MATERNAL PHYSIOLOGY IN PREGNANCY

Respiratory

- overall there is **~ 50%** loss of respiratory reserve,
  a. ↑ VO_2
  b. ↓ FRC
  c. ↓ CVS reserve
  d. airway changes

Alteration of Lung Volumes in Pregnancy		
Functional Residual Capacity	FRC	
Residual Volume	RV	**~ 20%** decrease
Expiratory Reserve Volume	ERV	
Vital Capacity	VC	
Inspiratory Reserve Volume	IRV	unchanged
Closing Volume	CV	
Total Lung Capacity	TLC	~ 5% decrease
Inspiratory Capacity	IC	~ 5% ***increase***

- the diaphragm is ***not*** splinted but is elevated and moves freely
- the transverse and AP diameter of the chest increases to compensate for the elevation of the diaphragm
- diaphragmatic breathing decreases in favour of thoracic excursion
- during normal tidal ventilation ~ 33% (≤ 50% ASA) have ***airway closure***, especially supine
- factors which do increase CV are advancing age, smoking and lung disease
- airway closure increases atelectasis, shunt flow and V/Q mismatch,

  → ↑ P_AO_2 and $P_{A\text{-}a}O_2$ gradient

- engorgement of the mucous membranes throughout the respiratory tract, causing swelling of the nasopharynx, oropharynx, larynx and trachea
- this may lead to difficulty in visualisation of the vocal cords, or to haemorrhage following manipulation of the airway
- increased levels of ***progesterone*** ± oestrogen sensitise the respiratory centre to CO_2

• ***dyspnoea*** is experienced by ~ 60-70% of women early in pregnancy, when ventilation is only mildly increased

1. ↑ minute ventilation ~ 50% at term
   i. ↑ tidal volume ~ 40%
   ii. ↑ respiratory rate ~ 15% → ↓ ***dead space*** ventilation
2. ↑ ***alveolar ventilation*** **~ 70%** above the nonpregnant state

• this far exceeds,

1. ↑ body weight ~ 20%
2. ↑ VO_2 ~ 15-20%

• several studies have shown a decrease in ***physiological dead space***, independent of tidal volume & rate changes
• this is believed to be due to more efficient mixing and distribution of ventilation, and possibly the increased CO of pregnancy → ***decreased*** $ETCO_2$ - $PaCO_2$ gradient
• pregnancy may actually be associated with a ***negative*** $ETCO_2$ - $PaCO_2$ gradient (CJA)

• progesterone → bronchodilatation and decreased airways resistance
• however, FEV_1, MBC and diffusing capacity remain unchanged
• pulmonary ***compliance*** is decreased ~ 30%,

1. C_L - unaltered
2. C_{CW} - decreased ~ 45%
   - returns to normal immediately following delivery

• oxygen consumption increases ~ 20% during pregnancy, and up to 100% during labour
• the HbO_2 curve is shifted to the ***right***, and arterial gas analysis reflects ***chronic hyperventilation***

→ pH ~ 7.44
PaO_2 ~ 95-105 mmHg
$PaCO_2$ ~ 32 mmHg
HCO_3^- ~ 21 mmol/l

• PaO_2 tends to be high early, falling as FRC encroaches upon CV, and may be normal or slightly subnormal at term
• plasma HCO_3^- decreases to ~ 21 mmol/l to compensate for the P_{aCO2}
• therefore, at term there is less ***buffer reserve***, and metabolic acidosis readily develops
• during labour ventilation may increase 300% with marked maternal ***hypocarbia & alkalaemia***,

→ P_{aCO2} ~ 20 mmHg
pH ~ 7.55

• between contractions women may hypoventilate, with periods of ***hypoxaemia***

- ***Respiratory: Importance for Anaesthesia***

a. intubation
   - mucosal bleeding
   - difficult intubation

b. respiratory reserve
   - rapid onset of hypoxia*
   - high VO_2 / low FRC ± low PaO_2
   - decreased CO supine

c. rapid gaseous induction
   i. ↓ MAC
   ii. ↓ FRC → less dilution
   iii. ↑ MV → rapid δ depth

d. foetal effects
   i. maternal respiratory alkalosis
      - umbilical/uterine vasoconstriction
      - ↑ maternal HbO_2 affinity (relative not absolute, ↑ DPG & curve → R)
   ii. maternal hypoventilation between contractions

NB: following adequate preoxygenation, the PaO_2 in apnoeic pregnant women falls ~ 80 mmHg/min more than in the nonpregnant state

Cardiovascular Changes

- ***Blood Volume***

a.	↑ plasma	~ 50%	∝	aldosterone & oestrogen
		~ 40	→	70 ml/kg
b.	↑ RBC mass	~ 20-30%	→	***dilutional*** ↓ [Hb] & haematocrit
		~ 25	→	30 ml/kg
c.	↑ ***blood volume***	~ 30-40%		
		~ 65	→	**100 ml/kg**

• ↑ RBC mass occurs slower than ↑ plasma, accounting for the relative ***anaemia*** of pregnancy
• ***autotransfusion*** of ~ 500 ml at delivery from the placenta into the maternal circulation
• this usually compensates, with the post-partum Hct. varying ± 5%

- ***Cardiac Output***

• increases by 8-10/52 gestation, reaching a peak at ~ 30/52, due to an increase in,

a. ↑ SV ~ 35%

b. ↑ HR ~ 15% → **- CO ~ 40-50%**

• CVP changes little, except during labor, or due to the effects of ***aortocaval compression***

→ ↓ CO ~ 40% in in the ***supine position***

• labour → ↑ catecholamines → ↑ SV and CO a further 40-45% above prelabour values
• uterine contraction further augments CO by ***autotransfusion***, ↑ blood volume ~ 10-25%
• ***BP*** increases with each contraction as PVR increases together with the increases in CO
• during the **3rd stage**, ***CO*** increases ~ 80% above prelabour values (NB: MCQ)
• CO returns to normal by the 2nd postpartum week

NB: ***aortocaval compression*** is of major importance for foetal well-being

• most women do not become overtly hypotensive, "concealed caval compression"
• ~ 10% of women become frankly hypotensive, "revealed caval compression"
• frequently with a superimposed ***reflex bradycardia***, despite the inability to maintain peripheral vascular tone

- ***Cardiac Work***

• increased, which may result in LVF when there is poor cardiac reserve
• changes found on clinical examination include,

a. ejection systolic murmur
b. a loud split first heart sound
c. occasionally a soft diastolic murmur
d. the apex beat is displaced to the left
e. the ECG axis shifts to the left
f. the heart may appear enlarged on CXR

- ***Blood Pressure***

a. ↑ CO ~ 50%
b. ↓ TPR - uterine AV shunt & decreased viscosity

→ slight ***decrease in MAP***

NB: a high BP in pregnancy, except during labour, is ***always abnormal***

• CVP and PAOP remain ***normal*** during pregnancy
• CVP increases 4-6 cmH_2O during contractions

- ***Electrocardiogram LAD***

• chamber volume and wall thickness increase during pregnancy
• upward displacement of the diaphragm and elevation of the heart
• arrhythmias occur more commonly during pregnancy, but are usually ***benign***

- ***Oxygen Flux***

• ***increases*** despite the slight ↓ [Hb] and O_2 content, due to,

a. ↑ CO
b. hyperventilation and ↑ PaO_2 (early)
c. ↑ 2,3-DPG → HbO_2 dissociation curve to the ***right***
→ **P_{50} ~ 30.4 mmHg** (cf. 26.7)

- ***Cardiovascular: Importance for Anaesthesia***

• patients undergoing spinal or epidural anaesthesia must,

a. be maintained in a ***lateral tilt*** position, with left uterine displacement

b. be adequately ***volume preloaded***

• regional anaesthesia attenuates some of the CVS changes which normally accompany labour, excepting those in the third stage which are not due to circulating catecholamines

NB: thus, epidural anaesthesia is recommended for any patient in whom an increase in myocardial work is undesirable

Blood Constituents

• there is a slight ***decrease*** in [Na^+], [K^+] and [Cl^-]
• albumin, globulins & total protein increase, but their plasma concentrations decrease
• the normal albumin:globulin ratio of ~ 1.6/1 → 1/1 at term
• colloid osmotic pressure progressively decreases, parallel with the fall in serum albumin
• further decreases in COP occur in the postpartum period, irrespective of the mode of delivery
• thus, the preeclamptic patient, or those on tocolytic therapy are prone to the development of ***pulmonary oedema***, despite near normal PAOP's
• changes in protein binding may lead to drug toxicity, due to changes in the unbound fraction

• pregnancy leads to a ***hypercoagulable state***, due to,

a. ↑ factors VII, VIII, X, XII (? IX)

b. ↑ fibrinogen (I) and FDP's

c. ↓ fibrinolytic activity - ↓ levels of plasminogen activators

d. ↓ antithrombin III

→ ***increased risk of thromboembolic disease***

Uterine Circulation

• nonpregnant blood flow parallels metabolic activity of the myometrium and endometrium, undergoing cyclic variations with menstruation
• during pregnancy, blood flow increases rapidly with the increasing uterus and foetus

→ £ **20** ***fold increase***

• early in pregnancy the O_2 ER of the uterus is low, therefore, some factor other than autoregulation increases flow ??oestrogen
• as the size and requirements of the foetus increase much greater than blood flow during pregnancy, the O_2 extraction ratio increases progressively with pregnancy

Central Nervous System

- LA requirements for subarachnoid or epidural anaesthesia are reduced in pregnancy
- possible causes include,
    a. increased diffusion of LA to the receptor site
    b. increased sensitivity of nerve fibres to LA
    c. ? raised CSF progesterone levels

- valsalva manoeuvres during delivery may increase CSF and epidural pressures, markedly increasing the spinal spread of anaesthetic
- the MAC for the volatile agents is also reduced ~ 40% during pregnancy
- this was thought to be due to progesterone, however, studies in rats have shown ***no correlation*** between plasma progesterone and MAC reduction
- there may be an upregulation of the ***endogenous opiate*** pathways and the endorphin system

Renal

- the ureters and renal pelvis progressively dilate from the 12th week
    → increased incidence of **UTI's**
- ↑ RBF and GFR ~ 60% at term ∝ ↑ CO and blood volume
- ***aldosterone*** levels are slightly increased, as are TBW and sodium
- plasma osmolality is decreased, with an effective "resetting" of the threshold for ADH secretion
- urine volume increases due to the need to excrete a greater mass of waste products
- both BUN and $[Cr]_{pl}$ decrease due to an ***increased creatinine clearance***
- during third trimester there may be alterations of renal function due to aortocaval compression

Hepatic & GIT Function

- ↑ LFT's due to ***enzyme induction***
- liver blood flow is not significantly altered and bilirubin levels are unaltered
- ¯ ***plasma cholinesterase* ~ 30%** and remains low for several weeks postpartum
- this generally doesn't affect the response to suxamethonium, as there is a larger V_{dSS} for the drug, which compensates for the decreased clearance
- during labour there is a greatly increased risk of ***aspiration*** and Mendelson's syndrome due to,
    1. ↓ gastric emptying
    2. ↓ lower oesophageal sphincter (LOS) tone
    3. ↑ gastric acidity
    4. ↑ intragastric pressure
    5. ↑ incidence of difficulty with intubation
    6. frequently require emergency anaesthesia in the "middle of the night" by junior staff

Endocrine

- endocrine disease is rare in pregnancy, as pre-existing disease usually results in infertility
- ***thyroid disease*** is the commonest endocrinopathy during pregnancy
- earliest changes are increased levels of,

    a. oestrogen

    b. progesterone

    c. βhCG

- normal pregnancy is associated with ***increases*** in the size of the,

    a. thyroid
        - ↑ BMR & PBI
        - FT_4 ***normal*** and patients remain ***euthyroid***
        - difficult as pregnancy symptoms mimic thyroid disease

    b. parathyroid
        - ↑ PTH → ↑ $Vit.D_3$
          ↑ Ca^{++} absorption
          ↓ Ca^{++} excretion
        - plasma [Ca^{++}] remains ***normal***, the increase supplies the foetus

    c. anterior pituitary
        - ↑ ACTH → cortisol
          aldosterone
          prolactin
        - ↑ MSH, β-END

    d. adrenals

FOETAL PHYSIOLOGY

Placental Circulation		
Normal Values	Average at Maturity	Adult Comparison
Weight	500 g	
Lobules	200 - each multiple villi	
Diffusion Distance	3.5 μm	~ 0.5 μm - lung
Surface Area	3-4 m^2	~ 70 m^2 - lung
Blood $Flow_{F/M}$	300 ml/min ~ 50% of CO	600 ml/min
$Blood\ Volume_M$	150 ml - intervillous spaces	
RBC Transit Time	15 secs	0.75 s - lung
P_MO_2	50 mmHg	
P_FO_2	30 mmHg	

Foetal Circulation

- ~ 55% of the foetal CO supplies the placenta via the umbilical arteries, where $SafO_2$ ~ 60%
- umbilical vein saturation, **$SuvO_2$ ~ 80%**, c.f. 98% of maternal arterial blood
- of this,

1. majority → passes through the liver
2. small fraction → passing directly into the IVC via the ***ductus venosus***

- the portal and systemic venous blood of the foetus, $SvfO_2$ ~ 26%
- the mixed venous blood in the **IVC** → **$SvfO_2$ ~ 67%**
- most 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

→ net effect being the head receives the better oxygenated blood

Foetal Respiration

- three factors aid in foetal transfer of O_2

1. $[Hb_F]$ ~ 50% greater than $[Hb_A]$ → greater CaO_2 /ml
2. Hb_F binds 2,3-DPG ***less*** effectively than Hb_A → left shift
3. Hb_F-CO_2 → Hb_A-CO_2 → "double" Bohr effect

NB: Hb_F-O_2 dissociation curve lies above and to the left
Hb_F-P_{50} ~ 19 mmHg Hb_A-P_{50} ~ 30.4 mmHg (cf. 26.7)

- the total ***diffusing capacity*** at term for O_2,
  a. across the placenta ~ 1.2 ml/O_2/min/mmHg
  b. across the lung ~ 20 ml/O_2/min/mmHg

- maternal 2,3-DPG level increases near term, increasing the P_{50} and improving unloading of O_2
- Hb_A begins to appear around the 20th week of intrauterine life
- no Hb_F is formed after birth,
  a. at birth Hb_A ~ 20%
  b. 4 months Hb_A > 90%

- CO_2 is 20 times more diffusible and concentration gradient is high, ∴diffusion not a problem
- the maternal $PaCO_2$ is reduced by hyperventilation of pregnancy

Other Placental Functions

a.	active nutrient absorption	- where [F] > [M] → amino acids, Cr, PO_4
b.	metabolism	- various drugs by MFO's and Plasma-ChE
c.	metabolic functions	- stores protein, Fe^{++}, Ca^{++} - acts $\equiv^t$ liver early, until foetal liver matures
d.	hormone synthesis	- βhCG - oestrogen - progesterone - hPL

Normal Values	Maternal	Foetal
Hb concentration	12 g/100 ml	18 g/100 ml
Blood flow	600 ml/min	300 ml/min
Uterine/Umbilical aa.		
• PaO_2	95 mmHg	15 mmHg
• SaO_2	97%	58%
• $PaCO_2$	35 mmHg	48 mmHg
Uterine/Umbilical vv.		
• PvO_2	33 mmHg	**30 mmHg**
• SvO_2	50%	**80%**

Bupivacaine Cardiotoxicity

• ***seizures***, presumably from accidental intravascular injection have been associated with ***cardiac arrests*** and difficult resuscitation ± death

• Moore & coworkers in the largest clinical survey reported,

a. seizures 2° to LA's were frequently associated with ***hypoxia*** or ***acidosis***

b. subsequently reported cases of bupivacaine induced convulsions managed with early ventilation with 100% O_2, ***without*** subsequent cardiac arrest

c. 21,000 administrations of bupivacaine, with 23 cases of convulsions ***not*** associated with cardiac arrest or neurological sequelae

• studies in awake sheep show that lignocaine and bupivacaine produce similar CNS toxicity when administered rapidly IV
• in the absence of,

1. hypoxia or hypercarbia
2. respiratory or metabolic acidosis
3. hyperkalaemia, or
4. hypotension

→ serious cardiac arrhythmias occurred following bupivacaine, but ***not*** lignocaine

• subsequent studies have shown bupivacaine cardiotoxicity is enhanced in the presence of hypoxia, hypercarbia or acidosis
• voltage clamp experiments with lignocaine and bupivacaine in guinea pig papillary muscles show,

a. both agents block fast inward Na^+ channels

b. both reduce $\delta V/\delta t$ of phase 0 to a similar degree

c. lignocaine dissociates from the channel ~ 1 sec

d. bupivacaine dissociation takes ~ 5x that of lignocaine

e. ***frequency-dependent block*** accumulates with bupivacaine, even at slow heart rates

→ bupivacaine is **~ 16x** as toxic as lignocaine to the myocardium

NB: as bupivacaine is ~ 4x as potent as lignocaine,
this gives it a ***relative toxicity ratio ~ 4 times***

• the net effect is that bupivacaine is potentially cardiotoxic at ~ 1.0 mg/kg if injected intravascularly

"Total Spinal" Anaesthesia

- subarachnoid injection of an epidural dose of local anaesthetic will result in,
    a. unconsciousness
    b. apnoea
    c. hypotension & bradycardia
    d. ***dilated*** pupils - brainstem hypoperfusion $\rightarrow$ fixed

- immediate management should include,
    a. airway maintenance & imediate endotracheal intubation
        + O_2 and IPPV (frequently required for ~ 2-3 hours)
    b. Trendelenberg position ± lateral tilt
    c. IV fluids
    d. atropine & ephedrine ± catecholamines
    e. assessment of foetal well-being ± emergent delivery

- the requirement for ***sedation*** is usually minimal, with most patients having no recall of the events
- more gradual onset of symptoms may be seen with subdural catheter placement, or with catheter migration following initial insertion

ASPIRATION PNEUMONITIS

• John Hunter provided the first description, giving evidence at a murder trial in 1781 (brandy & cats)
• James Simpson (1848) also indicted aspiration, rather than chloroform, as the cause of the first anaesthetic death of Hannah Greener
• Winternitz (1920) first described ***acid aspiration*** and Hall (1940) associated this with obstetrics
• ***Curtis and Mendelson*** (1946) described,

1. 66 cases of gastric aspiration in obstetric patients undergoing GA for vaginal delivery
2. an experimental aspiration syndrome in rabbits with acidic versus neutral fluids
3. the development of pulmonary oedema and CXR changes
4. the beneficial effects of neutralisation of the stomach contents

• the true ***incidence*** is difficult to determine, reported figures include,

a.	all anaesthetic deaths	~ 1-20%
b.	anaesthesia related deaths	~ 0.008-0.2 per 1,000 cases
c.	"silent" regurgitation subsequent aspiration	~ 4-26% of all general surgical cases ~ 10-20% of these
d.	Olsson *et al.* (1986)	- 185,358 anaesthetics - 38 cases of aspiration ~ 4.7 : 10,000 → **1 : 2,131** **~ 15 per 10,000** ***obstetric patients***
e.	subsequent ***mortality***	- reported ranges of 3-70% **~ 5%** is the most recent & reliable figure

NB: aspiration still a leading cause of ARDS & mortality from the later is still in the order of 50^{+}%

• a multitude of factors ***delay*** the rate of gastric emptying,

a. hyper/hypo-osmolar contents
b. high calorie solids > low calorie solids > liquids
c. acid within the duodenum & cholcystokinin
   • cf. gastrin, motilin and parasympathetic agents which increase emptying
d. pain, anxiety, opioids and labour
e. disease states, ie. inflammatory bowel disease, diabetes, hypothyroidism, peptic ulcer disease, electrolyte disorders, etc.

• ***gastric secretion*** continues to add volume to the gastric contents, mean ≤ 200 ml/hr,

a.	interdigestive phase	~ 1 ml/min
b.	digestive phase	~ 3-4 ml/min

Regurgitation & Vomiting

Def'n: ***regurgitation*** is the process whereby gastric contents ***passively*** flow through the gastro-oesophageal sphincter (lower oesophageal sphincter, LOS) into the oesophagus and the pharynx

- when the larynx is incompetent then "silent" ***aspiration*** can occur
- the pressure at the LOS is usually greater than intragastric pressure, preventing regurgitation
- the mechanism of action is multifactorial,

a. anatomical sphincter - doesn't exist *per se*, muscle is similar above & below
b. physiological sphincter - tonic contraction of the circular smooth muscle fibres
c. flap valve[§]
d. diaphragmatic action[§]
e. mucosal valve[§] [§]these act in unison
f. mechanical factors - lowermost 2-3 cm of the oesophagus are intra-abdominal

- despite these factors reflux does occur, but is rarely seen at intragastric pressures < **20 cmH_2O**

- numerous drugs affect the competency of the LOS,

a. ***decrease*** LOS tone
   i. anticholinergics: atropine, scopolamine, glycopyrrolate
   ii. opioids: morphine, pethidine, fentanyl
   iii. benzodiazepines: diazepam, midazolam
b. ***increase*** LOS tone
   i. gastrokinetics: metoclopramide, ? cisapride
   ii. hormones: motilin, gastrin, PGE_2
   iii. acetylcholinesterase inhibitors
   iv. increased ***alkalinity*** of gastric contents (MCQ)

Def'n: ***vomiting*** is the reflex action by which intragastric contents are ***actively*** expelled from the stomach, through the oesophagus and oropharynx, involving the use of both voluntary and involuntary muscles

- the ***vomiting centre*** in the medulla receives input from,
    a. the CTZ in the area postrema
    b. the vestibular & olfactory apparati, and other cortical areas
    c. almost the entirety of the GIT via the vagus nerve

- motor responses are mediated via,
    a. the cranial nerves V, VII, IX, XII
    b. phrenic and spinal motor nerves to the diaphragm and abdominal muscles

- the usual sequence of events in vomiting may include,
    a. prodromal tachycardia, sweating, tachypnoea, salivation and a sensation of nausea
    b. elevation of the hyoid bone & larynx, opening the crico-oesophageal sphincter
    c. closure of the glottis, elevation of the soft palate, closing the posterior nares
    d. respiration is held in *mid-inspiration*
    e. simultaneous strong downward contraction of the diaphragm & abdominal muscles

        → rapid elevation of intragastric pressure

    f. LOS relaxation & reverse peristalsis → expulsion of gastric contents

Risk Factors

1. depressed level of ***consciousness***
   - hypotension, hypoxia, hypercapnia
   - metabolic encephalopathy, coma
   - ETOH, drug overdosage, ***anaesthesia***
   - CVA
   - epilepsy
   - trauma
   - cardiac arrest
2. impaired ***airway reflexes***
   - ***drugs*** - CNS, NMJ, local anaesthesia
   - ***intubation / extubation***
   - bulbar/pseudobulbar palsy - MS, motor neurone disease, GBS, polio
     - CVA, brainstem infarction
   - elderly
   - local disease, post-surgical
3. increased ***regurgitation*** → LOS dysfunction
   → raised gastric pressure
   - ***pregnancy***
   - oesophageal disease - scleroderma, achalasia
   - hiatus hernia
   - obesity
   - bowel obstruction
   - NG tube

- an ***at risk*** has been defined as a patient having,
  1. a gastric volume **> 0.4 ml/kg** ~ 25 ml
  2. a gastric pH **< 2.5**

- these limits were based on a paper by *Roberts and Shirley (1974)*, who used unpublished data from Rhesus monkeys
- more recent work by *Raidoo (1988)* found that a much greater volume (~ 0.8 ml/kg) was required to produce classic Mendelson's syndrome
- animal models involved the ***direct installation*** of acid into the lungs, whereas clinical aspiration is almost never associated with the aspiration of the entire stomach contents
- subsequent studies of non-lethal aspiration support the concept that ***pH*** is the more important factor

• ***pregnancy*** is unique among the risk factors for aspiration as the risk is ***multifactorial***,

1.	↓ gastric ***emptying***	- displacement of the pylorus - increased progesterone (antagonises *motilin*)[§] - pain, anxiety, narcotic analgesics
2.	↓ ***LOS tone***	- anticholinergics, narcotics ?? loss of the cardio-oesophageal angle
3.	↑ gastric ***acidity***	- placental ***gastrin*** secretion
4.	↑ ***intragastric pressure***	- mechanical effects of the uterus - lithotomy

NB: ***barrier pressure*** (gastric - oesophageal) is normal,
except in those who experience "heartburn"

• some workers have shown changes starting in early pregnancy, whereas others have found no change until ~ 34 weeks
• there is equal lack of agreement as to when the risk decreases following delivery
• numerous studies showing up to 75% of patients having gastric contents > 0.4 ml/kg & pH < 2.5, up to ***48 hrs*** post-delivery
• however, this is no different from the general surgical population & the definition of "at risk" requires further clarification

NB: however, aspiration remains the major cause of maternal morbidity and mortality

■ ***Prevention***

1.	nil orally	- prevention of prolonged fasting with regular fluid intake
2.	non-particulate antacids	
3.	H_2 blocking agents	
4.	anticholinergic agents	- however, these reduce tone of the LOS
5.	metoclopramide	
6.	head-up position	
7.	avoid general anaesthesia	
8.	rapid sequence induction & cricoid pressure	
9.	endotracheal intubation with a cuffed ETT	
10.	awake extubation	
11.	alert, well trained recovery room staff	

FAILED ENDOTRACHEAL INTUBATION

• this is the leading cause of anaesthetic related maternal ***mortality***
• in Australia, Holland (AIC, 1984) **~ 69%** of anaesthesia related deaths were airway catastrophes
• the Confidential Enquiry into PeriOperative Deaths (UK 1987) found that 1 in 3 deaths attributable solely to anaesthesia was due to failure to intubate the larynx
• however, this report did not include obstetric patients, in whom the ***incidence*** of failed intubation is much higher,

a. general surgical population **~ 1 : 2,303**
b. obstetric population **~ 1 : 300** (~ 8x ↑ risk)

• reports of Confidential Inquiries into Maternal Deaths in England and Wales found that,

a. **13%** of all maternal deaths were associated with anaesthesia (1982-84)
b. **41%** of deaths arising from anaesthesia related to intubation difficulties (1973-1984)

Airway Assessment

■ ***Clinical Assessment***

• ***does not*** predict all cases
• bedside examination predictive of difficult intubation described by ***Mallampati*** *et al.* and modified by Samsoon and Young*
• assessment is made with the patient sitting upright and the head in the neutral position, with the mouth fully open and the tongue extended, ***without*** phonation,

Mallampati Classification - Class	
Class 1	faucial pillars, soft palate and uvula visible
Class 2	faucial pillars and soft palate visible but uvula obscured by the tongue
Class 3	only the soft palate is visible
Class 4*	the soft palate is not visible

• classification predicts ~ 50% of difficult airways, but has a high incidence of ***false positives***
• Tham *et al.* showed that assessment in the ***supine*** position is equally predictive

Assessment of Airway

1. ***history***
2. ***examination*** → **"MOUTHS"**
   - i. **M**andible
     - thyromental distance > 6 cm, 3 "finger-breadths"
     - alveolar-mental distance < 2 cm
     - "receeding", length - subluxation
     - obtuse mandibular angles
   - ii. **O**pening
     - incisor gap > 4 cm (Wilson > 5 cm)
   - iii. **U**vula
     - Mallampati grades I-IV - as per Samsoon & Young
   - iv. **T**eeth
     - prominent upper incisors, "buck" teeth
     - solitary incisors, nuisance teeth, loose teeth
     - crowns, caps, plates & dentures
   - v. **H**ead
     - flexion, extension, lateral flexion & rotation
   - vi. **S**ilhouette
     - obesity
     - "no neck", neck masses, Dowager's hump
     - craniofacial anomalies
3. ***investigations***
   - i. direct awake laryngoscopy
   - ii. indirect laryngoscopy
   - iii. fluoroscopy
   - iv. XRays (Bellhouse)
     - effective mandibular length
     - atlanto-occipital distance
     - C_1-C_2 interspace
     - anterior-posterior thickness of the tongue
   - v. CT scan
     - tracheal deviation, luminal diameter
     - intrathoracic trachea

PREGNANCY INDUCED HYPERTENSION

- ***Incidence***

  a. 5-10% of all pregnancies

  b. highest in primigravidas, though, the ***prevalence*** is greater in multiparous

  c. 0.05-0.2% of all deliveries progress to ***eclampsia*** (1:500-1:2,000)

  d. PIH is implicated in,
     i. ~ 20% of maternal deaths
     ii. ~ 6-10% of perinatal deaths

- ***Categories***

  1. ***gestational hypertension / proteinuria***
     i. hypertension without proteinuria
     ii. proteinuria without hypertension
     iii. proteinuric hypertension → ***preeclampsia***
        - developing ***after*** the 20th week of gestation
        - may occur earlier if associated with ***hydatidiform mole***
  2. ***chronic hypertension***
     i. incidentally associated with pregnancy
     ii. aggravated by pregnancy or preeclampsia
  3. ***unclassified hypertension***
     - found later than 20 weeks where the past hypertensive status is unknown
  4. ***eclampsia***
     - any form of hypertension accompanied by ***fitting***

Preeclampsia

- ***gestational hypertension*** is defined as,

  1. BP > 140/90 mmHg * on at least 2 occasions, > 6 hours apart, or
  2. ↑ BP above pre-pregnancy levels
     i. > 30 mmHg systolic
     ii. > 15 mmHg diastolic

- ***preeclampsia*** exists if any ***two*** of the following are present,

  1. gestational hypertension
  2. proteinuria > 300 mg/l per 24 hours (N: < 150 mg/l/24 hrs)
  3. oedema

• ***severe preeclampsia*** is denoted by ***any*** of the following,

1. systolic BP > 160 mmHg
   diastolic BP> 110 mmHg * on at least 2 occasions, > 6 hours apart
2. proteinuria > 5g / 24 hours * or rapidly increasing
   - "nephrotic" > 3.5 g / 24 hrs
3. oliguria < 400 ml / 24 hours
4. cerebral or visual disturbance
5. cyanosis or pulmonary oedema
6. epigastric pain

NB: ***eclampsia*** being the presence of any degree of hypertension, or proteinuria, with the occurrence of ***convulsions***

▪ ***Aetiology***

• unknown, though, it is generally agreed the underlying disorder relates to ***utero-placental ischaemia***
• some consider it a subset of TTP/HUS, being a generalised endothelial disorder, characterised by widespread vasospasm and platelet activation
• potential contributing factors,

a. genetic
b. acquired immune factors
   - immune reaction to ***trophoblastic*** tissue → placental vasculitis & ischaemia
   - more common amongst,
   i. nulliparas - no previous exposure to trophoblast
   ii. conditions with a large mass of trophoblast
      - hydatidiform mole
      - multiple pregnancy
      - diabetes
      - Rh incompatibility
c. imbalance in prostaglandin synthesis
   i. **PGI_2 / TXA_2** ***imbalance*** - Walsh (Am.J. O&G, 1985)
      - behind the advent of the "CLASP" (collaborative low dose aspirin) trial
   ii. angiotensin II / PGE_2 imbalance (PGE = vasodilator secreted by placenta)
d. abnormal (placental) activation of renin-angiotensin-aldosterone
e. nutritional disorders / deficiencies
f. a combination of these

Pathophysiology

NB: the majority of lesions are due to ***occlusive vascular spasm*** of arterioles

- ***Central Nervous System***

a. normal total CBF, however, there is ***focal*** vasospastic ischaemic injury
   - MRI, CT and angiographic evidence
   - postmortem studies → haemorrhagic necrosis around thrombosed precapillaries
   - petechial haemorrhages are common after the onset of convulsions
   - EEG shows diffuse slowing (δ/θ) ~ 50% of preeclamptic women; ~ 75% of eclamptic women

b. generalised oedema - does occur but usually 2° to ***seizures***, not a 1° event
   * papilloedema occurs rarely

c. headache, visual disturbance, other focal neurological signs

d. irritability, hyperreflexia

e. sensitive to central depressant drugs

f. ***convulsions***
   i. frequently have prodromal signs, but may be completely unheralded
   ii. often intractable leading to status epilepticus
   iii. ≥ 30% occur ***post-partum*** * most of these within the first 48 hours
   iv. may occur with only minimal increase in BP, cf. hypertensive encephalopathy

g. ***intracranial haemorrhage*** * leading cause of maternal death (~ 50%)

- ***Cardiovascular***

a. ↑ total body water

b. ↓ blood volume ~ 10 mild disease; ~ 30-40% in severe cases

c. ↓ RBC mass * masked by haemoconcentration

d. arteriolar vasoconstriction
   i. ↑ SVR * PVR remains ~ normal
   ii. ↑ sensitivity to vasoactive drugs
   iii. ↑ LVSWI ~ 25% show suboptimal myocardial function

e. ↑ vascular permeability
   i. fluid shifts from intravascular to extravascular space
   ii. hypoproteinaemia
   iii. generalised oedema

f. ↓ CO * one study suggested normal to increased, however, they used $MgSO_4$ first

g. CVP / PCWP low to normal
   i. ↓ CVP generally correlates with the severity of hypertension
   ii. there may be marked discrepancy between CVP & PCWP

NB: the initial presentation of low PCWP & CI, plus high SVR & HR responds well to initial ***volume expansion***, with elevation in filling pressures and CI, and a reduction in SVR & HR; subsequent infusion of hydrallazine resulted in further reduction in SVR without a reduction in PCWP (Finster)

- ***Respiratory***

a. frequently none

b. facial and laryngeal oedema * difficulty with ***intubation***

c. ↑ shunt and V/Q mismatch
   i. pulmonary arteriolar resistance is normal or low
   ii. ↑ $\delta P_{A\text{-}aO2}$ may occur, usually associated with a ***rise*** in PCWP
   iii. represents **LV *dysfunction*** more than ARDS

d. ***aspiration*** during eclamptic seizures

e. ***pulmonary oedema*** common at autopsy in fatal cases

- ***Renal***

a. ↓ ERBF and GFR

b. swelling of glomerular endothelial cells and luminal narrowing by ***fibrinoid*** deposition

c. ↑ glomerular permeability to large molecules

d. ***proteinuria*** → may reach nephrotic levels > 5 g/24 hrs

e. ↓ clearance of ***uric acid***, proportional to severity of hypertension

i.	normal	~ 0.18-0.21	mmol/l	~ 3-3.5	mg/dl
ii.	mild PIH	**> 0.24**	**mmol/l**	~ 4.0	mg/dl
iii.	severe PIH	**> 0.45**	**mmol/l**	~ 7.5	mg/dl

f. ↓ clearance of urea & creatinine in more severe cases ~ 30-50%

g. ***oliguria*** * frequently due to ***hypovolaemia* & ¯ RBF**

h. acute renal failure requiring dialysis,
   i. overenthusiastic hypotensive therapy
   ii. haemoglobinuria associated with HELLP
   iii. good prognosis if remainder of disease is appropriately managed

- ***Hepatic***

  a. hepatic swelling & epigastric pain
     i. subcapsular haemorrhages
     ii. ischaemic hepatic necrosis
     iii. fibrinoid deposits in venous sinusoids
  b. spontaneous hepatic rupture * rare, but mortality 55-75%
  c. ascites
  d. HELLP * elevated liver enzymes

- ***Coagulation***

  a. thrombocytopaenia ~ 20-30% of preeclamptic patients
     - usually in the range 100-150,000 / mm^3
     * associated ***platelet dysfunction*** ~ 10-25%
  b. DIC ~ 7% of all cases, more common with ***abruption***
  c. HELLP - haemolysis, elevated liver enzymes, low platelets
     - associated with a poor maternal & foetal outcome
     - no relationship between hypertension & HELLP

  NB: recent studies indicate the SBT is ***not*** a reliable test of clotting (Rodgers & Levin, 1990, Sem. Thrombosis Haemostasis)

- ***Foeto-Placental Unit***

  a. ↓ uterine and placental blood flow ~ 50-70%
  b. premature placental aging with,
     i. increased infarcts
     ii. uterine hypertonicity
     iii. increased sensitivity to oxytocic drugs
  c. ↑ frequency of,
     i. intrauterine growth retardation < 25^{th} percentile
     ii. intrauterine foetal death ≤ 23%
     iii. premature labour
     iv. placental abruption ~ 15x normal frequency
     v. LUSCS
     vi. neonatal hypoglycaemia & hyperbilirubinaemia

Management - General

NB: the cure for preeclampsia begins with ***delivery*** of the foetus,
early delivery has been stressed as crucial in avoiding serious sequelae,
all other treatment modalities are supportive only !

• conditions which mandate the ***delivery*** of the foetus, regardless of the gestational age, include

1. eclampsia
2. acute renal failure
3. HELLP syndrome
4. severe persistent hypertension

NB: delay rarely improves foetal survival and is detrimental to the mother

• standard ***obstetric management*** includes,

1. decreasing CNS irritability / control of convulsions
2. blood pressure control
3. improving end-organ perfusion → urine output ~ 1 ml/kg/hr
4. correction of coagulopathy

▪ *1. CNS Irritability*

a. **$MgSO_4$**

i. anticonvulsant
* administered parenterally ***is not*** an anticonvulsant itself
? effect is due to potent ***cerebral vasodilatation***
- also blocks NMDA glutamate receptors, ?protective
- cleared by the kidney, ∴ monitor level & $[Cr]_{pl}$

• therapeutic blood levels	~ **2-4**	**mmol/l**	
• loading dose	~ 40-80	mg/kg	(~ 3g / 70 kg)
• maintenance	~ 1.0-2.0	g/h	
• ampoules	~ 10	mmol/5 ml	(2.5g)

ii. muscle paralysis
- NMJ blockade is a ***linear*** function of plasma $[Mg^{++}]$
- ↓ release of ACh from motor neurones
- ↓ the sensitivity of the motor endplate
- ↓ the excitability of the muscle membrane
* diaphragmatic paralysis at ³ **7 mmol/l**

iii. cardiovascular
- ↓ SVR and ↑ CO ± reflex tachycardia
- ↑ conduction time
→ ↑PR, ↑QRS and ↑QT duration ≥ 5 mmol/l
- ↓ discharge rate of SA node
- may abolish digitalis induced VPC's
→ hypotension, conduction disturbances ± CHB

iv. uterine / foetal - reduces uterine hypercontractility → ***tocolytic***
- crosses the placenta & may cause ***foetal hypotonia***

b. other anticonvulsants

i. diazepam * treatment of choice for acute seizure control
~ 5-10 mg increments until effective

ii. ***phenytoin*** - more popular for prophylaxis due to lack of sedation
- side effects → rash, nausea and blurred vision

- therapeutic levels ~ 40-100 μmol/l
- loading dose ~ 10 mg/kg in 100 ml, over 20 minutes
  + 5 mg/kg in 100 ml, 2 hours later
- maintenance ~ 200 mg po/iv q8h, 12 hrs post-loading

NB: Eclampsia Trial Collaborative Group, Lancet 1995

- 1687 women with ***eclampsia***, in international multicentre randomised trial
- 2 arms of 2 groups, recurrence of ***convulsions***, $MgSO_4$ versus,

i. diazepam → ~ 52% ($p < 0.00001$)

ii. phenytoin → ~ 67% lower ($p < 0.00001$)

- ***mortality*** was not significantly different for either group versus $MgSO_4$
- foetal wellbeing was significantly better for $MgSO_4$ vs. phenytoin
  - better Apgar scores at 1 minute
  - less likely to be intubated
  - less likely to be admitted to neonatal ICU

■ *2. Control of Hypertension*

• good data to show that CVP may not reflect PCWP and there may be associated LV dysfunction
• James states that "as volume loading is frequently necessary in these patients, a CVP line represents minimum monitoring in any patient with severe PET"
• the case for PA catheters is less clear, Clark & Cotton 1988 recommended their use in,

1. hypertension unresponsive to conventional doses of hydrallazine
2. pulmonary oedema
3. oliguria unresponsive to volume challenge

NB: but the majority of patients could be managed ***without*** central catheterisation

• as the condition is one of vasospasm and there is usually associated volume depletion, most authorities recommend ***gradual*** reduction in BP to slightly ***supranormal*** values
• rapid, or profound reductions in MAP may have adverse effects upon both mother and foetus
• arteriolar vasodilators are the most popular agents, but provision of adequate volume expansion must be instituted ***prior*** to their use

- methods for controlling hypertension include,
    a. bed rest and hospitalisation
    b. avoidance of aortocaval compression
    c. adequate volume resuscitation
    d. epidural if in labour
    e. ***hydrallazine*** ~ 5 mg IV q20m (max ~ 10 mg)
       * maximal effect is in ~ 15 minutes, \ 20 minute intervals
       - ↑ RBF, CO, ***HR*** and uterine blood flow
    f. ***nifedipine*** - 10 mg SL q20m, up to 30 mg has been recommended
    g. b-***blockers***
       - esmolol - adverse effects in foetal sheep
         - adrenergic blockade and hypoxaemia
       - labetalol - used successfully, but caution if the foetus is premature
    h. ***methyldopa*** - usually used for chronic hypertension
       - long safe history in pregnancy up to 1-3 g/day in divided doses
       - may cause drowsiness, depression & postural hypotension
    i. nitroprusside - short-term control of refractory hypertension
    j. nitroglycerine - predominantly a venodilator & less effective with volume loading

3. Renal Protection

- despite the presence of ***oedema*** and ***oliguria***, the use of diuretics is not recommended
- ***volume expansion***, arteriolar dilatation with a slightly supranormal MAP are required
- aim for a urine output ~ 1 ml/kg/hr
- the use of low dose ***dopamine*** has not been widely investigated in PET

4. Respiratory

- involvement is generally minimal
- greatest problem is oedema of the upper airway and the potential difficulty in intubation
- pulmonary oedema is usually the result of overenthusiastic volume loading
- ARDS is ***uncommon***

5. Other Systems

- ***thrombocytopaenia*** is common but usually mild
- requirement for platelet transfusion is very uncommon
- low grade ***DIC*** also rarely requires active treatment
- management of ***liver dysfunction*** is purely supportive
- the rare complication of liver rupture requires emergency surgery for haemorrhage control

- ***Anaesthetic Management***

NB: the role of anaesthetic management includes,

1. pain relief during labour
2. anaesthesia for LUSCS
3. intensive management of life-threatening complications
4. consultive help in the routine obstetric management

OBSTETRIC HAEMORRHAGE

NB: major cause of maternal ***mortality***
significant bleeding occurs in **~ 3%** of all pregnancies

1. ***placental causes***
   - i. placenta praevia[§]
   - ii. abruptio placentae[§] [§] 50-70% of all ***antepartum haemorrhage***
   - iii. placenta accreta / increta / percreta
   - iv. retained placenta
   - v. advanced ectopic pregnancy
2. ***uterine & cervical causes***
   - i. uterine atony
   - ii. uterine rupture
   - iii. uterine inversion
   - iv. cervical or vaginal lacerations
   - v. uterine or cervical abnormalities * polyps, tumours, varicosities
   - vi. trauma
3. ***coagulopathy***
   - i. DIC
     - intrauterine foetal death
     - chorioamnionitis
     - amniotic fluid embolism
     - placental abruption
   - ii. preeclampsia
   - iii. HELLP syndrome
   - iv. coexisting haematological disease
   - v. drugs

Placenta Praevia

• implantation of the placenta in the lower uterine segment, either partially or completely overlying the cervical os, classified as ***total, partial*** or ***marginal***
• Clark (1985) reported an overall incidence ~ 0.3%
• increased incidence with,

1. advanced maternal age ~ 3x increase over 35 years
2. previous LUSCS * 10% with ≥ 4 previous sections
   ~ 0.26% without prior section

• classically presents as ***painless*** vaginal bleeding & accounts for 1/3 of all third trimester bleeding
• diagnosed on routine prenatal ultrasound with ≥ 95% accuracy
• maternal mortality has decreased to < 1%, but foetal mortality may be as high as 20%

Placenta Accreta

• placenta accreta, increta and percreta are conditions of ***abnormal placentation***
• frequently associated with ***placenta praevia***

1. placenta accreta - villi attach directly to the myometrium, without decidua basalis
   - there is ***no invasion*** of the myometrium
2. placenta increta - there is ***invasion into*** the myometrium
3. placenta percreta - there is ***invasion through*** the myometrium
   ± invasion of adjacent structures

• incidence has been reported as high as 1:2,562 pregnancies
• aetiology is ***unknown***
• predisposing factors,

1. placenta praevia * incidence of ~ 5% (Clark)
2. prior LUSCS * incidence of ~ 24% with 1 previous section
3. prior manipulation of the uterus - D&C, myomectomy, etc.
4. congenital malformations of the uterus
5. uterine tumours
6. multiparity
7. ? smoking

• the principal risk is that of ***haemorrhage***
• failure of conservative management may necessitate ***hysterectomy***
• diagnosis during vaginal delivery, 2° to haemorrhage, requires standard ABC management
• in the patient with placenta praevia & previous section, or in those with ultrasound evidence of placenta accreta, ***regional anaesthesia*** is permissible providing there is no suggestion of placenta increta or percreta
• actually difficult to tell on ultrasound, \ most would elect for GA

Abruptio Placentae

Def'n: premature separation of an abnormally implanted placenta, after the 20th week of gestation

- the incidence varies from 0.5-2.5%, and this constitutes 1/3 of antepartum haemorrhages
- maternal mortality is < 3%, however ***perinatal mortality*** is high, up to 60% in some studies
- associated factors include,

1. hypertensive disorders of pregnancy
2. chronic hypertension
3. multiparity
4. uterine abnormalities
5. previous abruption
6. premature rupture of the membranes

- vaginal bleeding is variable & frequently underestimates the degree of total loss
- blood tracks back into the myometrium and broad ligaments → ***concealed abruption***
- diagnosis is made clinically or by ultrasound

▪ ***Complications***

1.	hypotension ± haemorrhagic shock	
2.	coagulopathy (DIC)	~ 20-40% of severe abruptions
3.	pregnancy induced hypertension	~ 50% of severe abruptions
4.	acute renal failure	~ 1-4%
5.	postpartum haemorrhage	
6.	ischaemic organic necrosis	

- DIC occurs 2° to the release of ***tissue thromboplastin*** from necrotic placental tissue, with activation of circulating ***plasminogen***

- this leads to activation of fibrinolysis and a consumptive coagulopathy,

1. hypofibrinogenaemia - decreased factors V and VIII
2. thrombocytopaenia
3. ↑ APTT & INR
4. ↑ fibrinogen degradation products
5. widespread capillary damage and increased permeability

PREMATURITY

Def'n: birth of an infant between the 20th and 37th weeks of gestation

distinct from a ***small for gestational age*** infant → < 10th percentile

- the incidence ranges from 7-8% in the USA
- it accounts for ~ 80% of all ***perinatal deaths***, either directly or indirectly
- morbidity & mortality tends to be ***greater*** than for the SGA infants

Predisposing Factors

a. ***maternal factors***
   i. previous history of premature labour or abortion
   ii. systemic disease - diabetes, hyperthyroidism, CVS disease
   iii. trauma, surgery
   iv. coitus
   v. low socioeconomic status
   vi. drug abuse - smoking, cocaine, ? ETOH
   vii. general anaesthesia

b. ***uterine factors***
   i. premature ROM
   ii. incompetence of the cervix
   iii. malformations, tumours, retained IUCD
   iv. overdistension - polyhydramnios, multiple gestation

c. ***placental abnormalities*** - praevia, abruption

d. ***foetal problems***
   i. congenital malformations
   ii. infections
   iii. growth retardation
   iv. IUD

- ***Obstetric Problems***

a. breech presentation ~ 25% cf. 3% normally

b. maternal haemorrhage * associated problems
   i. placenta praevia
   ii. abruptio placentae
   iii. uterine atony from residual tocolytic agents

c. prolapsed cord / foetal distress

d. infection
   - association of prematurity with premature ROM
   - may be obscured by ***glucocorticoids*** given to enhance lung maturity

- ***Tocolysis***

- absolute contraindications,

a. significant maternal haemorrhage

b. acute foetal distress

c. chorioamnionitis

d. eclampsia / severe preeclampsia

e. foetal anomaly incompatible with life, or IUD

- relative contraindications,

a. mild / moderate preeclampsia

b. maternal disease
   i. cardiovascular
   ii. endocrine - uncontrolled diabetes or hyperthyroidism
   iii. renal disease

c. foetal growth retardation

- indications,

1. ***transfer*** to a high risk obstetric unit

2. enhancement of foetal ***lung maturity***
   - < 34 weeks production of ***surfactant*** by type II pneumocytes is insufficient
   - maternal glucocorticoids ***may*** decrease IRDS, mechanism unknown
   - requires 24 hours for effect & effective within 7 days of delivery
   - undesirable side-effects which may be increased by β-adrenergic tocolytics
   i. PIH
   ii. diabetes
   iii. possibly infection

Premature Rupture of the Membranes

- 80-90% of such patients will proceed into premature labour within 7 days
- risk of delaying these patients is the development of ***chorioamnionitis,***
    a. 4 fold increase in
        i. IRDS
        ii. neonatal sepsis
        iii. intraventricular haemorrhage
    b. prophylactic antibiotic therapy ***has*** been shown to reduce these complications
    c. tocolytic therapy is ***not*** more effective than expectant management
    d. relative contraindication to administration of glucocorticoids

Anaesthetic Considerations

a. labour and vaginal delivery in the event of failed tocolysis
b. elective caesarean section for maternal / foetal wellbeing
c. emergent caesarean section for foetal distress

- in addition to the usual requirements,
    1. to maintain maternal safety
    2. avoidance of foetal asphyxia, and
    3. provision of maternal comfort
        - during vaginal delivery it is important to inhibit the maternal "bearing-down" reflex, and thus a potentially traumatic delivery
        - uncontrolled, precipitous delivery increases the risk of ***intracranial haemorrhage***

- the preterm infant is also less tolerant of ***asphyxia***, which markedly increases the risk of,
    1. respiratory distress syndrome
    2. intraventricular haemorrhage
    3. necrotising enterocolitis

- however, premature labour is associated with a higher incidence of,
    1. placental abruption
    2. placenta praevia
    3. prolapsed cord, and
    4. infection

- therefore, a trial of premature labour is frequently associated with foetal distress and the need for urgent LUSCS

Side Effects of Tocolytic Agents

Drug	Maternal Effects	Foetal Effects
β-agonists	anxiety, nervousness nausea and vomiting hyperglycaemia hypokalaemia metabolic (lactic) acidosis hypotension, tachycardia chest pain, tightness arrhythmias pulmonary oedema, CCF	tachycardia foetal hyperglycaemia neonatal rebound hypoglycaemia increased free fatty acids foetal asphyxia (large doses) • maternal hypotension • increased uterine resistance
$MgSO_4$	anxiety, nervousness nausea and vomiting flushing drowsiness blurred vision sensitivity to muscle relaxants pulmonary oedema, CCF	hypotonia drowsiness decreased gastric motility hypocalcaemia
Phosphodiesterase inhibitors	tachycardia, arrhythmias narrow therapeutic index hypotension tremor nausea & vomiting hyperglycaemia hypokalaemia	tachycardia hyperglycaemia rebound hypoglycaemia
Prostaglandin synthetase inhibitors	GIT irritation inhibition of platelet function reduction in factor XII depressed immune function	? decreased uterine blood flow
Ethanol	CNS depression disorientation, agitation, headache nausea and vomiting hypotension gastric hypersecretion & acidity hypoglycaemia metabolic acidosis	foetal & neonatal CNS depression neonatal respiratory depression hypotonia metabolic acidosis hypoglycaemia temperature instability gastric irritation & vomiting foetal alcohol syndrome (withdrawal)

Tocolytic Agents

• the most commonly used agents are,

1. β_2-adrenergic agonists
2. $MgSO_4$

▪ ***Beta-Adrenergic Agonists***

• salbutamol, terbutaline and ritodrine are the commonly used agents
• although they are b_2-***selective***, they have significant β_1 activity which accounts for most of the undesirable effects
• tachycardia, often > 120 bpm is common
• ***pulmonary oedema*** £ **5%** of patients
• cause is not completely understood, but risk factors include,

a. prolonged therapy with / high doses of β-agonists
b. pre-existing cardiac disease
c. anaemia
d. inappropriate resuscitation & overhydration
e. multiple gestation
f. hypokalaemia
g. sepsis
h. ? combined therapy with $MgSO_4$

• concurrent use of glucocorticoids is no longer thought to be a risk factor
• opinion currently favours a ***noncardiogenic*** origin, in the absence of pre-existing cardiac disease
• ***hypoxic pulmonary vasoconstriction*** is impaired during β-adrenergic therapy
• this may account for ***hypoxia***, out of proportion to the degree of pulmonary oedema
• predominantly β-vasopressors, such as ***ephedrine***, will have reduced efficacy and may exacerbate the tachycardia
• recent human studies have shown that in the setting of maternal hypotension, the use of virtually ***pure*** a***-agonists*** (phenylephrine, metaraminol), ***does not*** produce any adverse neonatal outcome,

1. Apgar scores
2. acid-base balance
3. neurobehavioural examination

NB: these studies were in ***term*** pregnancies, still to be validated in preterm

- metabolic side-effects include,
    1. increased glycogenolysis, lipolysis, and gluconeogenesis
    2. ***hyperglycaemia*** and raised plasma insulin
        - may require additional insulin in the diabetic
        - may be exacerbated by glucocorticoids for foetal lung maturation
        - neonatal ***rebound hypoglycaemia*** may be severe
    3. intracellular shift of K^+, with ***hypokalaemia***
        - normal total body stores, therefore no treatment is required
        - hyperventilation / alkalaemia will enhance hypokalaemia
        - hypoventilation / acidaemia increase arrhythmias

- ***myocardial ischaemia*** and infarction have been associated with β-adrenergic use
- however, these are exceedingly rare in the absence of heart disease

- relative ***contraindications***,
    1. significant cardiac disease - AS, MS, IHSS
    2. uncontrolled hypertension
    3. severe PIH
    4. unstable diabetes mellitus
    5. hyperthyroidism
    6. ? asthma
    7. history of migraine headaches

■ ***Magnesium Sulphate***

• decreases uterine activity by membrane and intracellular competition with Ca^{++}
• efficacy is comparable to that of ritodrine, though many side-effects are similar,

a. decrease in MAP * decreased PVR

b. tachycardia * reflex, not direct chronotropic cf. β-agonists

c. depression of myocardial contractility

d. myocardial conduction blockade

e. neumomuscular junction blockade

i. ↓ ACh release from motor neurone

ii. ↓ sensitivity of the motor endplate to ACh

iii. ↓ excitability of the muscle membrane

- ***not*** reliably antagonised by administration of Ca^{++}

f. postpartum uterine atony and haemorrhage

g. nausea, vomiting, flushing, drowsiness and blurred vision

• toxicity is far more likely in the presence of abnormal ***renal function***
• in the absence of toxic plasma levels, the CVS effects are generally ***less*** than the β-agonists,

1. pulmonary oedema - seen less frequently
2. tachycardia - seldom significant

NB: however, some animal work suggests that Mg^{++} blunts the compensatory haemodynamic response to ***haemorrhage*** to a greater extent

\ ***hypotension*** should be treated promptly with volume / ephedrine

Clinical Manifestations of Hypermagnesaemia

Plasma Level		Clinical Features
2.0-4.0	mmol/l	anticonvulsant ?? sedation mild vasodilatation increased AV & ***intraventricular conduction***
~ 5.0	mmol/l	loss of ***monosynaptic reflexes*** (DTR's) increase in PR & QRS duration hypotension respiratory centre depression
~ 6.0	mmol/l	NMJ blockade, severe weakness
6.0-8.0	mmol/l	respiratory paralysis
8.0-12.0	mmol/l	cardiac arrest (asystolic)

AMNIOTIC FLUID EMBOLISM

- rare cause of maternal mortality
- first reported by Meyer in 1926, then subsequently in animal work by Warden in 1927
- clinical importance established by Steiner and Lushbaugh in 1941

a. incidence ~ 1:8,000 to 1:80,000

b. ***mortality*** **~ 86%**
~ 25-50% within the first hour

c. aetiology

i. predisposing factors
- advanced maternal age
- multiple pregnancies - majority > 3
- foetal macrosomia
- short duration labour with intense contractions
- oxytocic stimulation - intact membranes

ii. associated factors
- foetal demise ~ 40%
- meconium stained liquor
- amniotomy, amniocentesis
- PIH
- placenta praevia & placental abruption ~ 50%
- LUSCS
- pregnancy with an IUCD
- uterine rupture or cervical tears

■ ***Pathophysiology & Clinical Picture***

- classical descriptions are of the unheralded onset of ***shock, cyanosis, & coagulopathy***, typically in a multiparous patient
- the 2 life-threatening consequences of AFE are,

1. ***cardiopulmonary collapse***
   - acute pulmonary hypertension → cor pulmonale & RVF
   - V/Q mismatch, hypoxia, hypercarbia & acidaemia, further increasing PVR
   - ↓ LV preload & LV output, with peripheral vascular failure

2. ***DIC***
   - aetiology disputed
   - potent thromboplastic activity of amniotic fluid, deposition of fibrin clots and activation of fibrinolysis → hypofibrinogenaemia & coagulopathy
   - thromboplastic activity of trophoblastic tissue may play an integral role
   - toxicity of amniotic fluid is greatly dependent upon the ***particulate content***
   - this is especially true for meconium, **? *anaphylactoid*** response, however,

   i. ***absence*** of pruritis, urticaria & bronchospasm

   ii. requires "sensitisation", evidence for which is frequently lacking

- the most significant pathological finding are those in the lungs,
  1. pulmonary oedema ~ 70%
  2. alveolar haemorrhage
  3. pulmonary embolisation with amniotic materials

- prodromal symptoms of AFE include the sudden onset of,
  a. chills & shivering
  b. sweating, anxiety
  c. coughing, followed by signs of respiratory distress

  NB: these are followed by shock, cardiovascular collapse and convulsions

- respiratory difficulty is manifest by,
  a. cyanosis & tachypnoea*
  b. bronchospasm (?)
  c. pulmonary oedema

  NB: *2° to ***hypoxia***, which is also the cause of the ***convulsions***

- the definitive diagnosis is usually made at autopsy, however additional diagnostic aids include,

a.	CXR	- enlargement of the RA & RV - prominent proximal PA (cf. embolism) - pulmonary oedema (not seen in PTE, cf. the former)
b.	Lung scan	- isolated perfusion defects
c.	CVC catheter	- initially raised pressures 2° to pulmonary hypertension - later pressures may be low 2° to haemorrhage
d.	FBE / Coag's	- coagulopathy & anaemia later - cf. the normal procoagulant state of pregnancy

- ***Differential Diagnosis***

a.	pulmonary thromboembolism	- more common postdelivery - chest pain is a more common finding
b.	air embolism	- similar except for doppler / auscultation
c.	aspiration of gastric contents	- temporal relationship to general anaesthesia
d.	eclamptic convulsions	- presence of hypertension & proteinuria
e.	local anaesthetic toxicity	- temporal relationship & dose administered
f.	acute LVF	- presence of pre-existing heart disease
g.	cerebrovascular accident	- no cyanosis or coagulopathy
h.	haemorrhagic shock	- abruptio placentae, placenta praevia - ruptured uterus

- ***Management***

• no specific therapy, supportive only

a. ***respiratory***
   i. high F_IO_2
   ii. CPAP
   iii. intubation & ventilation - 100% O_2 ± PEEP
   iv. treatment of bronchospasm

b. ***cardiovascular***
   i. left uterine displacement
   ii. CVP / PCWP guided volume resuscitation
      • pulmonary oedema is variably ascribed to excessive volume therapy
   iii. inotropic support of MAP
   iv. treatment of pulmonary vasospasm ? inhaled NO

c. ***treatment of DIC***
   i. fresh whole blood, or packed cells plus FFP
   ii. cryoprecipitate - several reports of improvement (? fibronectin)
      * fibrinogen may act only to perpetuate coagulation
   iii. platelets
   iv. heparin * controversial, not recommended

d. other
   i. uterine massage and oxytocic stimulants (oxytocin ± methylergonovine)
   ii. PG's for control of uterine haemorrhage
      * may result in ***bronchospasm*** and/or ***pulmonary hypertension***
   iii. ***aprotinin*** for control of lysis prior to delivery
      * aprotinin doesn't cross the placenta & EACA is teratogenic

THROMBOEMBOLIC DISEASE

▪ ***Incidence***

a. ~ 0.05-1.8% of pregnancies (1:50 - 1:2000)
b. ~ 5x more common during pregnancy & postpartum period
c. ~ 3-6x more common ***postpartum*** cf. antepartum
d. ~ 3x more common with LUSCS cf. vaginal delivery
e. ~ 12% risk of repeat episode in the same pregnancy
f. ~ 5-10% risk during subsequent pregnancies

▪ ***Aetiology***

• three classically described factors,

1. ***vessel wall trauma***
2. ***venous stasis***
   - increased venous distensibility during first trimester
   - aortocaval compression from the second trimester
   - bed rest post-partum and with complications of pregnancy
3. ***altered coagulation status***
   - ↑ coagulation → ↑ all factors, except XI & XIII; ↓ antithrombin III
   - ↓ fibrinolytic activity → ↓ plasminogen activators; ↑ soluble fibrin-fibrinogen complexes
   - neither the platelet count, nor platelet adhesiveness is increased

NB: other risk factors,

i. increased maternal age
ii. obesity
iii. caesarean delivery
iv. prolonged bed rest
v. oestrogen therapy to suppress lactation
vi. blood group other than ***type O***
vii. * antithrombin III deficiency (autosomal dominant)

■ ***Pathophysiology***

- physiological disturbance depends upon,
  - a. the size of the embolus
  - b. the site of obstruction
  - c. the presence of pre-existing cardiopulmonary disease

- clinical syndromes range from,
  - a. asymptomatic
    - i. small multiple emboli traversing the pulmonary arteries
      - subsequent lysis and no adverse haemodynamic consequences
    - ii. isolated small emboli producing subsegmental obstruction
      - subclinical alteration of V/Q matching
  - b. chronic recurrent pulmonary emboli
    - pulmonary hypertension ± cor pulmonale and RVF
  - c. moderate-large single, or multiple emboli
    - i. clinically symptomatic - tachycardia, dyspnoea, mild fever, chest pain
    - ii. significant V/Q mismatch - hypoxaemia, ↑ A-a gradient
    - iii. ↑ RV afterload / ↓ LV preload
  - d. massive embolus
    - severe dyspnoea, hypoxaemia, chest pain
    - hypotension, cardiogenic shock, RVF ± sudden death

- the principal physiological derangement's with ***massive embolism*** are,
  - a. ↑ RV afterload
  - b. ↑ V/Q mismatch
    - i. ↑ V_D/V_T → dyspnoea & tachypnoea
    - ii. ↑ Q_S/Q_T
      - due to loss of ***surfactant*** and local mediator release
      - * ***hypoxaemia*** is frequently ***not*** totally corrected by O_2 administration
  - c. ↓ LV preload and CO with systemic hypotension

  NB: right coronary blood flow usually ***increases*** following PTE, due to ↑RVSWI and autoregulation

Diagnosis

- many of the clinical signs of DVT can be present in normal pregnancy

a. ***venography***
   - where PTE is suspected, is the most sensitive & specific test
   - suboptimal for detecting deep femoral or pelvic vein thromboses
   - there may be false positives with external vein compression, or poor technique

b. ***doppler sonography***
   - sensitivity ~ 90% and is most useful for popliteal, femoral and pelvic thrombi
   - however, far less sensitive at detecting thrombi below the knee
   - because of collateral venous channels ~ 50% of small calf thrombi are missed

c. impedance plethysmography
   - sensitivity/specificity similar to doppler
   - similarly, less effective below the popliteal vessels

d. thermography

e. fibrinogen scanning ($^{125}I^-$) * contraindicated in pregnancy (→ foetal thyroid)
   * also C/I in lactating mothers

f. radionuclide venography (^{99m}Tc) ~ 90% sensitivity

g. ***lung V/Q scan***
   - safe during pregnancy, though, ^{99m}Tc should be used with uterine shielding ??
   - a perfusion defect with normal ventilation is adequate for treatment
   - serious morbidity occur in ~ 2-4% of those having angiography

h. pulmonary angiography - avoided due to radiation hazard & the foetus

Clinical Presentation

- the first sign of DVT may be PTE, and the manifestations of PTE may be nonspecific or absent,

1. apprehension, altered sensorium
2. shortness of breath, dyspnoea, cough ± haemoptysis
3. sweating, syncope, tachycardia
4. chest pain, substernal tightness
5. CXR * usually normal
   - diminished vascular markings ("cut-off" sign)
   - elevated hemidiaphragm
   - pleural effusion
6. ECG - sinus tachycardia, other arrhythmias
   - RV strain: RAD, tall R in V_1, rarely S_1-Q_3-T_3

NB: CXR & ECG are frequently ***normal***, their main use is to rule out other pathology

Management

a. standard ABC in cases of massive embolism with collapse

b. supplemental F_IO_2 to maintain a P_{aO2} > 70 mmHg

c. IVT - access for drug administration
- volume expansion in the presence of hypotension

d. relieve anxiety with morphine

e. anticoagulation

▪ ***Anticoagulation***

• ***heparin*** is a large (x ~ 20,000D) mucopolysaccharide, which acts as an ***ATIII cofactor***

1. to increase the levels of activated **factor X inhibitor**
2. to inhibit the activation of **factor IX**

→ inhibiting the formation of ***thrombin*** from prothrombin

• prevents the formation of further thrombi but ***does not*** lyse existing clot
• plasma activity ***"half-life"* ~ 1.5 hrs** → better administrated by infusion
• heparin is not absorbed from the GIT and IM injection is contraindicated
• the greatest risk is ***haemorrhage*** **~ 4-33%** of patients
• other reactions include,

a. alopecia

b. osteoporosis

c. thrombocytopaenia - type I & II HITS

d. hypoaldosteronism - with prolonged therapy (? preservative)

• long-term therapy in the nonpregnant patient is usually with ***warfarin***
• however, this crosses the placenta readily and has a number of adverse effects,

a. 1st trimester → teratogenetic

b. 2nd trimester → severe CNS abnormalities in ~ 3%

c. 3rd trimester → foetal bleeding either before or after delivery

→ overall ***foetal mortality* ~ 15-30%**

• if the patient is on ***heparin*** at the time of labour, management is simpler,

1. heparin ***does not*** cross the placenta, thus the risk of foetal haemorrhage is low
2. the half-life is short, so if delivery is not anticipated for > 4-6 hours, there is no need to reverse the anticoagulation
3. in an emergency heparin can be reversed with protamine
   - approximate dose → ***protamine*** **~ 1 mg / 100^{U}** ***heparin***

• because of the ease of management, some advocate the use of heparin in these patients up to the time of delivery (150-250^{U} /kg q12h)

• ***thrombolytic agents*** are presently contraindicated during pregnancy
• tPA may be associated with a lower risk of haemorrhagic complications and may be useful under these circumstances

• ***surgical management*** is also limited during pregnancy, procedures used including,

1. femoral vein or vena caval interruption
2. thrombectomy
3. embolectomy * ~ 80% mortality in ***nonpregnant*** patients

VENOUS AIR EMBOLISM

• ***precordial doppler*** can detect as little as **0.1 ml** of intracardiac air & the correlation with TEE during caesarean section is ~ 100%
• the ***incidence*** of Doppler VAE during LUSCS is reported from,

a. 11 to 66% for epidural anaesthesia
b. 28 to 71% for general anaesthesia

NB: this may occur at any stage throughout the procedure,
however is most likely to occur during ***hysterotomy***, or repair of hysterotomy

- ***Aetiology***

a.	pneumoperitoneum	- for laparoscopy or hysteroscopy
b.	LUSCS	- especially with exteriorisation of the uterus
c.	surgery involving major veins	* classically sitting neurosurgery
d.	central venous cannulation	
e.	pump infusions	- CPB, haemofiltration / dialysis
f.	orthopaedic surgery	- especially THR

- ***Contributing Factors***

a. ***venous pressure gradient***
   - gradients ≤ -5 cmH_2O have been associated with significant entrainment
   - exteriorisation of the uterus increases this gradient & distends collapsed veins
   - ↓ CVP,
   i. relative / absolute hypovolaemia
   ii. prolonged labour with NPO status
   iii. pregnancy induced hypertension
   iv. regional anaesthesia with inadequate volume expansion

b. ***posture***
   - routine positioning with lateral tilt produces a gradient ≥ **-10 to -15 cmH_2O**
   - prone back operations, sitting neurosurgery, head-up ENT, etc.

c. ***volume*** & ***rate*** of entrainment
   - small volumes entrained slowly are usually asymptomatic
   i. ³ **0.5 ml/kg/min** → results in symptoms
   ii. ³ **2 ml/kg/min** → generally fatal

d. presence of an ASD * probe patent foramen ovale in **~ 10-25%**

- ***Associated Problems***

a. pulmonary hypertension± acute RV failure
b. systemic hypotension and tachycardia
c. increased alveolar dead space and P_{A-aO2} gradient
d. hypoxia
e. arrhythmias, cardiac arrest
f. systemic embolisation * coronary or cerebral

NB: rapid death following massive embolisation is 2° to obstruction to ***RV outflow***

- ***Monitoring***

1. poor sensitivity
   i. oesophageal stethoscope ~ 1.8 ml/kg/min
   ii. systemic hypotension ~ 0.7 ml/kg/min
   iii. ECG / tachyarrhythmias ~ 0.6 ml/kg/min
2. intermediate sensitivity ~ 0.5 ml/kg/min required for clinical symptoms
   i. $ETCO_2$ ~ 0.42 ml/kg/min
   ii. PA pressure rise ~ 0.42 ml/kg/min
   iii. continuous CVP ~ 0.4 ml/kg/min
3. high sensitivity
   i. ***doppler precordial stethoscope*** **~ 0.02 ml/kg/min** (1.5 ml/min)
   ii. transoesophageal echocardiography ~ 5-10x more sensitive than doppler

- ***Clinical Presentation***

- massive VAE, with EMD, hypotension, hypoxaemia and cardiac arrest is ***infrequent***
- only ~ 1% of maternal deaths are attributed to VAE
- the routine picture is less profound, presumably due to the slow rate of entrainment
- the aetiology of ***chest pain*** during LUSCS is unclear & probably multifactorial, however,

a. 20-50% of women ***with*** doppler VAE will complain of chest pain
b. < 2% ***without*** doppler VAE will complain of chest pain
c. SpO_2 < 92% has been reported in up to 25% with doppler VAE
d. ***dyspnoea*** is present in 20 to 40% with doppler VAE

NB: dyspnoea and SpO_2 < 92%, without doppler VAE is unusual

- ***Management***

• for symptomatic doppler evident VAE, or strongly suspected clinical VAE,

a. prevent further air embolisation
   - flood the operative field with saline if practicable
   - return the uterus to the abdominal cavity

b. 100% F_IO_2 (ie. cease N_2O)

c. usual recommendation is right lateral position, however,
   ? maintain left lateral tilt, as this decreases chance of RV outflow obstruction

d. IV volume expansion

e. place a ***multiorifice CVC*** line and attempt to aspirate air

f. if cardiovascular collapse occurs → immediate delivery of the baby

g. drugs
   - inotropes / vasoconstrictors
   - selective pulmonary vasodilators
   - antiarrhythmics

h. others

   i. thoracotomy

   ii. intracardiac needle aspiration
   ** must get RV & always get a ***pneumothorax***

NB: any patient who becomes ***comatose***, or fails to waken following GA, should have a CT head to exclude cerebral air embolism, as prompt management with ***hyperbaric oxygen*** is indicated

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CARDIAC DISEASE

Valvular Heart Disease

- the prevalence of heart disease during pregnancy ranges from 0.4 to 4.1%
- surgically amenable lesions should be corrected prior to pregnancy
- patients with valvular lesions should have ***antibiotic prophylaxis*** prior to operative procedures

Mitral Valve Prolapse

- prolapse of one or more of the MV leaflets (usually ***posterior***) into the LA during systole
- estimated incidence **~ 5%** general population
  ≤ **20%** in pregnancy
- clinical features include,
  a. a midsystolic snap
  b. a late systolic, bruit best heard at the ***apex***
  c. classically thin and tall patient, who may possess other Marfanoid features

- diagnosis is usually suspected from auscultation and confirmed by echocardiography
- aetiology is unknown, but thought to involve autosomal dominant inheritance, with reduced male expression
- few are symptomatic and even fewer are on medical therapy, usually for TIA's or frequent PCV's
- sudden death is commonly discussed but exceedingly ***rare*** and results from arrhythmia
- if severe these patients are managed as for mitral regurgitation (see below)

Mitral Regurgitation

- the second most common valvular anomaly during pregnancy
    a. soft S_1 and a widely split S_2
    b. holosystolic murmur, best heard at the apex, radiating to the axilla

- the increased blood volume of pregnancy is usually helpful for the MR patient
- in chronic MR, in contrast to acute MR,
    a. the LA dilates to accommodate the regurgitant volume
    b. LA stretch may result in AF
        - may precipitate ***pulmonary oedema***, with a maternal mortality ~ 17%
        - may result in ***systemic embolisation***
    c. the LV dilates and hypertrophies with the LA
    d. ↑ LVEDP
    e. ↓ LVEF

- techniques which decrease afterload are preferable, as they decrease the regurgitant fraction and increase forward cardiac output
- as these patients are ***preload dependent***, they require
    a. adequate volume expansion prior to establishment of regional block
    b. absolute avoidance of aortocaval compression

- if ***general anaesthesia*** is to be used, then the following principals apply,

    NB: "full, fast and loose"

    a. factors decreasing the regurgitant fraction,
        - decreasing afterload
        - vasodilators
        - regional anaesthesia
    b. factors increasing the regurgitant fraction,
        - ↑ afterload
        - ↑ SNS tone - pain, hypoxia, hypercarbia, acidosis
        - ↓ HR
        - N_2O
    c. volume expansion prior to induction, and prompt replacement of blood loss

Mitral Stenosis

NB: this is the most common of the ***rheumatic*** valvular lesions in pregnancy

a. diastolic pressure gradient LA-LV determined by mitral valve area & flow

b. ↑ LAP, pulmonary venous pressure ± pulmonary oedema

c. passive, reversible pulmonary hypertension & ↑ PVR
→ irreversible pulmonary hypertension later

d. ↓ CO ∝ ↓ LV filling & ***LV dysfunction***

• causes of sudden deterioration include,

1. AF
2. fever, infection, SBE
3. exercise, pregnancy

- ***Symptoms***

a. dyspnoea, orthopnoea, PND

b. acute pulmonary oedema

c. haemoptysis - may be severe

d. recurrent respiratory infection

e. fatigue - ↓ CO, development of PAH

f. chest pain ~ 10%

g. systemic thromboembolism

- ***Clinical Signs***

a. malar flush, peripheral cyanosis

b. small volume pulse ± AF

c. normal JVP ± loss of 'a' wave

d. heart - 'tapping' apex beat (palpable 1st HS)
- palpable RV impulse & loud P_2

e. auscultation * 4 cardinal signs →

i. loud S_1

ii. opening snap

iii. mid-diastolic rumble - supine ± left lateral

iv. pre-systolic accentuation

- ***Investigations***

a. ECG
   - P mitrale, biphasic P in V_1 ± AF
   - RV hypertrophy (PAH) ± "strain"

b. CXR
   - enlarged LA
   - pulmonary venous congestion - Kerley B lines
     ± pulmonary oedema
   - large pulmonary outflow tract
   - mitral valve calcification - lateral > AP

c. Echocardiography
   - assessment of severity - MV area, leaflet thickening
     - estimated MV gradient
   - exclusion of atrial myxoma
   - LA size and presence of thrombus
   - LV size and function
   - RA/RV size & function

d. Catheterisation
   - MV area & pressure gradient
   - PVR and pulmonary hypertension
   - LV function
   - * coronary artery anatomy
   - other valvular lesions

- ***Clinical Assessment of Severity***

a. severity of dyspnoea / exercise limitation
   - ie. NYHA classification, grades I-IV

b. systolic BP and pulse volume

c. signs of PAH - RV heave& loud P_2
   - ↑ JVP

d. murmur - duration of murmur ∝ degree of stenosis
   - interval between S_2-OS
   - ↓ S_2-OS interval due to higher LAP & earlier extension of valve, ∴ worse

e. loud S_1 and OS represent ***pliable valve***

f. CXR
   - valve calcification
   - LAH, PA prominence
   - CCF
   - ? LVH - implies other disease process

Treatment

- ***Medical***

1.	SBE prophylaxis	
2.	AF	- digoxin ± quinidine - cardioversion
3.	systemic emboli	- warfarin, heparin peripartum
4.	dyspnoea	- diuretics, fluid restriction, low Na^+ diet - ACE inhibitors

- ***Surgery***

1. commisurotomy
2. valve replacement

- ***Anaesthetic Considerations***

• Chesley claims that the mortality of paturients with MS is equal to that of those who have never conceived
• ***atrial fibrillation*** is a common sequelae of MS and ***does not*** result in an increased mortality in either pregnant or nonpregnant patients (Sullivan & Ramanathan NEJM 1985)

NB: "full, slow and tight"

a. primary goal is to maintain a slow HR
   - rates > 110 are poorly tolerated
   - avoid anticholinergics, sympathomimetics, vasodilators (reflex)
   - with recent onset AF consider DC cardioversion, or digoxin to control rate

b. relatively ***fixed CO***
   i. maintain SVR, avoid vasodilatation
   ii. maintain preload
      - within the constraints of pulmonary congestion
      - rapid infusions may precipitate AF or acute pulmonary oedema

c. avoid pulmonary vasoconstriction
   - hypoxia, hypercarbia, acidosis

AORTIC STENOSIS

a. ***aetiology*** - congenital bicuspid valve
- rheumatic
- calcific or degenerative

b. ***pathophysiology***

i. normal valve area ~ 2.5 - 3.5 cm^2

ii. LV / aortic root pressure gradient

iii. chronic pressure overload
- concentric LVH → ↑ LV mass
- LV failure / decompensation

iv. fixed low output state

v. ↓ LVEF and CO

vi. ↑ LVEDP → eventually ↑ LAP

vii. ↑ PCWP → eventually pulmonary hypertension

c. ***symptoms*** * late onset and indicate ***severe*** stenosis

i. angina - life expectancy ~ 5 yrs
~ 50% have CAD

ii. effort syncope - life expectancy ~ 3-4 yrs
- eventually LVF ± arrhythmias

iii. SOBOE - life expectancy 2 yrs

- ***Physical Examination***

a. pulse - regular if in SR
- slow upstroke, plateau, small volume

b. BP - narrow pulse pressure

c. heart - ↑ LV impulse + presystolic lift (S_4)
- sustained, basal systolic thrill
- harsh SEM → carotids
- decrease in A_2/P_2 + ***reverse splitting***
* normal heart size until late

NB: AS + cardiomegaly → AI, MI, CCF & severe end-stage disease

- ***Problems***

1. the murmur may disappear with the development of LVF
2. the pressure gradient is low with LVF
3. in the elderly
   i. murmur is often louder at the apex / LSE
   ii. arteriosclerosis obscures pulse changes
   iii. other causes of LVF are common

- ***Investigations***

a. ECG - SR, LVH ± strain
~ 10% LBBB

b. CXR - normal heart size
- convex LV border
- dilated ascending aorta (post-stenotic)
- valve calcification

c. Echo - AV disorganisation, LVH
- LV size and contraction
- LA size
- ***not*** good at quantifying severity

d. Catheterisation - assessment of LV function and other valves
- coronary anatomy

Catheter	AV gradient	AV area
normal	~ 0 mmHg	2.5-3.5 cm^2
mild	0-25 mmHg	1.2-2.0 cm^2
moderate	25-50 mmHg	0.8-1.2 cm^2
severe	> 50 mmHg	< 0.8 cm^2

- ***Medical Treatment***

1. SBE prophylaxis
2. digoxin & diuretics for LVF
3. balloon dilatation
4. vasodilators are ***contraindicated***, except in severe LVF
5. cardioversion for sudden onset AF

- ***Anaesthetic Considerations***

NB: "full, normal rate & tight"

• these patients tolerate the increase in plasma catecholamines better than MS/MI patients
• some will use a slow onset epidural block, though, decreases in afterload are contraindicated
• spinal anaesthesia remains contraindicated
• ***hypotension*** should be treated aggressively, using predominantly α_1-agonists (metaraminol) rather than ephedrine
• some recommend GA using thiopentone/volatile/N_2O/vecuronium
• irrespective of the technique used, the following are relevant,

a. good IV access * 2 x 16G or larger cannulae

b. ECG with II + V_5 to monitor for ***ischaemia***

c. prevent ischaemia * avoid AF, loss of atrial contribution to LV filling
- avoid tachycardia/bradycardia
- avoid decrease SVR

d. maintain - ***sinus rhythm***, HR ~ 70-80 bpm
- preload and SVR

Aortic Regurgitation		
	Acute	**Chronic**
Aetiology:	• SBE • aortic dissection • traumatic	• rheumatic • Marfan's • SBE • syphilis • RA, psoriasis, Reiter's • UC, Crohn's, ankylosing sp. • myxomatous degeneration
Symptoms:	• abrupt onset • pulmonary oedema • cardiogenic shock	• asymptomatic period • palpitations • fatigue, SOBOE • angina ~ 5-10%
Signs:	• rapid low volume pulse • hypotension • ***normal*** heart size[1] • soft or absent S_1 • loud S_3 • EDM (soft)	• 'water hammer' pulse • low diastolic pressure • LV enlargement • decrescendo DM at LSE • ESM with high CO • apical MDM (Austin Flint)
ECG:	• normal ± ischaemia	• LVH
CXR:	• LVF, pulmonary oedema • dilated aorta	• increased LV & aortic shadow • pulmonary oedema late

[1] NB: differential of acute pulmonary oedema & a small heart

- predominance of AI / AS determined clinically by,
    1. pulse characteristic
    2. pulse pressure
    3. heart size

- clinical severity is determined by,
    a. pulse character - bounding, collapsing, bisferens
    b. BP - systolic > 140 & diastolic < 60
    c. cardiomegaly
    d. LV heave
    e. Austin-Flint murmur
    f. ECG - LVH & strain
    g. loudness of the murmur is ***not*** a useful guide
    h. assessment of severity is via ***echocardiography*** and ***catheterisation***

- ***Anaesthetic Management***

  NB: "full, dilated and fast"

  a. maintain a HR > 80 bpm, with a low SVR
  b. avoid bradycardia & vasoconstriction
  c. regional anaesthesia, with sympathetic blockade, is the technique of choice
  d. if hypotension develops, ***ephedrine*** is the agent of choice
     → ↑ HR & ↑ vascular tone

IDIOPATHIC HYPERTROPHIC SUBAORTIC STENOSIS

- ***Features***

  a. hypertrophic cardiomyopathy
  b. marked asymmetrical septal hypertrophy
  c. autosomal dominant inheritance ~ 50% familial

- ***Pathophysiology***

  a. anatomical septal hypertrophy
  b. marked ↓ LV compliance
  c. ↑ LAP
  d. hypercontractile LV
  e. dynamic subaortic muscular stenosis
  f. systolic anterior motion of anterior MV leaflet ± occasionally with MR

- ***Symptoms***

  a. exertional angina
  b. effort syncope
  c. palpitations
  d. SOBOE
  e. sudden death

- ***Clinical Signs***

  a. sharp upstroke, often bifid pulse
  b. ESM at the LSE and apex → ↑ by valsalva manoeuvre
  c. MR in 50%
  d. normal S_1 and normal or split S_2
  e. ± S_3 and S_4

- ***Complications***

  a. sudden death, syncope
  b. arrhythmias
  c. LVF *murmur decreases markedly
  d. angina

- ***Exacerbating Factors***

  a. ↑ contractility
  b. ↓ preload
  c. ↓ afterload

- ***Factors Decreasing Dynamic Obstruction***

  a. ↓ contractility
  b. ↑ preload
  c. ↑ afterload

- ***Investigations***

  a. ECG - LVH + strain changes
     - septal Q-waves simulate AMI
     ± LA hypertrophy
  b. CXR - often no LVF or cardiomegaly
  c. Echo - anterior septal hypertrophy
     - ratio of septum:free wall ≥ **1.5:1**
     ± increase in size of LA

- ***Treatment***

a. β-adrenergic blockade
   - usually administered to all pregnant patients chronically
   - reduce contractility, decrease outflow obstruction
   - the slower HR allows increased diastolic filling which increases the LVEF

b. Ca^{++} entry blockers

c. ? diuretics

d. management of arrhythmias * amiodarone ***not*** digoxin

e. partial surgical resection of the septum

- ***Anaesthetic Considerations***

- as for MS & AS, Ostheimer believes slow onset epidural anaesthesia, instituted early in labour is not contraindicated, cf. spinal anaesthesia
- general anaesthesia considerations are,

NB: "full, slow and tight"

a. SBE prophylaxis

b. avoid
   - AF, tachycardia
   - falls in venous return or SVR
   - increases in contractility

c. maintain
   - slow HR, low contractility
   - high venous return & high SVR

ARRHYTHMIAS

• pregnancy is associated with an increased incidence of ***benign arrhythmias*** (PAC's / PVC's)
• investigation should focus on contributing factors, coexisting cardiac disease and the patient's haemodynamic status

Guide to Antiarrhythmics in Pregnancy

Drug	Route	Application	Use in Pregnancy	Comments
Lignocaine	IV	VT, VF digoxin toxicity	safe	• toxic doses and foetal acidosis → accumulation and neonatal CVS depression
Quinidine	oral	PAT	relatively safe	• high doses may lead to premature labour • rarely neonatal thrombocytopaenia
Procainamide	oral, IV	termination & prophylaxis in PAT	relatively safe	• maternal ANF & "lupus" syndrome chronically
Phenytoin	oral, IV	digoxin toxicity resistant VF/VT	not recommended ? OK acutely for digoxin toxicity	• "foetal hydantoin syndrome" • bleeding disorders
Amiodarone	oral, IV	SVT, VT, VF	**not recommended**	
Verapamil	oral, IV	SVT, chronic AF	probably safe	• IV may cause hypotension & foetal distress
Digoxin	oral, IV	SVT, chronic AF	safe	• monitor plasma levels • adjust dose with quinidine

Propranolol	oral, IV	atrial & ventricular tachyarrhythmias, chronic AF	relatively safe	• chronicly associated with
				  • IUGR, premature labour
				  • neonatal hypoglycaemia
				  • bradycardia
				  • respiratory depression

■ ***Sinus Arrhythmias***

• HR normally increases 10-20% during pregnancy
• in the absence of hypoxia, hypotension, anaemia, or fever, tachycardia requires no therapy
• ***bradycardia*** is rare in pregnancy in the absence of organic cardiac disease
• other underlying conditions include hypothyroidism, coronary artery disease, cardiomyopathy, or drug effects

Supraventricular Tachycardias

a. ***premature atrial contractions***
- increased in pregnancy & more likely to cause symptoms of anxiety etc.
- usually benign, often related to stress, fatigue, caffeine or alcohol consumption
- in rheumatic heart disease they may herald the onset of atrial flutter / fibrillation

b. ***paroxysmal atrial tachycardia*** ± block
- rapid reentry rhythm, beginning & terminating with a PAC
- HR ranges from 140-220 bpm
- increased susceptibility in pregnancy, or increased frequency of paroxysms
- usually well tolerated haemodynamically, unless underlying CVS disease
- ***sinus massage*** may help differentiate from,

i. sinus tachycardia - no effect or gradual slowing

ii. flutter with 2:1 block - increased degree of block

- massage may be therapeutic in PAT converting the rhythm to sinus
- R_X adenosine, edrophonium, metaraminol, digoxin, verapamil, β-blockade
- PAT + block = ***digoxin toxicity***→ check levels and treat hypokalaemia

c. ***multifocal atrial tachycardia***

d. ***atrial flutter***
- uncommon in pregnancy
- flutter waves ~ 220-340 bpm, with ventricular response ~ 150 bpm
- hyperthyroidism, chronic pulmonary disease & organic heart disease are common
- therapy for the underlying condition and slowing the ventricular rate
- R_X digoxin, verapamil, quinidine, procainamide

e. ***atrial fibrillation***
- rare in pregnancy, except in patients with,

i. mitral valve disease

ii. cardiomyopathy

iii. IHD

iv. chronic obstructive pulmonary disease, pulmonary embolism

v. hyperthyroidism

- ventricular rates ~ 140-200 untreated and 90-110 in chronic cases
- with chronic cases, left atrial thombus and systemic ***embolism*** is a major risk
- anticoagulation should be considered in these patients with heparin (not warfarin)
- R_X digoxin, verapamil, DC cardioversion for acute onset or if unstable

Ventricular Arrhythmia's

a. ***premature ventricular contractions***
- isolated, asymptomatic PVC's require no therapy
- symptomatic PVC's in patients without underlying CVS disease are best managed by removal of precipitating factors, such as alcohol or caffeine
- echocardiography to rule-out mitral valve prolapse or asymmetrical septal hypertrophy
- in the presence of underlying CVS disease, PVC's may herald the onset of LVF

b. ***ventricular tachycardia***
- rare in pregnancy, but does occur more frequently in those with frequent PVC's
- usually have underlying CVS disease, IHD, mitral valve disease, cardiomyopathy, valvular heart disease, mitral valve prolapse, asymmetrical septal hypertrophy, congenital long QT syndrome
- R_X = DC cardioversion if unstable, lignocaine for stable, slower patients
  bretylium and phenytoin are second line agents
  correction of underlying abnormalities (hypo-K^+/Mg^{++}, hypoxia)
  quinidine or procainamide are used for recurrent or chronic VT

c. ***ventricular fibrillation***
- though rare, this is the most common cause of maternal death
- R_X = immediate DC cardioversion & advanced life support
  failure to respond mandates ***immediate caesarean section***
- both cardioversion and defibrillation have been used successfully in pregnancy
- other than transient foetal arrhythmias, foetal outcomes have been good
- upward & lateral displacement of the mediastinum requires more lateral paddle placement

Conduction Abnormalities

Bundle Branch Blocks

- are rare in pregnancy, right being more common than left
- usually secondary to underlying CVS disease,
    a. cardiomyopathy
    b. coronary artery disease
    c. valvular heart disease
- in the absence of underlying disease, no specific therapy is required

Wolff-Parkinson White Syndrome

- characterised by a short PR interval, prolonged QRS and a δ-wave
- these patients are more likely to experience arrhythmias during pregnancy
- usually reentrant rhythms, ventricular rates up to 200 bpm, through an aberrant pathway (bundle of Kent most common)

NB: R_X = DCCV for unstable rhythms
procainamide & β-blockers for chronic therapy

- ***digoxin*** may increase conduction through the aberrant pathway & is contraindicated

- ***Atrio-Ventricular Block***

1. **1st Degree** = prolonged PR interval (> 0.20 s)
   * requires no specific therapy
   i. transient due to vagal tone
   ii. secondary to drugs - digoxin, β-blockers
   iii. AV nodal disease
2. **2nd Degree**
   i. **Mobitz I** = progressive lengthening PR interval, followed by a dropped beat
      - caused by disease ***within*** the AV node
      - rarely causes significant bradycardia, or progresses to higher degree block
      - associated with digoxin, increased vagal tone, inferior MI, or myocarditis
      - requires no specific therapy

   ii. **Mobitz II** = fixed PR interval (long) with regular dropped beats
      - caused by disease ***below*** the AV node
      - ventricular rates can be quite slow, with dyspnoea, syncope & fatigue
      - frequently progresses to a higher level of block
      - permanent pacemaker insertion is indicated
3. **3rd Degree** = complete AV dissociation
   - ventricular rates are frequently 40-50 bpm
   - rare in women of childbearing age
   - usually associated with,

   i. rheumatic heart disease
   ii. inferior MI
   iii. acute myocarditis
   iv. congenital heart block *often have associated VSD

   - R_X = permanent pacemaker insertion

CONGENITAL HEART DISEASE

Left to Right Shunts

- common causes are ASD, VSD and PDA
- all result in ***increased*** pulmonary blood flow, for as long as left heart pressures exceed right
- eventually results in progressive pulmonary hypertension, RVH and failure
- pregnancy related increases in blood volume, HR and CO may be tolerated with small shunts
- progression to R→L shunt, ***Eisenmenger's complex***, may be exacerbated by the decrease in SVR seen in pregnancy

▪ ***Anaesthetic Considerations***

a. baseline investigations
   - FBE, MBA_{20}
   - ECG, CXR, and echocardiogram

b. SBE prophylaxis

c. IV fluid precautions
   * paradoxical embolism

d. monitoring

   i. ECG
   - prone to arrhythmias, especially ASD

   ii. SpO_2
   - all lesions, but esp. those at risk of ***shunt reversal***

   iii. IABP
   * low threshold, any symptomatic patient

   iv. PA catheter
   - evidence of pulmonary hypertension
   - symptomatic CCF
   - shunt reversal
   ?? no data would be interpretable

e. maintain preload & afterload
   - volume preloading where required
   - prompt replacement of blood loss
   - avoidance of aortocaval compression

f. avoid raised PVR
   * avoid hypoxia, hypercarbia, acidosis

- for labour and delivery, CEA may be employed, however,

1. cautious volume loading should be employed
2. loss of resistance should employ ***saline***, not air
3. the sensory level should be raised slowly, and
4. hypotension should be aggressively treated
   * α_1-agonists preferably

Right to Left Shunts

- commonly include tetralogy of Fallot, transposition of the great arteries, tricuspid atresia
- most of these will have been surgically corrected
- most common R→L shunt in the childbearing years is L→R with Eisenmenger's syndrome
- many patients who have had a "functional" repair with no residual symptoms will tolerate pregnancy with minimal increased risk
- for these patients ***endocarditis prophylaxis*** is the principal concern
- uncorrected, or "palliated" patients, are at high risk and have an increased morbidity / mortality
- the decrease in SVR, which may be maximal immediately postpartum, increases shunt flow
- stress and pain with labour may lead to increases in PVR

Anaesthetic Considerations

a.	baseline investigations	- FBE, MBA_{20} - ECG, CXR, and echocardiogram
b.	endocarditis prophylaxis	
c.	IV fluid precautions	* paradoxical embolism
d.	monitoring	
	i. ECG, SpO_2	
	ii. IABP & CVP	* almost all cases
e.	maintain preload & afterload	- volume preloading where required - prompt replacement of blood loss - avoidance of aortocaval compression * left uterine displacement
f.	supplemental O_2	- but minimal effect with large shunt (> 30%)
g.	avoid raised PVR	* avoid hypoxia, hypercarbia, acidosis

- there is controversy over both pain relief during labour and anaesthesia for operative delivery
- if CEA is employed, the same considerations cf. L→R shunts apply, however, ***any*** decrease in SVR may be detrimental
- for labour, local / opioid mixtures are preferable due to the lesser sympathetic blockade
- any evidence of hypotension should be treated with α_1-agonists (metaraminol)
- if general anaesthesia is chosen, then the use of volatile agents should be limited
- usual rapid sequence induction may be poorly tolerated, and a carefully performed regional technique may be safer despite the theoretical problems with afterload

COARCTATION OF THE AORTA

- usually located just ***distal*** to the left subclavian artery
- associated conditions include cerebral aneurysms and other cardiac conditions
- most will have been surgically corrected prior to pregnancy, however in uncorrected lesions,

1. maternal mortality ~ 3-9%
2. foetal mortality ~ 20%

- cardiac output is rate limited, and although bradycardia is poorly tolerated, tachycardia may also result in LV decompensation
- due to the limited SV, the $\uparrow VO_2$ of pregnancy can only be met by an $\uparrow$ HR
- the progressive decrease in SVR may be poorly tolerated due to reflex tachycardia & CCF
- ***aortic rupture*** & dissection are possible distal to the stenosis, due to increased turbulent flow
- labour and delivery do not appear to increase the chance of rupture, although alterations of aortic anatomy have been documented in pregnancy
- most reported deaths from rupture have occurred ***prior*** to labour / delivery
- patients with surgically corrected lesions may undergo labour and delivery without increased risk

Anaesthetic Considerations

a. maintain "normal" HR & SVR

b. PA catheter and IABP monitoring
   - patients with symptoms of CCF or aneurysmal dilatation of the aorta
   - IABP pre & post-stenosis if severe disease

c. if a regional technique is chosen, then decreases in afterload and reflex increases in HR ***must*** be avoided

MYOCARDIAL INFARCTION

- in normal pregnancy this is a rare ~ 84 reported cases since 1922
- this corresponds to an incidence ~ 1:10,000
- the coronary anatomy of 30% of these cases was delineated, either angiographically or at PM,

a. ***thrombus formation & spasm*** are the 1° cause of AMI in pregnancy

b. atherosclerosis found in ~ 40% but not severe disease

c. AMI during pregnancy → mortality ≥ 30%

▪ ***Factors Affecting Risk***

a. ↑ maternal ***age*** - elevated cholesterol
- hypertension
? work related stress

b. ↑ in women ***smoking*** ? decreasing recently
- accentuates hypercoagulable state

c. ***drug abuse*** - cocaine & coronary spasm

d. cardiorespiratory changes of pregnancy
- most changes are maximal from 32 weeks on & this corresponds with ↑ risk
- majority of MI's occur in the third trimester & death is twice as likely

i. ↑ demand
- ↑ CO, HR, blood volume and VO_2
- stress of labour → CO may be 2-3x nonpregnant levels

ii. ↓ supply
- ↑ Q_S and arterial ***desaturation***
- ↓ FRC & IRV decreases reserve
- chronic mild hyperventilation & ↑ 2,3-DPG with ***right shift***
- ↓ SVR → ↓ mean diastolic BP and LV perfusion pressure
- thrombus formation 2° to the ***hypercoagulable*** state of pregnancy
- coronary spasm 2° to ***renin*** release from the chorion during ischaemia

▪ ***Medical Management***

a. relieve ongoing ischaemia and limit extension of infarction
- continuous NIBP/IABP, SpO_2 and foetal heart monitoring
- maximise oxygenation
- Ca^{++} blockers, nitrates, β-blockers & opioids have ***no*** adverse foetal effects
- Ca^{++} blockers are especially useful due to the ***vasospastic*** component
- cardioselective β-blockers are associated with fewer adverse foetal effects

b. manage complications of AMI *especially arrhythmias, CCF
- CCF is best managed with afterload reduction
- ***captopril*** may be teratogenic & limited experience precludes routine use
- digoxin is safe during pregnancy & first choice for SVT's
- SNP is relatively contraindicated due to potential ***thiocyanate*** toxicity
- lignocaine accumulates in the foetus but no lasting adverse effects demonstrated

c. ***anticoagulation***

i. low dose ***heparin*** for all patients

ii. prevention of systemic emboli
- large anterior infarcts
- CKMB ≥ 160
- CPK ≥ 8 times normal
- presence of AF or ventricular aneurysm

d. ***thrombolytic therapy*** - the role has not been established

e. ***percutaneous angioplasty*** or surgical revascularisation
- only if there is ongoing ischaemia and a large segment of myocardium is at risk

f. ***caesarean delivery***
- any ongoing foetal hypoxia unresponsive to resuscitative measures
- balance between,

i. avoiding the immediate 2 week post-infarct period, due to the risk of arrhythmias & haemodynamic instability, and

ii. the stresses of pregnancy, with the risk of rupture, aneurysm etc.

- ***Anaesthetic Management***

a. maximise myocardial O_2 supply / demand

b. avoid
- tachycardia, hypotension, hypertension
- pain, anxiety, shivering

c. monitoring - ECG, SpO_2 , NIBP/IABP, CVC ± PA catheter

d. regional analgesia / anaesthesia
- decreased LV afterload / preload
- blocks cardioaccelerator fibres & inhibits sympathetically mediated vasospasm
- decreases the surgical stress response & avoids the stress of intubation
- avoids the problems of a high dose opioid GA

e. high dose opioid general anaesthesia
- requires prolonged intubation of both mother & infant
- usually restricted for decompensated patient, or those with mixed valvular lesions in addition to AMI
- in unstable patients, retaining the ability to manipulate SVR may provide for greater haemodynamic stability
- control of ventilation may maximise VO_2 and remove pharmacological constraints

ASTHMA

a. incidence **~ 1:20** of general population
~ 1% of pregnant women
~ 10-15% of these will require hospitalisation
~ 50% will have no change in their asthma with pregnancy
~ 25% will improve & 25% worsen

b. conditions associated with maternal asthma
- preterm delivery, low birthweight infants & perinatal death occur more frequently
- haemorrhage, PIH, requirement for induced labour also more common

c. factors which affect asthma in pregnancy
- ↓ FRC ~ 20%
- ↑ VO_2
- ↑ progesterone - ↑ RR & MV
  ± bronchodilatation

Management

NB: 1. the aim of therapy is to prevent bronchospastic episodes & the subsequent maternal and foetal hypoxia
2. although some drugs may have adverse effects upon the foetus, there is generally ***less risk*** than if exposed to repeated episodes of ***hypoxia***

■ *b-**Sympathomimetics***

• little data relating to teratogenicity
• high doses used for ***tocolysis*** may result in tachycardia, hypotension, & pulmonary oedema
• ***albuterol*** has been associated with an increased incidence of uterine haemorrhage during spontaneous abortion

■ ***Steroids***

• safety is undetermined
• some studies showing an association with,

1. stillbirth, IUGR
2. cleft palate

NB: others show no such association

• the systemic effects of ***inhaled steroids*** are minimal in nonpregnant patients
• if systemic steroids are required, then use the minimal effective dose, or alternate day therapy
• the mechanism of action is believed to be ***direct bronchodilatation***, in addition to inhibition of synthesis of chemical mediators of inflammation

- ***Theophylline***

• narrow therapeutic range, ∴need to monitor & difficulty maintaining therapeutic plasma levels
• clearance is unchanged, or ***reduced*** in pregnancy
• no apparent teratogenic side effects
• potent tocolytic and may ***prolong labour***
• crosses the placenta easily and may result in,

a. ↓ foetal HR variability
b. transient tachycardia in the newborn ~ 10% even with normal plasma levels

• the elimination half-life is prolonged in neonates

- ***Cromolyn Sodium***

• not a bronchodilator & not efficacious in all patients
• difficult to predict those patients who will benefit from use, however, no adverse effects have been observed during pregnancy

- ***Antihistamines***

• in premature infants, there is a strong association with ***retrolental fibroplasia*** & maternal antihistamine use in the last 2 weeks of pregnancy

ENDOCRINE DISEASE

Thyroid Disease

NB: this is one of the most common endocrine disorders of pregnancy

- ***Nontoxic Goitre***

a. may increase in size due to relative ***iodine deficiency***
   - ↑ GFR and renal excretion

b. clinical manifestations - dyspnoea, altered phonation, dysphagia

c. anaesthesia * potential for intubation difficulty
   - regional anaesthesia by choice

- ***Hyperthyroidism***

a. aetiology
- Graves' disease, or ***diffuse toxic goitre*** most common
- toxic nodular goitre, toxic multinodular goitre
- hydatidiform moles, choriocarcinoma

b. manifestations
* usual signs frequently seen in euthyroid patients
- tachycardia, systolic ejection murmur
- heat intolerance, increased skin temperature
- diarrhoea, nervousness, weight loss (obscured by pregnancy)
- eye changes; exophthalmos, lid lag / retraction
- ***hyperemesis*** gravidarum may be the 1st sign

c. investigations
- difficult as oestrogen increases ***thyroxine binding globulin***
- plasma thyroxine elevated & T_3-uptake in hypothyroid range

- ***Anaesthesia***

• elective surgery should be postponed until rendered ***euthyroid***
• if hyperthyroid, avoid sympathomimetic agents & ensure an adequate depth of anaesthesia
• plasma catecholamines are ***not*** increased and the circulatory response is not due to increased sensitivity, however, they will exacerbate changes
• adequate premedication, ie. a benzodiazepine, is desirable
• anticholinergic agents should be avoided due to tachycardia & inhibition of heat loss
• the thiobarbiturates have antithyroid properties & are OK for induction, though, the antithyroid effect has not been demonstrated clinically
• ketamine and pancuronium are generally contraindicated
• CEA has the advantage of blocking adrenal and cardiac sympathetic innervation
• a potential problem is hypotension requiring pharmacological support

• superficial and deep cervical plexus blockade, combined with local infiltration is useful for thyroid surgery in the pregnant patient
• however, the addition of adrenaline may result in systemic effects
• β-blockers are generally useful for controlling the manifestations during surgery
• the increased VO_2 above the normal pregnant state further complicates the reduction in FRC & tendency to arterial desaturation

- ***Thyroid Storm***

a.	manifestations	- hyperpyrexia, tachycardia, AF, CVS instability ± collapse - severe dehydration, anxiety, altered consciousness * may mimic MH
b.	anaesthesia	- same cf. hyperthyroidism

- ***Hypothyroidism***

a.	aetiology	- rare in term pregnancy - associated with an increase in ***spontaneous abortion*** - usually ***iatrogenic***, surgery or radioactive iodine therapy
b.	manifestations	- fatigue, cold intolerance, cool dry skin, coarse hair - hoarseness, constipation - delayed DTR's, decreased mentation - oedema, cardiomegaly, CCF, pleural ± pericardial effusions - mild anaemia, hypercholesterolaemia, accelerated atherosclerosis - low voltages & sinus bradycardia on ECG

- ***Anaesthesia***

• more sensitive to opioids, sedatives and anaesthetic agents
• hypoxic ventilatory drive is diminished
• hypercapnic ventilatory drive is decreased in myxoedema coma, though not in hypothyroidism
• these factors may combine to predispose to ***respiratory failure***
• metabolism of drugs, especially opioids is delayed
• the bradycardia, decreased contractility & CO delay induction with IV agents but speed induction with volatiles
• typically have reduced intravascular volume, therefore are at greater risk of hypotension from blood loss or sympathectomy
• thus prehydration is advised & ephedrine is useful for treating hypotension
• NMJ blockade may be prolonged with standard doses
• they are prone to develop ***hypothermia***
• impaired free water clearance may result in ***hyponatraemia***
• ***hypoglycaemia*** may develop 2° to thyroid hormone replacement

DIABETES

NB: this is actually the ***most common*** medical problem encountered in pregnancy

- ***Pathophysiology***

a. placental insufficiency → major problem
   ~ 35-45% decrease blood flow
   - decrease worse with poor control (high HbA_{1c})

b. HbA_{1c}
   - poor carrier of oxygen
   - maternal P_{aO2} (? C_{aO2}) inversely related to levels

c. ketoacidosis
   - now a rare entity with good perinatal control
   - remains a significant cause of neonatal mortality
   - uncontrolled infection, steroids & β-mimetics for prematurity

d. susceptibility to infection

e. accelerated atherosclerosis

f. autonomic neuropathy

g. associated conditions
   i. pregnancy induced hypertension
   ii. premature labour
   iii. abruptio placentae
   iv. foetal macrosomia
   v. major foetal congenital malformations
   vi. rebound neonatal hypoglycaemia

Classification*	
Class A	• abnormal CHO tolerance nonpregnant • no insulin requirement before / during pregnancy
Class B	• duration of diabetes < ***10 years***
Class C	• duration of diabetes ***10-20 years***
Class D	• duration of diabetes > ***20 years***
Class F	• associated with diabetic ***nephropathy***
Class T	• associated with ***renal transplant***
Class R	• associated with ***retinitis proliferans***
Class H	• requiring insulin and associated with ***coronary artery disease***

* modified from White

- Datta & Brown (1977) found a higher incidence of foetal acidosis in infants of diabetic mothers
- in a subsequent study by Datta *et al.* using CEA, ***foetal acidosis*** was found to relate to both,
    1. the severity of the ***diabetes***
    2. the duration and severity of ***hypotension***

- the generation of foetal acidosis is multifactorial,
    a. increased lactate production from the hypoxic placenta
    b. increased placental glycogen $\rightarrow$ $\uparrow$ lactate production
    c. hyperglycaemia, in the presence of hypoxia further increases lactate production
    d. foetal hyperglycaemia may be associated with an increased O_2 utilisation

- in 1982, Datta *et al.* repeated their study, using ***spinal anaesthesia***, plus,
    1. tightly controlled maternal BSL levels * 80-120 mg/dl
    2. non-dextrose containing volume expansion - Hartmann's solution
    3. aggressive management of hypotension - MAP > 100 mmHg

    NB: neonatal pH's ***did not*** differ significantly from non-diabetic groups

- for ***general anaesthesia***, there are a number of important factors,
    1. increased ***gastric stasis***
    2. autonomic neuropathy
    3. "stiff-joint syndrome" in juvenile onset diabetics
    4. decreased insulin requirement immediately postoperatively
        - determination of BSL's in recovery

HEPATIC DISEASE IN PREGNANCY

NB: the most common cause of hepatic dysfunction in pregnancy is ***viral hepatitis***

▪ ***Cholestasis Of Pregnancy***

- ***intrahepatic cholestasis*** with deposition of bile acids in the skin & pruritis
- ? increased sensitivity to bile acids 2° to ***oestrogen*** production
- increased risk of ***prematurity*** (~ 50% ↑) and foetal death
- foetal distress may occur in up to 30%, with a caesarean rate of 30-60%
- clinical manifestations include,

a. ***pruritis*** - classical presenting symptom, usually 3rd trimester
- involving the palms, soles of the feet and the trunk

b. dark urine, light stools & ***mild jaundice***

c. ***prothrombin time*** is usually normal
- may be increased with vitamin K malabsorption
- this may occur 2° to ***cholestyramine*** used to alleviate the jaundice

d. increased risk of ***postpartum haemorrhage***

▪ ***Acute Fatty Liver Of Pregnancy***

- aetiology is unknown, but there may be some link to ***tetracyclines***
- in the untreated patient maternal & foetal morbidity / mortality **~ 80-90%**
- immediate delivery has reduced ***maternal mortality*** **~ 10-33%**
- ***foetal mortality*** remains high due to a high incidence of stillbirths
- untreated the disease may progress to,

a. fulminant hepatic failure & encephalopathy

b. DIC with uncontrolled GIT bleeding

c. death

- the incidence is higher in ***young primiparas*** giving birth to twins or male infants
- typically presents between the 36-40th weeks of gestation,

a. headache, fatigue, malaise

b. diffuse, or right upper quadrant, abdominal pain & severe persistent vomiting

c. jaundice & fever ~ 50%

d. mild hypertension & peripheral oedema suggest PIH

e. there is usually evidence of DIC

f. plasma electrolyte & glucose abnormalities

g. encephalopathy & coma occur late

- ***Hepatic Involvement in Other Conditions***

1. PIH, preeclampsia, eclampsia ~ 50% abnormal LFT's
2. HELLP syndrome

RENAL DISEASE

- normal physiological changes in pregnancy,
  a. ↑ RBF & GFR ~ 50%
  b. ↓ BUN & creatinine ∝ GFR & protein uptake across the placenta
  c. ↑ tubular reabsorption ∝ GFR → maintains water & sodium balance
     - however, commonly see ***glycosuria***, amino-aciduria & ***proteinuria***
     - serum ***uric acid*** levels decrease significantly in normal pregnancy & are a sensitive marker of ***tubular function***
  d. dilatation of the collecting system extends to the pelvic brim

- in the absence of associated factors, such as hypertension or proteinuria,
  a. creatinine
     i. female ~ 45-95 µmol/l
     ii. pregnancy ~ 30-80 µmol/l
  b. creatinine < 140 µmol/l - no adverse effect
  c. creatinine > 200 µmol/l - decreases the likelihood of conception
     ~ 20% deliver prior to 36 weeks
     - ↑ stillbirths, IUGR, neonatal deaths

  NB: 1. levels > 200 µmol/l may be associated with a decrease in maternal renal function which does ***not reverse*** after the pregnancy
  2. the presence of ***hypertension*** may be the most important determinant of maternal & foetal outcome
  3. the majority of renal disease occurs in females after their childbearing years, however, there are a number of conditions which may affect young females

■ ***Glomerular Disease***

- may result from infection, inflammation, or systemic diseases such as SLE or diabetes
- frequently accompanied by ***hypertension & proteinuria***
- associated incidence of ***preeclampsia* ~ 50%**
- ***nehprotic syndrome*** commonly results from glomerular disease
- however, the commonest cause of this *de novo* in pregnancy is preeclampsia

- ***hypertension*** is the single most common medical complication of pregnancy
- concurrent hypertension may result in further deterioration of renal function
- diastolic pressures > 85 mmHg require differentiation, though, this may be difficult

Acute Renal Failure

- incidence ~ 1:10,000
- usually related to late complications of pregnancy,
    a. maternal haemorrhage - placental abruption, placenta praevia, other causes
    b. preeclampsia / eclampsia
    c. postpartum HUS
    d. amniotic fluid embolism
    e. progression of pre-existing renal disease

- factors requiring consideration during anaesthesia include,
    1. pericardial effusion, CCF
    2. pulmonary infiltrates / oedema
    3. CNS depression with uraemia
    4. platelet dysfunction, anaemia

Renal Transplant

- factors relevant to management include,
    1. natural history of the primary renal disease
    2. current renal function ~ 25% suffer deterioration in pregnancy
    3. time of conception relative to the time of surgery
    4. immunosuppressive drugs used for rejection control
        - predisposition to infection in the mother
        - premature rupture of the membranes
        - foetal malformation, IUGR
        - adrenal insufficiency
        - neonatal lymhpopaenia within the first few weeks

- maternal and foetal outcome is good in ~ 70% who are otherwise healthy
- the risk of ***prematurity*** may be as high as 45%

Anaesthetic Considerations

- CEA remains the method of choice for most patients, providing no coagulopathy is present
- generally results in ***increased*** uterine and renal perfusion, providing hypotension is avoided
- relatively contraindicated with long-term β-blockers, due to risk of hypotension/bradycardia
- general anaesthesia should be avoided unless regional contraindicated, due to the reduction of 30-50% in RBF/GFR with the volatile agents

Adrenal Disorders

▪ ***Adrenocortical Insufficiency Addison's***

• may result from,

1. 1° destruction of the adrenal
   - autoimmune
   - tumour
   - haemorrhagic necrosis
   - infection (TB)
2. 1° hypofunction of the pituitary
   - tumour, infection (TB), sarcoid
   - haemorrhagic necrosis
3. 2° suppression of the pituitary
   - exogenous steroid administration
   - steroid secreting tumours

• presentation may be indolent, or acute life threatening collapse
• clinical features,

a. weakness, fatigue, vomiting, diarrhoea, abdominal pain
b. excess pigmentation
c. hypotension ± hypovolaemia
d. biochemical abnormalities
   - mild ***hyponatraemia***, hypoosmolality
   - ***hyperkalaemia*** (Na^+/K^+ ratio < 25:1)
   - ***hypoglycaemia***
   - mildly elevated urea
   - mild anion gap ***acidosis***

NB: mild hypotension, pigmentation, N&V are all common in normal pregnancy

• may be better tolerated in pregnancy due to foetal → maternal transfer of ***glucocorticoids***
• the post-partum diuresis & dehydration may precipitate an ***adrenal crisis***
• anaesthetic considerations include,

1. correction of hypovolaemia
2. steroid supplementation
3. correction of biochemical abnormalities
   i. glucose supplementation
   ii. Na^+/K^+ balance
4. increased susceptibility to
   - drug induced myocardial depression
   - muscle paralysis
5. decreased responsiveness to catecholamines
6. monitoring + IABP and CVP

Phaeochromocytoma

• rare in pregnancy, but high maternal / foetal mortality
• symptoms include,

a. anxiety, palpitations, tachyarrhythmias
b. headache, diaphoresis, blurred vision
c. heat intolerance
d. excessive weight loss
e. paroxysmal or sustained hypertension, usually ***not*** associated with proteinuria
f. episodic attacks triggered by
   - uterine contractions
   - foetal movements
   - changes in posture

• prolonged α-adrenergic stimulation results in,

a. decreased plasma volume with elevation of the haematocrit
b. reflex hypotension / tachycardia

• the safety of adrenergic blocking drugs has not been established, however foetal survival is undoubtedly improved with their use
• the α-blocking agents ***phentolamine*** and ***phenoxybenzamine*** are combined with *b-**blockade*** to prevent the reflex tachycardia
• β-blockade may result in decreased foetal HR and increased uterine contractility
• avoidance of factors which increase catecholamine release,

1. hypoxia, hypercarbia and acidosis
2. hypotension *poorly controlled epidural anaesthesia

• drugs known to have a pressor or tachycardic response should be avoided,

a. droperidol
b. anticholinergics
c. succinylcholine
d. histamine releasing agents - dTC, atracurium, ? morphine
e. pancuronium
f. halothane *ventricular arrhythmias

• patients with ***cardiomyopathy*** may require infusion of catecholamines following tumour removal, pending up-regulation of receptors and decay of sympathetic blockade

Cushing's Syndrome

- ovulation and pregnancy are rare with this condition
- increased incidence of spontaneous abortion, stillbirths, and premature labour
- effects 2° to excess circulating glucocorticoids
- common caused by,

a.	***iatrogenic steroid administration***	=	most common
b.	pituitary adenoma	~ 80%	(of remainder)
c.	ectopic ACTH	~ 15%	
d.	adrenal adenomas, hyperplasia		

- classical features may closely resemble normal pregnancy,

a. weight gain, truncal obesity, plethoric face, hirsuitism, bruising, striae
b. weakness, osteoporosis, poor wound healing
c. hypertension
d. psychosis
e. hypernatraemia, hypokalaemia and hyperglycaemia

- objectives of management,

a.	control of hypertension	
b.	normalisation of volume status	- spironolactone
c.	correction of biochemical abnormalities	- hyperglycaemia - hypernatraemia/hypokalaemia
d.	perioperative steroid supplementation	
e.	potential for airway difficulty	

Hyperparathyroidism

- ***parathyroid adenoma*** is the commonest cause in pregnancy
- normal pregnancy → ↑ PTH and Vit.D_3
- however, serum Ca^{++} levels are normally ***decreased***,
    1. ↑ foetal demands
    2. ↑ RBF/GFR and renal excretion
    3. hypoalbuminaemia of pregnancy → ↓ total Ca^{++} > ↓ ionised Ca^{++}

    NB: serum Ca^{++} levels may be ***normal*** in the hyperparathyroid patient

- labour and delivery usually proceed uneventfully
- there is an increased incidence of,
    1. stillbirths, spontaneous abortion, premature labour
    2. ***neonatal tetany***

▪ ***Clinical Manifestations***

1. generalised weakness, malaise, lethargy
2. anorexia, hyperemesis, constipation
3. polyuria, polydipsia (nephrogenic DI)
4. hypertension

▪ ***Complications***

1. renal calculi
2. pancreatitis
3. psychiatric disorders
4. hypercalcaemic crisis
    - mental deterioration ± coma
    - arrhythmias, CCF
    - renal failure

▪ ***Anaesthetic Considerations***

1. maintenance or normovolaemia and renal output
2. ECG monitoring
    - ↑ Ca^{++} & ↓ $\boldsymbol{QT_C}$
    - arrhythmias
3. osteoporosis and risk of pathological fractures
4. unpredictable response to NMJ blocking drugs, ***∴monitor***

Hypoparathyroidism

- rare in pregnancy, usually resulting from unintentional parathyroidectomy at thyroid surgery
- borderline cases may present due to increased demands of the foetus

- ***Clinical Manifestations***

1. fatigue, lethargy
2. paraesthesias, numbness
3. muscle weakness, tetany
4. carpopedal spasms, laryngeal stridor
5. altered mental status, convulsions
6. dry, rough skin, patchy hair loss, cataracts
7. ***long QT*** and decreased myocardial contractility

- ***Anaesthetic Considerations***

1. plasma ionised Ca^{++} can be rapidly reduced by ***respiratory alkalosis***
2. CEA may prevent the hyperventilation associated with labour

   → decreased likelihood of ***tetany***

Pituitary Disorders

- postpartum pituitary necrosis, ***Sheehan's syndrome***, following shock or haemorrhage, is the commonest cause of anterior pituitary insufficiency
- the clinical picture relates to the degree of damage, and relates to the deficiency of hormones secreted by the ovaries, adrenal gland, and thyroid gland
- the presentation may be insidious, with the first sign being failure of ***lactation*** with breast involution
- more dramatic presentation may follow with hypoadrenalism & hypothyroidism

HAEMATOLOGICAL DISEASES

Haemoglobinopathies

▪ *Thalassemia*

• mixed disorders resulting in the diminution of production of the protein chains of Hb_A

a. α-thalassaemia - thalassaemia minor

b. β-thalassaemia - autosomal codominant

i. heterozygous - β-thalassaemia minor
- half normal haemoglobin

ii. homozygous - β-thalassaemia major (Cooley's anaemia)

• most patients with α-thalassaemias and β-thalassaemia minor require ***no treatment***
• patients with b-***thalassaemia major*** have,

1. little or no production of β-globin
2. ***anaemia*** - average Hct < 20%
3. multiple transfusions with the potential for ***iron overload***,
   i. cardiomyopathy - CCF & arrhythmias
   ii. pancreatic dysfunction - bronze diabetes
   iii. hepatic dysfunction - cirrhosis
   iv. hepatomegaly & splenomegaly
4. skeletal malformations in association with ***marrow hyperplasia***

▪ *Sickle Cell Disease*

• most common in Negroes and people of Mediterranean descent
• heterozygotes (sickle cell trait) are usually asymptomatic
• single gene mutation encoding for β-globin, substituting ***valine*** for ***glutamate*** at position 6

$$HbS = HbA_{\beta}^{\,6\ glu \rightarrow val}$$

1. polymerisation of Hb under conditions of low P_{O2} or acidosis
2. RBC distortion, decreased plasticity and decreased survival time
   → ***hyperbilirubinaemia & anaemia***
3. ***vaso-occlusive*** phenomena
   i. placental infarction / insufficiency
   ii. splenic infarction, sepsis
   iii. pulmonary infarction, infiltrates, chest pain
   iv. CVA's
   v. avascular bone necrosis

Disorders of Coagulation

• normal pregnancy is associated with a ***hypercoagulable state***,

1. ↑ Factors I, VII, VIII, IX, X
2. expansion of blood volume
3. platelet count remains normal but ↑ TXA_2 with ↑ platelet aggregation
4. ↓ proteins S & C, and plasminogen activators

▪ *Iatrogenic Coagulopathy*

• usually patients with prior veno-occlusive disease or with prosthetic heart valves
• usually on warfarin but are changed to heparin due to the teratogenic effects of the former
• some would continue warfarin as it is more effective prophylaxis in the presence of prosthetic heart valves, converting to heparin only for labour and delivery

▪ *Idiopathic Thrombocytopenic Purpura*

• commonest haematological disorder in pregnancy
• usual F:M ratio ~ 3:1
• autoimmune disorder due to ***antiplatelet antibodies***, with accelerated platelet destruction

→ thrombocytopenia & splenomegaly

• often asymptomatic, or may present with bleeding diathesis
• ***CNS haemorrhage*** is the most serious consequence
• anti-platelet Ab's cross the placenta and may result in ***neonatal thrombocytopaenia***,

1. ~ 50% have platelet counts < 100,000
2. risk of ICH during vaginal delivery
3. no good evidence LUSCS is safer than NVD for the baby

• usual management includes ***steroids*** and ***splenectomy***
• high dose ***gamma-globulin*** has been used for resistant cases
• however, maternal response ***does not*** correlate with that of the foetus

▪ *Von Willebrand Disease*

• autosomal dominant, variable penetrance mode of inheritance, characterised by,

1. reduced factor VIII activity
2. impaired aggregation of platelets & prolonged bleeding time

• most patients increase factor VIII levels with pregnancy and deliver normally
• if factor VIII levels/activity remain below 25% then consideration for cryoprecipitate or FFP at the time of delivery should be given

NEUROLOGICAL DISORDERS

▪ ***Multiple Sclerosis***

• relatively common disease in young people, ***incidence* ~ 1:2000**
• results in ***demyelination*** within the CNS, it ***does not*** involve the peripheral nerves
• characterised by unpredictable ***relapsing course*** and the incidence of exacerbation in the first 3 postpartum months is **~ 3x** the nonpregnant population
• conditions in the perioperative period are known precipitants, eg. ***pyrexia***, surgery itself
• studies in both obstetric and nonobstetric patients have shown no significant increase with spinal or epidural anaesthesia

> ***NB:*** there is ***no evidence*** that women who receive epidural or spinal anaesthesia have a higher relapse rate, however, the patient should be warned there is a higher relapse rate in the peripartum period, ***irrespective*** of the use of anaesthesia

▪ ***Epilepsy***

• increased risk of complications,

a. prematurity
b. preeclampsia
c. obstetric haemorrhage
d. uterine hypotonia

• these may be 2° to medications or to the seizures themselves
• LEA & regional techniques are safe
• if GA is required, then avoid ketamine & enflurane
• phenytoin & phenobarbitone interfere with vit.K metabolism & require coagulation studies

- ***Myasthenia Gravis***

a. history
   - course of the disease
   - previous surgery, thymectomy, plasmapheresis
   - daily muscle strength & functioning
   - bulbar involvement
   - presence of CAL

b. medications
   - anticholinesterase dosage
   - immunosuppressives

c. lung function tests
   - spirometry
   - arterial gas analysis if indicated

d. optimisation of condition prelabour / anaesthesia

e. regular assessment during labour for changing anticholinesterase requirement
   - peak flows
   - sequential vital capacity estimations

f. LEA *preferred technique where possible

g. GA
   - avoid CNS depressant medication
   - increased risk of aspiration
   - unpredictable response to neuromuscular blocking agents, usually,

   i. increased sensitivity to nondepolarising agents

   ii. resistance to suxamethonium - ED_{95} up to 2.5x normal

   - duration of action of SCh is prolonged
   - requirement for elective postoperative ventilation

Elective Postoperative Ventilation[1]		
Factor		Points[2]
• long history of myasthenia	> 6 yrs	12
• moderate to severe CAL	* not 2° to MG	10
• high pyridostigmine dose	> 750 mg/day	8
• diminished vital capacity	< 2.9 l < 40 ml/kg	4

[1] figures for non-pregnant patients

[2] total score **> 10 points** = post-operative ventilation for > 3 hours

AUTOIMMUNE DISEASE

• mechanisms of immune host damage include,

1. circulating antigen-antibody activation of C', T-cells and macrophages (type II)
2. Ag-Ab immune complex deposition, with subsequent tissue damage (type III)
3. cell mediated, sensitised T-cell destruction of tissue (type IV)

• immunosuppression at the level of the foetoplacental unit allows ongoing pregnancy
• ***progesterone*** inhibits T-lymphocyte function
• several protein species have been isolated and appear to be associated with exacerbation or remission of a number of autoimmune diseases,

1. pregnancy-associated globulin 2-PAG
   - also called pregnancy associated plasma protein A (PAPP-A)
   - immunosuppressive glycoprotein affecting C' and lymphocyte transformation
2. pregnancy zone protein PZP
3. uromodulin
   - immunosuppressive glycoprotein isolated from urine which inhibits T-cell and macrophage function

Rheumatoid Arthritis

• chronic, systemic, non-organ-specific autoimmune disease of unknown aetiology
• ? infectious synovitis that induces antigenic change which stimulates autoimmune response
• Ab's are formed against a myriad of gamma globulins and EBV related antigens
• frequency in young women ~ 3x young males
• rarely occurs during, and is generally suppressed by pregnancy, possibly due to increased concentrations of circulating ***cortisol***
• may relapse severely in the post-partum period (~ 2-4/12)
• lactation appears to prolong remission

■ ***Anaesthetic Considerations***

1. airway problems
   i. mandibular hypoplasia
   ii. TMJ synovitis / arthritis
   iii. cervical spine instability, fusion, subluxation
   iv. cricoarytenoid arthritis
   v. laryngeal rotation

2. cardiovascular
   i. pericardial effusion, pericarditis
   ii. rheumatoid nodules - valvular
   - epicardial or myocardial
   iii. coronary arteritis & focal interstitial myocarditis (rarely)
3. respiratory
   i. CAL
   ii. pleuritis
   iii. interstitial fibrosis
   iv. nodular lung disease - Caplan's disease
   v. pneumonitis
   vi. pulmonary arteritis - PAH rare
   vii. intrapulmonary rheumatoid nodules (spontaneous rupture)

Systemic Lupus Erythematosus

- Ab formation against,
  1. intranuclear
     i. single and double stranded DNA
     ii. Sm1 ribonucleoprotein
  2. lymphocytes, erythrocytes
  3. neurons
  4. gamma globulins

- ***anticardiolipin antibody*** is one of many phospholipid Ab's present in SLE (20-65%)

- ***Clinical Features***

  a. incidence ~ 4-250 / 100,000
  ~ 8-10:1 F:M ratio
  b. peak onset 2^{nd}-4^{th} decades
  c. ~ 20% of cases are diagnosed at the onset of pregnancy during ***routine screening***
  d. severity & frequency of exacerbation increases in ~ 50% of pregnancies
  e. usual presentation in pregnancy
     i. fever, general malaise
     ii. symmetric arthritis
     iii. myalgias and muscle weakness
  f. occasional "preeclampsia-like" syndrome, with hypertension, proteinuria & oedema

- ***Anaesthetic Considerations***

1. CVS
   i. pericardial effusions ~ 25%
   ii. acute or constrictive pericarditis
   iii. tachyarrhythmias
   iv. Libman-Sacks endocarditis & valvular malfunction (check Echo preop.)
   v. rarely AMI
2. respiratory ~ 75%
   i. interstitial pneumonitis
   ii. fibrinous pleuritis ± bilateral pleural effusions
   iii. acute pulmonary vasculitis, or advanced arteriosclerosis
   iv. focal alveolar haemorrhages
   v. bronchopneumonias
   vi. massive pulmonary haemorrhage - rarely
3. renal
   i. lupus nephritis ~ 50%
   ii. nephrotic syndrome
   iii. chronic renal failure
4. other
   i. ***coagulopathy*** - ↑ APTT due to circulating ***lupus anticoagulant***
      - either a phospholipid or an anticoagulant Ab
   ii. anticardiolipin - thrombocytopaenia (but increased adhesiveness)
      - arterial thromboses
      (CVA, gangrene, MI, avascular necrosis of bone)
      - venous thromboses & intravascular clot formation
   iii. Raynaud's phenomenon ~ 15%

- ***Foetal & Neonatal Considerations***

1. increased incidence of premature labour, miscarriage & stillbirth
   - especially with antiphospholipid Ab's
   - survival may be improved by antiplatelet or anticoagulant drugs
2. neonatal lupus syndrome
   i. cytopaenias
   ii. discoid rash
   iii. cardiac conduction abnormalities