KCL Division of Women's Health

KING'S HEALTH PARTNERS

An Academic Health Sciences Centre for London

Pioneering better health for all

Medical Problems in Pregnancy:

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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**

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

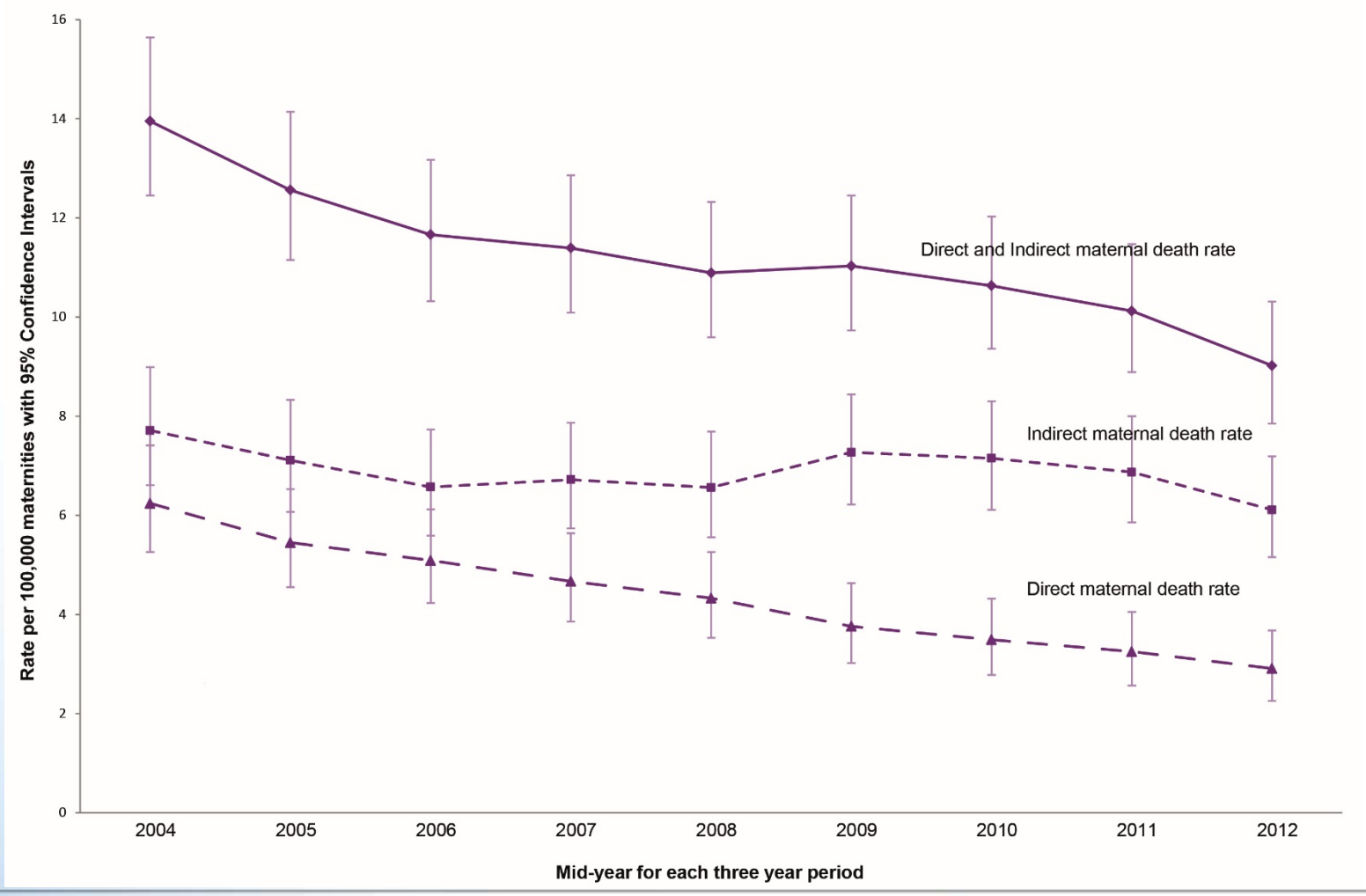
Hyperemesis gravidarum

Acute Fatty Liver of Pregnancy

Coincidental

Pneumonia, Malaria, Hepatitis

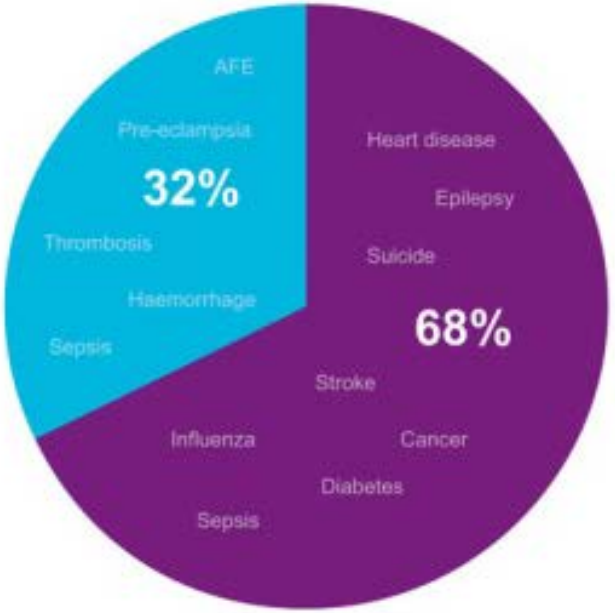
Maternal Mortality 2011-13



Causes of maternal death

Causes of mothers' deaths

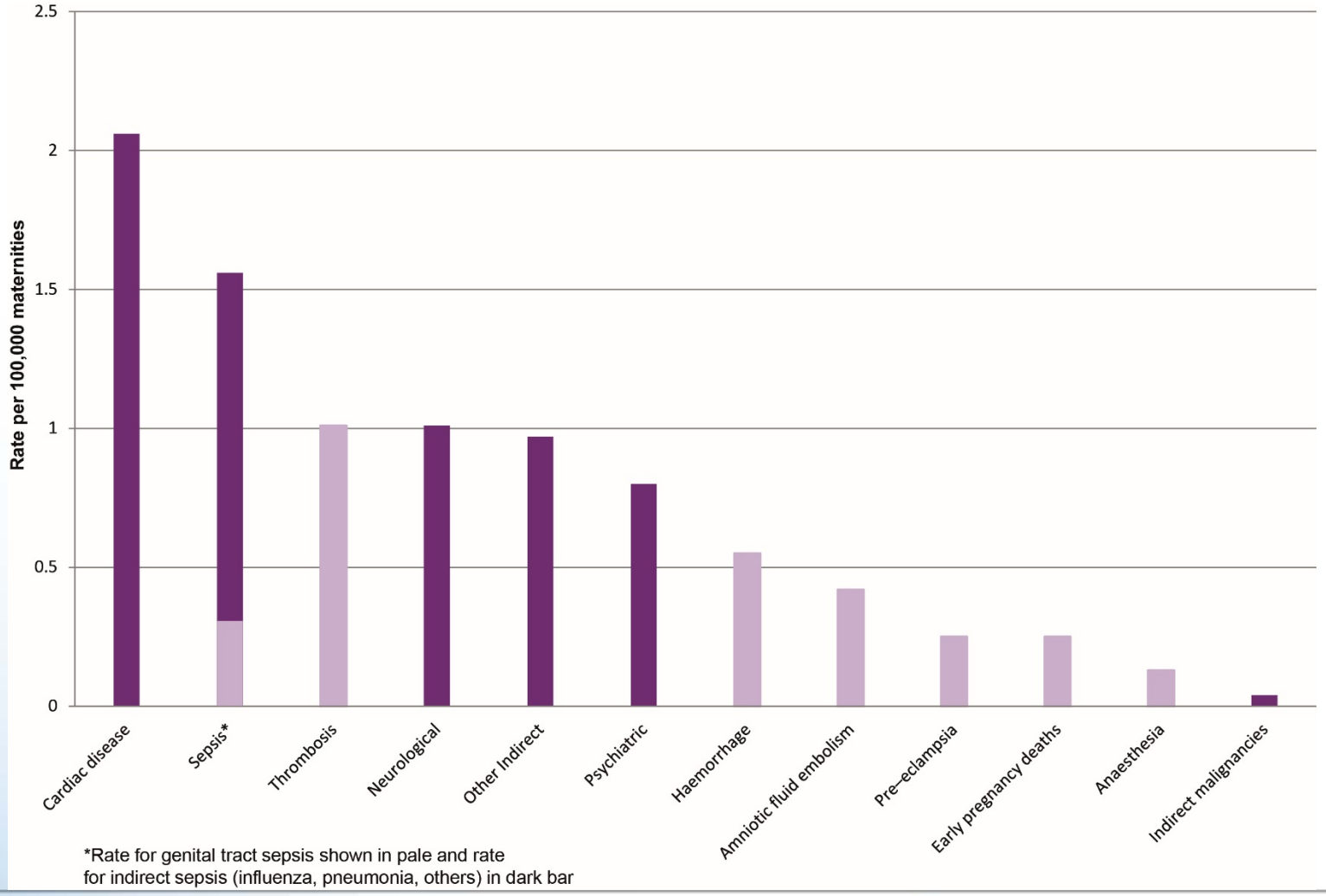
Two thirds of mothers died from medical and mental health problems in pregnancy and **only one third** from direct complications of pregnancy such as bleeding.



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

- Pre-pregnancy advice
- Joint specialist and maternity care

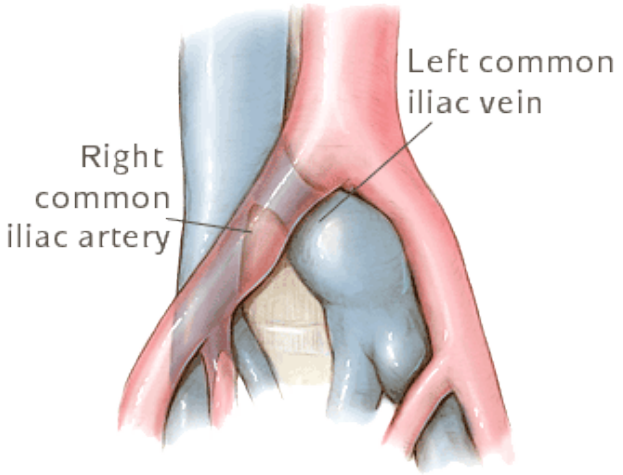
Causes of maternal death 2011-13



Dark bars show indirect causes, pale bars direct causes

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

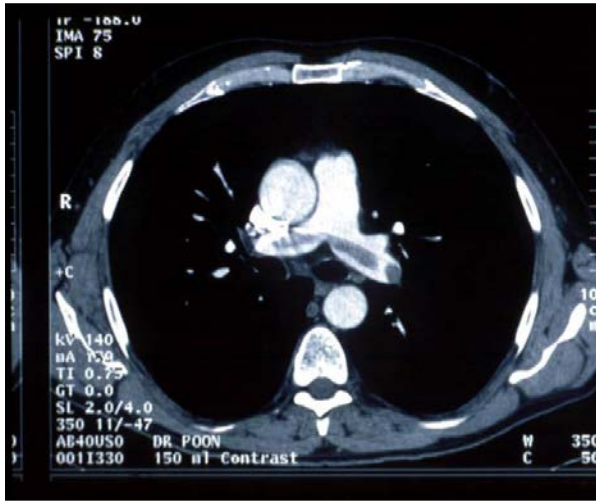
- CXR
- V/Q Lung scan
- CTPA

D dimers are useless!!

Unless higher pregnancy specific normal ranges are used

Radiation exposure

	Rads	mGy
CXR	<0.001	<0.01
Perfusion scan	<0.08	<0.8
Ventilation scan	<0.01	<0.1
CTPA / Helical CT	<0.013	<0.13
Max recommended	<0.5	5



Radiation in pregnancy

Table 7
Radiation Exposure of Various Imaging Examinations Performed for Pulmonary Embolism

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

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 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).

Ridge CA, et al. Am J Roentgenol 2009;193:1223–7.

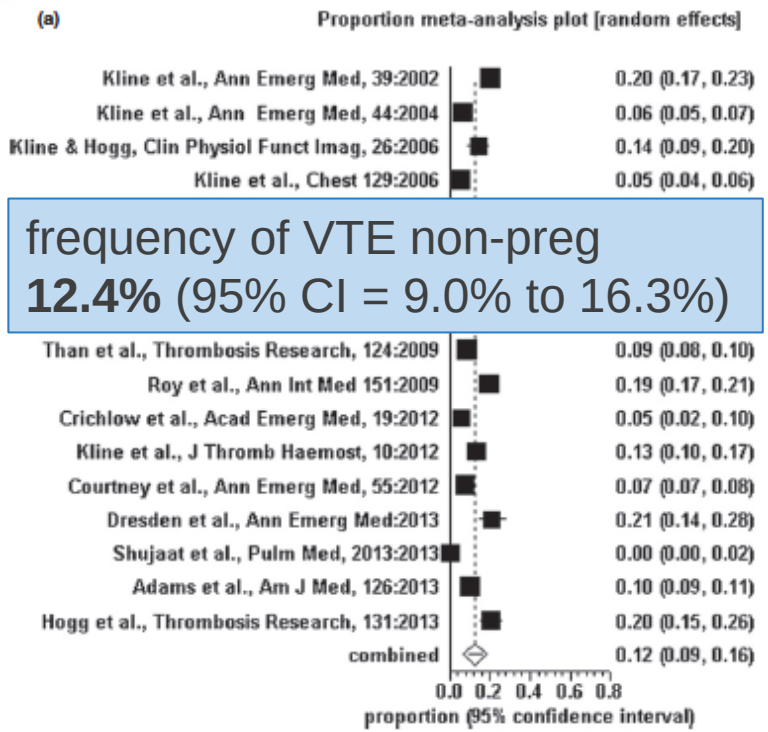
Academic Emergency Medicine
Official Journal of the Society for Academic Emergency Medicine

EVIDENCE-BASED DIAGNOSTICS

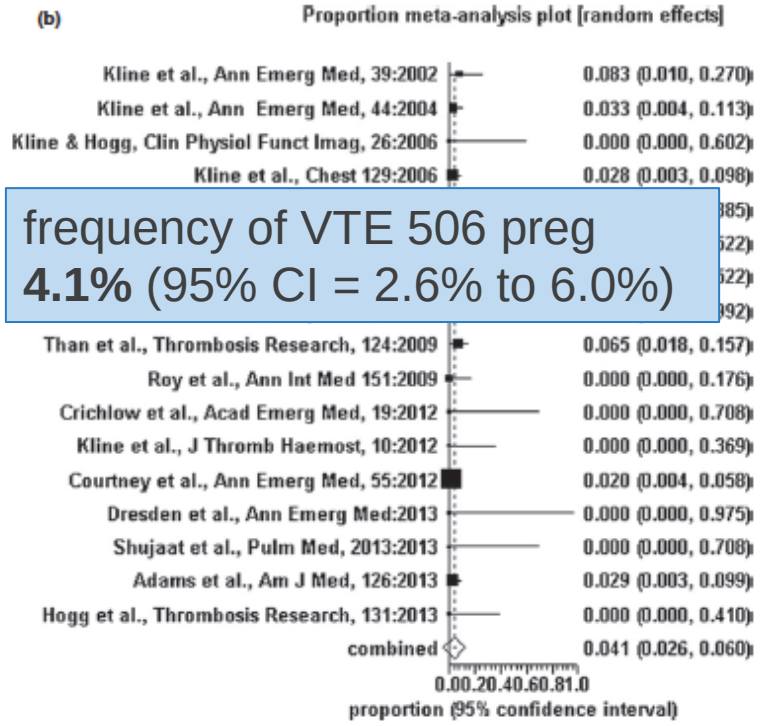
2014;21:949–959

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

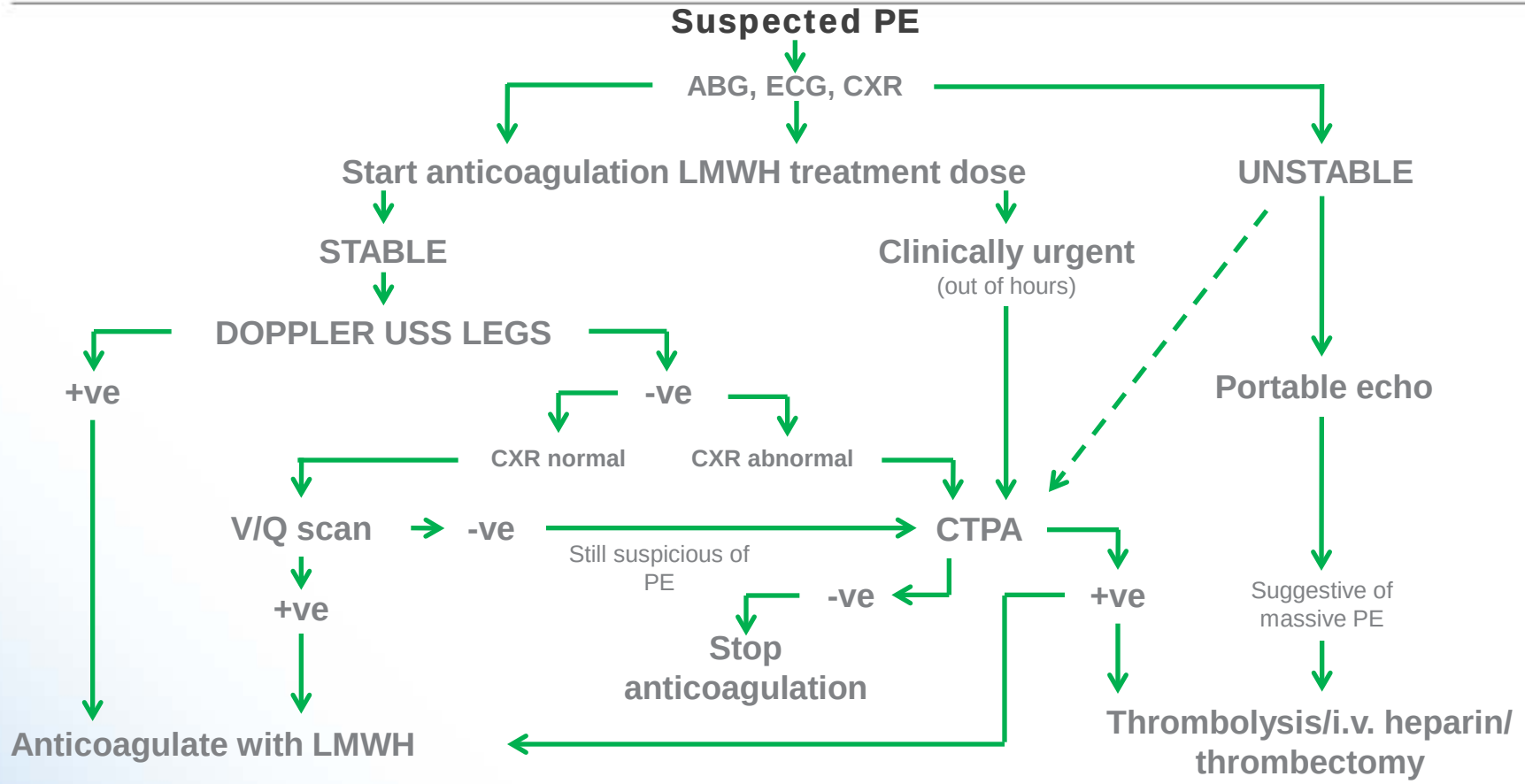


frequency of VTE non-preg
12.4% (95% CI = 9.0% to 16.3%)



frequency of VTE 506 preg
4.1% (95% CI = 2.6% to 6.0%)

Diagnosis of PE in pregnancy



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

Modified from: Scarsbrook *et al*. *Clin Radiol* 2006;61:1–12

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

BMJ. 2007 Feb 24;334(7590):418-9. Scarsbrook AF, Gleeson FV.

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'.

Patel J P et al. Circulation. 2013;128:1462-1469

Thrombolysis:

SHOULD NOT BE WITHELD in massive PE, with haemodynamic instability

Ahearn et al. 2002;

Leonhardt G et al. J Thromb Thrombolysis. 2006;21:271-6

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

Deaths from cardiac disease 2011-13 (UK)

49 women died from a cardiac condition

- 12 (25%) were classified as Sudden Adult Death Syndrome (SADS),
- 10 (20%) had an aortic dissection,
- 10 (20%) had an acute coronary syndrome,
- 6 (12%) died from cardiomyopathy
- 11 (22%) had other cardiac conditions

Peripartum Cardiomyopathy

Heart Failure Association of the European Society of cardiology Working Group on PPCM 2010

PPCM is an idiopathic cardiomyopathy presenting with heart failure secondary to LV systolic dysfunction toward the end of pregnancy or in the months following delivery, where no other cause of heart failure is found. It is a diagnosis of exclusion. The left ventricle may not be dilated but the ejection fraction is nearly always reduced below 45%.

Sliwa K, Hilfiker-Kleiner D, Petrie MC, et al. Eur J Heart Fail 2010;12:767-78.

Predictors of cardiac events in pregnancy: Toronto study

Cardiac Events predicted by:

Prior cardiac event or arrhythmia

NYHA classification > II or cyanosis

LV Ejection fraction < 40%

Left heart obstruction

Mitral valve area < 2 cm^2

Aortic valve area < 1.5 cm^2

Aortic valve gradient > 30mmHg

Siu et al Circulation 2001;104:515

European Heart Journal (2011) **32**, 3147–3197
doi:10.1093/eurheartj/ehr218

ESC Guidelines on the management of cardiovascular diseases during pregnancy

The Task Force on the Management of Cardiovascular Diseases during Pregnancy of the European Society of Cardiology (ESC)

Table 6 Modified WHO classification of maternal cardiovascular risk: principles

Risk class	Risk of pregnancy by medical condition
I	No detectable increased risk of maternal mortality and no/mild increase in morbidity.
II	Small increased risk of maternal mortality or moderate increase in morbidity.
III	Significantly increased risk of maternal mortality or severe morbidity. Expert counselling required. If pregnancy is decided upon, intensive specialist cardiac and obstetric monitoring needed throughout pregnancy, childbirth, and the puerperium.
IV	Extremely high risk of maternal mortality or severe morbidity; pregnancy contraindicated. If pregnancy occurs termination should be discussed. If pregnancy continues, care as for class III.

Conditions in which pregnancy risk is WHO I
• Uncomplicated, small or mild - pulmonary stenosis - patent ductus arteriosus - mitral valve prolapse
• Successfully repaired simple lesions (atrial or ventricular septal defect, patent ductus arteriosus, anomalous pulmonary venous drainage).
• Atrial or ventricular ectopic beats, isolated
Conditions in which pregnancy risk is WHO II or III
WHO II *(if otherwise well and uncomplicated)*
• Unoperated atrial or ventricular septal defect
• Repaired tetralogy of Fallot
• Most arrhythmias
WHO II–III *(depending on individual)*
• Mild left ventricular impairment
• Hypertrophic cardiomyopathy
• Native or tissue valvular heart disease not considered WHO I or IV
• Marfan syndrome without aortic dilatation • Aorta <45 mm in aortic disease associated with bicuspid aortic valve
• Repaired coarctation
WHO III
• Mechanical valve
• Systemic right ventricle
• Fontan circulation
• Cyanotic heart disease (unrepaired)
• Other complex congenital heart disease
• Aortic dilatation 40–45 mm in Marfan syndrome • Aortic dilatation 45–50 mm in aortic disease associated with bicuspid aortic valve

Advise against pregnancy

Pulmonary arterial hypertension

Systemic ventricular dysfunction

LVEF < 30%,

NYHA III/IV

Previous PPCM with any residual LV impairment

Severe mitral stenosis

Severe symptomatic aortic stenosis

Aorta > 45mm Marfan

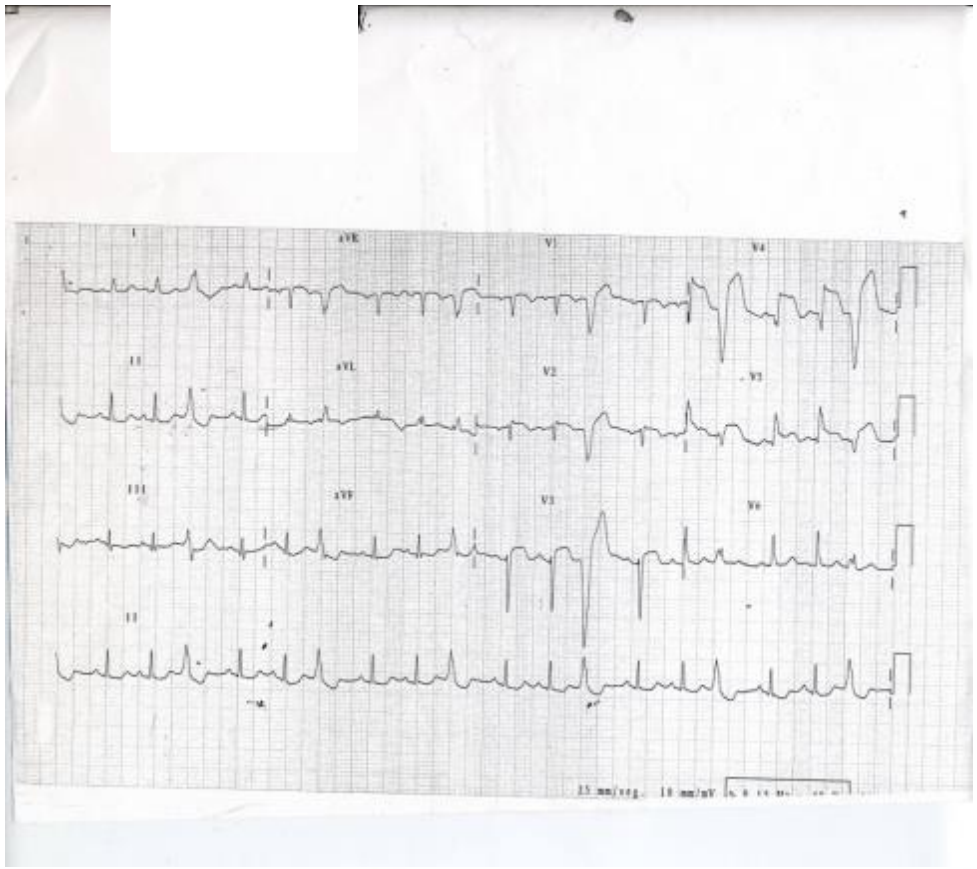
Aorta > 50 mm bicuspid

Severe coarctation

CONTRACEPTION

Case 1

- 39 yr old asian, 37 weeks pregnant
- c/o dizziness and epigastric pain
- o/e sweaty, BP 94/68, HR 84



Case 1: 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 2

- 38 year old primip, 39 weeks pregnant
- C/o chest and back pain
- O/e BP 165/85, HR 124, O_2 sats 97%
- Urinalysis NAD
- ‘Writhing around the bed’, ‘won’t lie down to be examined’
- Not in labour!

Case 2: What investigations would you request?

A. **CXR**

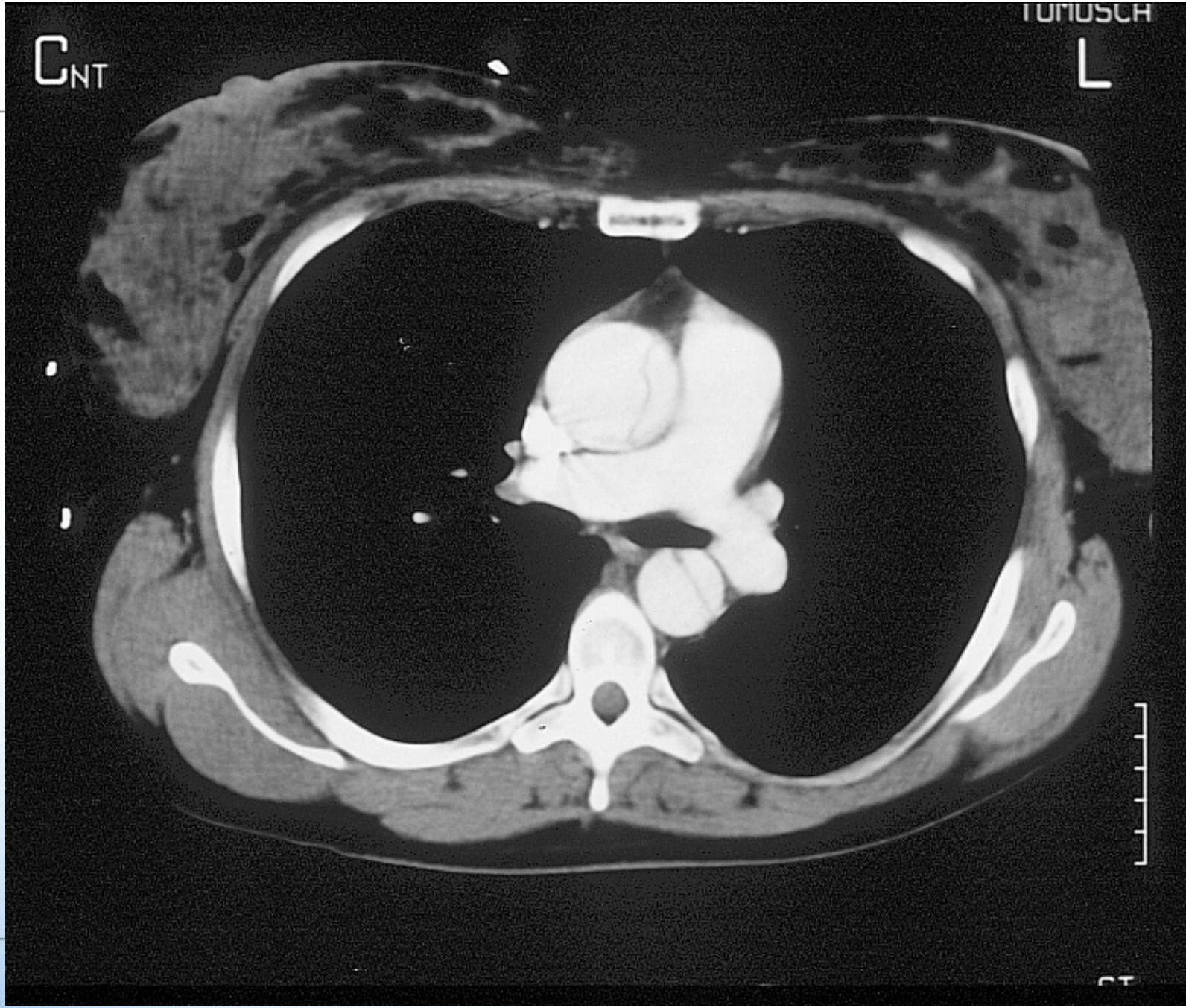
B. **back XR**

C. **TTE**

D. **TOE**

E. **abdo US**

F. **CTPA**


CNT
L

- **Not all chest pain and breathlessness = PE**
- **Beware the hypertensive (systolic) woman with chest pain**
- **CXR**
- **Echo**

Case 3

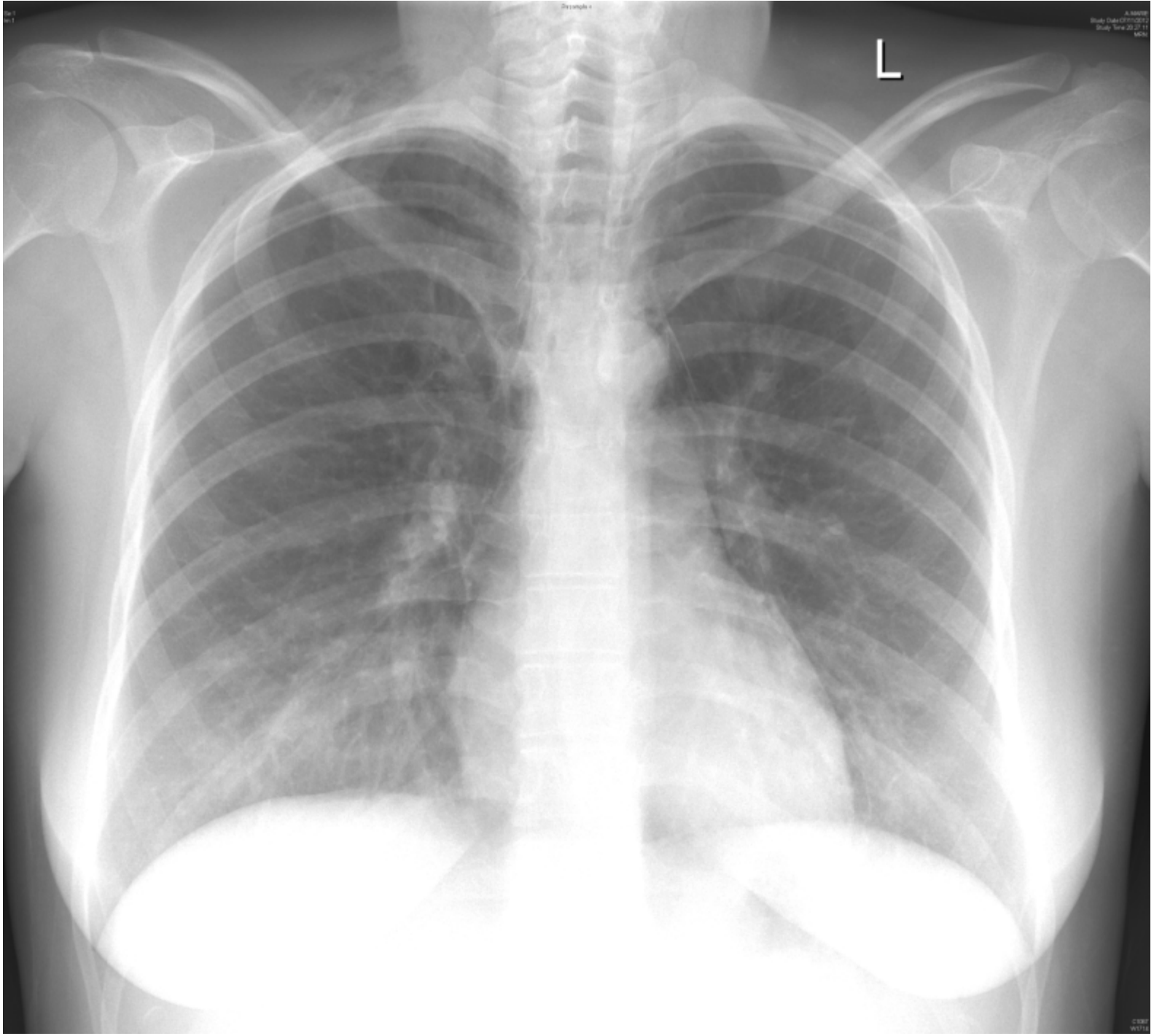
35 year old

1 day post first normal vaginal delivery

C/O chest pain

Obstetric SHO requests CTPA

Medical registrar asked to review - told CXR normal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Acute asthma

Cydulka et al. Am J Resp Crit Care Med 1999;160:887-892

- 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 2weeks later

CHEST

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 4] Unadjusted and Adjusted Analyses for Outcomes Comparing Pregnant and Nonpregnant Women in the 1996 to 2001 and 2011 to 2012 Time Periods

Outcomes	Pregnant Women, No. (%)	Nonpregnant Women, No. (%)	Unadjusted		Adjusted With Propensity Score[a]		Adjusted With Use of Inverse Probability Weighting[b]	
			OR (95% CI)	*P* Value	OR (95% CI)	*P* Value	OR (95% CI)	*P* Value
1996-2001 period								
Systemic corticosteroids in the ED	45 (51)	841 (64)	0.50 (0.32-0.79)	.002	0.52 (0.33-0.81)	.004	0.35 (0.18-0.69)	.002
Systemic corticosteroids at ED discharge	28 (42)	592 (59)	0.43 (0.26-0.73)	.002	0.44 (0.26-0.76)	.003	0.30 (0.13-0.68)	.004
2011-2012 period								
Systemic corticosteroids in the ED	28 (78)	633 (76)	1.03 (0.46-2.31)	.94	1.11 (0.50-2.49)	.80	0.98 (0.42-2.26)	.95
Systemic corticosteroids at ED discharge	19 (63)	481 (71)	0.83 (0.37-1.86)	.64	0.87 (0.38-1.96)	.73	0.81 (0.34-1.95)	.64

[a]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).
[b]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.

CHEST 2015; 147 (2): 406 - 414

Table 2 Risk of any major congenital malformation in children born to mothers with asthma

	Cases (n = 5124)	Controls (n = 30053)		
	n (%)†	n (%)†	Adjusted OR‡ (95% CI)	p Value
Maternal asthma status				
No asthma diagnosis or medications before delivery	4420 (86.3)	26235 (87.3)	Reference	
Asthma diagnosis or medication§ before delivery	704 (13.7)	3818 (12.7)	1.10 (1.01 to 1.20)	0.032
Diagnosis with no medication before delivery	171 (3.3)	881 (2.9)	1.17 (0.99 to 1.39)	0.071
Asthma medication§ but no diagnosis before delivery	183 (3.6)	968 (3.2)	1.13 (0.96 to 1.33)	0.132
Diagnosis and asthma medication§ before delivery	350 (6.8)	1969 (6.6)	1.06 (0.94 to 1.20)	0.329
⩾1 asthma exacerbation during pregnancy	18 (<0.5)	94 (<0.5)	1.09 (0.65 to 1.82)	0.754
*⩾1 medication exposure during pregnancy**				
Any asthma medication	410 (8.0)	2240 (7.5)	1.05 (0.94 to 1.18)	0.367
Short-acting β agonist	375 (7.3)	2085 (6.9)	1.06 (0.94 to 1.19)	0.336
Inhaled corticosteroid	220 (4.3)	1209 (4.0)	1.07 (0.92 to 1.24)	0.407
Long-acting β agonist	25 (<0.5)	131 (<0.5)	1.12 (0.72 to 1.75)	0.614
Oral corticosteroid	46 (0.9)	216 (0.7)	1.23 (0.89 to 1.69)	0.201
Other bronchodilator medication¶	13 (<0.5)	72 (<0.5)	1.05 (0.59 to 1.87)	0.872
Other anti-inflammatory medication**	9 (<0.5)	27 (<0.5)	2.02 (0.96 to 4.28)	0.065

*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, titropium or ipratropium.
**Cromoglicate, nedocromil, montelukast or zafirlukast.

Tata et al. Thorax 2008

Hviid A, Molgaard-Nielsen D. CMAJ 2011;183(7):796-804.

RESEARCH CMAJ

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
    - 1232 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

Hviid A, Molgaard-Nielsen D. Corticosteroid use during pregnancy and risk of orofacial clefts. CMAJ 2011;183(7):796-804.

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

		Cleft lip with or without cleft palate		Cleft palate alone	
Corticosteroid use	No. of live births	No. (prevalence*)	Adjusted OR† (95% CI)	No. (prevalence*)	Adjusted OR‡ (95% CI)
Any use	51 973	57 (1.10)	1.05 (0.80–1.38)	27 (0.52)	1.23 (0.83–1.82)
No use	780 663	818 (1.05)	1.00	330 (0.42)	1.00
Route of administration					
Oral					
Yes	2 195	0 (0.00)	NA	0 (0.00)	NA
No	830 441	875 (1.05)	1.00	357 (0.43)	1.00
Inhalant					
Yes	7 421	6 (0.81)	0.75 (0.34–1.68)	3 (0.40)	0.94 (0.30–2.92)
No	825 215	869 (1.05)	1.00	354 (0.43)	1.00
Nasal spray					
Yes	11 245	6 (0.53)	0.52 (0.23–1.16)	5 (0.44)	1.07 (0.44–2.58)
No	821 391	869 (1.06)	1.00	352 (0.43)	1.00
Dermatologic					
Yes	22 480	34 (1.51)	1.45 (1.03–2.05)	14 (0.62)	1.45 (0.85–2.48)
No	810 156	841 (1.04)	1.00	343 (0.42)	1.00
Other topical form					
Yes	12 091	13 (1.08)	1.04 (0.60–1.79)	5 (0.41)	0.97 (0.40–2.34)
No	820 545	862 (1.05)	1.00	352 (0.43)	1.00

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

	Maternal concentration	Cord blood concentration
Prednisolone	10	1
Hydrocortisone	6	1
Betamethasone	3	1

‘OK’ drugs in pregnancy

All antiemetics

All H2 blockers

All PPIs

NSAIDs < 32 weeks if good indication

Beta blockers for heart disease / thyrotoxicosis

Antihistamines cetirazine and loratidine

Metformin

Drugs for renal / IBD / CTD

YES - OK

- Cyclosporin
- Tacrolimus
- Azathioprine
- Prednisolone
- Sulfasalazine
- Mesalazine
- Hydroxychloroquine
- Biologics (Etanercept / infliximab) Adalimumab)
- IVIG
- Metronidazole

NO

- NSAIDs (1st and 2nd trim OK)
- (Mycophenolate mofetil)
- Rapamycin
- Tetracycline
- ACE Inhibitors (oligohydramnios/renal dysplasia/pulmonary hypoplasia/ cardiac)
- AT II receptor blockers
- Methotrexate
- Cyclophosphamide
- Statins

Ostensen M et al. Arthritis Research & Therapy 2006; 8: 209

Update: Rheumatology (Oxford). 2008 Jun;47 Suppl 3:iii28-31.

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

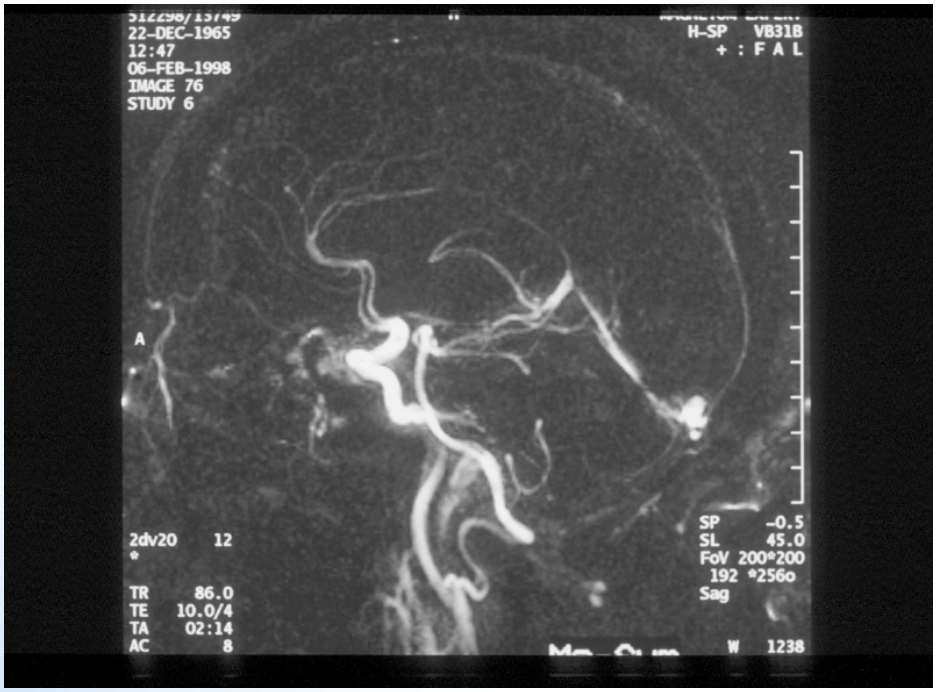
Thrombotic Thrombocytopenic Purpura

Meningitis

Drug / ETOH withdrawal

Hypoglycaemia / hypercalcaemia

Related to dural puncture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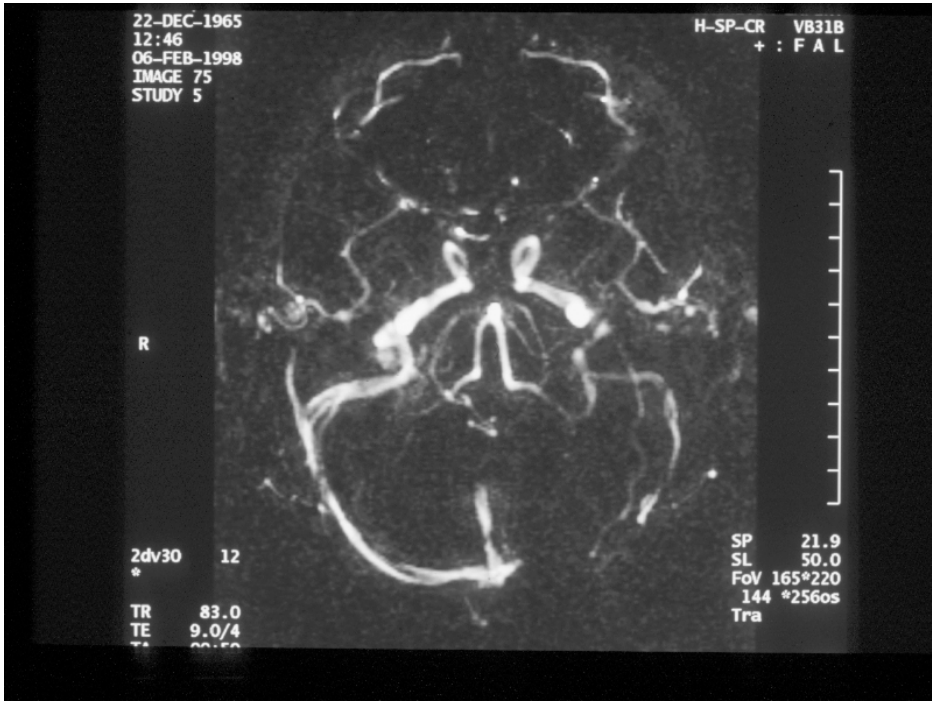
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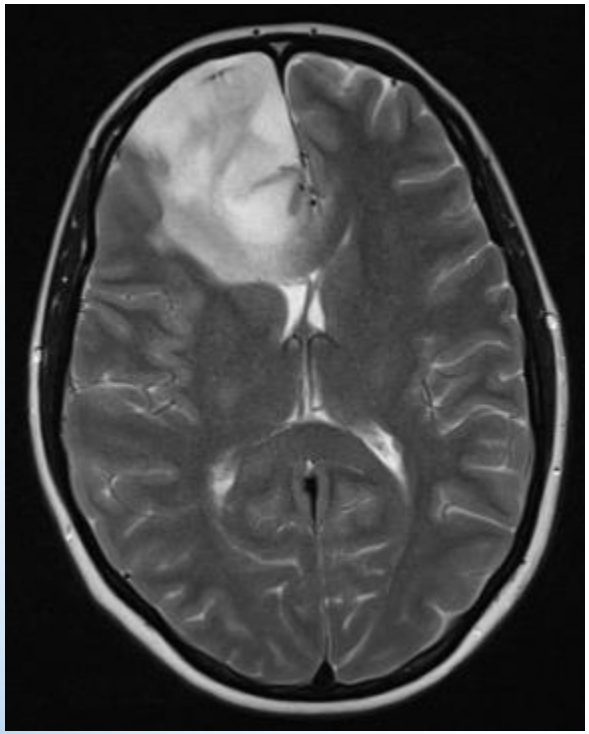
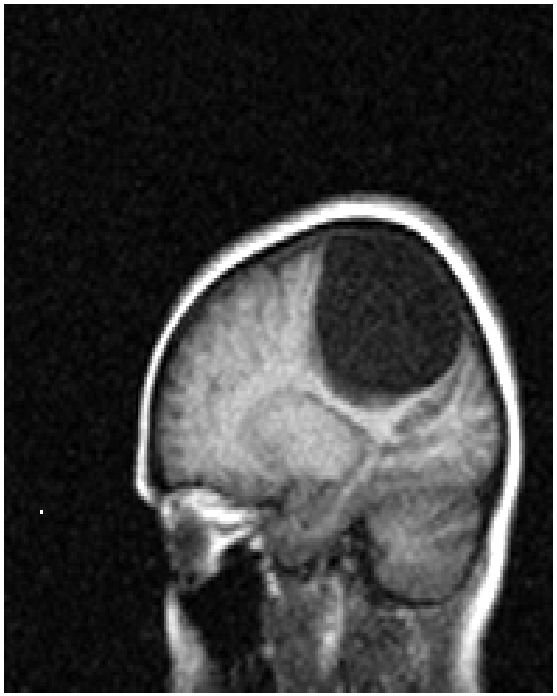
Seizures in Pregnancy

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





Headache: Who to scan?

Signs

Severe / persistent (CVT)

Sudden onset / thunderclap (SAH)

Post partum Headache

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

RCVS - Reversible cerebral vasoconstriction syndrome

Rare - Approximately 10% of cases occur in the post-partum period

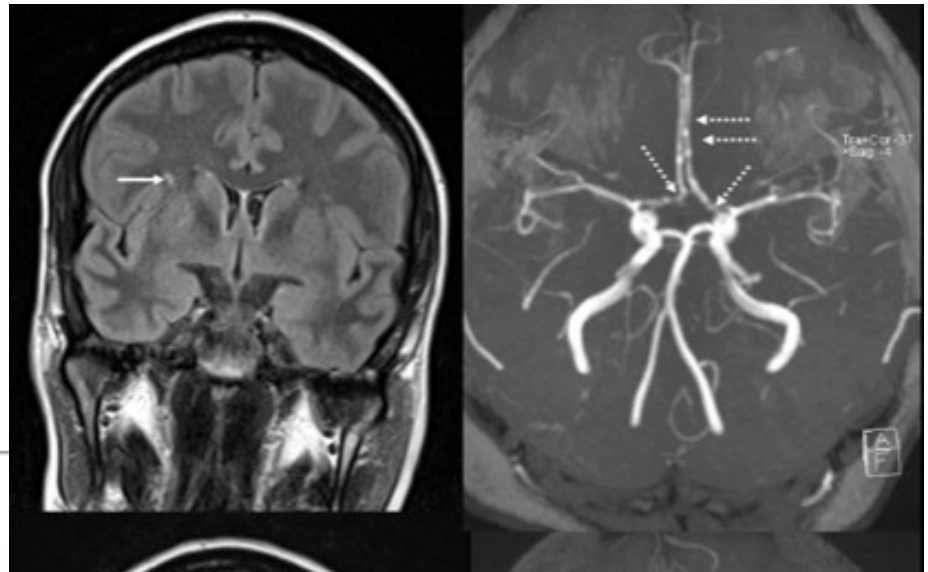
Presents with explosive-onset, ‘worst-ever’ headache

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



Summary

- Medical problems in pregnancy are common and potentially fatal
- Medical conditions are responsible for two thirds of all 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
- VTE is the commonest direct cause of maternal death
- Control of medical disease is important and improves pregnancy outcomes
- Most drugs do not have a licence for use in pregnancy but much harm can result if they are omitted

Key Messages from MBRRACE

Women with pre-existing medical conditions should have pre-pregnancy counselling by doctors with experience of managing their disorder in pregnancy.

Women with medical disorders in pregnancy should have access to a coordinated multidisciplinary obstetric and medical clinic, thereby avoiding the need to attend multiple appointments and poor communication between senior specialists responsible for their care.

Key messages

Pregnant women with medical conditions require an individualised care plan made together by members of the multidisciplinary team including an obstetrician, obstetric anaesthetist, obstetric or specialty physician, surgeon and members of the allied health professions as appropriate.

Appropriately trained senior physicians should be involved in the care of pregnant and post partum women with new onset symptoms suggestive of or known underlying medical disorders.

The way forward

High level actions are needed to ensure that physicians are appropriately trained in, and engaged with, the care of pregnant women, and that services are designed for women with medical conditions which provide appropriate and evidence-based care across the entire pathway, including pre-pregnancy, during pregnancy and delivery, and postpartum.

http://www.e-lfh.org.uk/programmes/medical-problems-in-pregnancy/

e-LfH
e-Learning for Healthcare

NHS
Health Education England

e-LMpP { e-learning for Medical Problems in Pregnancy

Royal College of Physicians
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WELLBEING OF WOMEN

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Leading specialists from the UK and overseas will discuss the most important and common medical problems which complicate pregnancy, delivery and the puerperium. The management of medical disorders pre-dating pregnancy as well as those arising during pregnancy will be covered.

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