There is so much we don't know in medicine that could make a difference, and often we focus on the big things, and the little things get forgotten. To highlight some smaller but important issues, we've put together a series of pearls that the Red Whale found at the bottom of the ocean of knowledge!

Red Whale GP-Update

Hypertension in pregnancy: NICE guidelines

The use of aspirin for the prevention of pre-eclampsia in high-risk pregnant women was introduced by NICE in 2010 (NICE 2010,CG107). New evidence has recently been published about the risks of chronic hypertension in pregnancy and the benefit of aspirin for the prevention of pre-eclampsia. This is detailed within the relevant sections of the summarised NICE guidelines below.

The NICE guidance categorises pregnant women with hypertension into three groups:

Women with chronic hypertension = women with hypertension ***prior*** to conception.

Women with gestational hypertension = women who develop hypertension after 20 weeks.

Women with pre-eclampsia = gestational hypertension + proteinuria.

All pregnant women with any form of hypertension need shared care. In addition, it is important to educate ALL pregnant women about the symptoms of pre-eclampsia, and explain they must seek immediate medical advice if they experience them.

- Symptoms include:
  - Severe headache.
  - Visual disturbance, e.g. blurring, flashing before eyes.
  - Severe pain below the ribs.
  - Vomiting.
  - Sudden swelling of the face, hands or feet.

Chronic hypertension

Pre-conception counselling

For women of child-bearing age with chronic hypertension:

- There is an increased risk of congenital malformations with ACEI, ARB and chlorothiazide if taken during pregnancy.
- There is no known increased risk with other anti-hypertensives.
- **ACEI and ARB should be stopped within 2 days of notification of pregnancy. Offer an alternative.**

A recent large systematic review and meta-analysis looked at pregnancy outcomes in women with chronic hypertension (BMJ 2014;348:g2301). It included 55 studies from 25 countries with a total of 795 221 pregnancies.

- It confirmed that chronic hypertension was associated with adverse pregnancy outcomes.
- In the US, compared with normotensive women, those with chronic hypertension had an increased risk of superimposed pre-eclampsia, C-section, premature delivery, birth weight <2500g, neonatal ITU admission and perinatal death.
- The linked editorial suggests strategies to prevent these adverse outcomes that are relevant to GPs and midwives (BMJ 2014;348:g2655):
  - Primary prevention: reduce obesity, encourage women to have children at a younger age, smoking cessation (to reduce the risk of superimposed pre-eclampsia).
  - Secondary prevention: low-dose aspirin, antihypertensives if BP >150/100mmHg (reduces the risk of severe hypertension but no effect on perinatal outcomes (NEJM 2015;372:407-17)).
  - Tertiary prevention: evaluation for secondary causes of hypertension prior to pregnancy and assessment for end organ involvement. Increased surveillance during pregnancy – USS monitoring of foetal growth, more frequent antenatal clinic visits, consideration of home BP monitoring, consideration of induction of labour.

Managing chronic hypertension in pregnancy

- Reassess medication (as above). The limited available evidence does not show increased risk of congenital malformation with other drugs. A recent large retrospective cohort study suggests it may be the hypertension itself rather than the drug used that is the risk factor, but, for now, this should not change our practice (BMJ 2011;343:d5931).
- Aim for blood pressure targets:
  - <150/100 for uncomplicated hypertension.
  - <140/90 for hypertension with end organ damage, e.g. renal.
- For uncomplicated hypertension, do not increase treatment to lower diastolic below 80mmHg.
- **Refer for shared care with obstetricians** because additional foetal monitoring is required and early delivery *may* be recommended if BP >160/110 despite treatment.
- Review long-term treatment 2w after delivery, and offer full medical review at post-natal check.

Gestational hypertension

Managing gestational hypertension

Here we consider women diagnosed with hypertension after 20w gestation who do not have proteinuria.

- **Refer all pregnant women with BP >140/90 for assessment in secondary care.**
- Management depends on severity of hypertension, and will be determined by obstetricians *(see table below).*
- Bed rest should not be part of treatment as there is no evidence it helps!
- Additional foetal monitoring, e.g. growth, amniotic fluid volume and umbilical artery Doppler, may be required.

Pre-eclampsia

Prevention of pre-eclampsia

Identify women at high risk of pre-eclampsia and advise them to take 75mg aspirin daily.

NICE identifies high and moderate risk factors for developing pre-eclampsia:

High risk factors	Moderate risk factors
Hypertension in previous pregnancy	First pregnancy
Chronic kidney disease	Age 40 or older
Autoimmune disease, e.g. SLE, antiphospholipid	Pregnancy interval >10y
Type 1 or type 2 diabetes	BMI >35 at first visit
Chronic hypertension	Family history of pre-eclampsia

- **Advise women with one high risk factor or 2 or more moderate risk factors to take 75mg aspirin daily from 12w until the baby is born** *(this is an unlicensed indication and should be discussed and documented appropriately).*
- **DO NOT** recommend magnesium, folic acid, antioxidants (vitamins C and E), fish oil or garlic for the purposes of preventing hypertensive disorders during pregnancy *(though all pregnant women should still be encouraged to take folic acid pre-conceptually and for first trimester to prevent neural tube defects).*
- **DO NOT** use nitric oxide donors, progesterone, diuretics or low molecular weight heparin to prevent hypertensive disorders in pregnancy as there is insufficient evidence that they are effective.

Evidence for aspirin in the prevention of pre-eclampsia

NICE uses two key meta-analyses as its basis for recommending 75mg aspirin for women with one high or two moderate risk factors. Cochrane reviewed 59 RCTs which had addressed the role of aspirin in reducing the risk of pre-eclampsia (Cochrane 2007; (2) CD004659). The studies included more than 37 000 women.

- Aspirin offered a small reduction in the risk of pre-eclampsia compared with placebo (RR 0.83 (CI 0.77–0.89)). It also reduced preterm births.
- There was no difference in the risk of gestational hypertension.
- There were no additional adverse pregnancy events, e.g. placental abruption, haemorrhage.
- 2 studies followed infants to 18m of age. One showed no adverse events; the other (which was non-blinded and had high drop-out rates) showed a small increase in gross and fine motor developmental delay.

Aspirin reduced the relative risk of pre-eclampsia equally for all women, with a pooled NNT of 72. However, in terms of absolute risk, high-risk women stand to gain the most benefit, with an NNT of 19 to prevent one episode of pre-eclampsia. This is why NICE targets this group.

A follow-up study (Lancet 2007;369:1791) looked at individual patient data, and provides the basis for the risk factors identified by NICE. It found that high-risk women potentially benefited the most, and that the benefits for moderate-risk women were more equivocal, so NICE has determined that a woman needs 2 moderate risk factors to warrant aspirin.

A more recent systematic review (Ann Intern Med 2014;160:695) supports the use of aspirin in women at high risk of pre-eclampsia, but the absolute benefit may be small. It found a reduced risk of preterm delivery (RR 0.86, 95% CI 0.76-0.98), intrauterine growth restriction (RR 0.8, 95% CI 0.65-0.99) and pre-eclampsia (RR 0.76 95% CI 0.62 – 0.95) in high-risk women taking aspirin. There was no difference in mean blood loss or risk of post-partum haemorrhage between groups.

Testing for proteinuria

When assessing for proteinuria, NICE only makes recommendations in the context of secondary care. It says:

- Use an automated reagent-strip reading device OR a spot protein:creatinine ratio.
- If ≥1+ proteinuria, use spot PCR to quantify.
- PCR >30mg/mmol or 24-hour urine collection >300mg protein suggest significant proteinuria.

NICE does not make any specific recommendations for primary care. At present, usual practice would be to use a visually interpreted dipstick and to consider ≥1+ significant and warranting further assessment.

Managing pre-eclampsia

Women diagnosed with hypertension who also have dipstick proteinuria:

- **Refer to secondary care for same day assessment and probable admission.**
- Monitoring, treatment and delivery time will be determined by the obstetricians *(see table below).*
- Additional foetal monitoring including growth, amniotic fluid volume and umbilical artery Doppler imaging may be required.

	Mild (140/90–149/99)	**Moderate (150/100–159/109)**	**Severe (≥160/110)**
Management of gestational hypertension			
Admit to hospital?	No	No (same day outpatient)	Yes
Treat?	No	Oral labetalol first line (alternatives include methyldopa/nifedipine)	Oral labetalol first line (alternatives include methyldopa/nifedipine)
BP monitoring	Once weekly	At least twice weekly	At least four times daily
Test for proteinuria	At each visit	At each visit	Daily
Blood tests	As per routine antenatal care	U&E, FBC, LFT at initial presentation. No further blood tests indicated if no proteinuria subsequently	U&E, FBC and LFT at presentation then weekly
Management of pre-eclampsia (hypertension + proteinuria)			
Admit to hospital?	Yes	Yes	Yes
Treat?	No	Oral labetalol first line (alternatives include methyldopa/nifedipine)	Oral labetalol first line (alternatives include methyldopa/nifedipine)
BP monitoring	At least four times daily	At least four times daily	More than four times daily
Test for proteinuria	Once confirmed, do not repeat	Once confirmed, do not repeat	Once confirmed, do not repeat
Blood tests	U&E, FBC, LFT three times weekly	U&E, FBC, LFT three times weekly	U&E, FBC, LFT three times weekly

Post-natal care and follow-up

- All women should have a medical review at their post-natal check.
- If a woman needs ongoing antihypertensive treatment in the post-natal period, the following antihypertensives have no known adverse effects on babies receiving breast milk:

Labetalol	Captopril
Nifedipine	Atenolol
Enalapril	Metoprolol

- Avoid diuretics in women who are breast-feeding or expressing breast milk.
- There is insufficient evidence to comment on the safety of ARBs, amlodipine and other ACEI for breast-feeding mothers.
- There is also an increased risk of the same problems in subsequent pregnancies.
- Women with pre-eclampsia should aim for a BMI within the healthy range before their next pregnancy.

Risk of developing hypertension in later life?

It is well known that women who have hypertensive disorders in pregnancy (gestational hypertension, pre-eclampsia, eclampsia or HELLP syndrome) are at increased risk of developing hypertension later in life. A massive cohort study has now quantified the risks and looked at how quickly hypertension recurs (BMJ 2017:358:j3078).

- About one-third of women with hypertension in pregnancy developed hypertension in later life.
- The hypertension may present as soon as 1y after delivery.

Another cohort study looked at women who had had hypertension in pregnancy, to identify what factors increased the risk of hypertension in later life (BMJ 2017;358:j30240).

- The main risk identified was obesity: the researchers estimated that 25% of all cases of hypertension in later life were attributable to obesity, and that modifying lifestyle to reduce obesity would reduce the number of women who developed hypertension in later life.

The accompanying editorial reminds us these women need regular monitoring (but doesn't specify what this means!) (BMJ

2017;358:j3245).

Do you code hypertensive disorders in pregnancy? Do you ensure you monitor these women for hypertension? Do you do this ad hoc or do you want to be more proactive?

NICE on hypertension in pregnancy

- Offer all women with 1 high risk or 2 moderate risk factors 75mg aspirin daily from 12w of gestation to reduce the risk of pre-eclampsia.
- Educate all pregnant women about the symptoms and signs of pre-eclampsia.
- Avoid prescribing ACEI and ARBs for women with chronic hypertension who are hoping to start a family.
- Gestational hypertension is BP >140/90 in the absence of proteinuria. All women with a BP >150/100 require same-day assessment in secondary care.
- Pre-eclampsia is hypertension and at least 1+ proteinuria. All women with BP >140/90 and proteinuria need same-day assessment in secondary care.
- Review anti-hypertensive medication in the post-natal period, and adjust to take account of breast-feeding.
- Remember women with gestational hypertension and pre-eclampsia are at increased risk of hypertension later in life.

Discuss these guidelines with your community midwife and PHCT. How will you identify women eligible for aspirin treatment?
Do you have, or could you design, information for recognising the symptoms of pre-eclampsia, and to explain why a woman has been offered aspirin?

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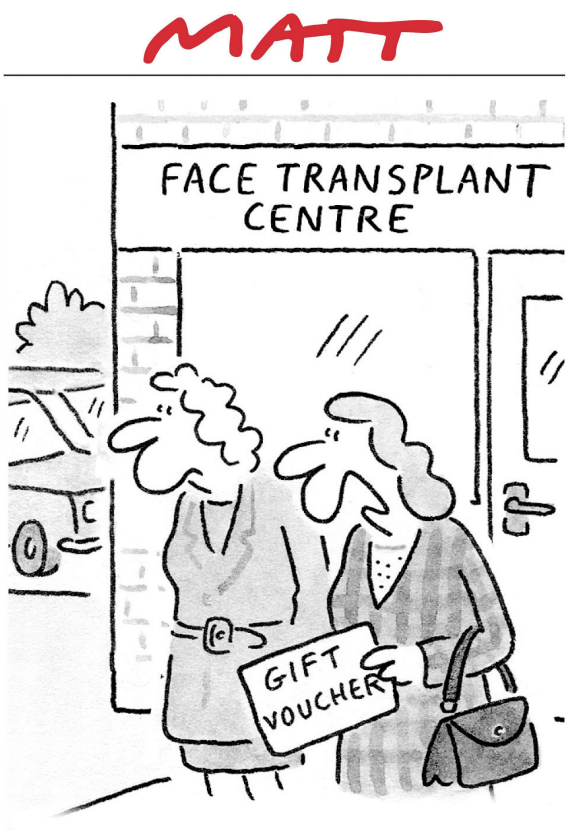

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www.gp-update.co.uk

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RCGP CPD ACCREDITED

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London	Fri 18 May 2018
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Newcastle	Wed 6 Jun 2018
Sheffield	Thur 7 Jun 2018
Manchester	Fri 8 Jun 2018
Birmingham	Sat 9 Jun 2018
Norwich	Wed 13 Jun 2018
London	Thur 14 Jun 2018
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Oxford	Fri 28 Sep 2018
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Glasgow	Fri 9 Nov 2018
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MSK problems are the most common reason for seeing a GP and represent 30% of repeat GP visits. We want to help build your confidence. On the course we will tackle:

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- Diagnosis: why waddling like a duck might help; and what to do when there is no diagnosis!
- Why chronic pain is 'in the brain' – and more importantly, what we and our patients can do about it.

We will provide you with a new narrative and a tool box of strategies you can take back to the surgery and start using the next day.

London	Thur 17 May 2018
Manchester	Wed 6 Jun 2018
Leeds	Thur 11 Oct 2018
Birmingham	Fri 12 Oct 2018
London	Thur 18 Oct 2018
Brighton Red Whale SEE BACK PAGE	Wed 21 Nov 2018

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London	Fri 18 May 2018
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Nottingham	Wed 17 Oct 2018
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London	Thur 24 May 2018
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London	Thur 4 Oct 2018
Leeds	Thur 11 Oct 2018
Birmingham	Fri 12 Oct 2018
Manchester	Thur 15 Nov 2018
Bristol	Fri 16 Nov 2018
Brighton Red Whale	SEE BACK PAGE — Thur 22 Nov 2018

The Cancer Update Course

Within the next 15 years the need for cancer care will double and you will look after as many cancer survivors as diabetics. Shared care follow up will become the norm, and secondary care will pass responsibility to us. A key 2015 Lancet Oncology commission paper warned that: "GPs are inadequately trained and resourced to manage the growing demand for cancer care in high income countries".

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London	Wed 23 May 2018
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London	Thur 28 Jun 2018
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The Effective Consultation Course

London	Fri 18 May 2018
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Leeds	Fri 16 Nov 2018
London	Fri 23 Nov 2018

The Medically Unexplained Symptoms Course

Manchester	Thur 7 Jun 2018
London	Thur 18 Oct 2018

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NOVEMBER 2018

21	Wednesday	The MSK and Chronic Pain Update Course
22	Thursday	The Women's Health Update Course The Telephone Consultation Course
23	Friday	The GP Update Course
24	Saturday	The Cancer Update Course Lead. Manage. Thrive!

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- ☐ The Women's Health Update Course (location)..... (date).....
- ☐ The Telephone Consultation Course (location)..... (date).....
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