State if the document is a Trust Policy/Procedure or a Clinical Guideline / Drugs Therapeutic Committee Document	**Guideline**

Document Title:	Headache in Pregnancy
Document Number	
Version Number	V1
Name and date and version number of previous document (if applicable):	
Document author(s):	Dr Anna Cohen - Consultant Neurologist, Dr Saadia Waheed – Consultant Obstetrician
Document developed in consultation with:	Dr Marian Chan - Ambulatory Care Consultant Trish Ryan – Head of Midwifery Ilene Ngwenya – Clinical Midwifery Manager Rebecca Daniels – Clinical Midwifery Manager
Staff with overall responsibility for development, implementation and review:	
Development / this review period:	

Date approved by the Policy Approval Group/Clinical Guidelines Committee / DTC on behalf of the Trust Board:	
Chief Executive / Chair Clinical Guidelines /Chief Pharmacist Signature:	
Date for next review:	
Date document was Equality Analysed:	

Target Audience:	Midwives, Obstetricians
Key Words:	
Associated Trust Documents:	
Reason for current amendments:	

CONTENTS PAGE

INTRODUCTION

Headache is common in women of childbearing age. The headaches can either be primary or secondary in nature.

Key causes of headache in pregnancy

Primary:

- Migraine
- Tension headache
- Cluster Headache

Secondary:

- Hypertension/Pre-Eclampsia
- Subarachnoid haemorrhage
- Drug-related, e.g. nifedipine, medication overuse
- Postdural tap
- Meningitis
- Cerebral venous thrombosis
- Caffeine withdrawal
- Idiopathic intracranial hypertension
- Stroke (rare)
- Arteriovenous malformation (can enlarge/bleed in pregnancy)
- Enlargement of a pituitary tumour
- Enlargement of a hormone-sensitive tumour, e.g. meningioma
- Bleeding into a pre-existing tumour
- Cerebral metastasis or choriocarcinoma
-

Assessing headaches in pregnancy:

The history alone often distinguishes the benign and more sinister causes of headache, particularly by eliciting the presence or absence of 'red flag' features i.e. duration, location, frequency, severity, family history, associated symptoms and relationship to this and previous pregnancies should all be established. It is often helpful, to the patient and doctor, to ask what the patient believes to be the cause of the headache.

Red flag features for potential secondary headache:

- Thunderclap: rapid time to peak headache intensity (seconds to 5 minutes), e.g. with a subarachnoid haemorrhage
- Focal neurological symptoms (e.g. limb weakness, aura <5 minutes or >1 hour)
- Non-focal neurological symptoms (e.g. cognitive disturbance) – seen in central venous thrombosis
- Change in headache frequency, characteristics or associated symptoms
- Abnormal neurological examination
- Headache that changes with posture – a sign of high or low cerebrospinal fluid pressure

- Headache awakening the patient – associated with migraine and raised intracranial pressure
- Headache precipitated by physical exertion or Valsalva manoeuvre – consider subarachnoid haemorrhage or raised intracranial pressure
- Patients with risk factors for cerebral venous thrombosis
- Jaw claudication or visual disturbance – associated with giant cell arteritis (women over 50 years)
- Fever – consider meningitis
- Neck stiffness – indicative of meningeal irritation
- New onset of headache in a patient with a history of HIV infection
- New-onset headache in a patient with a history of cancer

A neurological examination is usually essential and needs to include the following:

- Fundoscopy – looking for papilledema
- Cranial nerve assessment, in particular:
    - Pupil reaction to light and accommodation
    - Visual fields – looking for lesions affecting visual processing, such as pituitary tumours
    - Eye movements **–** a sixth nerve palsy presents with binocular horizontal diplopia with in-turning of the eye and decreased lateral movement; a third nerve palsy, with or without pupillary dilatation, can point to an aneurysm in the posterior communicating artery
    - Speech and swallowing
- Tone, power, reflexes and coordination in all four limbs
- Plantar response (an upward extensor plantar response is seen in upper motor neurone lesions)
- Assessment of gait, including heel–toe walking.
- Blood pressure, proteinuria and clonus should be assessed and pre-eclampsia considered, especially after 20 weeks of gestation.

Migraine

The lifetime prevalence of migraine is 22% in women and 10% in men. The discrepancy is thought to be due to the effect of oestrogens, as pre-pubertally there is no difference between the sexes. It is generally agreed that migraine can worsen during first trimester, then resolved during second and third trimesters, due to the stabilisation and increase of oestrogen. 67-89% of patients report migraine improvement during the second and third trimesters, and in 20% the attacks disappear. There can be a resurgence of migraine in the post-partum period within 3-6 days, again due to falling oestrogen levels and sleep disturbance.
Migraine without aura is more likely to be associated with oestrogen fluctuations; therefore is more likely to be menstrually related and also more likely to resolve during pregnancy. Migraine can also occur de novo in pregnancy. New onset transient neurological symptoms can occur, often reflecting migraine aura, but these must be managed appropriately to rule out other causes.

History

Of paramount importance is the history. The International Headache Classification (IHCD) of migraine involves unilateral or bilateral, throbbing headache lasting 4-72 hours, with nausea, vomiting, photophobia, osmophobia, movement making the pain worse. An aura is a reversible neurological deficit lasting 5-60 minutes which can be visual, sensory, rarely motor. The aura has a gradual onset and offset over minutes, thus distinguishing it from vascular lesions such as stroke or venous sinus thrombosis. Most helpful in the history is the patient's personal or family history of migraine.

Examination

Neurological examination in migraine, including fundoscopy and blood pressure, is generally normal. There is often temporal and occipital tenderness during a migraine attack, which reflects the sensitisation of second order neurons and the development of allodynia.

Investigations

No investigations are required if the diagnosis is secure.

Treatment

Initial first-line management of migraine includes avoidance of precipitants, rest, hydration, regular meals and relaxation. Paracetamol and anti-emetics may be all that is required but further analgesia or specific anti-migraine preparations may be needed. Triptans (see below) or a non-steroidal anti-inflammatory drug (in the first and second trimesters) may be used after discussing with the patient the risks associated with use of these drugs in pregnancy.

Outside of pregnancy $5HT_1$-receptor agonists (triptans) are commonly used and effective. Sumatriptan is the most extensively studied of the triptans during pregnancy and data from the Sumatriptan Pregnancy Registry show no increase in adverse outcomes in women exposed to this drug during pregnancy. The use of triptans in pregnancy, however, may still be best reserved for severe migraine that does not respond to simple analgsics.

Women experiencing three to four headaches a month may be considered for prophylactic treatment, especially when the headache is unresponsive to simple analgesia. If prophylaxis is required, propranolol (10–40 mg three times a day) has the best evidence of safety in pregnancy and lactation. Amitriptyline in the lowest effective dose (25–50 mg at night) may also be used

Tension-type headache

Tension-type headache is extremely common, and may be exacerbated in pregnancy due to a number of factors, including muscle tension, dehydration, poor sleep. Tension-type headaches are not severe, not throbbing, and generally not associated with nausea, photophobia, or worsening with movement. Neurological examination is normal. No specific investigations are required. Treatments include paracetamol acutely. Preventive medications are best avoided, but alteration of lifestyle, including relaxation and avoidance of trigger factors, is helpful.

SECONDARY HEADACHES:

A major concern of new onset or worsening headaches in pregnancy is due to secondary causes. 90% of headaches in pregnancy are benign. The risk of a secondary headache increases in the second and third trimester, and post-partum, reflecting the altered physiology of the pregnant woman. However even in the post-partum period, 50-75% are primary headaches. The management of these syndromes depends on the underlying pathology. Differential diagnosis of a primary or secondary headache syndrome is vital, as is prompt and appropriate treatment of the underlying cause. In MBRRACE report 2017, 12 women died from intracranial haemorrhage 2013-2015 and in 25% of cases different care would have made a difference in outcome.

When to consider a secondary headache?

A history is paramount in differentiating primary from secondary headaches. Patients with a previous history of migraine or family history of migraine, with headaches matching the phenotype of migraine can be reassured AS LONG AS THERE IS NO OTHER CAUSE IDENTIFIED. Migraine can present de novo in pregnancy, as can migraine auras or reversible neurological deficits.

Secondary headaches, or those with an underlying structural cause, should be considered in the following cases: (SNOOP mnemonic)

1) Systemic symptoms or signs: these include fever (infection) and neck stiffness (meningitis), hypertension (pre-eclampsia), abnormal blood tests including liver function
2) Neurological symptoms or signs: seizures, loss of consciousness or obtundation, pupil or eye movement abnormality, papilledema on fundoscopy, weakness in face or limbs, abnormal tendon reflexes or plantars, cranial nerve, motor or cerebellar dysfunction
3) Onset sudden: thunderclap headaches, sudden onset headache or weakness (as opposed to migraine and aura which develop over minutes)
4) Onset recent: in a patient with no prior history of headaches (although with the caveat that migraine can present de novo in pregnancy)
5) Particular or persistent headache: in patients with a previous headache history, but the current headache is markedly different, or headaches which are persistent or progressive

Pre-eclampsia

The International Headache Society diagnostic criteria for headache attributed to preeclampsia are

Headache in a woman who is pregnant or in the puerperium fulfilling criterion

1. Pre-eclampsia or eclampsia has been diagnosed
2. Evidence of causation demonstrated by at least two of the following:
    - Headache has developed in temporal relation to the onset of the preeclampsia or eclampsia
    - Either or both of the following: headache has significantly worsened in parallel with worsening of the preeclampsia or eclampsia or headache has significantly improved or resolved in parallel with improvement in or resolution of the preeclampsia or eclampsia
3. Headache has at least two of the following three characteristics:

- bilateral location
- pulsating quality
- aggravated by physical activity

4. Not better accounted for by another ICHD-3 diagnosis

Please refer to the guideline on management of preeclampsia and eclampsia

Posterior reversible encephalopathy syndrome:

Posterior reversible encephalopathy syndrome (PRES) is a clinical–neuroradiological entity associated with preeclampsia. It is characterised by headache, vomiting, visual disturbances, seizures and altered mental state, with radiological findings of oedema in the posterior circulation of the brain

Cerebral blood flow is maintained despite changes in blood pressure by an auto regulatory mechanism facilitated by changes in vascular resistance. In PRES, this auto regulatory response is impaired, leading to breakdown of the normal blood–brain barrier and culminating in vasogenic brain oedema. Because of a partial lack of sympathetic innervation of the vasculature that emerges from the basilar artery, oedema tends to occur in the posterior regions of the central nervous system. Oedema leads to progressive brain compression within the skull and the symptoms of headache, nausea, vomiting and seizures. So why does pre-eclampsia lead to a breakdown in this autoregulation? Cases of PRES without hypertension have been reported associated with immunosuppressant drug use, nephrotic states, sepsis and systemic lupus erythematosus. In these cases a common aetiological pathway leading to vasogenic oedema is endothelial damage. Endothelial dysfunction is associated with the pathophysiology of pre-eclampsia. Studies have also shown that pregnancy alone predisposes the brain to the neurological complications of eclampsia by promoting hydrostatic brain oedema when blood pressure is acutely elevated.

Prompt recognition and management of PRES is required to avoid the risk of irreversible lesions. When PRES is associated with pre-eclampsia, management follows the treatment algorithm for severe pre-eclampsia with blood pressure control, prevention and/or treatment of seizures and prompt delivery of the baby.

Analgesic Overuse

Medication overuse in the setting of migraine is the use of analgesics such as paracetamol or aspirin on more than 15 days per month, or triptans on more than 10 days per month. A medication overuse headache can occur in patients with a previous or family history of migraine who are using regular analgesics for any indication. This headache can take the phenotype of the migraine, or it can be more dull and featureless, but the drug history is vital in making the diagnosis. If women in the pre-conception phase or in early pregnancy have stopped their migraine preventives and rely more on acute abortive medications, then it is possible that a medication overuse headache may arise. Management is withdrawal of the medication of overuse.

Idiopathic Intracranial Hypertension (IIH):

Idiopathic intracranial hypertension is increasing in frequency, in line with the national epidemic of obesity. It mainly affects obese women of childbearing age (19.3/ 100 000). It may present for the first time in pregnancy and pre-existing disease tends to worsen during pregnancy. The headache is generalised, non-throbbing, aggravated by coughing or straining and is associated with diplopia (38%) and visual loss (31%) with papilledema. Diagnosis requires excluding other

causes and finding abnormally elevated cerebrospinal fluid pressure (>20 cmH_2O) on lumbar puncture.

Management includes monitoring of the visual fields and visual acuity because of the risk of optic nerve involvement or infarction. Women should be encouraged to limit weight gain. Treatment with therapeutic lumbar puncture or acetazolamide (500 mg twice daily) is directed towards improving the headache and preventing visual loss.

Cerebral Venous Sinus Thrombosis CVT:

CVT can occur in the third trimester up to 6 weeks post-partum, due to the hypercoaguable state of pregnancy The highest risk is in third trimester and postpartum. The headache of venous sinus thrombosis can be a thunderclap headache, reflecting the vascular aspect of the pathophysiology. Alternatively there can be a more gradual onset with signs of raised intracranial pressure. Patients typically present with seizures (40%) (focal or generalised), visual obscuration's, VI nerve palsy, and can have papilledema. Signs can be progressive and bilateral, with bilateral hemispheric involvement. CVT occurs in the absence of hypertension and proteinuria- if these are present then the diagnosis is more likely pre-eclampsia. Investigations include MRI, MRV, clotting screen, phospholipid antibodies, and Factor V Leiden. Treatment is with low molecular weight heparin for 6 months duration of no underlying clotting abnormality is found, and with prophylactic low molecular weight heparin in subsequent pregnancies. Antiepileptic drugs are indicated only for 6 months if seizures present early, but seizures can occur up to a year post event in 32%.

Post Dural Puncture headache

The risk of dural puncture in patients who have epidural anaesthesia is around 1.5%, and around half of these patients will experience a post-dural puncture headache. 90% will develop within 3 days, and 2/3 within the first 48 hours of procedure, although some can be delayed for up to 14 days. The history is of headache which may be occipital, but with significant worsening on sitting or standing up, and resolution on lying down. Tinnitus and muffled hearing may also be present, as lowering of CSF pressure lowers the perilymphatic pressure in the inner ear canal. Factors increasing the risk of post dural puncture headache include: younger age, female, lower weight, previous history of post dural puncture headache, previous headache history. 72% will improve in one week, but 13% remain persistent.

The history alone is often adequate to make a diagnosis. Differential diagnoses include migraine, pre-eclampsia in the puerperium, septic and aseptic meningitis, cerebral vein thrombosis, and pneumocephalus (sudden headache due to injection of air into the subdural space, which is relieved by lying down and usually resolves after a few hours). If investigations are necessary, then an MRI may show evidence of low CSF pressure, and myelography can localise the leak (although not often required).

Treatment for the mainstay is conservative, with, in ascending order: bed rest and oral hydration, oral caffeine 300mg, IV caffeine 500mg if available, or epidural blood patch.

Tumour

Brain tumours are rare, and rarely present with headaches alone. The headache may be one of raised intracranial pressure (worse on lying down, worsened with coughing bending or straining, false localising VI palsy with diplopia and visual obscurations). Often they will present with seizures or a neurological deficit which will be found on examination, as will papilledema. Any patient presenting with these symptoms de novo in pregnancy must have cranial imaging to rule

out a space occupying lesion. Meningiomas, which are commoner in women, have some hormone-dependent qualities, and their rate of growth may be increased with pregnancy.

Reversible Cerebral Vasoconstriction syndrome (RCVS):

Reversible Cerebral Vasoconstriction syndrome is rare, often presenting as a thunderclap headache or series of thunderclap headaches. Seizures and cortical strokes, either ischaemic or haemorrhagic, can also occur. There is segmental constriction of cerebral arteries which normally resolves within 3 months. Half of the cases of RCVS occur in the post-partum period, or after exposure to adrenergic or serotonergic drugs.

Diagnosis can be difficult to the dynamic changes in vessels it requires the demonstration of diffuse arterial beading on cerebral angiography with resolution within 1–3 months. Stroke can occur a few days after normal imaging, and cerebral vascoconstriction is maximal 2-3 weeks after onset.

Treatment includes IV magnesium and labetalol, as the pathophysiology may be on the same spectrum of endothelial dysfunction as pre-eclampsia. Calcium channel blockers are beneficial for the headache and blood pressure, but have no proven effect on haemorrhagic or ischaemic complications.

Pituitary Apoplexy

This is a rare but potentially life threatening condition due to haemorrhagic infarction of the pituitary gland, more likely with an underlying adenoma or rapidly growing adenoma or stimulation of the gland due to the oestrogenic state of pregnancy. Fluctuations in blood pressure and a concomitant coagulopathy may also be precipitating factors. Symptoms are of a thunderclap headache which is often orbital. There can also be visual field or acuity disturbance; and involvement of eye movements due to III IV VI nerves in the cavernous sinus. There are changes to the mental or conscious state in 20%. This is a neuroendocrine emergency due to the loss of ACTH and subsequent hypotension.
Management includes rapid diagnosis with MRI brain, then acute fluid and electrolyte correction. Intravenous hydrocortisone is given IV initially, and the patient is monitored for other pituitary-dependent hormones, such as thyroid function, cortisol, prolactin, LH FSH and oestradiol. Visual fields and eye movements should be monitored, and consider neurosurgical referral if any deterioration.

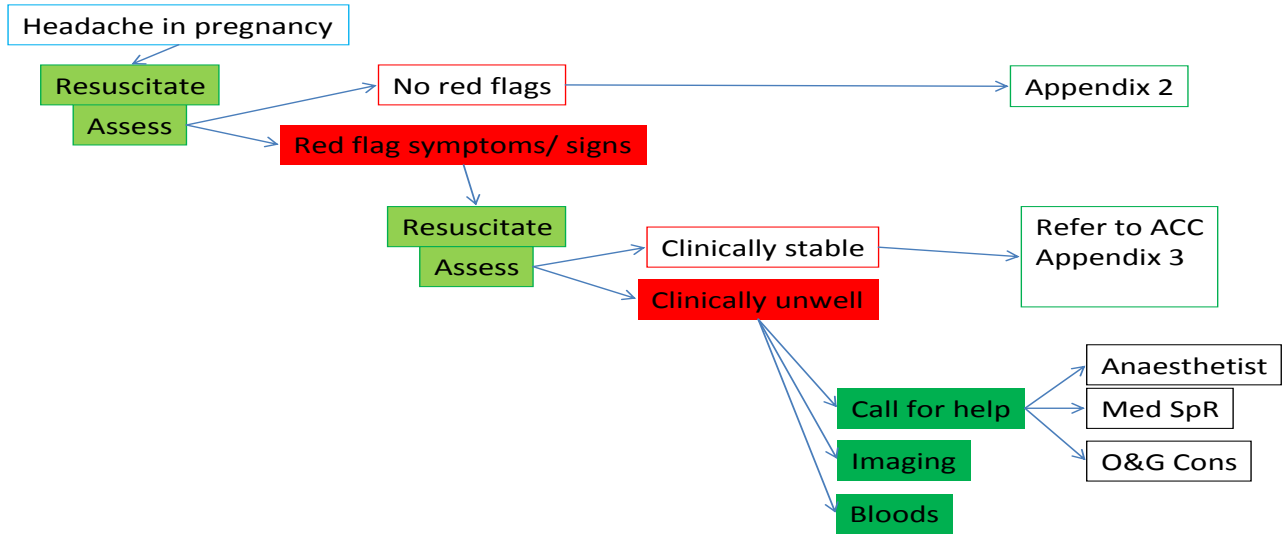
Table 1: Acute medications in Pregnancy

Drug	First trimester	Second trimester	Third Trimester	Lactation
Paracetamol	√	√	√	√
Ibuprofen/Naproxen	(√)	√	Until 32 weeks	Ibuprofen
Sumatriptan	√	√	√	√
Metoclopramide	√	√	√	√ May increase lactation
Aspirin 100mg	√	√		Reye's syndrome

Table 2. Preventive Medications in Pregnancy

Medication	First trimester	Second Trimester	Third Trimester	Lactation
Propranolol	√	√	Neonatal bradycardia, hypoglycaemia, Resp depression	√
Amitriptyline/ Nortriptyline	√	√	Neonatal withdrawal	√
Valproate	X	X	X	Does not cross breast milk but limited evidence of efficacy
Topiramate/ Candesartan	X	X	X	X
Melatonin	No evidence	No evidence	No evidence	No evidence

Appendix 1:



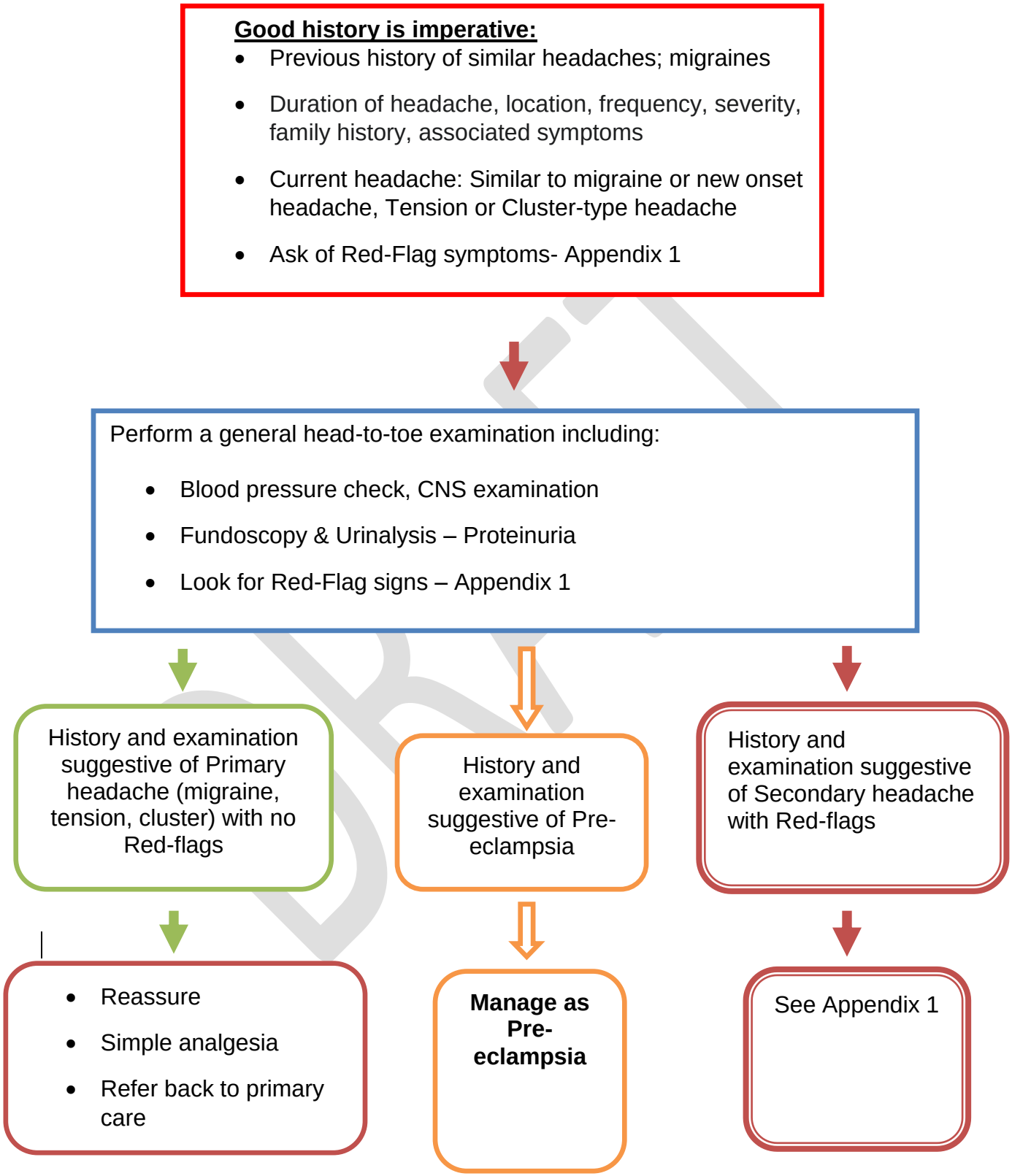
Red Flag Symptoms:

- Sudden onset or thunderclap onset
- Associated systemic symptoms
- Focal neurological symptoms (e.g. limb weakness, aura <5 minutes or >1 hour)
- Other Neurological symptoms (e.g. cognitive disturbance)
- De novo headache
- Headache different to usual
- Persistent or worsening headache
- Change in headache frequency, characteristics or associated symptoms
- Headache that changes with posture
- Headache awakening the patient
- Headache precipitated by physical exertion or Valsalva manoeuvre
- Jaw claudication or visual disturbance
- Fever – consider meningitis
- Neck stiffness – indicative of meningeal irritation

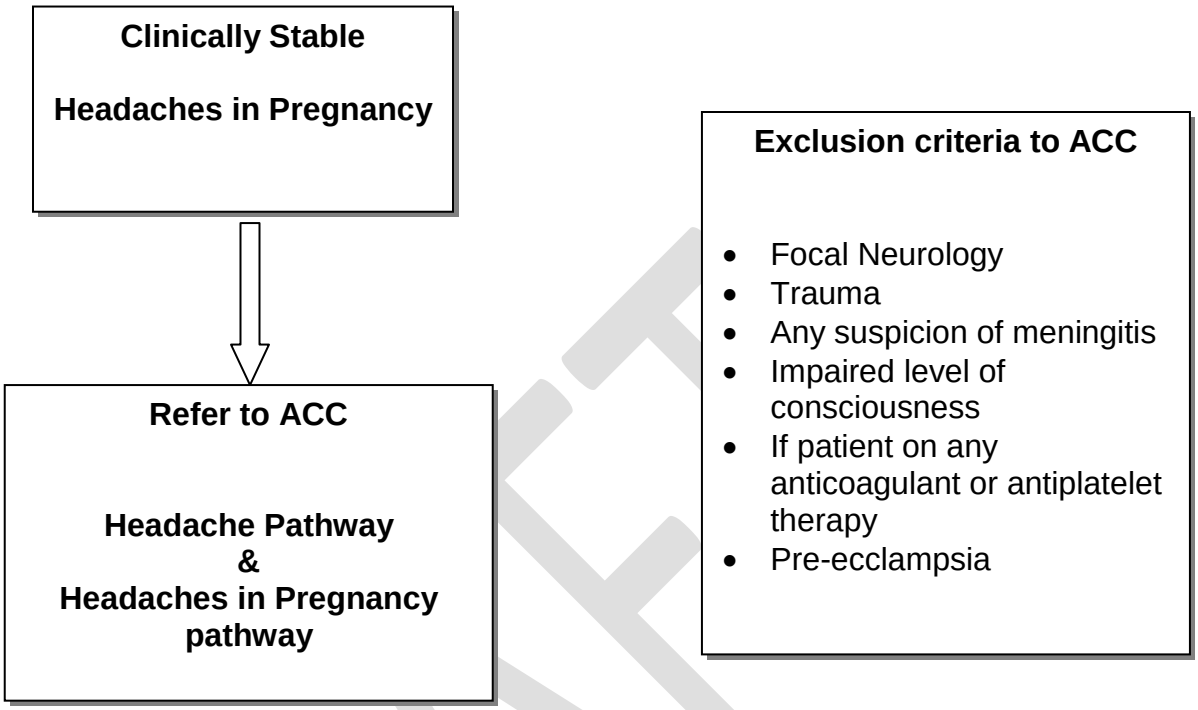
Red Flag Signs

- Moribund/Obtunded
- Stiff neck
- Any neurological abnormality
- Papilledema
- Hypertension
- Fever – consider meningitis

Appendix 2: Management of Headaches with no red flags



Appendix 3: ACC



Selected References

1. Lieberman et al. Natural course and pathogenesis of transient focal neurologic symptoms during pregnancy. Arch Neurol 2008; 65(2): 218-220.
2. International headache Classification IHCD-3 2017 https://www.ichd-3.org/
3. Afridi S. Current concepts in migraine and their relevance to pregnancy. Obstetric Med 2018.
4. Calhoun etal. Treatment of cluster headache in pregnancy and lactation. Curr Pain Headache Rep 2010; 14: 164-173.
5. O'Neal. Headaches complicating pregnancy and the post-partum period. Practical Neurology 2017:17: 191-202.
6. Falardeau et al. The use of acetazolamide during pregnancy in intracranial hypertension patients. J Neuroophthalmol 2013;33: 9-12.
7. Gurcay. Diagnosis, Treatment, and Management Strategy of Meningioma during Pregnancy. Asian J Neurosurg 2018;13: 86-89.
8. Ducros. Reversible cerebral vasoconstriction syndrome. Lancet Neurol 2012;11: 906-17.
9. Raffaelli et al. Characteristics and diagnoses of acute headaches in pregnant women- a retrospective cross-sectional study. J Headache Pain 2017;18:114.
10. Macgregor EA. Headache in Pregnancy. Neurol Clin 2012;30:853-66.
11. Rajasekeran et al. UK guidelines for the management of pituitary apoplexy. Clin Endocrinol 2011;74:9-20.
12. Revell et al. Headaches in Pregnancy. The O&G 2014;16:179-84.
13. Pearce CF, Hansen WF. Headache and Neurological Disease in Pregnancy. Clinical Obstetrics and Gynaecology. 2012;55(3):810–828.
14. Nelson-Piercy C. Handbook of Obstetric Medicine. 4th edition. 2010
15. Scottish Intercollegiate Guidelines Network. Diagnosis and Management of Headache in Adults. A National Clinical Guideline. Edinburgh: SIGN; 2008.
16. National Institute for Health and Care Excellence. Headaches. Diagnosis and Management of Headaches in Young People and Adults. NICE clinical guideline 150. London: NICE; 2012.
17. Cunnington M, Ephross S, Churchill P. The safety of sumatriptan and naratriptan in pregnancy: what have we learned? Headache 2009;49:1414–22.
18. Marcus DA. Pregnancy and chronic headache. Expert Opin Pharmacother 2002;3:389–393.
19. Revell K, Morrish P. *Headaches in pregnancy*. The Obstetrician & Gynaecologist 2014 ... DOI: 10.1111/*tog*.12101.