Hypertension in pregnancy - Management

Scenario: Identification and management of women at high risk of pre-eclampsia

CKS safe practical clinical answers - *fast*

Who is at high risk of developing pre-eclampsia?

- Women are at high risk of pre-eclampsia if they have:

- **One of the following high risk factors:**

- A history of hypertensive disease during a previous pregnancy.

- Chronic kidney disease.

- Autoimmune disease, such as systemic lupus erythematosus or antiphospholipid syndrome.

- Type 1 or type 2 diabetes.

- Chronic hypertension.

- Thrombophilia.

- **Two or more of the following moderate risk factors:**

- First pregnancy.

- Aged 40 years or older.

- Pregnancy interval of more than 10 years.

- Body mass index (BMI) of 35 kg/m^2 or greater at the first visit.

- Family history of pre-eclampsia.

- Multiple pregnancy.

Basis for recommendation

- Having reviewed the available evidence, the National Institute for Health and Clinical Excellence (NICE) defined high-risk and moderate-risk groups [National Collaborating Centre for Women's and Children's Health, 2008; National Collaborating Centre for Women's and Children's Health, 2010].

How do I manage a woman at high risk of developing pre-eclampsia?

For women at high risk of pre-eclampsia:

- **Give advice about a healthy lifestyle.**

o Advice should be the same as for healthy pregnant women and should include advice regarding rest, work, exercise, and weight. Beginning or continuing a moderate course of exercise during pregnancy is not associated with adverse outcomes.

- **Prescribe aspirin 75 mg daily from 12 weeks of gestation until the birth of the baby:**

o If the woman has either:

o One or more high risk factors for developing pre-eclampsia.

o Two or more moderate risk factors for developing pre-eclampsia.

o Seek specialist advice before prescribing aspirin:

o For girls younger than 16 years of age.

o If blood pressure is uncontrolled or if the woman has thrombophilia.

- **Dipstick the urine for protein** at initial presentation and each subsequent antenatal visit.

- **Warn about symptoms of pre-eclampsia** and advise the woman to seek immediate advice if she develops any of the following (including during the postpartum period):

o Severe headaches (increasing frequency unrelieved by regular analgesics).

o Vision problems, such as blurred vision, flashing lights, double vision, or floating spots.

o Persistent new epigastric pain or pain in the right upper quadrant.

o Vomiting.

o Breathlessness.

o Sudden swelling of the face, hands, or feet.

Basis for recommendation

Advice about a healthy lifestyle

- The National Institute for Health and Clinical Excellence (NICE) looked at the evidence on lifestyle in women at risk of hypertensive disorders during pregnancy [National Collaborating Centre for Women's and Children's Health, 2010].

- **Rest**

- NICE reviewed the available evidence and concluded that there is insufficient evidence for the use of rest in any form to prevent hypertensive disease in pregnancy.

- **Exercise**

- NICE concluded that there is evidence from a Cochrane systematic review that exercise has no significant effect on reducing the incidence of pre-eclampsia.

- **Work**

- NICE found six studies on working hours and physical activity, including lifting heavy weights, and concluded that generally poor-quality evidence showed no effect.

- **Weight**

- NICE identified no evidence on maintaining a healthy weight during pregnancy.

- NICE concluded that advice on rest, exercise, and work for women at risk of hypertensive disorders of pregnancy should be the same as the advice given to healthy pregnant women in their guideline *Antenatal care, routine care for the healthy pregnant woman* [National Collaborating Centre for Women's and Children's Health, 2008].

Advice about moderate exercise

- This recommendation is based on expert advice from NICE [National Collaborating Centre for Women's and Children's Health, 2008].

Use of aspirin for women at high risk of pre-eclampsia

- The recommendations to use aspirin is based on expert advice from NICE [National Collaborating Centre for Women's and Children's Health, 2010]. NICE reviewed evidence from a Cochrane systematic review and a large meta-analysis of individual patient data and concluded that:

- The use of low-dose aspirin was consistent with a small risk reduction for pre-eclampsia, and there is a clear benefit in their defined high-risk groups.

- Moderate risk has been poorly defined in studies. However, the presence of two moderate risk factors would confer a greater risk that any risk factor considered individually.

- Data on the safety of aspirin in the doses used for the prevention of pre-eclampsia are sufficient.

- The recommendation to start aspirin at 12 weeks' gestation is based on expert advice from NICE, as this is the earliest gestational age for which there is available evidence concerning the use of aspirin for the prevention of pre-eclampsia [National Collaborating Centre for Women's and Children's Health, 2010].

▪ Most of the CKS expert reviewers recommended that aspirin should be given to girls younger than 16 years of age on specialist advice only.

▪ Some of our expert reviewers warned against prescribing aspirin to women with uncontrolled blood pressure. CKS recommends that in such women, it is best to seek specialist advice about whether or not to prescribe aspirin.

Women with thrombophilia

▪ NICE has stated that evidence on the association between thrombophilia and hypertensive disorders remains unclear. Only women with certain types of thrombophilia are at an increased risk of pre-eclampsia. These thrombophilias include women with hyperhomocysteinaemia, prothrombin heterozygosity, anticardiolipin antibodies, and Factor V Leiden heterozygosity. CKS therefore recommends that specialist advice is sought before prescribing aspirin.

Testing for proteinuria

▪ Expert opinion in the NICE guideline *Antenatal care, routine care for the healthy pregnant woman* states that when blood pressure is measured at each antenatal check, a urine sample should be tested at the same time for proteinuria [National Collaborating Centre for Women's and Children's Health, 2008]. NICE based this recommendation on evidence from a retrospective study of 53 women that found that those with proteinuria greater 500 mg per day had a high risk of pre-eclampsia [Stettler and Cunningham, 1992].

▪ Proteinuria is an important sign of pre-eclampsia after a gestation of 20 weeks. However, throughout pregnancy proteinuria may also be caused by an underlying medical condition [National Collaborating Centre for Women's and Children's Health, 2008].

Symptoms of pre-eclampsia

▪ These recommendations are based on expert advice from NICE [National Collaborating Centre for Women's and Children's Health, 2010] and three narrative reviews [Sadovsky, 2002; Duley et al, 2006; Young et al, 2010].

▪ A key recommendation from the 1998 Confidential Enquiry into Maternal Deaths that is accepted good clinical practice is that all women should receive antenatal education so that they are aware of the symptoms associated with pre-eclampsia (such as headache or epigastric pain), its importance, and the need to obtain medical advice [DH, 1998].

Measures not recommended for the prevention of hypertensive disorders of pregnancy

▪ A review of the literature for all of the following was undertaken by NICE [National Collaborating Centre for Women's and Children's Health, 2010].

- **Nitric oxide**

  - NICE concluded that there is limited high-quality evidence from a Cochrane systematic review that there is no reduction in hypertensive disorders during pregnancy following the use of nitric oxide donors, such as glyceryl trinitrate.

- **Progesterone**

  - NICE concluded that there is limited high-quality evidence from a Cochrane systematic review that there is no reduction in hypertensive disorders during pregnancy following the use of progesterone.

- **Diuretics**

  - NICE concluded that there is limited high-quality evidence from a Cochrane systematic review that there is no reduction in hypertensive disorders during pregnancy following the use of diuretics.

- **Low-molecular-weight heparin**

  - NICE reviewed the evidence from an open-label randomized controlled trial involving 80 women with the angiotensin converting enzyme DD genotype who had a history of pre-eclampsia [Mello et al, 2005]. This genotype is associated with thrombophilia and fetal loss. Although this study showed a clinically significant reduction in pre-eclampsia and its sequelae, NICE concluded that the study was of poor quality, and therefore the evidence is limited. NICE therefore have not recommended the use of low molecular weight heparin because of the risks associated with its use.

- **Calcium**

  - NICE concluded that there is high quality evidence from a Cochrane systematic review that calcium supplementation reduces the risk of pre-eclampsia in women who have a low dietary intake of calcium (which does not generally apply to women in the UK). The benefits of calcium supplementation are greatest in women who are at high risk of pre-eclampsia. If calcium intake is known to be adequate then there is no statistically significant benefit. Therefore, NICE decided that routine calcium supplementation in the UK could not be justified.

- **Magnesium**

  - NICE identified no evidence on the use of magnesium.

- **Antioxidants**

  - NICE concluded that there is high-quality evidence from a Cochrane systematic review that there is no reduction in hypertensive disorders during pregnancy following the use of antioxidants. There is evidence from two randomized trials done since this review that there is no benefit from the use of antioxidants [Roberts et al, 2010; Xu et al, 2010]. One of the trials has suggested that there might be an increased risk of fetal loss and perinatal death associated with their use [Xu et al, 2010].

- **Folic acid**

- NICE found only poor-quality evidence from a large prospective cohort study involving 2951 women that investigated whether folic acid started early in the second trimester of pregnancy reduced the risk of pre-eclampsia. Although the results did suggest a possible benefit, NICE concluded that the results were likely to be confounded by other factors, including the use of other vitamins. There was no statistically significant evidence that folic acid alone reduced the risk of pre-eclampsia. Although folic acid is recommended in pregnancy for other reasons, it is not recommended for use to prevent hypertensive disorders of pregnancy.

- **Fish oils**

- NICE concluded that there is high-quality evidence from a Cochrane systematic review that there is no reduction in hypertensive disorders during pregnancy following the use of fish or algal oils.

- **Garlic**

- NICE concluded that there is limited good quality evidence from a Cochrane systematic review for the use of garlic to prevent pre-eclampsia, but increasing the intake of garlic is not recommended, as no significant effect was found.

- **Dietary salt restriction**

- NICE reviewed evidence from a randomized controlled trial involving 361 women and concluded that there is limited good-quality evidence that a low sodium diet does not prevent subsequent development of pre-eclampsia in women with weight gain and mild hypertension. However, although NICE does not recommend salt restriction to prevent pre-eclampsia, it stresses the importance of a healthy lifestyle and the importance of salt reduction in chronic hypertension.

Prescriptions

For information on contraindications, cautions, drug interactions, and adverse effects, see the electronic Medicines Compendium (eMC) (http://emc.medicines.org.uk), or the British National Formulary (BNF) (www.bnf.org).

Low-dose aspirin

Age from 16 years onwards

Aspirin dispersible tablets: 75mg once a day

Aspirin 75mg dispersible tablets
Take one tablet once a day.
Supply 28 tablets.

Age: from 16 years onwards
NHS cost: £0.83
Licensed use: no - off-label indication

Scenario: Proteinuria and no hypertension in pregnancy

CKS safe practical clinical answers - *fast*

How do I manage women with new proteinuria without hypertension at less than 20 weeks' gestation?

If the woman is 20 weeks' gestation or less and is found to have proteinuria but is not hypertensive:

- Consider possible urinary tract infection (UTI):

o If a woman has symptoms of a UTI, or urinary dipstick test is positive for nitrite, or is positive for both leukocyte esterase and blood, make a working diagnosis of UTI and manage appropriately. Urine should be sent for culture and sensitivity.

o For detailed information on the diagnosis and management of UTI in pregnancy, see the CKS topic on Urinary tract infection (lower) - women.

- If there is no evidence of a UTI and the woman has 1+ protein or more on repeat dipstick testing, consider underlying medical conditions and assess for chronic kidney disease. For more information, see the CKS topic on Chronic kidney disease - not diabetic.

Basis for recommendation

- **Considering possible urinary tract infection (UTI)**

o It is good clinical practice to consider possible UTI in a woman who is pregnant and has a positive dipstick for protein. However, it should be noted that although protein may occur in the urine of women with a UTI, the presence of protein does not independently predict a UTI [Little et al, 2009]. For detailed information on the diagnosis of UTI, see the CKS topic on Urinary tract infection (lower) - women.

- **Assessing for chronic kidney disease**

o National guidelines on early identification and management of chronic kidney disease recommend that all people with an incidental finding of proteinuria or haematuria (not due to UTI) should be tested for possible chronic kidney disease, and underlying medical conditions should be considered [NICE, 2008a]. For further information, see the CKS topic on Chronic kidney disease - not diabetic.

How do I manage women with new proteinuria without hypertension after 20 weeks' gestation?

If the woman is over 20 weeks' gestation and has new proteinuria but no hypertension:

- **If she has symptoms of pre-eclampsia,** arrange same-day hospital assessment.
- **If there are no symptoms of pre-eclampsia:**

o Consider possible urinary tract infection (UTI).

o If there is 1+ protein: if the woman has symptoms of a UTI, or the dipstick test is positive for nitrite or is positive for both leukocyte esterase and blood, make a working diagnosis of UTI and manage appropriately. Urine should be sent for culture and sensitivity. Ensure follow up within 1 week and reassess. For detailed information on the diagnosis and management of UTI, see the CKS topic on Urinary tract infection (lower) - women.

o If there is 2+ protein or more on dipstick testing: even if the woman has symptoms of a UTI or the dipstick test is positive for nitrite, or is positive for both leukocyte esterase and blood, seek same day specialist advice.

o If there is no evidence of a UTI:

o If there is 1+ protein on dipstick testing of urine, review 1 week later. If proteinuria is persistent, seek specialist advice.

o If there is 2+ protein or more on dipstick testing, seek same day specialist advice.

Symptoms of pre-eclampsia

- **Symptoms of pre-eclampsia**

o Severe headaches (increasing frequency unrelieved by regular analgesics).
o Vision problems, such as blurred vision, flashing lights, double vision, or floating spots.
o Persistent new epigastric pain or pain in the right upper quadrant.
o Vomiting.
o Breathlessness.
o Sudden swelling of the face, hands, or feet.

Basis for recommendation

- **Admitting to hospital if there is proteinuria and symptoms of pre-eclampsia, even if the woman is not hypertensive**

o The Pre-eclampsia Community Guideline (PRECOG) development group reviewed the available evidence and concluded that proteinuria may be the first clinical indication of pre-eclampsia [PRECOG, 2004b]. Therefore, if the woman has symptoms suggestive of pre-eclampsia and proteinuria, then she should be assumed to have pre-eclampsia until proven otherwise.

- **Considering possible urinary tract infection (UTI)**

o It is good clinical practice to consider possible UTI in a woman who is pregnant and has a positive dipstick test for protein. However, although protein may occur in the urine of women with a UTI, the presence of protein does not independently predict a UTI [Little et al, 2009]. For detailed information on the diagnosis of UTI, see the CKS topic on Urinary tract infection (lower) - women.

- **Reassessment of normotensive women with 1+ protein who are well within 1 week, and seeking specialist advice if there is persistent proteinuria**

o The recommendation to re-assess in 1 week is based on expert advice from PRECOG [PRECOG, 2004a].

o PRECOG does not give specific advice on what action to take if a woman has persistent 1+ protein and is otherwise well [PRECOG, 2004a]. However, there is evidence that significant proteinuria is predictive of developing pre-eclampsia and poor pregnancy outcomes, and national guidelines advise that the presence of proteinuria should alert the healthcare professional to the need for increased surveillance [National Collaborating Centre for Women's and Children's Health, 2008]. In the absence of guidance to inform management, CKS recommends seeking specialist advice if proteinuria persists, as specialist assessment and increased monitoring may be necessary.

▪ Seeking same day specialist advice if there is 2+ proteinuria

o PRECOG recommends that all women with 2+ protein or more on dipstick testing who are over 20 weeks' gestation should have early assessment in secondary care, as this may indicate impending pre-eclampsia or an underlying medical problem [PRECOG, 2004a]. Many of the CKS expert reviewers advised that all women with 2+ protein or more on dipstick testing should have hospital assessment within 48 hours regardless of whether or not a urinary tract infection may be the cause. Therefore CKS recommends that same-day specialist advice should be obtained.

▪ Quantification of proteinuria by a 24-hour urine collection or spot albumin: creatinine ratio

o CKS has not recommended that GPs initiate a 24-hour collection of urine or spot albumin:creatinine ratio for quantification of protein, as this will usually be initiated in secondary care. GPs should note that:

o The National Institute for Health and Clinical Excellence (NICE) recommends that a 24-hour urine collection or a spot urinary protein:creatinine ratio are the only reliable methods for quantification of proteinuria in women at risk of pre-eclampsia [National Collaborating Centre for Women's and Children's Health, 2010].

Hypertension in pregnancy - Management

Scenario: Chronic (pre-existing) hypertension, or new hypertension before 20 weeks' pregnancy

CKS safe practical clinical answers - *fast*

How do I assess a woman with chronic hypertension?

- **Take a history.**

o Length of time that the woman has had known hypertension and her level of control.

o Past and current medication.

o Problems in previous pregnancies, their management, and the outcome of these pregnancies.

• **Consider whether investigation is required for possible secondary causes of hypertension.** For more information, see the section on Secondary hypertension in the CKS topic on Hypertension - not diabetic.

• **Perform a dipstick urine for proteinuria at presentation and at each antenatal visit.** Use an automated dipstick if available.

• **Ask about symptoms of pre-eclampsia at each review after 20 weeks' gestation.**

o Severe headaches (increasing frequency unrelieved by regular analgesics).

o Vision problems, such as blurred vision, flashing lights, double vision, or floating spots.

o Persistent new epigastric pain or pain in the right upper quadrant.

o Vomiting.

o Breathlessness.

o Sudden swelling of the face, hands, or feet.

Basis for recommendation

Take a history and assess if investigation for secondary causes is required

• CKS has based these recommendations on accepted clinical practice.

Dipstick urine for proteinuria

• Proteinuria in women with chronic hypertension may be:

o Due to underlying renal disease.

o Due to the development of pre-eclampsia if it is new and occurs after 20 weeks' gestation.

• The National Institute for Health and Clinical Excellence (NICE) recommends the use of automated dipstick testing in secondary care. Evidence from a meta analysis of six trials and a prospective study showed that visual dipstick analysis of urine with a 1+ threshold is not accurate at detecting clinically significant proteinuria. Its use in clinical decision making is therefore limited. Accuracy is improved by using an automated dipstick device. Primary care clinicians should use automated dipsticks if they have access to them.

Assessing for symptoms of pre-eclampsia

• This recommendation is based on expert advice [National Collaborating Centre for Women's and Children's Health, 2010] and three narrative reviews [Sadovsky, 2002; Duley et al, 2006; Young et al, 2010]. Women with chronic hypertension are at increased risk of pre-eclampsia [National Collaborating Centre for Women's and Children's Health, 2010].

How should I manage a woman with chronic hypertension?

- **Advise the woman** that:

o She should restrict her dietary intake of salt (sodium). For more information, see the section on Lifestyle advice in the CKS topic on Hypertension - not diabetic.

o Bed rest is not recommended.

o She will require regular monitoring of her blood pressure throughout her pregnancy, and is likely to require more frequent antenatal checkups than usual.

o The aim of treatment is to adequately control her blood pressure throughout her pregnancy.

▪ For uncomplicated hypertension, keep the blood pressure less than 150/100 mmHg (but diastolic pressure no less than 80 mmHg).

▪ If there is evidence of target-organ damage (for example kidney disease), keep the blood pressure less than 140/90 mmHg.

- **Warn about symptoms of pre-eclampsia** and that she should seek immediate advice if she develops any symptoms after 20 weeks' gestation (including during the postpartum period).
- **Prescribe aspirin 75 mg daily from 12 weeks' gestation.** Explain that this is believed to help prevent the development of pre-eclampsia.

o Seek specialist advice before prescribing aspirin if blood pressure is uncontrolled.

- **If she is taking an angiotensin-converting enzyme (ACE) inhibitor or angiotensin-II receptor antagonist (AIIRA), stop this immediately** and prescribe an alternative treatment if necessary.

o Explain that there is an increased risk of congenital abnormalities if these drugs are taken during pregnancy.

- **Refer the woman to a specialist in hypertensive disorders if the woman has secondary hypertension,** or a renal physician, an endocrinologist, or a specialist in connective tissue disease as appropriate.
- **Otherwise, refer the woman to an obstetric physician.**

o While the woman is waiting to see a specialist, continue her usual antihypertensive treatment (unless she is taking an ACE inhibitor or AIIRA).

o If the woman is not currently taking antihypertensive treatment:

▪ If her blood pressure is high, discuss management with a specialist.

▪ If her blood pressure is normal (which may be because of the physiological drop in blood pressure that occurs in early pregnancy), monitor her blood pressure regularly.

- **If the woman develops proteinuria after 20 weeks' gestation then her care becomes that of a woman with pre-eclampsia.**

Basis for recommendation

Low salt diet

- On the basis of expert opinion, the National Institute for Health and Clinical Excellence (NICE) recommends that pregnant women with chronic hypertension should follow the same general advice in relation to dietary salt intake as women with hypertension who are not pregnant [National Collaborating Centre for Women's and Children's Health, 2010]. This is because the pathogenesis is the same and reducing the intake of salt can lower blood pressure.

Bed rest

- NICE reviewed the literature on the benefits of bed rest during pregnancy in women with chronic hypertension [National Collaborating Centre for Women's and Children's Health, 2010]. NICE reviewed a randomized controlled trial (RCT) done in 218 women in Zimbabwe. This study examined the effectiveness of hospital bed rest compared with normal activities at home on the risk of developing severe hypertension in women with chronic hypertension or gestational hypertension [National Collaborating Centre for Women's and Children's Health, 2010]. Thirty-three women in the chronic hypertension group were randomized to normal activities at home (18 women) or hospital bed rest (15 women). There was no statistically significant difference between the two groups with regard to the development of severe hypertension, proteinuria, or severe proteinuria. NICE concluded that there is no evidence that bed rest is beneficial. There is also concern that prolonged bed rest may increase the risk of venous thromboembolism.

Frequency of monitoring of blood pressure

- There is no evidence on which to base recommendations regarding frequency of antenatal contacts for women with chronic hypertension. The view of NICE, however, is that the routine schedule for antenatal care monitoring of blood pressure is inadequate for pregnant women with chronic hypertension [National Collaborating Centre for Women's and Children's Health, 2010].

Target blood pressure

- NICE reviewed the literature and found that [National Collaborating Centre for Women's and Children's Health, 2010]:

o There is evidence from two good-quality studies that there is less risk of severe hypertension with 'tight' blood pressure control but no other differences in maternal or perinatal outcomes, including fetal growth.

o A meta-regression of RCTs found that the more blood pressure is reduced in pregnant women with hypertension, the more the birthweight of their infants is reduced. This meta-regression included women taking methyldopa, acebutolol, atenolol, labetalol, metoprolol, oxprenolol, pindolol, propranolol, bendroflumethiazide, chlorothiazide, hydrochlorothiazide, ketanserin, hydralazine, isradipine, nicardipine, nifedipine, verapamil, and clonidine.

o On the basis of these studies, NICE recommends that:

▪ Treatment should aim to lower blood pressure from the moderate or severe range, but excessive reduction of blood pressure should be avoided as this may affect fetal growth.

▪ Women with target-organ damage would need a lower blood pressure target than women without target-organ damage.

Advising about symptoms of pre-eclampsia

- This recommendation is based on expert advice from NICE and three narrative reviews [Sadovsky, 2002; Duley et al, 2006; Young et al, 2010]. Women with chronic hypertension are at increased risk of pre-eclampsia [National Collaborating Centre for Women's and Children's Health, 2010].
- A key recommendation from the 1998 Confidential Enquiry into Maternal Deaths that is accepted good clinical practice is that all women should receive antenatal education so that they are aware of the symptoms associated with pre-eclampsia (such as headache or epigastric pain), its importance, and the need to obtain medical advice [DH, 1998].

Aspirin to prevent pre-eclampsia

- NICE concluded that there is evidence from a meta-analysis that aspirin is effective in reducing the risk of pre-eclampsia, including in women who have chronic hypertension [National Collaborating Centre for Women's and Children's Health, 2010].
- Some CKS expert reviewers warned against prescribing aspirin to women with uncontrolled blood pressure. CKS recommends that in such women, it is best to seek specialist advice about whether or not to prescribe aspirin.

Stopping angiotensin-converting enzyme (ACE) inhibitors or angiotensin-II receptor antagonists (AIIRA)

- There is limited evidence regarding the use of ACE inhibitors or AIIRAs during pregnancy. Studies suggest that ACE inhibitors are associated with congenital malformations, intrauterine growth retardation, and premature delivery, and that AIIRAs are associated with congenital malformations.
- NICE states that there is sufficient concern, despite the relatively poor quality of the studies, to recommend avoiding ACE inhibitors and AIIRAs during pregnancy [National Collaborating Centre for Women's and Children's Health, 2010].

Chlorothiazide is also possibly teratogenic but is not prescribable in the UK

- NICE noted a possible association with congenital abnormalities, neonatal thrombocytopenia, neonatal hypoglycaemia and hypovolaemia, and possible maternal electrolyte imbalance [National Collaborating Centre for Women's and Children's Health, 2010].

Other antihypertensive drugs during pregnancy

- NICE reviewed studies of other antihypertensive drugs and found:

o No obvious association with congenital abnormalities for the following drugs: methyldopa, labetalol, atenolol, metoprolol, oxprenolol, pindolol, prazosin, nifedipine, verapamil, bendroflumethiazide, furosemide, and hydralazine. No or very little information about other antihypertensive drugs is available.

o Antihypertensives reduce the risk of severe hypertension but not of proteinuria.

o From the limited available evidence, it is not possible to determine the best antihypertensive treatment for pregnant women with chronic hypertension.

Referral to a specialist

- NICE states that the evidence from trials on the treatment of blood pressure does not make it possible to determine the best antihypertensive treatment for a pregnant woman [National Collaborating Centre for Women's and Children's Health, 2010]. CKS recommends seeking specialist advice before starting treatment. If the woman's blood pressure is normal, then it should be checked regularly.

Prescriptions

For information on contraindications, cautions, drug interactions, and adverse effects, see the electronic Medicines Compendium (eMC) (http://emc.medicines.org.uk), or the British National Formulary (BNF) (www.bnf.org).

Low-dose aspirin

Age from 16 years onwards

Aspirin dispersible tablets: 75mg once a day
Aspirin 75mg dispersible tablets Take one tablet once a day. Supply 28 tablets. **Age**: from 16 years onwards **NHS cost**: £0.83 **Licensed use**: no - off-label indication

safe practical clinical answers - *fast*

How should I assess a woman with new hypertension after 20 weeks' gestation?

- **Check urine for protein (subsequent frequency of monitoring will be determined by secondary care).** If available, use automated dipstick testing.
- **Ask about symptoms of pre-eclampsia at presentation and each subsequent antenatal check.**

o Severe headaches (increasing frequency unrelieved by regular analgesics).

o Vision problems, such as blurred vision, flashing lights, double vision, or floating spots.

o Persistent new epigastric pain or pain in the right upper quadrant.

o Vomiting.

o Breathlessness.

o Sudden swelling of the face, hands, or feet.

Basis for recommendation

Testing for proteinuria by dipstick estimation

- This is based on expert advice in the National Institute for Health and Clinical Excellence (NICE) guideline *Antenatal care: routine care for the healthy pregnant woman* [NICE, 2008b] which recommends testing for protein at each antenatal visit. This is particularly important in women with new hypertension who are at an increased risk of pre-eclampsia [National Collaborating Centre for Women's and Children's Health, 2010]. Rarely, pre-eclampsia may present atypically without proteinuria [Sibai et al, 1993].
- There is good evidence from a systematic review and a subsequent prospective study that automated dipstick testing is more accurate than visually read dipstick testing [National Collaborating Centre for Women's and Children's Health, 2010].

Assessing for symptoms of pre-eclampsia

- This recommendation is based on expert advice from NICE [National Collaborating Centre for Women's and Children's Health, 2010] and three narrative reviews [Sadovsky, 2002; Duley et al, 2006; Young et al, 2010]. Women with new hypertension are at increased risk of pre-eclampsia [National Collaborating Centre for Women's and Children's Health, 2010].

How should I manage a woman with new hypertension after 20 weeks' gestation?

- **If urine is negative for protein:**

o **Admit immediately if the woman has severe hypertension (blood pressure 160/110 mmHg or higher) or if she has symptoms of pre-eclampsia.**

o Otherwise, discuss with the local maternity unit to arrange urgent assessment.

- **If urine is positive for protein (1+ protein or more on automated dipstick testing, or a trace or more on visual dipstick testing):**

o Discuss immediately with the local maternity unit, to arrange urgent assessment or admission.

Basis for recommendation

Management of gestational hypertension (new hypertension presenting at 20 weeks' gestation or more without proteinuria)

- These recommendations are based on expert opinion from the National Institute for Health and Clinical Excellence (NICE) [National Collaborating Centre for Women's and Children's Health, 2010], which recommends:

o That all women with gestational hypertension should be offered an integrated package of care that may include hospital admission, regular measurement of blood pressure, testing for proteinuria, and relevant blood tests.

o Admission to hospital if blood pressure is 160/110 mmHg or greater.

- Expert assessment is also recommended as pre-eclampsia may present atypically; 20% of women with atypical eclampsia have minimal or absent proteinuria [Young et al, 2010].

Management of pre-eclampsia

- These recommendations are based on expert opinion from NICE [National Collaborating Centre for Women's and Children's Health, 2010], which recommends:

o That all women with pre-eclampsia should be offered immediate admission and an integrated package of care, regular measurements of blood pressure, testing for proteinuria, and relevant blood tests.

Dipstick analysis of proteinuria and decision to refer

- NICE reviewed the evidence and recommended that an automated dipstick is used for diagnosing pre-eclampsia in secondary care and that a 1+ protein result or more on an automated dipstick should be quantified by using a 24-hour urine collection or a spot urinary protein:creatinine sample [National Collaborating Centre for Women's and Children's Health, 2010]. There are no recommendations for primary care clinicians who may only have access to visual dipstick testing. NICE based its decision on a review of the available evidence and concluded that:

o Visual dipstick testing is a poor test for the diagnosis of pre-eclampsia.

o A negative dipstick result does not exclude significant proteinuria.

- NICE based its recommendation mainly on evidence from a meta analysis of six trials and a subsequent prospective study that showed visual dipstick analysis of urine with a 1+ threshold is unreliable for detecting clinically significant proteinuria [Waugh et al, 2004]. Its use in clinical decision making is therefore of limited usefulness. Although accuracy may be improved by using a higher cut-off point (such as 2+), there are only limited data of poor methodological quality for this threshold. Accuracy was improved by using an automated dipstick device.
- Most primary care physicians will only have access to visual dipstick analysis of urine and will need to make a clinical decision taking into account the result. In addition, accurate quantification of proteinuria by collection of a 24-hour urine sample or by urinary protein:creatinine ratio would take an unacceptable length of time. Therefore, CKS recommends that primary care clinicians seek immediate specialist advice for pregnant women who are more than 20 weeks' gestation who present with new hypertension and a trace or more of protein in their urine on visual dipstick urinalysis. If access to the more accurate automated dipstick testing is available, then a threshold of 1+ protein is recommended, in keeping with NICE guidelines.

How will gestational hypertension be managed in secondary care?

The following is a summary of secondary care management recommended by the National Institute for Health and Clinical Excellence (NICE).

- **Women with severe hypertension will be admitted.**

o Blood pressure will be measured four times a day. The woman will be kept in hospital until her blood pressure is 159/109 mmHg or lower.

o Blood will be taken to test for kidney function, electrolytes, full blood count, transaminases and bilirubin on presentation.

o Urine will be tested for protein using automated dipsticks or urinary protein:creatinine ratio.

o Antihypertensive medication will be prescribed:

▪ Labetalol is the first choice.

▪ Methyldopa and nifedipine are alternatives after consideration of the adverse effect profile for the mother and the fetus.

o **Follow up**

▪ Once blood pressure has fallen to 159/109 mmHg or lower, women will be followed up in outpatients/an early pregnancy assessment centre with twice-weekly blood pressure monitoring; twice-weekly automated dipstick testing for protein: and once-weekly blood tests for urea and electrolytes, full blood count, transaminases, and bilirubin.

▪ Birth before 37 weeks will only be offered to women with refractory severe hypertension after a course of antenatal steroids (if required) has been completed.

- **Women with moderate hypertension will be managed and followed up in an outpatient setting or at a pregnancy assessment centre.**

o Blood will be taken for urea and electrolytes, full blood count, transaminases, and bilirubin, if not already done by the GP on presentation.

o Antihypertensive medication will be prescribed:

▪ Labetalol is the first choice.

▪ Methyldopa and nifedipine are alternatives after consideration of the adverse effect profile for the mother and the fetus.

o **Follow up**

▪ Will be in outpatients/a pregnancy assessment unit with twice-weekly blood pressure monitoring, and twice-weekly testing of urine for protein using automated dipsticks or urinary protein:creatinine ratio.

▪ Further blood tests will not be performed unless the woman develops proteinuria.

- **Women with mild hypertension will be managed and followed up in an outpatient setting or at a pregnancy assessment centre.**

o Blood tests other than those done for routine antenatal care will not be needed.

o Monitoring will be as follows:

▪ If presenting before 32 weeks, or if at high risk of pre-eclampsia, the woman will have blood pressure monitoring and testing of urine for protein using automated dipsticks or urinary protein:creatinine ratio twice a week.

▪ If presenting after 32 weeks and not at high risk of pre-eclampsia, the woman will have blood pressure and urine checked for protein using automated dipsticks or urinary protein:creatinine ratio not more often than once per week.

- **Bed rest** in hospital is not recommended as a treatment for gestational hypertension.
- **Aspirin 75 mg daily will be prescribed until the birth of the baby only if the woman** has either:

o One or more high risk factors for pre-eclampsia.

o Two or more for moderate risk factors for pre-eclampsia.

Basis for recommendation

Referral to secondary care

- Expert opinion from the National Institute for Health and Clinical Excellence (NICE) is that all pregnant women with any degree of new-onset hypertension require a full assessment in secondary care by a healthcare professional who is trained in the management of

hypertensive disorders [National Collaborating Centre for Women's and Children's Health, 2010].

Monitoring and review

- NICE found [National Collaborating Centre for Women's and Children's Health, 2010]:

o No studies that provided evidence on the frequency of blood pressure measurements. It recommends that the frequency of monitoring will be determined by the degree of hypertension and may be influenced by medical history and the presence of risk factors.

o The evidence regarding the gestational age at diagnosis and the subsequent development of severe pre-eclampsia or fetal growth restriction difficult to interpret. NICE agreed that the development of gestational hypertension before 35 weeks deserves special consideration and monitoring.

o Only poor-quality evidence about the role of haematological and biochemical blood tests. NICE suggests the limited use of the recommended blood tests to help to rule out disease progression.

Drug treatment of gestational hypertension

- NICE studied the Cochrane systematic review [Abalos et al, 2007] on the use of antihypertensive therapy for mild to moderate hypertension in pregnancy [National Collaborating Centre for Women's and Children's Health, 2010]. Realizing that this review did not specifically address the treatment of women with gestational hypertension, NICE looked at all of the individual studies. In many of the studies either the population investigated was not clearly defined or it included a mixed population. NICE concluded that:

o There is limited good-quality evidence about treatment for gestational hypertension. This evidence does not support blood pressure-lowering treatment for mild or moderate gestational hypertension with the aim of improving pregnancy outcomes, but it does support starting treatment once severe hypertension has developed.

o There is not enough evidence to know whether antihypertensive treatment prevents rare serious events, such as a stroke or placental abruption.

o There is insufficient evidence about the target blood pressure; it must be low enough to prevent secondary damage, such as stroke, without being excessively low and thereby potentially affecting fetal growth.

o There is good evidence to show that beta-blockers and labetalol reduce the risk of severe hypertension. One small, poor-quality, quasi-randomized trial found a statistically significant reduction in the risk of pre-eclampsia/proteinuria with labetalol compared with methyldopa. However, proteinuria was not defined.

o There was little evidence regarding calcium-channel blockers.

- NICE reached a consensus that the association between beta-blockers and reduced fetal growth was likely to be the result of excessive lowering of blood pressure and related to the dose.
- Taking the above into account, NICE recommends that:

o Labetalol should be used first line as it seems to be as effective and safe as other antihypertensive drugs and it is licensed for use in pregnancy.

o Alternative treatment including methyldopa and nifedipine should be offered after considering adverse effect profiles for the woman, fetus, and newborn baby. NICE recommends using these treatments in women of Afro–Caribbean origin as it is not known if this group of women responds well to beta-blockers in pregnancy (a poor response to beta-blockers has been recognized in people of Afro–Caribbean origin who are not pregnant).

Timing of the birth

- NICE reviewed the evidence from a large, open-label, randomized controlled trial (RCT) done in the Netherlands [National Collaborating Centre for Women's and Children's Health, 2010]. Although NICE concluded that because of different clinical practice the results are not directly applicable to the UK, their expert view was that if gestational hypertension becomes severe (160/110 mmHg or greater) even though the women is being treated with antihypertensive drugs, then the woman should be offered immediate birth after a course of antenatal steroids.

Bed rest

- NICE recommends that bed rest in hospital should not be offered as a treatment for gestational hypertension. NICE reviewed the evidence in relation to bed rest in an RCT carried out on 218 women in Zimbabwe. This study examined the effectiveness of hospital bed rest compared with normal activities at home on the risk of severe hypertension in women with chronic hypertension or gestational hypertension [National Collaborating Centre for Women's and Children's Health, 2010].

o There were 185 women in the gestational hypertension group who were randomized to normal activities at home (90 women) or hospital bed rest (95 women).

o Although the study found that hospital bed rest was more effective than continuing normal activities at home (OR 0.52, 95% CI 0.27 to 0.99), NICE pointed out that that the study was small and also conducted in a healthcare setting which was not applicable to the UK. NICE were also concerned that prolonged bed rest may increase the risk of venous thromboembolism.

Use of aspirin in women with gestational hypertension

- NICE reviewed the evidence from [National Collaborating Centre for Women's and Children's Health, 2010]:

o A Cochrane systematic review that reported a 40% reduction in the relative risk of progressing to pre-eclampsia in women with gestational hypertension taking aspirin compared with placebo or no treatment.

o A small RCT that found no statistically significant difference for progression to moderate or severe pre-eclampsia between 23 women who were randomized to take 100 mg of aspirin a day and 24 women who received a placebo.

- Considering the above, NICE did not consider the evidence sufficient to support the use of aspirin in women with gestational hypertension unless they have additional risk factors for pre-eclampsia.

How will pre-eclampsia be managed in secondary care?

The following is a summary of secondary care management recommended by the National Institute for Health and Clinical Excellence (NICE).

- **Women with pre-eclampsia will be admitted.**

o Blood pressure will be measured at least four times a day.

o The amount of protein in the urine will be quantified but once a diagnosis of significant proteinuria has been made the quantification will not be repeated.

o **Women with severe or moderate pre-eclampsia** will be prescribed labetalol as first-choice treatment to keep diastolic blood pressure less than 80–100 mmHg and systolic blood pressure less than 150 mmHg. Methyldopa and nifedipine are alternatives after consideration of the adverse effect profile for the mother and the fetus.

o **Blood tests**

▪ Blood tests for urea and electrolytes, full blood count, transaminases, and bilirubin will be done three times a week for women with moderate or severe pre-eclampsia, and twice a week for women with mild pre-eclampsia.

o **Timing of birth**

▪ Birth will be offered to women presenting with pre-eclampsia before 34 weeks, after discussion with neonatal and anaesthetic teams and a course of antenatal steroids has been given, if severe hypertension develops which is refractory to treatment, or if maternal or fetal indications for urgent intervention develop.

▪ Birth will be offered to women who develop severe pre-eclampsia after 34 weeks when their blood pressure has been controlled and a course of antenatal steroids has been completed (if appropriate).
▪ Birth will be offered to women with mild or moderate pre-eclampsia at 34+0 to 36+6 weeks depending on their maternal and fetal condition, risk factors, and availability of neonatal intensive care.
▪ Birth within 24–48 hours will be offered to women with mild or moderate pre-eclampsia after 37+0 weeks.

Basis for recommendation

Management in secondary care

• The expert opinion of the National Institute for Health and Clinical Excellence (NICE) is that assessment of women with pre-eclampsia should always be done by a healthcare professional trained in the management of hypertensive disorders of pregnancy [National Collaborating Centre for Women's and Children's Health, 2010].
• NICE recommends that all women with pre-eclampsia with a blood pressure of 140/90 mmHg or greater be admitted.

Monitoring and review

• NICE reviewed the available evidence and concluded that [National Collaborating Centre for Women's and Children's Health, 2010]:
o There are no data to inform the frequency of blood pressure monitoring, and this should depend on the severity of hypertension and the presence of risk factors. There is no evidence to support a change from the routine practice of measuring blood pressure at least four times a day in women with mild or moderate new hypertension and proteinuria while an inpatient. Blood pressure should be recorded more frequently in women with severe pre-eclampsia to detect rises in blood pressure and to monitor response to therapy. The risk of stroke is increased if hypertension is severe.
o Once the diagnosis of significant proteinuria has been made, there is little benefit from repeating the analysis. There is only a weak association between more than 5 g of protein in the urine per 24 hours and stillbirth, admission to neonatal intensive care unit, and small-for-gestational-age infants. The degree of protein in the urine does not seem to be related to outcome for the mother. Therefore, NICE considers that the evidence does not support repeated measurement of urinary protein once significant proteinuria is established.
o There is sufficient evidence that in women with pre-eclampsia, measuring platelet count, serum creatinine, and transaminases is useful in monitoring progression to more severe

disease. Although rising serum uric acid is associated with severe pre-eclampsia this test has not been shown to be of additional value. Available evidence shows that a coagulation screen is not helpful if the platelet count is above 100 x 10^9/L.

Drug treatment of pre-eclampsia

- NICE reviewed the available evidence and concluded that [National Collaborating Centre for Women's and Children's Health, 2010]:

o There is limited good-quality evidence about treatment of pre-eclampsia. There is no evidence that lowering blood pressure in women with mild or moderate pre-eclampsia improves pregnancy outcomes compared with starting treatment once the woman has developed severe hypertension. However, there is insufficient evidence to know whether antihypertensive treatment prevents rarer outcomes such as a stroke or placental abruption.

o There is some evidence about appropriate target blood pressure. There seems to be an increased risk of severe hypertension with less tight control (diastolic values above 90 mmHg or 100 mmHg).

o There is some evidence from a randomized controlled trial that labetalol reduces the risk of progression to severe hypertension.

o There is little evidence on the use of calcium-channel blockers.

o NICE considered that the association of beta-blockers with reduced fetal growth was a result of excessive lowering of blood pressure.

- Expert opinion from NICE is that:

o Labetalol seems to be as effective and safe as other drugs used for hypertension for managing pre-eclampsia and it is licensed for use in pregnancy.

o Labetalol should be used as first-line treatment.

o Alternative treatment includes methyldopa and nifedipine, and these should be offered after considering adverse effect profiles for the woman, fetus, and newborn baby. NICE recommends using these treatments in women of Afro–Caribbean origin, as it is not known whether they respond well to beta-blockers in pregnancy (a poor response to beta-blockers has been recognized in people of Afro–Caribbean origin who are not pregnant).

Timing of the birth

- These recommendations are based on expert advice from NICE after their review of the available evidence [National Collaborating Centre for Women's and Children's Health, 2010].

Scenario: Postpartum follow-up for hypertensive disorders in pregnancy

CKS safe practical clinical answers - fast

How should I follow up a woman with chronic hypertension postpartum?

- **Measure blood pressure:**

o Daily for the first 2 days after birth.

o At least once between day 3 and day 5 after birth.

o As clinically indicated if the woman's antihypertensive treatment is changed after birth.

- **Aim to keep blood pressure lower than 140/90 mmHg.**
- **For the first 2 weeks after the birth:**

o Continue the antihypertensive treatment used during pregnancy, unless the woman is taking methyldopa.

o If she is taking methyldopa, this should be stopped 2 days after the birth, as it may increase the risk of depression. Antihypertensive treatment that the woman took before planning a pregnancy should be restarted unless there are contraindications to a particular drug because the woman is breastfeeding or is planning further pregnancies.

- **Review antihypertensive treatment.**

o Review long-term antihypertensive treatment 2 weeks after the birth.

▪ Consider restarting the woman's pre-pregnancy hypertensive treatment unless there are contraindications to a particular drug because she is breastfeeding or planning further pregnancies.

▪ Target blood pressures will be those used in the long-term treatment of hypertension. For more information, see the CKS topic on Hypertension - not diabetic, or for women with diabetes, see the CKS topic on Diabetes type 2.

o Ensure that future antihypertensive treatment and monitoring is discussed in primary care 6–8 weeks after the birth at her postnatal review.

Basis for recommendation

Monitoring and control of blood pressure after the birth

- These recommendations are based on the expert opinion of the National Institute for Health and Clinical Excellence (NICE) [National Collaborating Centre for Women's and Children's Health, 2010].

o NICE identified no evidence about the frequency of postnatal observations or investigations.

o Its recommendations are, therefore, based on the knowledge that blood pressure peaks between 3–5 days after birth, and that it is sensible to monitor blood pressure if changes are made to treatment.

Choice of antihypertensive drug

- NICE identified no evidence about the choice of antihypertensive treatment postpartum. As there is no evidence for any particular antihypertensive, NICE considered that antenatal antihypertensive treatment should continue in the post-natal period unless methyldopa has been used (because of the risk of depression with methyldopa) [National Collaborating Centre for Women's and Children's Health, 2010].

Stopping methyldopa

- NICE is aware of a Medicines and Healthcare products Regulatory Agency (MHRA) report that considers methyldopa to be the drug of choice during pregnancy and breastfeeding [MHRA, 2009]. The MHRA states that methyldopa may not be suitable for some women. However, NICE considers that this drug should not be used during the post-natal period, as women are already at risk of depression, and if possible, it should be stopped and the antihypertensive treatment that the woman was taking before her pregnancy be restarted.

Review of antihypertensive treatment

- NICE recommends that long-term antihypertensive treatment is reviewed 2 weeks after the birth [National Collaborating Centre for Women's and Children's Health, 2010]. CKS recommends that former antihypertensive treatment be restarted, unless there are contraindications such as the woman is breastfeeding or planning another pregnancy.
- It is the opinion of NICE that women with chronic hypertension should be offered a formal medical review of their hypertension at their routine post-natal review [National Collaborating Centre for Women's and Children's Health, 2010].

How should I follow up a woman with gestational hypertension postpartum?

The following is a summary of secondary care management recommended by the National Institute for Health and Clinical Excellence (NICE).

- Most women will be followed up by the maternity unit until their blood pressure has returned to normal or until the woman has been referred to a specialist for a medical review should her blood pressure remain elevated. The woman should be given a care plan by the hospital detailing:
  - Who will provide follow-up care, including medical review if needed.
  - Frequency of blood pressure monitoring.
  - Thresholds for reducing or stopping treatment.
  - Indications for referral to primary care for blood pressure review.

o Self-monitoring for symptoms of pre-eclampsia.

- The woman should have her blood pressure measured:

o Daily for the first 2 days after birth.

o At least once between day 3 and day 5 after birth.

o As clinically indicated if antihypertensive treatment is changed after birth.

- **If the woman has not taken any antihypertensive treatment during pregnancy:**

o Aim to keep her blood pressure lower than 140/90 mmHg.

o Antihypertensive treatment will be started if blood pressure rises above 149/99 mmHg.

- **If antihypertensive treatment has been used during the antenatal period:**

o The same treatment will be continued, unless the woman has been taking methyldopa which should be stopped 2 days postpartum because of the risk of depression.

o If blood pressure falls below 140/90 mmHg, reducing antihypertensive treatment will be considered.

o Antihypertensive treatment will be reduced or stopped if the woman's blood pressure falls below 130/80 mmHg.

- **If the woman has gestational hypertension she should be offered a medical review either in the community or at the hospital:**

o If she remains on antihypertensive treatment 2 weeks after transfer to community care.

o At her post-natal review 6–8 weeks after the birth.

▪ Women who still need antihypertensive medication at the time of this review should be offered a specialist assessment of their hypertension.

Basis for recommendation

Monitoring and review by a specialist

- The National Institute for Health and Clinical Excellence (NICE) is aware that a few women with presumed gestational hypertension will have undiagnosed chronic hypertension [National Collaborating Centre for Women's and Children's Health, 2010]. NICE has therefore recommended an individualized care plan before transfer to community care.

Monitoring and control of blood pressure postpartum

- These recommendations are expert opinion from NICE [National Collaborating Centre for Women's and Children's Health, 2010].

o NICE identified no evidence about the frequency of postnatal observations or investigations.

o Its recommendations are therefore based on the knowledge that blood pressure peaks between 3–5 days after birth and that it is sensible to monitor blood pressure if changes are made to treatment.

Choice of antihypertensive drug

- NICE identified only one small randomized controlled trial that compared timolol with methyldopa, and therefore concluded that there is no evidence for any particular antihypertensive. NICE recommends that antenatal antihypertensive treatment should continue in the postnatal period unless methyldopa has been used.

Stopping methyldopa

- NICE is aware of a Medicines and Healthcare products Regulatory Agency (MHRA) report that considers methyldopa to be the drug of choice during pregnancy and breastfeeding [MHRA, 2009]. The MHRA states that methyldopa may not be suitable for some women. However NICE considers that this drug should not be used during the post-natal period, as women are already at risk of depression, and if possible, it should be stopped.

Advice on review and referral

- These recommendations are expert opinion from NICE [National Collaborating Centre for Women's and Children's Health, 2010]. NICE also considers that all women with gestational hypertension should have a review of their blood pressure at the post-natal review 6–8 weeks after the birth. Who carries out this review will depend on local circumstances and expertise, and NICE were not prescriptive about this. However NICE recommend that if the woman still requires antihypertensive treatment 6–8 weeks after the birth, then she should be offered a specialist assessment.

How should I follow up a woman with pre-eclampsia postpartum?

The following is a summary of secondary care management recommended by the National Institute for Health and Clinical Excellence (NICE).

- The woman should not be discharged home until she has no symptoms of pre-eclampsia, her blood pressure is 149/99 mmHg or lower, and her blood tests are improving.
- **All women should be given a care plan** that includes information about:
  - Who will provide follow-up care, including medical review if needed.
  - Frequency of blood pressure monitoring.
  - Thresholds for reducing or stopping treatment.
  - Indications for referral to primary care for blood pressure review.
  - Self-monitoring for symptoms of pre-eclampsia.
- **Women with pre-eclampsia who did not take antihypertensive treatment and have given birth and who have been discharged home** will have:

- Their blood pressure measured:
  - At least once between day 3 and day 5 after birth.
  - On alternate days until their blood pressure normalizes, if their blood pressure was abnormal between day 3 and day 5.
- If blood tests are stable or improving but not in the normal range they will be repeated as clinically indicated.
- The aim is to keep blood pressure lower than 140/90 mmHg.
- Antihypertensive treatment will be started if blood pressure is 150/100 mmHg or higher.

- Symptoms of pre-eclampsia, such as severe headache and epigastric pain, will be asked about each time blood pressure is measured.

- **Women with pre-eclampsia who took antihypertensive treatment and have given birth** will have:
  - Their blood pressure measured every 1–2 days for up to 2 weeks after transfer to primary care until the woman is off treatment and has no hypertension.
    - If blood tests are stable or improving but not in the normal range, they will be repeated as clinically indicated.
    - The antihypertensive treatment used during the pregnancy will be continued, unless the woman has been taking methyldopa, which should be stopped 2 days postpartum because of the risk of depression. Antihypertensive treatment that the woman took before planning a pregnancy will be restarted unless there are contraindications to a particular drug because the woman is breastfeeding or is planning further pregnancies.
    - A reduction in antihypertensive treatment will be considered if their blood pressure falls below 140/90 mmHg.
    - Antihypertensive treatment will be reduced if their blood pressure falls below 130/80 mmHg.
  - Symptoms of pre-eclampsia, such as severe headache and epigastric pain, will be asked about each time blood pressure is measured.

- **Women with pre-eclampsia will be offered a medical review either in the community or at the hospital:**
  - If they remain on antihypertensive treatment 2 weeks after transfer to community care.
  - At their post-natal review 6–8 weeks after the birth.
    - Women who still need antihypertensive medication at the time of this review should be offered a specialist assessment of their hypertension.
    - Perform dipstick testing of the urine. Women with 1+ proteinuria or more but normal blood pressure should be reviewed 3 months postpartum to assess kidney function and to consider referral to a renal specialist.

Basis for recommendation

Monitoring and review by a specialist

- The National Institute for Health and Clinical Excellence (NICE) recommends that an individualized care plan should be established before transfer to community care [National Collaborating Centre for Women's and Children's Health, 2010].

Monitoring and investigations postpartum

- These recommendations are expert opinion from NICE [National Collaborating Centre for Women's and Children's Health, 2010].
  - NICE identified no evidence about investigations and treatment and, therefore, recommends that the investigations and observations relevant to the antenatal period also applied to the post-natal period, taking into account that blood pressure peaks between 3–5 days after birth.
  - Women may develop pre-eclampsia after birth and NICE recommends that symptoms of pre-eclampsia be enquired about at each assessment.

Choice of antihypertensive drug

- NICE found a lack of good-quality evidence about choice of drug and whether antihypertensive treatment should be given routinely to women with pre-eclampsia. It therefore recommends that antihypertensive treatment used during the pregnancy should be continued, unless this was methyldopa.

Stopping methyldopa

- NICE is aware of a Medicines and Healthcare products Regulatory Agency (MHRA) report that considers methyldopa to be the drug of choice during pregnancy and breastfeeding [MHRA, 2009]. The MHRA states that methyldopa may not be suitable for some women. However NICE considers that this drug should not be used during the postnatal period, as women are already at risk of depression, and if possible, it should be stopped.

Advice on review and referral

- These recommendations are based on expert opinion from NICE [National Collaborating Centre for Women's and Children's Health, 2010]. NICE also considers that all women with pre-eclampsia should have a review of their blood pressure at the postnatal review 6–8 weeks after the birth. Who carries out this review will depend on local circumstances and expertise, and NICE were not prescriptive

about this. However, NICE recommends specialist referral for women with persistent hypertension or proteinuria or both.

How do I manage a woman with postpartum pre-eclampsia or eclampsia?

- Consider the possibility of imminent pre-eclampsia/eclampsia in a woman up to 4 weeks postpartum (even if she has not had previous hypertension or pre-eclampsia) if she develops *any* of the following:
  - Severe headaches (increasing frequency unrelieved by regular analgesics).
  - Vision problems, such as blurred vision, flashing lights, double vision, or floating spots.
  - Persistent new epigastric pain or pain in the right upper quadrant.
  - Vomiting.
  - Hypertension.
  - Proteinuria.
  - Breathlessness due to pulmonary oedema.
  - Sudden swelling of the face, hands, or feet.
- Consider the possibility of eclampsia in any woman who has a seizure within 4 weeks of delivery.
- **All women with suspected postpartum pre-eclampsia or eclampsia should be admitted to hospital for immediate assessment.**

Basis for recommendation

Importance of considering the possibility of pre-eclampsia/eclampsia even if the woman has not had antepartum or intrapartum pre-eclampsia

- Pre-eclampsia and eclampsia may both present for the first time after delivery [Mathew et al, 2003; Duley et al, 2006].
- In a study of 23 women with late postpartum eclampsia, only five had been previously diagnosed with pre-eclampsia [Chames et al, 2002].
- A prospective descriptive study of every case of eclampsia in the UK in 1992 found that 44% of cases occurred postpartum [Douglas and Redman, 1994].

Possibility of presenting up to 4 weeks after delivery

- A multicentre, retrospective analysis of data involving 89 women with eclampsia found that 29 women had postpartum eclampsia and 23 (79%) of these women had late-onset eclampsia (developing more than 48 hours after delivery) [Chames et al, 2002].
- In a multicentre, retrospective analysis of 3988 women diagnosed with pre-eclampsia, 229 (5.7%) were diagnosed during the postpartum period [Matthys et al, 2004]. Of these, 151 women were

studied and 29 (16%) developed eclampsia. The average time from delivery to readmission was 7 days and ranged from 1 day to 24 days.

Importance of considering the possibility of eclampsia in any woman who has a seizure within 4 weeks of delivery

- Symptoms and signs of pre-eclampsia usually precede eclampsia, but not always, which can make diagnosis difficult.
- Case studies of three women report eclampsia developing without preceding hypertension or proteinuria [Dziewas et al, 2002].

Importance of considering pre-eclampsia if the woman develops a headache, vision symptoms, abdominal pain, or typical symptoms

- In a multicentre, retrospective analysis of data involving 89 women with eclampsia, 29 women had postpartum eclampsia, and 21 of these had at least one prodromal symptom that heralded the onset of eclampsia: 20 women had headache, 10 women had vision changes, 5 women had nausea or vomiting, and 2 women had epigastric pain [Chames et al, 2002].
- Case studies have shown that acute severe headache, vision disturbances, and gastrointestinal symptoms may herald impending eclampsia [Veltkamp et al, 2000; Dziewas et al, 2002; Mathew et al, 2003; Graeber et al, 2005; Munjuluri et al, 2005].
- A case-control study of 53 women admitted in the postpartum period found that headache, a blind spot, cortical blindness, malaise, nausea, and vomiting were more likely to occur in women with postpartum severe pre-eclampsia or eclampsia than in women with intrapartum pre-eclampsia [Atterbury et al, 1998].

Immediate referral to hospital

- This is accepted good clinical practice.

Which antihypertensive drugs can be used during breastfeeding?

- **The following are considered to be safe during breastfeeding:**
  - Labetalol
  - Nifedipine
  - Enalapril
  - Captopril
  - Atenolol
  - Metoprolol

o Methyldopa

- **Do not prescribe the following:**

o Angiotensin-converting enzyme inhibitors, other than captopril and enalapril.

o Angiotensin-II receptor antagonists.

o Amlodipine.

Basis for recommendation

- The National Institute for Health and Clinical Excellence (NICE) reviewed the available evidence on use of antihypertensive drugs in breastfeeding women [National Collaborating Centre for Women's and Children's Health, 2010]. The studies identified measured non-clinical endpoints, such as secretion of the drug in the mother's milk or detection of the drug in the infant's plasma. No studies were found on whether antihypertensive drugs taken while breastfeeding had adverse effects on the infants.

Use of labetalol, nifedipine, and methyldopa

- NICE concluded that:

o The drugs mostly likely to be used by breastfeeding women seem to be suitable: labetalol, nifedipine, and methyldopa.

o However, NICE does not recommend the use of methyldopa in the postnatal period due to the risk of depression. This view conflicts with advice from the Medicines and Healthcare products Regulatory Agency (MHRA), which recommends methyldopa as the drug of choice during breastfeeding [MHRA, 2009].

Use of atenolol and metoprolol

o NICE commented that there are no known adverse effects.

Use of angiotensin-converting enzyme (ACE) inhibitors

- There is conflicting advice about the use of ACE inhibitors:

o NICE recommends that if ACE inhibitors are needed, then captopril or enalapril should be used because of the quality and quantity of associated safety data.

o However, the MHRA recommends that ACE inhibitors should not be used by breastfeeding mothers in the first few weeks after delivery. This is because, although amounts of the drug transferred to the infant by breastfeeding are unlikely to be clinically relevant, data are insufficient to exclude the possibility of profound hypotension in the infant. The MHRA considers that pre-term infants may be at particular risk. The MHRA suggests that the use of captopril, enalapril, or quinapril may be considered in older infants who are being breastfed.

Use of angiotensin-II receptor antagonists (AIIRAs)

- Both NICE and the MHRA agree that AIIRAs should not be used as there are no data on their use and their effects on breastfeeding infants.

Use of amlodipine

- NICE found insufficient evidence of safety and, therefore, does not recommend the use of amlodipine.

Use of diuretics

- NICE make no statement regarding the use of diuretics for treating hypertension in a woman who is breastfeeding.
- Although the amount of bendroflumethiazide excreted in breast milk is too small to be harmful, care is needed that the diuresis does not cause dehydration, leading to inhibition of breastfeeding. However, this is less likely if a low dose of 2.5 mg daily is used [LactMed, 2007].