural veins into azygous system → SVC) maintains VR/C.O. and MAP
            - 15% of ♀ – "Supine hypotension syndrome" occurs as compensatory mechanisms are insufficient → results in ↓ VR/C.O. and MAP → causes hypotension, bradycardia, pallor, syncope, N/V, sweating
        - (ii) Partial compression of abdominal aorta → causes ↓ uteroplacental BF by 20% (causing foetal distress) and ↓ renal BF
    - This is prevented by positioning mother on left side



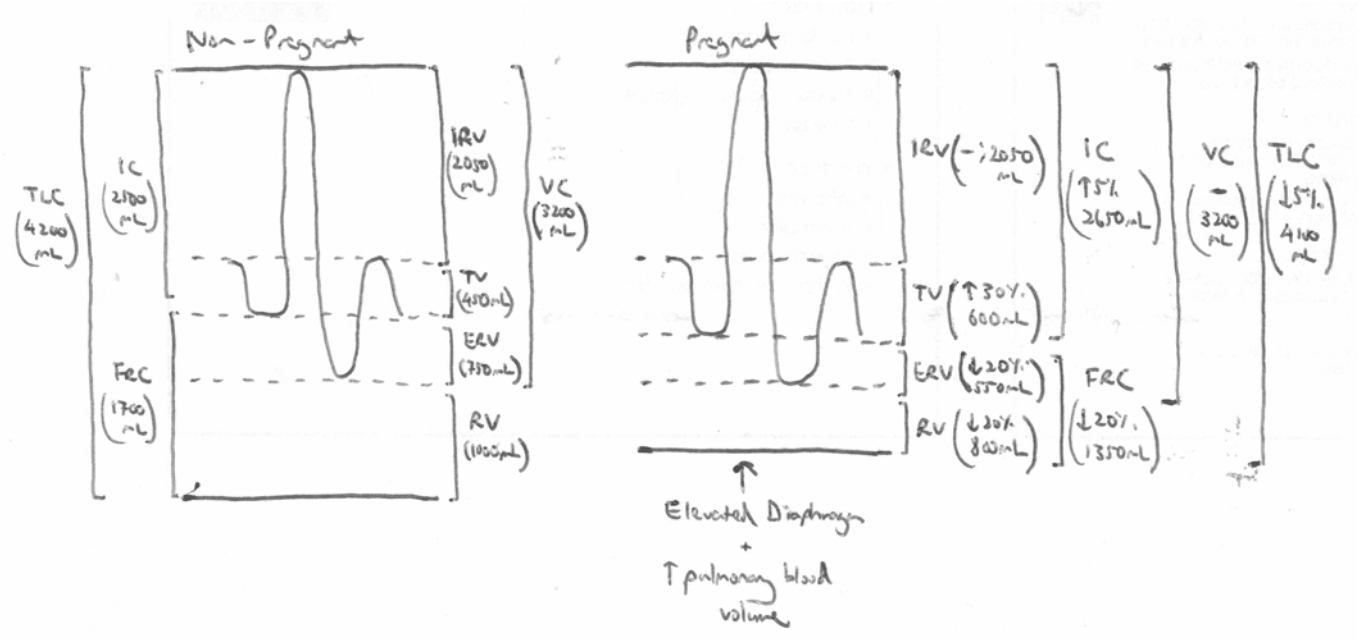
Note – During labour:

- (i) C.O. – ↑ 15% (early labour),↑ 30% (1st stage), ↑ 45% (2nd stage), ↑ 65% (post-partum), then normalizes 2/52 post-partum
- (ii) Uterine contractions and uterine involution post-partum squeezes 300 mL of blood out of uterus into circulation ("Autotransfusion") causes ↑ VR → ↑ SV/C.O.
- (iii) BP – ↑ 10-20 mmHg with uterine contractions. Normalises 2/52 post-partum
- (iv) CVP ↑ (4-6 cmH_2O) due to ↑ VR a/w autotransfusion

<u>Respiratory changes during pregnancy</u>:

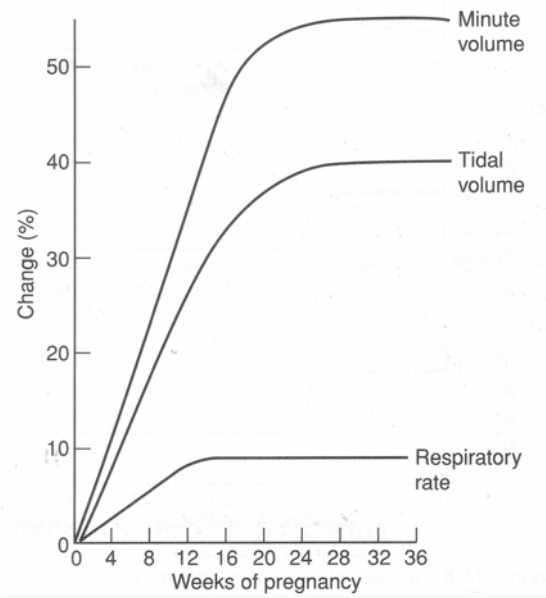
- (1) Anatomical changes to thorax and airway:
  - (i) Diaphragm displaced up 4 cm by gravid uterus → but contractility not markedly restricted
  - (ii) ↑ AP and transverse diameter by 2-3 cm (so ↑ circumference by 5-7 cm) → due to "Relaxin" (from corpus luteum) that relaxes ligaments of ribs
  - (iii) Upper respiratory tract (Ie. vocal cords, nasal mucosa) swollen → due to capillary engorgement
- (2) Changes in lung volumes:
  - Occur early in pregnancy and continue to change progressively during pregnancy (esp from 20/40) → normalize 2-5 days post-partum
  - ↓ ERV and RV (incl FRC and TLC) → due to (i) elevated diaphragm (2° gravid uterus) and (ii) ↑ pulmonary blood volume

IRV (u/c; 2050 mL)	IC (↑ 5%; 2500 to 2650 mL)	VC (u/c; 3200 mL)	TLC (↓ 5%; 4200 to 4100 mL)
TV (↑ 30%; 450 to 600 mL)			
ERV (↓ 20%; 750 to 550 mL)	FRC (↓ 20%; 1700 to 1350 mL)		
RV (↓ 20%; 1000 to 800 mL)			



Note – FRC ↓ by 70% of sitting value when supine (due to effects of gravid uterus on diaphragm)

- (3) ↑ minute and alveolar ventilation:
  - ↑ early (esp after 10/40) and continues to ↑ gradually during pregnancy (↑ by 50-70% at term) → due to (i) ↑ TV (by 40% at term) and (ii) ↑ RR (by 15% at term)
  - Caused by progesterone-mediated stimulation of medullary respiratory centres → ↑ sensitivity to $PaCO_2$ (left shift in CO_2 response curve)



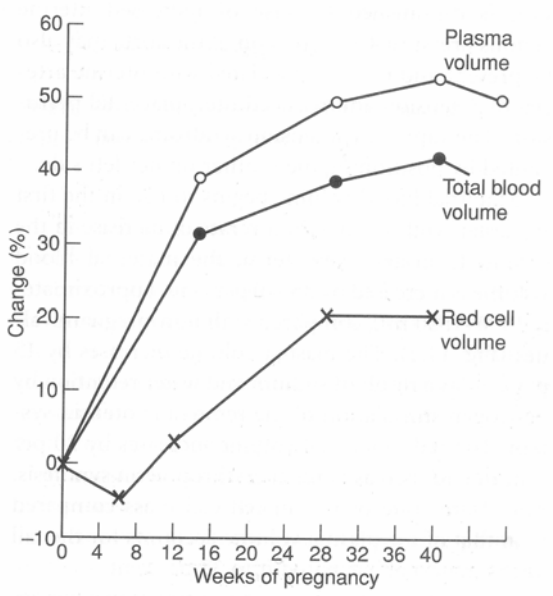
  - During labour – ↑ MV/AV further (by 160%) due to pain and ↑ MRO_2 a/w uterine contractions → can cause transient ↓ $PaCO_2$ (to 20 mmHg!)
- (4) ABG changes:

	Normal ABG	Pregnancy ABG	Important points
pH	7.40	7.42	- ↑ MV (esp at end of 1st TM → causes (i) ↓ PCO_2 and (ii) ↑ PO_2 → this creates favourable pressure gradients of O_2/CO_2 across placenta for exchange with foetus! - ↓ PCO_2 causes a respiratory alkalosis BUT Δ pH is compensated renally (by ↑ HCO_3^- excretion/↓ BE) → this prevents a shift in Hb ODC (despite ↓ PCO_2) BUT ↓ maternal buffering capacity - ABG changes normalize rapidly post-partum
PCO_2 (mmHg)	40	30	
PO_2 (mmHg)	95	105	
HCO_3^- (mmol/L)	24	20	
BE (mmol/L)	0	-2	

- (5) Changes in lung mechanics:
  - (a) Work of breathing unchanged → due to balance b/t (i) Non-elastic forces (↓ AWR) and (ii) Elastic forces (↓ total compliance of respiratory system)
  - (b) ↓ AW resistance (by 35%) and ↑ anatomical DS (by 45%) → due to progesterone-mediated large AW dilation
  - (c) ↓ total compliance of respiratory system → due to ↓ CW compliance 2° to elevation of diaphragm by gravid uterus (Nb. lung compliance is unchanged)
  - (d) F-V curves unchanged (while sitting)
  - (e) AW closure (and atelectasis) when supine only → up to 50% ♀ have FRC < CC when supine (otherwise FRC remains > CC when sitting)
- (6) ↑ tissue O_2 delivery to tissues:
  - ↑ O_2 flux (by 10% at term) → due to (i) ↑ C.O. (main), (ii) ↑ PO_2, and (iii) ↑ tissue BF (a/w regional vasodilation) → despite limitations in $CaCO_2$ by (i) Anaemia of

pregnancy, (ii) Right shift in Hb ODC (due to ↑ 2,3-DPG), and (iii) Hb being maximally saturated
    - ↑ tissue MRO_2 during pregnancy (by 20% at term)

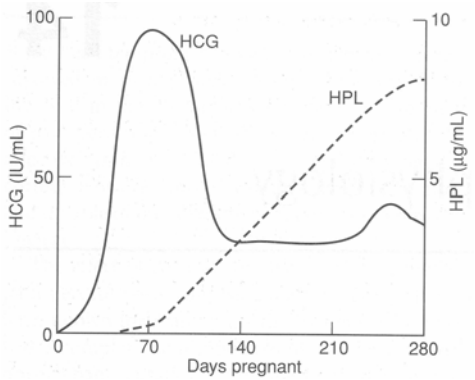
Haematological changes during pregnancy:
- (1) Physiological anaemia of pregnancy:
    - From 6-8/40 to 28-32/40 → ↑ BV by 40% (1.2-1.5 L) due to (i) ↑ PV by 50% (due to Na^+/H_2O retention by oestrogen activation of RAAS) and (ii) ↑ RCV by 30% (due to renal EPO synthesis)
    - BUT ↑ PV > ↑ RCV and ↑ PV occurs faster than ↑ RCV → thus, ↓ RBC count (4.6 to 3.6 x $10^6/mm^3$), ↓ Hb (140 to 120 g/L) and ↓ Hcrit (41 to 35%) by 28-32/40

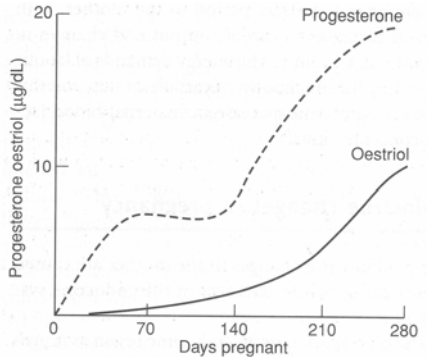


- (2) ↓ platelets (5-20%) due to haemodilution (can result in gestational thrombocytopaenia
- (3) ↑ WCC (9000/mm^3) due to ↑ PMNL and monocytes
- (4) Acquired hypercoagulable state → prepares for blood loss at delivery
    - ↑ coagulation – ↑ CF VII, VIII, IX, X, XII and fibrinogen, but ↓ ATIII → ↓ APTT/PT (20%) and bleeding time (10%)
    - ↑ fibrinolysis – ↑ plasminogen and fibrin/FDP formation, but ↓ tPA and CF XIII (fibrin-stabilising factor)
- (5) ↑ total amount of proteins BUT [ ]'s are variable:
    - ↓ [ ] – Total proteins, γ-globulins and albumin → due to haemodilution
    - ↑ [ ] – Total globulins (esp α and β-globulins), fibrinogen and CRP
- (6) ↓ plasma oncotic pressure (14%) due to ↓ [albumin] → ↑ oedema
- (7) ↑ ESR due to ↑ plasma globulin/fibrinogen
- (8) ↓ pseudocholinesterase activity (20-30%) at end of 1st TM

Endocrine changes during pregnancy:
- (1) Placenta produces 4 hormones:
    - (i) Human chorionic gonadotrophin (hCG)
        - Peptide hormone synthesized by syncytiotrophoblast cells) → ↑ until it peaks at 10-12 weeks, then ↓ till term
        - Role – Maintains corpus luteal function during 1st TM (oestrogen and progesterone production) that maintains pregnancy until placenta takes
    - (ii) Human placental lactogen (hPL)

        - Peptide hormone → ↑ throughout pregnancy and it peaks near term
        - Role – Promotes foetal growth by regulating maternal metabolism → secretion is ↑ by ↓ maternal BGL → exerts "insulin antagonist" effect (favours lipolysis and FFA usage in mother to spare glucose for use in foetus)
    - (iii) Oestrogen and progesterone
        - Steroid hormones produced by corpus luteum in 1st TM and then the placenta using precursors derived from foetal adrenal cortex → levels ↑ gradually until term
        - Role – Responsible for several maternal physiological changes





- (2) Pituitary gland:
    - ↑ PRL, ↑ ACTH, ↑ MSH
    - ↓ GH (by HPL) and ↓ FSH/LH (by oestrogen/progesterone)
- (3) Others:
    - ↑ cortisol (due to ACTH)
    - ↑ renin/AII and ↑ aldosterone (due to ACTH/progesterone)
    - ↑ T3/T4
    - ↑ PTH (due to Ca^{2+} transfer to foetus)
    - ↑ prostaglandins (PGA ↑ in 1st TM; PGE ↑ in 3rd TM)

<u>Metabolic changes during pregnancy</u>:

- (1) ↑ BMR and MRO2 by 20% at 36/40, then ↓ to 15% above baseline at term → due to ↑ demands of foetus, hypertrophy of maternal tissues (breast/uterine), ↑ cardiorespiratory work a/w pregnancy
- (2) Metabolism of metabolic fuels
    - (a) CHO
        - ↑ BGL due to ↑ HPL (causes ↓ insulin sensitivity/glucose intolerance due to "insulin antagonist" effects), ↑ cortisol, ↑ oestrogen/progesterone → causes ↑ placental glucose transfer for foetal use, gestational DM and glycosuria
        - ↑ insulin levels from end of 1st TM to 32/40, then ↓ to baseline at term → due to ↑ BGL
    - (b) Fat
        - Fat is stored in 1st half of pregnancy (for use later in pregnancy)→ ↓ plasma [ ] of FFA/glycerol, cholesterol and phospholipids
        - Fat is mobilized in 2nd half of pregnancy (due to ↑foetal growth in 3rd TM) → ↑ plasma [ ] of FFA/glycerol, cholesterol and phospholipids → ↑ placental transfer for foetal use (esp fat synthesis in foetal liver)
    - (c) A.a. → ↓ maternal plasma [a.a] due to ↑ hepatic gluconeogenesis (to ↑ BGL), placental transfer for foetal use (energy/protein synthesis) and urinary losses

- (3) ↑ maternal weight → due to ↑ uterine/breast tissue mass (progesterone/oestrogen), ↑ ECFV (by 3 L at term), and ↑ fat stores (3 kg)

GI changes during pregnancy:
- (1) ↑ gastro-oesophageal reflux (all 3 trimesters) due to:
  - (a) Incompetent LOS function → (i) ↓ LOS tone (progesterone, narcotics, anticholinergics, diazepam) and/or (ii) changes in angle of gastro-oesophageal junction by pressure effects of gravid uterus
  - (b) ↑ IGP (gravid uterus effect)
- (2) ↓ GI motility
  - (a) ↓ gastric motility and emptying at 12-14/40 (end of 1st TM) due to progesterone-mediated GI SM relaxation (4-8 hrs) → during labour, gastric emptying esp prolonged (4-8 hrs) due to anxiety, pain, narcotic effects
  - (b) ↓ intestinal motility due to effects of progesterone and ↓ motilin
  - (c) ↓ GB contraction (2nd and 3rd TM) due to progesterone-mediated ↓ in CCK
- (3) ↑ gastric acid volume (> 25 mL) and acidity (pH < 2.5), esp during 3rd TM and labour → due to ↑ gastrin (by placenta)
- (4) Cephalad displacement of stomach/intestines by gravid uterus → ↑ IGP
- (5) Hepatic changes:
  - HBF unaltered during pregnancy
  - Fatty changes, glycogen depletion, lymphocytic infiltration, SER proliferation (↑ CYP450 activity) and ↑ ALP levels

Renal changes during pregnancy:
- (1) ↑ GFR (50%) and RBF (75%) during 1st TM due to ↑ C.O. → a/w ↓ plasma [ ] of urea and creatinine in 1st and 2nd TMs
- (2) Glycosuria → due to ↑ GFR, ↑ BGL and ↓ renal threshold (↓ tubular reabsorption)
- (3) Proteinuria (due to ↑ renal venous pressure ↓ renal threshold (↓ tubular reabsorption)) and ↑ excretion of a.a. (due to ↑ plasma [a.a.])
- (4) ↑ HCO_3^- excretion (plasma [ ] 18-21 mmol/L; BE -2) → compensation for respiratory alkalosis
- (5) ↑ RAAS effects on kidneys
- (6) Dilation of renal pelvis, calyces and ureters (from 2nd/3rd month of pregnancy) → due to obstruction of urine flow by gravid uterus

CNS changes during pregnancy:
- (1) Analgesia from β-endorphins and enkephalins (from placenta) → levels ↑ significantly with uterine contractions during labour/delivery
- (2) ↑ sedation due to progesterone
- (3) ↑ EDV engorgement due to ↑ IAP → ↑ pressures to + 1 cmH_2O during pregnancy, + 4-10 cmH_2O during labour, up to + 60 cmH_2O when bearing down
- (4) CSF unaltered during pregnancy (but ↑ 70 cmH_2O when bearing down)

Musculoskeletal changes during pregnancy:
- Relaxin from placenta → causes ligament relaxation and lumbar lordosis

(II) **<u>Anaesthetic Implications of Maternal Physiological Changes</u>**:

(1) ↑ risk of hypoxaemia and desaturation:
- (a) ↓ maternal O_2 reserve due to – (i) ↓ FRC (by 20% at term), and (ii) ↑ MRO_2 (by 20% at term) a/w ↑ metabolic rate → causes rapid desaturation/hypoxaemia (even with brief period of apnoea) → thus, very good preoxygenation is required prior to a GA!
- (b) Difficult intubation due to anatomical changes (Ie. UAW swelling, large breasts) → risk of prolonged period of apnoea → risk of desaturation/hypoxaemia

(2) Changes in anaesthetic requirements:
- GA:
  - (a) Rapid induction/recovery from volatile anaesthesia due to ↑ wash-in/wash-out → (i) ↑ alveolar ventilation (by 50-70% at term) and (ii) ↓ FRC (by 20% at term), although this is partly offset by ↑ C.O. (by 30-40% at term)
  - (b) ↓ dose of anaesthetic agents → (i) MAC ↓ 40% (due to progesterone/β-endorphins, (ii) ↓ induction dose of STP by 35% (due to ↑ Vd and elimination), (iii) ↑ sensitivity to vecuronium (as ED_{50} ↓ by 50%)
- Neuraxial block:
  - (a) ↓ LA dose required (by 25-30% at any stage of pregnancy) due to → (i) ↑ spread of LA (esp at 2nd TM due to distension of EDV), (ii) ↑ sensitivity of nerve fibres to LA, and (iii) ↑ diffusion of LA to membrane receptor sites
  - (b) ↑ risk of bloody tap due to distension of EDV (esp during contractions)

(3) Risk of aorto-caval compression:
- Abdominal aorta and IVC may be occluded by effects of gravid uterus as early as 2nd TM (max. effect at 36-38/40), especially when supine → characterised by:
  - (i) Complete compression of IVC:
    - 85% of ♀– Compensatory vasoconstriction, tachycardia and collateral blood flow (venous return diverted via paravertebral and epidural veins into azygous system → SVC) maintains VR/C.O. and MAP
    - 15% of ♀ – "Supine hypotension syndrome" occurs as compensatory mechanisms are insufficient → results in ↓ VR/C.O. and MAP → causes hypotension, bradycardia, pallor, syncope, N/V, sweating
  - (ii) Partial compression of abdominal aorta → causes ↓ uteroplacental BF by 20% (causing foetal distress) and ↓ renal BF
- This is prevented by positioning mother on left side

(4) ↑ aspiration risk during GA:
- (a) ↑ gastro-oesophageal reflux (all 3 trimesters) due to → (i)↓ LOS tone (progesterone, narcotics, anticholinergics, diazepam), (ii) ↑ IGP (effect of gravid uterus) and (iii) altered gastro-oesophageal junction angle (due to effects of gravid uterus)
- (b) ↓ GI motility/emptying (at 12-14/40; end of 1st TM) due to progesterone → prolonged further during labour (by 4-8 hrs) due to anxiety, pain, narcotics
- (c) ↑ gastric acid volume (> 25 mL) and acidity (pH < 2.5), esp during 3rd TM and labour → due to ↑ gastrin (by placenta)
- (d) Difficult intubation due to anatomical changes

(III) **Physiology of the Placenta**:

Functions of the placenta:

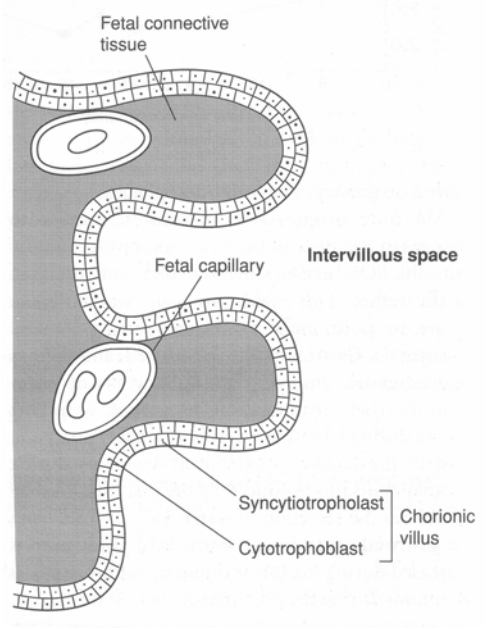
- (1) Endocrine organ of pregnancy → produces hCG, HPL, oestrogen, progesterone (see above for details)
- (2) Immunological function
    - (a) Immunological barrier function
        - Protects foetus from rejection by maternal immune system
        - Mechanism – (i) Inability of trophoblasts to present Ag to maternal lymphocytes (as they do not express MHC), (ii) Acquired defects in maternal immunocompetence
    - (b) Protects foetus from infection
        - Permits transport of maternal IgG to foetus (Nb. IgG is the ONLY Ab class that can cross placenta) → provides passive immunity to foetus for first few months post-birth
        - Mechanism – Syncytiotrophoblast contains receptors for Fc fragment of IgG → IgG is endocytosed into a vesicle → then released into foetal blood

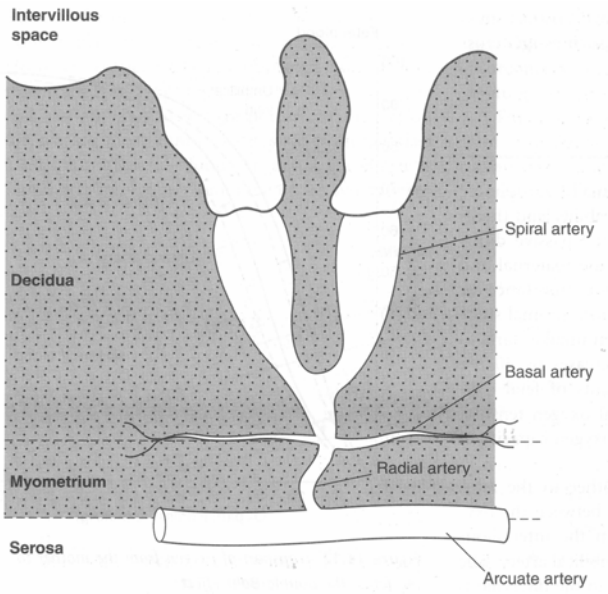
> Note – Issues:
> - (i) Rh isoimmunisation – Maternal Ab against foetal RBC can cross placenta → cause foetal haemolysis
> - (ii) Foetal autoimmune diseases (Eg. myasthenia gravis, thrombocytopaenia, thyroid diseases) can occur as maternal autoimmune IgG Ab's can cross placenta

- (3) Transport substances b/t maternal and foetal plasma
    - Gas exchange (O_2/CO_2), nutrient transfer (glucose, a.a., lipids, vitamins), wastes removal (urea/bilirubin), H_2O/electrolyte exchange and drug transfer across placental barrier via various transport mechanisms (see below for details)
- (4) Metabolic functions → synthesizes glycogen, FA, cholesterol and various enzymes (Eg. sulfatase, pseudocholinesterase, ALP, MAO and COMT)

Anatomy of the placenta:

- "Chorionic villus" is the basic structural unit of the placenta → it is a vascular projection of foetal tissue that is bathed by maternal blood within the "Intervillous space". It consists of:
    - (i) Foetal connective tissue containing foetal capillaries
    - (ii) Chorion → outermost layer of foetal tissue that is made of 2 layers → (a) Syncytiotrophoblast (directly contacts maternal blood in intervillous space) and (b) Cytotrophoblast (b/t syncytiotrophoblasts and foetal CT)





Important to note – Substances traverse between foetal and maternal blood via the following layers: Maternal blood (intervillous space) ↔ Chorion (2x layers of trophoblasts) ↔ Foetal connective tissue ↔ Endothelium of foetal capillaries ↔ Foetal blood

- Uteroplacental blood supply:
  - Uterine and Ovarian arteries → form Arcuate arteries → form Radial arteries that arise and penetrate myometrium
  - Radial arteries then divide into → (i) Spiral arteries (ejects blood into intervillous space), and (ii) Basal arteries (supply myometrium and deciduas)
  - Maternal blood within "Intervillous space" bathes the chorionic villi → then drains into venous openings that lead into the Uterine veins
- Foetal blood flow in chroionic villi → derived from paired Umbilical arteries → flows into capillaries within chorionic villi → then into Umbilical vein

Aside – Efficiency of foetal-intervillous blood flows:
- Should act as an efficient "counter-current system" (Ie. flow on both sides run in opposite directions) → BUT due to shunting it is no more efficient than a "concurrent system" (Ie. flow on both sides run in same direction)
- This inefficiency in placental barrier transfer is attenuated by maternal blood flow being 2x > than umbilical blood flow

<u>Factors determining placental transfer of substances</u>:
- (1) Mechanism of placental membrane exchange:
  - (a) Simple passive diffusion
    - Small and/or lipid soluble substances (such as respiratory gases (O_2/CO_2), electrolytes (Na^+/Cl^-), lipids (FA, steroids, fat-soluble vitamins) and most drugs) diffuse across the placental barrier down their [ ] gradients without use of energy
    - Rate of transfer follows "Fick's Law of Diffusion":

$$J = \frac{D \times A \times dC}{dT}$$

Where:
- [ ] gradient across placental barrier (dC) – determined by:
  - (i) Maternal-foetal arterial [ ]$_{GRADIENT}$
  - (ii) Maternal intervillous space and foetal placental blood flows
  - (iii) Diffusing capacity of placenta for the substance
  - (iv) Protein binding/dissociation rates of substance
  - (v) Metabolism of substance by placenta (Eg. O_2)
- Surface area of placental barrier (A) – Exchange area = 1.8 m^2 (Nb. total villous area = 16 m^2)
- Thickness of placental barrier (dT) – 3.5 um
- Diffusion capacity of substance by placenta (D) – determined by substance's:
  - (i) MWT – Impermeable if > 6 kDa; diffusion related to other factors if < 1 kDa
  - (ii) Lipid solubility – Diffusion rate α to lipid solubility
  - (iii) Degree of ionization – Electrical charge deters placental transfer → Nb. "Ion trapping" of basic drugs can occur on foetal side due to ↑ acidity there (cf. maternal side of placenta)
  - (iv) Protein binding/dissociation rate – diffusion α to % free form

  - (b) Facilitated transport – Substances (such as glucose, lactate, a.a., electrolytes (Na^+, H^+)) are transported across the placental barrier via a membrane protein carrier down their [ ] gradients without use of energy → rate of transfer is determined by Fick's Law of Diffusion (see above), BUT occurs much faster than simple passive diffusion
  - (c) Active transport – Substances (such as H_2O-soluble vitamins, a.a., I_2, Fe^{2+}, and electrolytes (K^+, Ca^{2+}, PO_4^{3-})) are transported across the placental barrier via a membrane protein carrier against their [ ] gradients with the use of energy (as ATP)
  - (d) Endocytosis – Large/non-lipid soluble substances that are not transported by a carrier protein (such as IgG, globulins, lipoproteins) are taken up in small vesicles and then exocytosed on the other side of the placental barrier
  - (e) Bulk flow – H_2O (and solutes via "solvent drag") moves across the placental barrier according to Starling forces ($P_{HYDROSTATIC}$ and $P_{OSMOTIC}$) across the barrier
  - (f) Breaks – Delicate parts of chroionic villi break off within IVS and release contents into maternal circulation (Eg. foetal RBC)
- (2) Uteroplacental blood flow
  - At term → uteroplacental BF is 500-700 mL/min (10% maternal C.O.) of which:
    - (i) 70-90% of this BF enters the intervillous space (via the spiral arteries) → NOT autoregulated as blood flow is "pressure-dependent" (see factors below)
    - (ii) 10-30% of this BF supplies the myometrium/deciduas (via the basal arteries) → autoregulated blood flow
  - Blood flow to the intervillous space (which participates in substance exchange with foetal blood) is affected by the following factors:

$$UBF = \frac{(UAP - UVP)}{UVR}$$

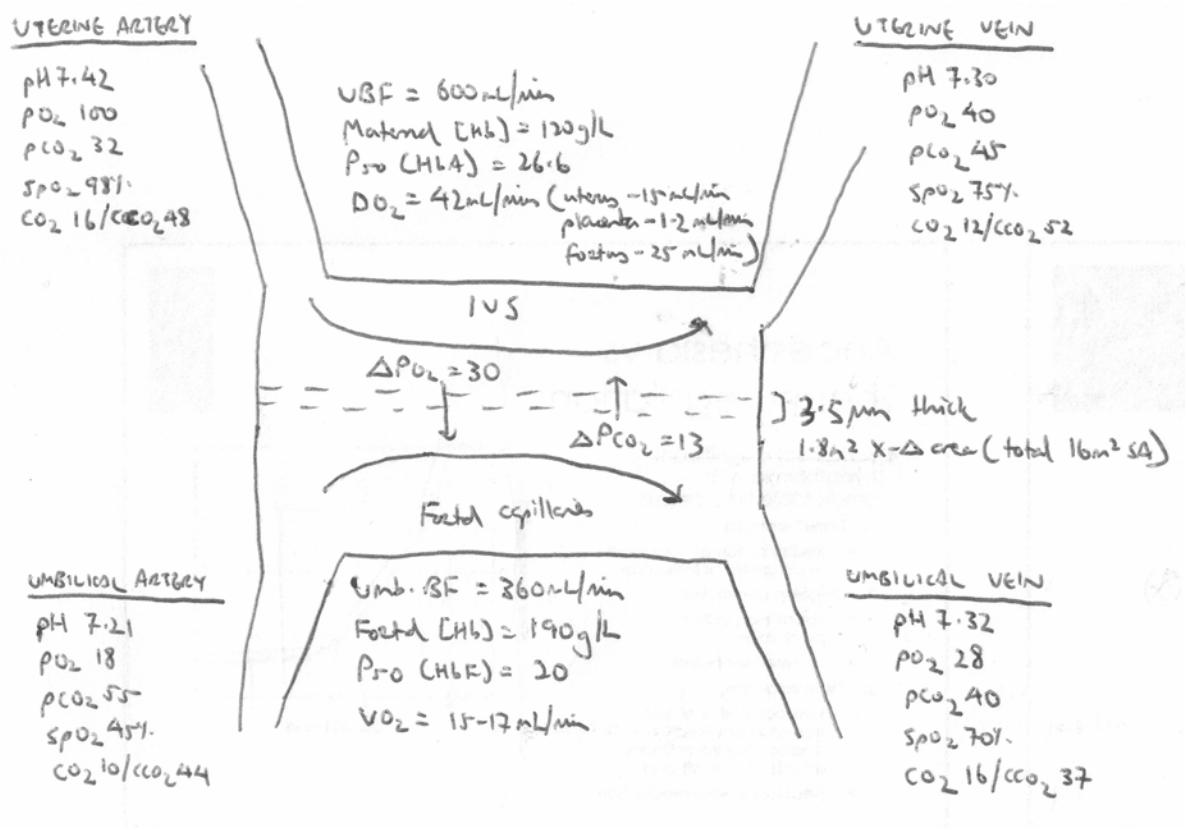
(1) Uterine arterial pressure (UAP):
- Maternal arterial BP → ↓ MABP (Ie. due to SNS block 2° neuraxial block, hypovolaemia, supine hypotension syndrome, Etc.) causes ↓ UAP → ↓ UBF

(2) Uterine venous pressure (UVP):
- Uterine tone and contractions → ↑ tone/contractions (Ie. due to contractions, oxytoxics, ketamine, Etc.) causes ↑ UVP → ↓UBF

(3) Uterine vascular resistance (UVR):
- Uterine arteriolar tone → ↑ vasoconstriction (Ie. a/w essential HT and PET, α-adrenoceptor stimulation (by endogenous SNS innervation, catecholamines or sympathomimetics), and vasopressin) causes ↑ UVR → ↓ UBF

- (3) Umbilical blood flow
  - At term → umbilical BF is 360 mL/min (25-50% of foetal C.O. (≈ 1000 mL/min))
  - It is "autoregulated" (cf. uterine BF) → involves vasodilators (PCI-2/NO) derived from vascular endothelium
  - BF is ↓ with severe hypoxia, ↑ BGL, catecholamine and cord compression
- (4) Placental surface area available for exchange
- (5) Placental metabolism
  - Consumption of substance by placenta (Eg. O_2) → ↓ amount available for transfer

Placental gas exchange:



- O_2/CO_2 exchange across the placenta occurs by "flow-limited passive diffusion" (as they are small hydrophobic molecules that are very permeable within the placental barrier) → the rate of diffusion is thus determined by "Fick's law of diffusion" (See above)

> Important to note – Gas exchange across the placenta is very inefficient cf. that in an adult lung (Ie. placenta only exchanges 1/10th the amount of O_2 as the adult lung) → due to:
> - (1) ↑ diffusion distance in the placenta → 3.5 um (vs 0.5 um in the lung)
> - (2) ↓ gas permeability in the placenta → permeability of blood-blood barrier of placenta is much less than the blood-gas barrier of lung
> - (3) ↓ total surface area of the placenta → 16 m^2 at term (vs 50-60 m^2 in the lung)

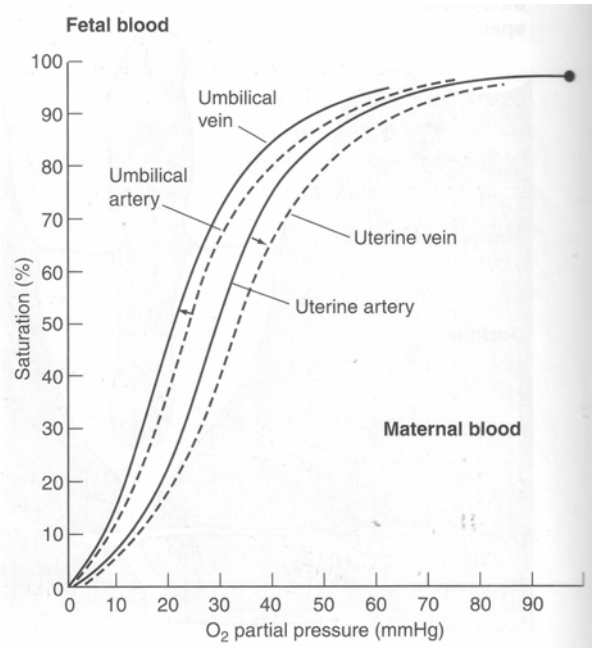
- O_2 exchange across the placenta → determined by the following factors:
  - (1) Rates of maternal and foetal blood flows → MAIN factors
    - (i) Maternal (intervillous space) blood flow → determined by factors that influence Uterine BF (see above)

- (ii) Foetal (placental) blood flow → determined by factors that influence Umbilical BF (see above)

- (2) Maternal-foetal PO_2 gradient
  - PO_2 gradient of ≈ 30 mmHg exists between maternal blood in intervillous space (~ 50 mmHg) and foetal blood in umbilical artery (~ 20 mmHg) → O_2 diffuses down its [ ] gradient from maternal to foetal blood
- (3) Maternal-foetal Hb O_2 affinity
  - (i) Double Bohr effect → 2-8% of transplacental O_2 transfer

> Note – "Bohr Effect" → ↑ PCO_2/↓ pH causes a right shift in Hb O_2 dissociation curve → conformational change in Hb resulting in ↓ affinity for O_2

    - When foetal blood releases CO_2 → ↑ pH (7.21 to 7.32) and ↓ pCO_2 (from 55 to 40 mmHg) of foetal blood → left shift in O_2 Hb DC → ↑ affinity for O_2 → ↑ O_2 uptake across placenta from maternal blood
    - CO_2 released from foetus is taken up by maternal blood → ↓ pH (7.42 to 7.3) and ↑ pCO_2 (from 32 to 45 mmHg) of maternal blood → right shift in O_2 Hb DC → ↑ O_2 unloading → ↑ O_2 crosses placenta to foetal blood



  - (ii) Hb type
    - HbF (in foetal blood) has a ↑ O_2 affinity than HbA (in maternal blood) → P_{50} 20 mmHg (HbF) vs P_{50} 26.6 mmHg (HbA) → assists O_2 unloading in maternal blood and O_2 uptake across placenta into foetal blood

> Note – HbF has a relative left shift in O_2 Hb DC and ↑ O_2 affinity (cf. HbA) → b/c it lacks β-chains (Ie. HbF is $\alpha 2\gamma 2$ cf. HbA which is $\alpha 2\beta 2$) and thus cannot bind 2,3-DPG

- (4) Maternal-foetal O_2 carrying capacity in blood
  - Foetal blood has a ↑ O_2 carrying capacity cf. maternal blood → due to 40% ↑ in [Hb] (190 g/L vs 120 g/L)
- (5) Placental O_2 consumption
  - Placenta consumes 20-30% of transferred O_2

- CO_2 exchange across the placenta → determined by the following factors:

> Note – CO_2 exists as HCO_3 (60%), carbamino- Hb (30%), dissolved CO_2 (10%) → dissolved CO_2 and HCO_3 are the main forms of CO_2 placental transfer

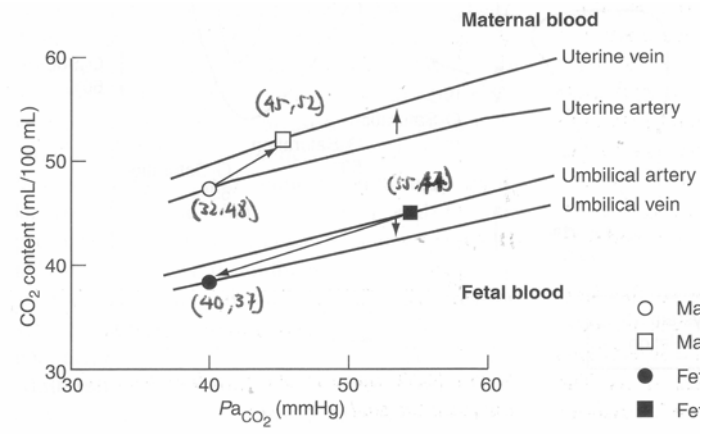
  - (1) Rates of maternal and foetal blood flows → MAIN factors
    - (i) Maternal (intervillous space) blood flow → determined by factors that influence Uterine BF (see above)
    - (ii) Foetal (placental) blood flow → determined by factors that influence Umbilical BF (see above)

> Note – CO_2 is 20x more diffusible than O_2 (as it is more soluble) → thus, CO_2 exchange is influenced more by rates of maternal-foetal BF (cf. O_2)

  - (2) Maternal-foetal PCO_2 gradient
    - PCO_2 gradient of ≈ 13 mmHg exists between foetal blood in umbilical artery (~ 50 mmHg) and maternal blood in intervillous space (~ 37 mmHg) → CO_2 diffuses down its [ ] gradient from foetal to maternal blood
  - (3) Maternal-foetal Hb CO_2 affinity
    - "Double Haldane effect" → accounts for 46% of transplacental CO_2 transfer

> Note – "Haldane Effect" → Hb can ↑ capacity for CO_2 carriage (as HCO_3^-) for a given PCO_2 when it is in its deoxygenated state

    - ↑ O_2 unloading from maternal blood → causes ↑ CO_2 carriage capacity of maternal blood (as carbamino-Hb) for a given PCO_2 → results in ↑ CO_2 transfer from foetal blood across placenta
    - ↑ O_2 loading of foetal blood → causes ↓ CO_2 carriage capacity of foetal blood for a given PCO_2 → facilitates further CO_2 transfer to maternal blood



  - (4) Maternal-foetal CO_2 carrying capacity in blood
    - Foetal blood has a ↑ CO_2 carrying capacity cf. maternal blood (as carbamino-Hb) → due to 40% ↑ in [Hb] (190 g/L vs 120 g/L)
  - (5) LeChatelier effect
    - CO_2 transfer from foetal to maternal blood favours a equilibrium shift in the "carbonic anhydrase" reaction → results in ↑ CO_2 production from association H^+ and HCO_3^- in foetal blood → results in more CO_2 for transfer!

$$H^+ + HCO_{3-} \leftrightarrow H_2CO_3 \leftrightarrow CO_2 + H_2O$$