Medical Problems in Pregnancy

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CMACE 2011: Saving Mother’s Lives

- Failure to take symptoms seriously (‘healthy’ females)
- Reluctance to investigate (perceived risks of radiation)
- Fear of prescribing appropriate drugs

Overall mortality rate 11.39/100,000 pregnancies (2006-2008 data)
Considerations in pregnancy

- Two patients rather than one
- Physiological changes in normal pregnancy
- Differences in blood test parameters
- Radiation exposure
- Drug considerations
- Differential diagnoses may be different
- Effects of pregnancy on pre-existing conditions
- Conditions unique to pregnancy
- Early involvement of multispecialty team and ITU mandatory
Physiological changes in pregnancy

- Peripheral vascular resistance falls by 50%
- MAP falls by 10mmHg by 22-24w then slowly rises to term
- Cardiac output and circulating volume increase by 50% (haemodilution)
- Resting HR increases by 10-20/minute
- Renal blood flow and GFR increase by 70-80%
- Glycosuria, proteinuria (<300mg/d), bicarbonaturia, aminoaciduria, calciuria
- Physiological hydronephrosis/hydronephrotic; kidney length increases by 1cm and renal pelvis dilates (AP diameter ≤2cm normal)
- Hyperventilation/respiratory alkalosis due to progesterone-mediated stimulation of respiratory centre
Which of the following are abnormal in a 34w pregnant patient?

- Hb 104g/l
- WCC 14.3x10⁹/l
- CRP 34
- ESR 49
- TnI 0.39
- ALT 48
- ALP 320
- Creatinine 92
- Uric acid 0.39
- Cholesterol 7.1
Which of the following are **abnormal** in a 34w pregnant patient?

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Blood tests in pregnancy

Which of the following are **abnormal** in a 34w pregnant patient?

- **Hb 104g/l**
  - LLN 100g/l in pregnancy (haemodilution)
- **WCC 14.3x10^9/l**
  - 6-16x10^9/l in 3rd trimester
- **CRP 34**
  - normal ranges apply in pregnancy
- **ESR 49**
  - 30-70mm/h in 3rd trimester
- **TnI 0.39**
  - normal ranges apply in pregnancy
- **ALT 38**
  - ULN reduced by ~20% (e.g. 40 → 32)
- **ALP 320**
  - ULN 400 in 3rd trimester
- **Creatinine 92**
  - ULN reduced to 70µmol/l (increased GFR)
- **Uric acid 0.39**
  - ULN = weeks pregnant / 10 (0.34 in this case)
- **Cholesterol 7.1**
  - ULN 8.3mmol/l in 3rd trimester
Radiology in pregnancy

- Need to consider radiation dose to fetus AND mother

- **Deterministic effects:** dose threshold for clinical effect (IUD, CNS malformation, IUGR, mental retardation) below which no clinical effect occurs = 50-1000mGy

- **Stochastic effects:** no threshold for clinical effect (genetic damage, cancer esp. Leukaemia); absorbed dose influences probability but not severity of effect

- Effects may be greater during early pregnancy/1st trimester
Radiology in pregnancy

<table>
<thead>
<tr>
<th>Radiological Investigation</th>
<th>Mean fetal radiation dose (mGy)</th>
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<tbody>
<tr>
<td>CXR</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AXR</td>
<td>1.4</td>
</tr>
<tr>
<td>CT head</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>CT chest</td>
<td>0.06</td>
</tr>
<tr>
<td>CT abdomen</td>
<td>8.0</td>
</tr>
<tr>
<td>V/Q</td>
<td>0.9</td>
</tr>
<tr>
<td>CTPA</td>
<td>0.13</td>
</tr>
</tbody>
</table>

- No specific counselling for estimated fetal radiation doses <5mGy
- Annual background radiation is 1.8mGy in UK
- CXR = 9d background radiation or one-way flight from London to New York
Drugs in pregnancy

Which of the following are UNSAFE in pregnancy?

- Paracetamol
- NSAIDs
- Amoxicillin
- Clarithromycin
- Doxycycline
- Trimethoprim
- Gentamicin
- Cephalosporins
- Prednisolone
- PPIs
- Valproate
- Phenytoin
- Lamotrigine
- Carbamazepine
- Levetiracetam
- Tacrolimus
- Ciclosporin
- Azathioprine
- Cyclizine
- Metoclopramide
- Antihistamines
- ACE-i
- β-blockers
- α-blockers
- ARBs
- Diuretics
- CCBs
- Statins
- Antidepressants
Drugs in pregnancy

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- Paracetamol
- **NSAIDs (in 3rd trimester)**
- Amoxicillin
- Clarithromycin
- **Doxycycline**
- **Trimethoprim**
- Gentamicin
- Cephalosporins
- Prednisolone
- PPIs
- **Valproate**
- Phenytoin
- Lamotrigine
- Carbamazepine
- Levetiracetam

- Tacrolimus
- Ciclosporin
- Azathioprine
- Cyclizine
- Metoclopramide
- Antihistamines
- **ACE-inhibitors**
- **β-blockers**
- **α-blockers**
- ARBs
- **Diuretics**
- CCBs
- **Statins**
- Antidepressants
Hypertension in pregnancy

1. Chronic (essential) hypertension
   - BP >140/90mmHg PRIOR to pregnancy or occurring <20w gestation
   - persists >3m post-partum

2. Pregnancy-induced (gestational) hypertension
   - BP >140/90mmHg (or increase ≥30/15mmHg from earliest recorded BP in pregnancy) occurring >20w gestation
   - No proteinuria (increased risk of pre-eclampsia with earlier onset during pregnancy)
   - May persist for up to 3m post-partum and recur in subsequent pregnancies
   - Risk increases with advancing maternal age, obesity, T2DM, insulin resistance, PCOS
   - Remember to consider secondary causes of HTN

3. Pre-eclampsia (PET)
   - BP >140mmHg (or increase of ≥30/20mmHg from earliest recorded reading in pregnancy on 2 separate occasions >4h apart or any BP reading >160/110mmHg) occurring >20w gestation
   - Proteinuria (dipstick ≥2+, >300mg/24h, P:Cr >30mg/mmol on 2 occasions in absence of UTI)
Complications of PET

- Eclampsia
- Cerebral haemorrhage due to hypertension
- DIC or VTE
- HELLP
- Renal failure
- Hepatic failure or liver capsule rupture
- Pulmonary oedema or ARDS (avoid aggressive fluids if oliguric)
- Cortical blindness/RPLS
- Placental abruption
- IUGR, IUD or iatrogenic pre-term delivery
## Assessing severity of PET

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mild-Moderate PET</th>
<th>Severe PET</th>
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<tbody>
<tr>
<td>CNS</td>
<td>Headache, hyperreflexia, visual disturbance</td>
<td>Seizures</td>
</tr>
<tr>
<td>Renal</td>
<td>Proteinuria 0.3-4.9g/24h</td>
<td>Proteinuria ≥5.0g/24h (or dipstick 4+)</td>
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<tr>
<td>Hepatic</td>
<td>Normal LFTs</td>
<td>Elevated liver enzymes</td>
</tr>
<tr>
<td>Haematological</td>
<td>Platelets &gt;100</td>
<td>Platelets &lt;100</td>
</tr>
<tr>
<td>BP</td>
<td>&lt;160/110mmHg</td>
<td>≥160/110mmHg</td>
</tr>
<tr>
<td>Feto-placental</td>
<td>-</td>
<td>IUGR, fetal distress</td>
</tr>
</tbody>
</table>
Rx of HTN in pregnancy

- Indicated if BP ≥160/110mmHg to reduce risk of ICH and placental abruption
- **Labetalol 100mg BD – 600mg QDS** (first line as reduces cardiac output)
- **Methyldopa 250mg BD – 1G TDS** (avoid post-partum)
- **Nifedipine SR 10-40mg BD** (first line in PET due to vasoconstriction)
- Hydralazine 25mg TDS – 75mg QDS
- Doxazosin 1mg OD – 8mg BD (unsafe in breastfeeding)
- ACE-i, ARBs and thiazides CI during pregnancy (IUGR, oligohydramnios, neonatal anuric renal failure, congenital malformations)
- ACE-i (enalapril 5-20mg BD) OK during breastfeeding (avoid thiazides, methyldopa and α-blockers)

**Urgent induced delivery if severe PET**

- Check for persisting HTN and proteinuria at 6w post-partum; screen for renal disease and other secondary causes if present; screen for APLS if PET <34w; prophylactic ASA
Clinical Case

- 35-year-old female presents to ED following generalized seizure
- 3-weeks post-partum (uncomplicated pregnancy and NVD)
- Second seizure whilst being assessed in ED
- BP 190/126mmHg

What is the diagnosis?

How are you going to treat this patient?
Eclampsia

• 1/3000 pregnancies (incidence 0.03%) in UK
• Case fatality 2%
• Up to 44% of cases occur post-partum (usually within 4w)
• 60% have history of PET, 15% isolated HTN, 15% isolated proteinuria and 10% have no history of PET/HTN/proteinuria
• IV MgSO4 4G (16mmol) over 10min then 1G (4mmol)/h for 24h (avoid loading dose if already taking CCB due to risk of hypotension)
• Stop or reduce infusion if absent reflexes or RR <12/min
• IV labetalol 50mg bolus then 20-160mg/h for severe HTN (insert arterial line)
• Exclude other causes of seizure (ICH, CVT) with neuroimaging
• Cautious fluid replacement (risk of pulmonary oedema/ARDS)
• LMWH once BP controlled (providing no coagulopathy)
Headache/Seizures in pregnancy

- **Migraine** usually improves during pregnancy, may rebound after delivery
- **PET/eclampsia**
- **CVST** often post-partum, risk increased by thrombophilia, PET, dehydration e.g. HG
- **Stroke** often SAH/ICH (also dissection), risk increased by HTN/PET/thrombophilia
- **Pituitary apoplexy** headache, vomiting, hypotension and visual field defects
- **RCVS** thunderclap headaches early post-partum
- **TTP** thrombocytopenia, MAHA, normal clotting, renal failure
- **IIH** early pregnancy, obesity, may resolve after delivery
- **PDPH**
- **Gestational epilepsy**
- **Others** e.g. meningoencephalitis, alcohol/drugs, hypoglycaemia, hyponatraemia
Clinical Case

- 24-year-old female
- 28 weeks pregnant (first pregnancy)
- pleuritic chest pain and dyspnoea
- ECG sinus tachycardia, $S_1Q_3T_3$
- respiratory alkalosis on ABG

HOW WOULD YOU INVESTIGATE FOR PE?

HOW WOULD YOU TREAT IF PE WAS CONFIRMED?
‘The patient was discharged from ED after presenting with pleuritic chest pain and breathlessness. The medical registrar believed that CXR and anticoagulation were contraindicated in pregnancy. The patient was later found dead at home. Coroner’s post-mortem revealed she had died from a massive pulmonary embolus.’ *CEMACH 2007*
VTE in pregnancy: the facts

- up to 50% with VTE in pregnancy have heritable thrombophilia (esp. FVL)
- other RF include previous VTE, obesity, dehydration, smoking, age >35, twins, multiparity, pre-eclampsia, OHS
- 85% of DVTs occur on left (55% outside pregnancy)
- 72% of DVTs are ileofemoral/proximal (9% outside pregnancy)
- leg oedema and calf pain are common in normal pregnancy
- long-term complications in young healthy women; severe PTS (10%) and chronic pulmonary HTN (4%)
Investigating VTE in pregnancy

- d-dimer positive in 80% by 2nd trimester and 100% by 3rd trimester
- negative d-dimer should NOT be used to exclude VTE in pregnancy (high risk)
- sinus tachycardia, rightward axis and S₁Q₃T₃ on ECG and respiratory alkalosis on ABG are NORMAL findings in pregnancy
- CXR is safe and mandatory in ALL pregnant patients with ?PE; alternative pathologies, suitability for V/Q

Bilateral leg USS;

- no radiation risk
- very low yield in the absence of clinical DVT
- 3% risk of false +ves in pregnancy
- may delay definitive lx/expose patients to unnecessary antioagulation for longer
CTPA vs V/Q in pregnancy

Sequential combination of CXR, V/Q, CTPA and conventional pulmonary angiography together give <9/12 background radiation dose to fetus

- Significantly more radiation to lactating maternal breast (20mGy)
- Lifetime risk of breast cancer 1/8
- Excess risk from CTPA 1/1200 at age 20 decreasing to 1/3500 by age 40
- Overall increases relative risk of breast cancer by 1.004
Treating VTE in pregnancy

- warfarin is teratogenic in (early) pregnancy (safe during breastfeeding)
- LMWH is safe during pregnancy
- different dosing e.g. enoxaparin 1mg/kg BD
- check platelet count after 2 weeks of Rx (HIT)
- anti-factor Xa monitoring only if ↓↓ or ↑↑ BMI or GFR <30ml/min
- discontinue LMWH temporarily 24h prior to delivery; restart after 6-12h
- continue anticoagulation for ≥6w after delivery and for ≥6m in total
- switch to warfarin 1w after delivery
- prophylactic LMWH antenatally in subsequent pregnancies
- case reports of successful thrombolysis for massive PE in pregnancy
Breathlessness in pregnancy

- Physiological ‘air hunger’ (progesterone-induced increase in respiratory drive, increased cardiac output, diaphragmatic splinting)
- Anaemia
- PE
- Asthma
- Pneumothorax
- Pneumonia
- Pulmonary oedema/ARDS
- Arrhythmia
- Peripartum cardiomyopathy
- Amniotic fluid embolus
Asthma in Pregnancy

- Improvement or no change in asthma in 70%
- Asthma worsens in 30%, peak at 6m gestation, discontinuation of Rx
- Poorly controlled asthma associated with prematurity, IUGR and PET
- Pregnant patients less likely to be discharged on oral steroids and 3x more likely to have ongoing symptoms at 2w post-discharge
- Acute attacks rare in labour (high levels of endogenous corticosteroids)
- CXR is mandatory, screen for and treat infection (including H1N1)
- $\beta_2$-agonists, inhaled and oral steroids, theophyllines and magnesium are all safe during pregnancy
- Avoid starting leukotriene antagonists but continue if severe asthma and taking them prior to pregnancy
Peripartum Cardiomyopathy

- Heart failure with onset from last month of pregnancy to 5m postpartum in the absence of previous heart disease or alternative cause
- Multiple pregnancy, HTN, PET, multiparity, older maternal age, Afro-Caribbean
- Markedly reduced LVEF and global dilatation on ECHO
- Induce delivery if antenatal presentation
- Furosemide, β-blockers, digoxin, hydralazine, nitrates (ACE-i postpartum)
- Anticoagulate (most deaths due to PE or cerebral/systemic embolism from mural thrombus)
- Immunosuppression if myocarditis (prednisolone +/- AZT), inotropes, IABP, LVAD, cardiac transplantation
- 50% make full spontaneous symptomatic recovery, LV function normalizes in 30%, mortality up to 25%
Clinical Case

- 34-year-old multiparous female
- 32 weeks pregnant
- Admitted to AMU with 24h of chest pain
- Central, sharp, radiating to right shoulder
- Associated dyspnoea and tachycardia
- BP 158/94mmHg
- ECG sinus tachycardia

WHAT IS THE DIFFERENTIAL DIAGNOSIS?

HOW SHOULD SHE BE INVESTIGATED?
Aortic dissection in pregnancy

- 90% antenatal, usually 3\textsuperscript{rd} trimester
- Hypertension, older maternal age, bicuspid AV, Marfan’s, coarctation
- Often misdiagnosed as PE
- CXR, ECHO and CTA or MRA
- 80% type A (ascending aorta): Rx surgically with induction of delivery if >28w or involvement of descending aorta
- 20% type B (descending aorta): conservative Rx
IHD in pregnancy

• 3rd trimester or postpartum
• Older mothers with conventional CVD risk factors
• Atypical symptoms e.g. epigastric pain, vomiting
• Coronary dissection > spasm > embolus > atherosclerotic
• TnI is not elevated in normal pregnancy or puerperium
• Low threshold for angiography and PCI
• Aspirin, opiates, nitrates, β-blockers and LMWH safe
• Clopidogrel OK but needs to be stopped prior to delivery (may necessitate use of BMS rather than DES)
• Avoid ACE-i and statins
Clinical Case

- 31-year-old pregnant female
- 35 weeks pregnant
- General malaise, anorexia, loss of appetite
- Mildly confused, jaundiced
- BP 145/90mmHg
- Hb 10.1, WCC 21, plts 147
- Urea 8.8, creatinine 144
- Bil 87, ALT 166, ALP 320, albumin 30, INR 1.4, glucose 3.8
- Urate 0.77
- Urine dip – proteinuria 2+

WHAT IS THE DIAGNOSIS/DIFFERENTIAL?
Abnormal LFTs in pregnancy

1. Diseases coincidental to pregnancy
   - Viral hepatitis
   - Gallstones
   - Drug-induced liver reaction
   - Alcohol or drug abuse

2. Diseases with increased risk during pregnancy
   - Budd-Chiari syndrome

3. Diseases specific to pregnancy
   - Hyperemesis Gravidarum
   - Obstetric Cholestasis
   - HELLP syndrome
   - AFLP
Hyperemesis Gravidarum

- Severe/prolonged vomiting in pregnancy resulting in inability to maintain hydration/nutrition
- Usually presents <12w
- Diagnosis of exclusion (DKA, UTI, cholecystitis, pancreatitis, alcohol, drugs, molar/twin pregnancies, Addisons etc.)
- Very high $\beta$-HCG, suppressed TSH with high fT4 (clinically euthyroid), transaminitis, hypokalaemia/natraemia, hypochloraemic metabolic alkalosis
- Risk of AKI, VTE, Mallory-Weiss, anaemia (B12 def.), peripheral neuropathy (B6 def.), seizures, Wernicke’s, central pontine myelinolysis, IUGR and IUD
- Pyridoxine supplements, IV fluids and thiamine, LMWH, antiemetics, PPI, steroids, enteral nutrition or TPN
Obstetric cholestasis (OC)

- 1/130 pregnancies, SE Asians, S Americans, second half of pregnancy
- Severe pruritus with mildly abnormal LFTs (jaundice and epigastric pain rare)
- Hx of similar symptoms with OCP in 15%, FHx of OC or gallstones common
- Exclude viral hepatitis, gallstone disease, CAH and PBC
- Emollients, antihistamines, ursodeoxycholic acid, vitamin K, deliver at 37w
- Risk of preterm labour, meconium staining and IUD (<2%, usually >37w in those with high bilirubin)
- 90% recurrence in subsequent pregnancies (especially if twins)
HELLP syndrome

- 30% postnatal, 70% antenatal, mortality <1%
- Complicates 20% of severe PET but HTN & proteinuria may be absent
- N&V, epigastric pain (liver capsule oedema, may rupture with subcapsular haematoma)
- Intravascular haemolysis, raised bilirubin and modestly elevated LFTs, platelets <100, renal failure may occur
- Distinguish from AFLP and TTP/HUS
- Antihypertensives, FFP/platelets as required, delivery, high-dose dexamethasone postnatally
Acute Fatty Liver of Pregnancy (AFLP)

• 1/10,000 pregnancies, late pregnancy or early postpartum, case fatality 2%

• More common in twin and male pregnancies

• 20% of cases associated with inborn errors of mitochondrial fatty acid oxidation (higher risk of recurrence in subsequent pregnancies)

• Rapidly progressive liver failure, encephalopathy and renal failure

• Urate raised out of proportion to any associated PET

• Fatty liver on USS and microvesicular steatosis on liver Bx (rarely done)

• Delivery is the only cure

• Supportive care on ITU (fluids, NAC, vasopressors, blood/platelets/FFP, dextrose, haemofiltration, plasmapheresis) +/- liver transplantation
Distinguishing HELLP from AFLP*

<table>
<thead>
<tr>
<th>Feature</th>
<th>HELLP</th>
<th>AFLP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systemically unwell</td>
<td>Not usually</td>
<td>Yes</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>Common</td>
<td>Less common</td>
</tr>
<tr>
<td>WCC</td>
<td>Usually normal</td>
<td>Very high</td>
</tr>
<tr>
<td>Urate</td>
<td>Mildly elevated</td>
<td>Very high</td>
</tr>
<tr>
<td>Low platelets</td>
<td>Always</td>
<td>May occur with DIC</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>Only if severe/DIC</td>
<td>Common</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>Rare</td>
<td>Common</td>
</tr>
<tr>
<td>Encephalopathy</td>
<td>Rare</td>
<td>Common</td>
</tr>
</tbody>
</table>

*Both may cause vomiting, epigastric pain, jaundice, abnormal LFTs and renal failure in late pregnancy/early postpartum*
You are called to ED resus where a pregnant female has just collapsed...

**WHAT IS THE DIFFERENTIAL DIAGNOSIS?**

- Postural hypotension
- Massive PE
- Concealed haemorrhage – ectopic, placental abruption
- Aortic dissection
- Amniotic fluid embolus
- Seizure
- Stroke/SAH/CVST
CPR in pregnancy

- Access to thorax restricted by gravid uterus and ‘pregnant’ breasts

- Place wedge under RIGHT hip to achieve LEFT LATERAL TILT (relieves IVC obstruction by gravid uterus increasing cardiac output by up to 25%)

- Perimortem C-section if CPR unsuccessful after 5min (may restore circulation when all else fails)
Key learning points

- Pregnancy places otherwise healthy females at high risk of medical problems – symptoms should not be dismissed
- Two patients to consider
- Awareness of changes in physiology and blood tests
- Most radiology is safe in pregnancy – consent re. risks vs. benefits
- Most drugs are safe in pregnancy (important exceptions)
- Consider differential diagnoses CAREFULLY
- Involve specialists and critical care EARLY
- Under-investigation and under-treatment COSTS LIVES