General Principles

- Pregnant women are more predisposed to certain acute medical problems
- Those with chronic medical conditions can worsen / flare
- Pregnant women can suffer pregnancy specific medical problems
- Pregnant and postpartum women deserve the same attention to diagnosis and treatment and appropriate management plans as the non-pregnant patient
- Most drugs do not have a licence for use in pregnancy
- Errors of omission are common
Maternal death rate 2003-12
(Three year rolling averages)
Indirect maternal deaths 1985-2011
(Three year periods)
Causes of maternal death

Causes of mothers’ deaths

Two thirds of mothers died from medical and mental health problems in pregnancy and only one third from direct complications of pregnancy such as bleeding.

Women with pre-existing medical and mental health problems need:

- Pre-pregnancy advice
- Joint specialist and maternity care
Table 2.5: UK Maternal deaths and mortality rates by cause 1985–2011

<table>
<thead>
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<td><strong>Rates per 100,000 maternities</strong></td>
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<tr>
<td>Genital tract sepsis*</td>
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<tr>
<td>Amniotic fluid embolism</td>
<td>0.43</td>
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<td>0.80</td>
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<td>Early pregnancy deaths</td>
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<td>Other Direct¹</td>
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<td>0.33</td>
<td>0.40</td>
<td>0.19</td>
<td>0.17</td>
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<td></td>
</tr>
<tr>
<td><strong>All direct</strong></td>
<td>6.13</td>
<td>5.53</td>
<td>6.10</td>
<td>4.99</td>
<td>5.31</td>
<td>6.24</td>
<td>4.67</td>
<td>3.49</td>
<td></td>
</tr>
</tbody>
</table>

*Including early pregnancy deaths as a result of sepsis

²Acute fatty liver and genital tract trauma; included with pre-eclampsia and eclampsia and haemorrhage respectively from 2009 onwards

¹Deaths from these causes not included in reports from earlier years

Source: CMACE, MBRRACE-UK
Causes of maternal death

74% of women who died 2009-12 had a pre-existing medical disorder

Solid bars show indirect causes, hatched bars show direct causes
## Medical Problems in Pregnancy

### Pre-existing
- Asthma
- Epilepsy
- Hypertension
- Diabetes
- Thyroid
- SLE / RA / CTD
- Renal
- Cardiac

### Pregnancy - specific
- Pre-eclampsia
- Thromboembolism
- Gestational Diabetes
- Obstetric cholestasis
- Acute Fatty Liver of Pregnancy

### Coincidental
- Pneumonia, Malaria, Hepatitis
Case 1

- 39 yr old multip, 12 weeks, 76kg
- Secondary infertility; IVF pregnancy
- Admission for ovarian hyperstimulation syndrome
- A+E: C/O swollen, painful left leg for 3 weeks
- Sudden onset left sided pleuritic pain last night
- SOB since
- O/E dyspnoeic, RR 34, SOBOE undressing
- Pulse 118, BP 104/66
- Oxygen saturation 92%
Case 1: Which of the following is/are appropriate?

A. D dimers
B. leg dopplers
C. Enoxaparin (Clexane) 80mg bd
D. Enoxaparin (Clexane) 120mg od
E. V/Q
F. CTPA
Diagnosis of DVT in Pregnancy

- 88% on left (vs. 55% in non pregnant)
- 71% proximal (vs. 9% in non pregnant)
  - 64% were restricted to the iliac and/or femoral vein.

*Chan WS et al. CMAJ 2010; 182:657-60*
Diagnosis

DVT
  Doppler US

PE
  CXR
  V/Q Lung scan
  CTPA

D dimers are useless!!

Unless higher pregnancy specific normal ranges are used
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Rads</th>
<th>mGy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Perfusion scan</td>
<td>&lt;0.08</td>
<td>&lt;0.8</td>
</tr>
<tr>
<td>Ventilation scan</td>
<td>&lt;0.01</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>CTPA / Helical CT</td>
<td>&lt;0.013</td>
<td>&lt;0.13</td>
</tr>
<tr>
<td>Max recommended</td>
<td>&lt;0.5</td>
<td>5</td>
</tr>
</tbody>
</table>
### Table 7
Radiation Exposure of Various Imaging Examinations Performed for Pulmonary Embolism

<table>
<thead>
<tr>
<th>Examination</th>
<th>Effective Whole-Body Dose (mSv)</th>
<th>Fetal Dose (mGy)</th>
<th>Effective Dose per Breast (mGy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PA/lateral CXR</td>
<td>0.06–0.25</td>
<td>0.01</td>
<td>...</td>
</tr>
<tr>
<td>Low-dose perfusion scintigraphy</td>
<td>0.6–1.0</td>
<td>0.1–0.37</td>
<td>0.11–0.3</td>
</tr>
<tr>
<td>V/Q scintigraphy</td>
<td>1.2–6.8</td>
<td>0.1–0.8</td>
<td>0.22–0.28</td>
</tr>
<tr>
<td>CTPA</td>
<td>2–20</td>
<td>0.01–0.66*</td>
<td>10–70</td>
</tr>
<tr>
<td>Low-dose CTPA</td>
<td>2.7</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>Pulmonary DSA</td>
<td>3.2–30.1</td>
<td>0.5</td>
<td>...</td>
</tr>
<tr>
<td>Evaluation of background radiation</td>
<td>2.5</td>
<td>1.1–2.5</td>
<td>...</td>
</tr>
</tbody>
</table>

Note.—Variation in reported doses is largely related to CT settings, number of CT detectors, trimester, patient age, body mass index, and method of dose calculation. CTPA = CT pulmonary angiography, CXR = chest radiography, DSA = digital subtraction angiography, PA = posteroanterior.

*Data from Winer-Muram et al (3) not included due to outdated CT parameters and generation of CT scanner used in their study.

---

Mammogram is associated with 3-4.4 mSv
V/Q versus CTPA

Increased risk of fatal childhood cancer to the age of 15 following in utero radiation exposure = 0.006% per mGy, (1 in 17 000 per mGy).

The fetal radiation exposure associated with CTPA = 0.1 mGy

\[ V/Q = 0.5 \text{ mGy} \]

CTPA: Radiation to mother’s breasts = 65-250 (70-100) x greater than V/Q, 10-20 times greater than 2 view mammogram.

- 10 mGy radiation (CTPA) to a woman’s breast increases lifetime risk of developing breast cancer by 13.6% above her background risk
- V/Q investigation of first choice for young women especially if FH of breast CA or patient has had previous chest CT scan
- Higher rate of nondiagnostic scans in pregnancy with CTPA (37.5%) V/Q (4%)

(may be related to the imaging protocol employed).

Systematic Review and Meta-analysis of Pregnant Patients Investigated for Suspected Pulmonary Embolism in the Emergency Department

Jeffrey A. Kline, MD, Danielle M. Richardson, Martin P. Than, MBBS, Andrea Penaloza, MD, PhD, and Pierre-Marie Roy, MD

**Frequency of VTE non-preg**

12.4% (95% CI = 9.0% to 16.3%)

**Frequency of VTE 506 preg**

4.1% (95% CI = 2.6% to 6.0%)
Diagnosis of PE in pregnancy

**Suspected PE**

- ABG, ECG, CXR
- Start anticoagulation LMWH treatment dose
- **START ANTICOAGULATION LMWH TREATMENT DOSE**

**Stable**

- DOPPLER USS LEGS
- **DOPLER USS LEGS**
  - +ve
  - V/Q scan → -ve
  - Anticoagulate with LMWH

**Unstable**

- Clinically urgent (out of hours)
  - Portable echo
  - Suggestive of massive PE
  - Thrombolysis/i.v. heparin/thrombectomy

+ve

CXR normal

CXR abnormal

Still suspicious of PE

CTPA

- Still suspicious of PE
- Stop anticoagulation

ABG, arterial blood gas;
ECG, electrocardiogram;
CXR, Chest X-ray;
USS, ultrasound sonography;
CTPA, computerised tomography pulmonary angiography

Learning points - Investigating suspected PE in pregnancy.

- Physiological changes during pregnancy can mimic pulmonary embolism, making clinical diagnosis unreliable

- Imaging is essential to avoid inappropriate treatment and can be performed without exposing the fetus to any specific risks

- A chest x ray should always be performed to exclude other causes

- Half dose perfusion scintigraphy can be used in most patients

- Computed tomographic pulmonary angiography should be used only in patients with lung disease such as asthma—which makes scintigraphy less likely to be diagnostic—or an abnormal chest x ray, because it exposes maternal breast tissue to high doses of radiation

**Treatment of acute PE in pregnancy**

High dose LMWH:

*eg. Enoxaparin 1mg/kg/bd (= ACS dose)*

**NOT 1.5 mg/kg od (= non-pregnant dose)**

*RCOG Green Top Guideline no. 37b*

‘Increase in volume of distribution during pregnancy leads to a prolongation of enoxaparin half-life, so once-daily dosing is adequate’.


Thrombolysis:

**SHOULD NOT BE WITHELD** in massive PE, with haemodynamic instability


56 articles, 231 patients; *Gartman EJ. Obstetric medicine 2013*
Case 2

24 year old, P0
27 weeks pregnant

c/o palpitations

Associated dizziness and breathlessness

o/e tachycardic HR – 240

BP 94/68
Case 2
SVT

Vagotonic manoeuvres are safe

Adenosine – safe

Verapamil is effective second line therapy
  Up to 10mg can be given without affecting fetal HR

Beta-blockers also safe
Case 3

• 39 yr old asian, 37 weeks pregnant
• c/o dizziness and epigastric pain
• o/e sweaty, BP 94/68, HR 84
Case 3: which of the following are appropriate?

A. Troponin
B. Thrombolysis
C. Transfer to catheter lab
D. Primary angioplasty
E. Aspirin
F. Clopidogrel

If normal coronaries consider CMRI.

Bubble test also safe in pregnancy
Case 4

- 38 year old primip, 39 weeks pregnant
- C/o chest and back pain
- O/e BP 165/85, HR 124, O\textsubscript{2} sats 97%
- Urinalysis NAD
- ‘Writhing around the bed’, ‘won’t lie down to be examined’
- Not in labour!
Case 4: What investigations would you request?

A. CXR
B. back XR
C. TTE
D. TOE
E. abdo US
F. CTPA
• Not all chest pain and breathlessness = PE
• Beware the hypertensive (systolic) woman with chest pain
• CXR
• Echo
Case 5

35 year old

1 day post first normal vaginal delivery

C/O chest pain

Obstetric SHO requests CTPA

Medical registrar asked to review - told CXR normal
Acute asthma


• 51 pregnant, 500 non-pregnant presenting to ED with acute asthma.
• No difference in severity or duration of symptoms, initial PEFR (51% vs 53% predicted)
• 40% using inhaled steroids month prior to admission
• Less likely to be given systemic steroids (44% vs 66%)
• Equally likely to be admitted (24% vs 21%)
• Steroids if sent home (38% vs 64%)
• x3 Ongoing exacerbation 2 weeks later
Table 2  Risk of any major congenital malformation in children born to mothers with asthma

<table>
<thead>
<tr>
<th>Maternal asthma status</th>
<th>Cases (n = 5124)</th>
<th>Controls (n = 30053)</th>
<th>Adjusted OR† (95% CI)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No asthma diagnosis or medications before delivery</td>
<td>4420 (86.3)</td>
<td>26235 (87.3)</td>
<td>Reference</td>
<td></td>
</tr>
<tr>
<td>Asthma diagnosis or medication§ before delivery</td>
<td>704 (13.7)</td>
<td>3818 (12.7)</td>
<td>1.10 (1.01 to 1.20)</td>
<td>0.032</td>
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<tr>
<td>Diagnosis with no medication before delivery</td>
<td>171 (3.3)</td>
<td>881 (2.9)</td>
<td>1.17 (0.99 to 1.39)</td>
<td>0.071</td>
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<tr>
<td>Asthma medication§ but no diagnosis before delivery</td>
<td>183 (3.6)</td>
<td>968 (3.2)</td>
<td>1.13 (0.96 to 1.33)</td>
<td>0.132</td>
</tr>
<tr>
<td>Diagnosis and asthma medication§ before delivery</td>
<td>350 (6.8)</td>
<td>1969 (6.6)</td>
<td>1.06 (0.94 to 1.20)</td>
<td>0.329</td>
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<tr>
<td>≥1 asthma exacerbation during pregnancy</td>
<td>18 (&lt;0.5)</td>
<td>94 (&lt;0.5)</td>
<td>1.09 (0.65 to 1.82)</td>
<td>0.754</td>
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<table>
<thead>
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<th>≥1 medication exposure during pregnancy*</th>
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<td>Any asthma medication</td>
<td>410 (8.0)</td>
<td>2240 (7.5)</td>
<td>1.05 (0.94 to 1.18)</td>
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<td>Short-acting β agonist</td>
<td>375 (7.3)</td>
<td>2085 (6.9)</td>
<td>1.06 (0.94 to 1.19)</td>
<td>0.336</td>
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<td>Inhaled corticosteroid</td>
<td>220 (4.3)</td>
<td>1209 (4.0)</td>
<td>1.07 (0.92 to 1.24)</td>
<td>0.407</td>
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<tr>
<td>Long-acting β agonist</td>
<td>25 (&lt;0.5)</td>
<td>131 (&lt;0.5)</td>
<td>1.12 (0.72 to 1.75)</td>
<td>0.614</td>
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<tr>
<td>Oral corticosteroid</td>
<td>46 (0.9)</td>
<td>216 (0.7)</td>
<td>1.23 (0.89 to 1.69)</td>
<td>0.201</td>
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<tr>
<td>Other bronchodilator medication§</td>
<td>13 (&lt;0.5)</td>
<td>72 (&lt;0.5)</td>
<td>1.05 (0.69 to 1.67)</td>
<td>0.872</td>
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<td>Other anti-inflammatory medication**</td>
<td>9 (&lt;0.5)</td>
<td>27 (&lt;0.5)</td>
<td>2.02 (0.96 to 4.28)</td>
<td>0.065</td>
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</tbody>
</table>

*Reference groups are mothers with no prescriptions for the selected drug group in pregnancy.
†Proportion of cases or controls whose mothers had a diagnosis or at least one selected drug prescription in pregnancy.
‡Odds ratios (95% confidence intervals) adjusted for maternal age at birth of case or control child; maternal smoking status, body mass index, socioeconomic status, sex of the child, gestation of pregnancy had no confounding effects.
§Any asthma medication except oral corticosteroids during pregnancy or in the year before the pregnancy.
¶Aminophylline, theophylline, ephedrine, orciprenaline, tiotropium or ipratropium.
**Cromoglicate, nedocromil, montelukast or zafirlukast.
Corticosteroid use during pregnancy and risk of orofacial clefts

Anders Hviid MSc DMSc, Ditte Mølgaard-Nielsen MSc

- Cohort study of all live births in Denmark 1996 to 2008.
- 832,636 live births
  - 51,973 exposures to corticosteroids during the first trimester
  - 1,232 isolated orofacial clefts (i.e., cleft lip, cleft palate, or cleft lip and cleft palate) diagnosed within first year of life
  - 84 in which the infant had been exposed to corticosteroids during the first trimester

Table 3: Association between corticosteroid use during first trimester of pregnancy and isolated orofacial clefts among 832 636 live births

<table>
<thead>
<tr>
<th>Corticosteroid use</th>
<th>No. of live births</th>
<th>Cleft lip with or without cleft palate</th>
<th>Cleft palate alone</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No. (prevalence*)</td>
<td>Adjusted OR† (95% CI)</td>
</tr>
<tr>
<td>Any use</td>
<td>51 973</td>
<td>57 (1.10)</td>
<td>1.05 (0.80–1.38)</td>
</tr>
<tr>
<td>No use</td>
<td>780 663</td>
<td>818 (1.05)</td>
<td>1.00</td>
</tr>
<tr>
<td>Route of administration</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>2 195</td>
<td>0 (0.00)</td>
<td>NA</td>
</tr>
<tr>
<td>No</td>
<td>830 441</td>
<td>875 (1.05)</td>
<td>1.00</td>
</tr>
<tr>
<td>Inhalant</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7 421</td>
<td>6 (0.81)</td>
<td>0.75 (0.34–1.68)</td>
</tr>
<tr>
<td>No</td>
<td>825 215</td>
<td>869 (1.05)</td>
<td>1.00</td>
</tr>
<tr>
<td>Nasal spray</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>11 245</td>
<td>6 (0.53)</td>
<td>0.52 (0.23–1.16)</td>
</tr>
<tr>
<td>No</td>
<td>821 391</td>
<td>869 (1.06)</td>
<td>1.00</td>
</tr>
<tr>
<td>Dermatologic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>22 480</td>
<td>34 (1.51)</td>
<td>1.45 (1.03–2.05)</td>
</tr>
<tr>
<td>No</td>
<td>810 156</td>
<td>841 (1.04)</td>
<td>1.00</td>
</tr>
<tr>
<td>Other topical form</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>12 091</td>
<td>13 (1.08)</td>
<td>1.04 (0.60–1.79)</td>
</tr>
<tr>
<td>No</td>
<td>820 545</td>
<td>862 (1.05)</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Note: CI = confidence interval, NA = not applicable, OR = odds ratio.
*Per 1000 live births.
†Odds ratio adjusted for year of birth, maternal place of residence at start of pregnancy, maternal place of origin, smoking status during pregnancy, history of orofacial clefts among offspring and history of any birth defects among offspring.
‡Odds ratio adjusted for year of birth, maternal place of residence at start of pregnancy and history of orofacial clefts among offspring.
Transfer of steroids across the placenta

<table>
<thead>
<tr>
<th>Steroid</th>
<th>Maternal concentration</th>
<th>Cord blood concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prednisolone</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>Hydrocortisone</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Betamethasone</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>
Women should be advised of the importance of maintaining good control of their asthma during pregnancy to avoid problems for both mother and baby.

Counsel women with asthma regarding the importance and safety of continuing their asthma medications during pregnancy to ensure good asthma control.
National asthma audit

Asthma deaths occurring between February 2012 and January 2013 (n = 195)

Highlights lack of education amongst women and healthcare providers as a key failing
Improved Management of Acute Asthma Among Pregnant Women Presenting to the ED

Kohei Hasegawa, MD, MPH; Rita K. Cydulka, MD; Ashley F. Sullivan, MPH; Mark I. Langdorf, MD; Stephanie A. Nonas, MD; Richard M. Nowak, MD, MBA; Nancy E. Wang, MD; and Carlos A. Camargo Jr, MD, DrPH

4895 patients with acute asthma, 125 pregnant women in 48 EDs

<table>
<thead>
<tr>
<th>TABLE 4</th>
<th>Unadjusted and Adjusted Analyses for Outcomes Comparing Pregnant and Nonpregnant Women in the 1996 to 2001 and 2011 to 2012 Time Periods</th>
</tr>
</thead>
<tbody>
<tr>
<td>Outcomes</td>
<td>Pregnant Women, No. (%)</td>
</tr>
<tr>
<td>----------</td>
<td>-------------------------</td>
</tr>
<tr>
<td><strong>1996-2001 period</strong></td>
<td></td>
</tr>
<tr>
<td>Systemic corticosteroids in the ED</td>
<td>45 (51)</td>
</tr>
<tr>
<td>Systemic corticosteroids at ED discharge</td>
<td>28 (42)</td>
</tr>
<tr>
<td><strong>2011-2012 period</strong></td>
<td></td>
</tr>
<tr>
<td>Systemic corticosteroids in the ED</td>
<td>28 (78)</td>
</tr>
<tr>
<td>Systemic corticosteroids at ED discharge</td>
<td>19 (63)</td>
</tr>
</tbody>
</table>

*Propensity score adjustment for the potential confounding factors (age, history of hospitalization for acute asthma, and respiratory rate and peak expiratory flow at ED presentation).

*Inverse probability weighting based on the computed propensity score to adjust for the differences in patient characteristics and acute asthma severity between pregnant and nonpregnant women.
Appropriate antibiotic therapy

A. Amoxycillin and doxycycline
B. Amoxycillin and erythromycin
C. Augmentin and doxycycline
D. Cefuroxime
E. Amoxycillin and clarithromycin
‘OK’ drugs in pregnancy

All antiemetics
All H2 blockers
All PPIs
NSAIDs < 32 weeks if good indication
Beta blockers for heart disease / thyrotoxicosis
Antihistamines cetirizine and loratidine
Metformin
Case 5

- 39 year old, A/C, P₂
- Essential hypertension
- 8/40 headache and worsening hypertension
- Rx analgesia, increased methyldopa
- 10/40 headache severe, worse on bending
- 2 episodes of numbness right hand - 15 mins
- Fundoscopy papilloedema
Case 7: What investigations would you do?

A. CT
B. MRI
C. MRV
D. PET scan
E. LP
F. CT venogram
Epilepsy

- The death rate from epilepsy in pregnancy (0.40 per 100 000) is now higher than the death rate from hypertensive disorders in pregnancy (0.38 per 100 000)
Differential diagnosis of seizures in pregnancy

- Eclampsia
- Epilepsy
- Cerebral venous thrombosis
- CVA / ICH / SAH / SOL
- Thrombotic Thrombocytopenic Purpura
- Meningitis
- Drug / ETOH withdrawal
- Hypoglycaemia / hypercalcaemia
- Related to dural puncture
Seizures in Pregnancy

A first seizure in pregnancy that cannot readily be attributed to eclampsia or epilepsy warrants investigation with CT or MRI scan of brain.
Who to scan?

Signs

Severe / persistent (CVT)

Sudden onset / thunderclap (SAH)
Pressure (blood pressure for pre-eclampsia/eclampsia)
Anaesthetic (post-dural puncture headache)
Reversible (vasoconstriction syndrome)
Thrombosis (cerebral venous sinus thrombosis, ischaemic stroke)
Use your brain (there are so many other causes of headache)
Migraine.

Lim S Y et al. Pract Neurol 2014;14:92-99
Rare - Approximately 10% of cases occur in the post-partum period

Presents with explosive-onset, ‘worst-ever’ headache

Thunderclap – peaks 1 min, intense

2/3 occur in the first week post partum

Multiple thunderclap headaches over 1-4 weeks ~ pathognomonic

Background headache in between
Maternal Cardiac Arrest: Remember

AIRWAY
BREATHING
CIRCULATION

WEDGE (25% increase in CO)

DELIVER
Perimortem caesarean section is part of the resuscitation procedure in any women who arrests in the second half of pregnancy. It should be undertaken to facilitate maternal resuscitation within 5 minutes of the arrest if there is no initial response to advance life support in the tilted position.
Medical problems in pregnancy are common and potentially fatal.

Medical conditions are responsible for over half the direct and nearly all indirect maternal deaths and much maternal morbidity in the UK.

Cardiac disease is the leading cause of maternal mortality in the UK.

- ACS / aortic dissection / cardiomyopathy

Most drugs do not have a licence for use in pregnancy but much harm can result if they are omitted.
RCP course
Nov 18-20\textsuperscript{th} 2015

http://www.symposia.org.uk
sympreg@imperial.ac.uk

E-learning: