14.12 Neurological conditions in pregnancy 2642

14.12 Neurological conditions in pregnancy 2642

ESSENTIALS Pregnancy can influence the clinical course of an underlying neuro- logical problem or precipitate the first presentation of a neurological disease. Epilepsy—sodium valproate is associated with higher risk of major congenital malformations and impaired neuropsychological devel- opment than other antiepileptic drugs: lamotrigine or levetiracetam are preferred. Women taking antiepileptic drugs can breastfeed. Multiple sclerosis—relapse rate is reduced in pregnancy but substantially increased for three months post-partum. Cerebrovascular disease—stroke syndromes specific to pregnancy in- clude pre-eclampsia, which can lead to posterior reversible vasoconstric- tion syndrome. Reversible cerebral vasoconstriction syndrome presents after delivery and has many similarities to posterior reversible vasocon- striction syndrome. Cerebral venous thrombosis accounts for approxi- mately 20% of all strokes occurring in pregnancy and puerperium. There are conflicting opinions as to whether pregnancy or delivery increases the risk of cerebral aneurysm or arteriovenous malformation rupture. Introduction Neurological conditions in pregnancy are an important cause of mor- tality and morbidity in the United Kingdom. From 2010 to 2015, there were 50 maternal deaths in the United Kingdom related to diseases of the central nervous system. The commonest causes identified were subarachnoid haemorrhage, intracerebral haemorrhage, and epilepsy. During pregnancy, a range of haemodynamic and biochemical changes occur in the mother, and these can significantly impact and influence the natural history of an underlying neurological problem or precipitate the first presentation of neurological disease in preg- nancy. This chapter will cover the management of common neuro- logical diseases during pregnancy. Imaging in pregnancy This causes safety concern during pregnancy, but the clinician should put maternal well-being at the centre of all decision-making. Computed tomography

Computed tomography (CT) can be performed in pregnancy. The fetal exposure dose from a head CT scan is less than 0.1 mGy, which is low. The patient should be informed that no association has been proven between radiation exposure of less than 50 mGy and risk of spontaneous miscarriage or developmental malforma- tions. Iodinated contrast should only be given if required in pregnancy: it does cross the placenta, but no teratogenic effects have been described. Magnetic resonance imaging This is the modality of choice in pregnancy. Despite theoretical concerns, there is no evidence to suggest that magnetic resonance imaging (MRI) exposure, irrespective of trimester, is associated with fetal harm. Contrast agents such as gadolinium are avoided in pregnancy because of an increased risk of harm; including still- birth and neonatal death. Headaches Headaches are common in women of childbearing age and preg- nancy is no exception to this. The commonest headache presenta- tions encountered in pregnancy include, tension headaches, and migraines. However, it is important to always be mindful of any red flag features, suggestive of a more sinister pathology, necessitating urgent evaluation (Box 14.12.1). Migraine Migraines usually improve during pregnancy and 60–70% of women report fewer migrainous attacks during pregnancy. In women who are troubled by headaches in pregnancy, nonpharmacological steps 14.12 Neurological conditions in pregnancy Pooja Dassan Box 14.12.1 Red flags in headache presentation • Headaches of sudden onset • Headaches associated with neck stiffness • Patient reports worst headache ever • Headache with abnormal neurological signs

14.12 Neurological conditions in pregnancy 2643 are usually advocated as part of the first line management. This in- cludes advising patients to improve hydration, reduce consumption of caffeinated drinks, avoid sleep deprivation, and adopt regular eating patterns. Approaches to drug treatment should involve using nonopioid analgesics, such as paracetamol and nonsteroidal anti-inflammatory drugs, although the latter should be avoided after 30 weeks' gesta- tion. A prokinetic agent such as domperidone is a helpful adjunct to these abortive medications. Opiates, although safe to use during pregnancy, are usually avoided in migrainous patients as they can exacerbate nausea and, if anything, worsen gastric motility prob- lems. If despite these initial measures the headaches are still trouble- some, then a preventative medication is usually prescribed. Both propranolol and amitriptyline are reasonable first line options and should be used at the lowest effective dose. Epilepsy An important aspect of the consultation with any female patient of childbearing age with epilepsy is preconception counselling (see Box 14.12.2). As approximately 50% of pregnancies are un- planned, clinicians must approach this subject at the earliest opportunity to ensure that the patient's therapy has been optimized and folic acid 5 mg per day has been initiated for at least three months preconception. Antiepileptic drugs Lamotrigine Lamotrigine's teratogenic profile is more favourable than other antiepileptic drugs, in particular when compared with valproate. However, one drawback with lamotrigine use in pregnancy is that the apparent clearance increases steadily through pregnancy and notably peaks at 32 weeks, when it can be as high as 330% as compared with nonpregnant baseline. This can result in quite a significant fall in lamotrigine levels in the third trimester, with deterioration in seizure control as a consequence. This change in lamotrigine's pharmacokinetics during pregnancy does revert back to pre-pregnancy conditions within a few days of delivery. In our practice, we advocate checking serum lamotrigine level either pre-pregnancy or in very early pregnancy and treating this as the mother's baseline. Thereafter, the clinician should consider increasing the lamotrigine dose to prevent significant reduction of levels from baseline. Whether such increases should be based on clinical assessment or therapeutic drug monitoring is currently the subject of a multicentre randomized trial. Levetiracetam Levetiracetam is a newer generation antiepileptic mediation with a

favourable side effect profile and is widely used to treat seizures. The emerging data suggest that the risk of major congenital mal- formation for mother's taking levetiracetam is between 2 to 3%, which is comparable to the background risk. In addition, current evi- dence suggests that taking levetiracetam during pregnancy does not have a negative impact on the child's cognitive and language develop- ment. Levetiracetam metabolism also increases in pregnancy and in our practice, we advocate checking drug levels once every trimester. Management of pregnancy and labour Several antiepileptic drugs, including phenytoin and carbamaze- pine, are hepatic enzyme inducers and thus lead to a reduction in vitamin K-dependent clotting factors in the fetus. Previously oral vitamin K was prescribed for women taking hepatic enzyme- inducing antiepileptic drugs from 36 weeks' gestation until de- livery, to prevent hemorrhagic disease of the newborn. This is no longer necessary as all babies receive intramuscular (IM) vitamin K after birth. Women with epilepsy should be encouraged to deliver in hospital as it is recognized that 3% will have a seizure within 24 hours of de- livery. The reasons behind this include fatigue and sleep deprivation, failure to adhere to usual antiepileptic drug regime during labour, and impaired absorption. If a mother is felt to be at particular risk of seiz- ures during this period, then short-term clobazam (a benzodiazepine derivative) can be used as an effective adjunct to her usual medication. Breastfeeding All antiepileptic drugs are excreted in varying degrees into breast milk. Despite this, it is the opinion of experts to support breast- feeding in women using antiepileptic drugs, as the benefits of breast- feeding are likely to outweigh any theoretical risks. Multiple sclerosis Most women with multiple sclerosis (MS) can safely conceive, give birth, and breastfeed without any significant ill-effects to the mother or baby. Important aspects to discuss during pre-pregnancy counselling in women with MS are detailed in Box 14.12.3. Use of disease-modifying drugs in pregnancy is de- scribed in Table 14.12.1. Box 14.12.2 Pre-pregnancy counselling issues • Reassure the patient that most women with epilepsy give birth to a healthy child. • Aim to maintain the mother pre-pregnancy on a single agent, at the lowest effective dose. Higher risk of malformations with polytherapy and dose-related effects are likely to be observed with most antiepileptic drugs (e.g. valproate). • Teratogenicity is defined in the following categories: — Structural malformations and these can be either major or minor; — Impaired neuropsychological development; — Reduced intrauterine growth. • Sodium valproate—The MHRA (Medicines and Healthcare products Regulatory Agency) recently updated their guidance in March 2018 re- commending that valproate must no longer be used in any woman of childbearing age, unless she has a pregnancy prevention programme in place. This is designed to make sure patients are fully aware of the risks and the need to avoid becoming pregnant. If valproate is taken during pregnancy, up to 4 in 10 babies are at risk of developmental disorders, and approximately 1 in 10 are at risk of birth defects. • The magnitude of the risk of maternal seizures on the fetus is dif- ficult to quantify. Overall, women with epilepsy who are having generalized seizures during pregnancy should be informed that the fetus may be at risk of harm with multiple or prolonged seiz- ures, but the actual absolute risk—particularly of a single seizure—is probably low.

Section 14 Medical disorders in pregnancy 2644 Myasthenia gravis Myasthenia gravis affects skeletal muscles and does not affect the smooth muscles of the myometrium, thus uterine contractions are not impaired. The key to managing myasthenia gravis in pregnancy is the same as with any other autoimmune condition; to optimize control pre-pregnancy. It is important to remember that several of the drugs used to treat myasthenia gravis (see Table 14.12.2) are safe in pregnancy and it is imperative that women are reassured of this. The issues pertaining to the management of myasthenia in the pre- conception stage, during pregnancy, and thereafter are

covered in Table 14.12.3. Cerebrovascular disease Ischaemic strokes The estimated incidence of stroke in pregnancy is 4–7 cases per 100 000. The three common aetiologies accounting for most cases of pregnancy-related ischaemic strokes are cardioembolism, pre- eclampsia/eclampsia and cerebral venous thrombosis. If a stroke is suspected, urgent imaging should be carried out, as in nonpregnant patients (see Fig. 14.12.1). In nonpregnant in- dividuals, intravenous recombinant tissue plasminogen activator (t-PA) is the recommended treatment for an acute ischaemic stroke presenting within 4.5 hours of onset. There is very little evidence relating to the use of this treatment in pregnant women but, overall, the evidence suggests that treatment with t-PA should be con- sidered in all pregnant patients with disabling strokes. Stroke syndromes specific to pregnancy Pre-eclampsia This is a multisystem disorder, primarily thought to be a disorder of placental implantation and presents with a constellation of symp- toms including pregnancy-induced hypertension and proteinuria. In approximately one-third of cases of stroke diagnosed in preg- nancy or the puerperium, pre-eclampsia/eclampsia is also concomi- tantly diagnosed. Haemorrhagic strokes occur most commonly. The pathophysiology underpinning this is complex but appears to be re- lated to impaired endothelial function. In addition, pre-eclampsia can lead to posterior reversible vaso- constriction syndrome, which is radiologically characterized with bi-lateral, symmetrical subcortical changes, often seen predominantly in the occipital and parietal areas (see Fig. 14.12.2). The imaging characteristics of this condition are of vasogenic oedema, although in a few patients areas of cytotoxic oedema have been identified, suggestive of irreversible ischaemic damage. It classically presents with a severe, often thunderclap, headache. Other clinical features include seizures, cortical blindness, fixed neurological deficits, and alteration in level of consciousness with eventual stupor. Urgent identification of these patients is paramount. Management entails adequate control of seizures (primarily with IV magnesium sulphate in patients with eclampsia), control of blood pressure and, on occasions, urgent delivery of the fetus is required. Reversible cerebral vasoconstriction syndrome This condition, like posterior reversible vasoconstriction syndrome, is recognized as a self-limiting condition, occurring within the first week after delivery, often following an uncomplicated preg- nancy and delivery. This condition characteristically presents with Box 14.12.3 Key issues to discuss during pre-pregnancy counselling in women with multiple sclerosis • Fertility is not affected in multiple sclerosis (MS). • There is no single genetic cause of MS. The risk of MS in the general population is 0.13%. However, when a parent has MS, risk to the child is 2–2.5%. • Safety of disease-modifying drugs (DMDs)—see Table 14.12.1 • Relapse rate is reduced by up to 70% in pregnancy, especially during the third trimester. • This is followed by a substantial increase in risk of relapses in the im- mediate post-partum period and for up to three months thereafter. • Vitamin D supplementation (up to 4000 IU/day) can be used safely during pregnancy to reduce the relapse rate. • Mild relapses during pregnancy can be managed conservatively, but significant relapses leading to new disability can be treated with ei-ther intravenous methylprednisolone or oral prednisolone. Less than 10% of the maternal dose of methylprednisolone or prednisolone reaches the fetus as a result of metabolism to the inactive form by the placenta. • Mode of delivery should be guided by obstetric reasons and there is no documented adverse effect of regional anaesthesia. Table 14.12.1 Use in pregnancy of disease-modifying drugs for multiple sclerosis (MS) Disease-modifying drugs (DMDs) FDA pregnancy category Advice in pregnancy β-interferon C—animal studies have shown adverse fetal effects; there are no adequate studies in humans; benefits of treatment may outweigh risks • Large molecule, does not cross placenta • Emerging data suggest, it is safe to continue until at least conception and that the benefits of breastfeeding outweigh any associated risks. Glatiramer acetate B—animal studies have not shown adverse fetal effects; there are no adequate studies in

pregnant women • Large molecule, does not cross placenta • Emerging data suggest, it is safe to continue until at least conception and that the benefits of breastfeeding outweigh any associated risks. Natalizumab C—animal studies have shown adverse fetal effects; there are no adequate studies in humans; benefits of treatment may outweigh risks • Large molecule which crosses placenta via active transport after first trimester • During pre-conception counseling, the MS team should discuss the pros and cons of stopping vs continuing on this treatment during pregnancy. Evidence shows that women who stop Nataizumab can experience a rebound of their MS (severe relapse) during pregnancy.

14.12 Neurological conditions in pregnancy 2645 recurrent thunderclap headaches and other clinical features can in- clude seizures, confusion, or a fixed neurological deficit. Reversible cerebral vasoconstriction syndrome can occur in conjunction with pre-eclampsia or posterior reversible vasoconstriction syndrome, and in fact, these three conditions are likely to be underpinned by similar pathophysiological processes. The characteristic feature of this condition is the reversible narrowing of the intracerebral vasculature and this can be identified via dedicated intracranial vascular imaging (see Fig. 14.12.3). Patients are expected to recover spontaneously within one to three months and treatment is gen- erally supportive. In some cases, complications can occur, and patients are left with permanent damage due to subarachnoid haemorrhage or parenchymal damage from infarction or intracerebral haemorrhage. Table 14.12.2 Use in pregnancy and when breast feeding of drugs for myasthenia Drug Pregnancy Breastfeeding Pyridostigmine • Very little crosses the placenta, no reports of fetal harm • <0.1% passes into breast milk Corticosteroids • Prednisolone can be used and usually at the lowest maintenance dose • Due to placental metabolism of prednisolone, only 10% is transferred
to fetal circulation • There is increased risk of gestational diabetes • Can be continued during breastfeeding Azathioprine • Safe to continue in pregnancy • Can be continued during breastfeeding Methotrexate and mycophenolate mofetil (MMF) • Contraindicated in pregnancy • Contraindicated in breastfeeding Table 14.12.3 Management of myasthenia gravis
during pregnancy and delivery Pre-pregnancy • Optimize management • Switch from teratogenic DMD to safer option (e.g. azathioprine) • Plan thymectomy pre-pregnancy to optimize control • Check thyroid function tests and thyroid antibody status Pregnancy • Most patients who are stable preconception are unlikely to experience a relapse while pregnant • Reassure patient re concerns related to taking myasthenia gravis medications • Avoid drugs that can precipitate myasthenia gravis • Arthrogryposis in the fetus is rare but a well-recognized complication of maternal myasthenia gravis Delivery • In stable patients, plan spontaneous vaginal delivery • Assisted delivery may be required to prevent maternal exhaustion • The mother should take usual myasthenia gravis medications throughout labour • If the mother’s maintenance dose of prednisolone is

> “ 7.5 mg/day, the consensus is to give a stress dose of hydrocortisone 100 mg TDS intravenously in labour • Care with anaesthetic agents which can precipitate myasthenia gravis Baby • Transient neonatal myasthenia gravis is a well- recognized consequence of maternal myasthenia gravis and is independent of the severity of maternal myasthenia gravis • Presents within the first week of life • Occurs due to transplacental transfer of anticholinesterase receptor

(AChR) antibodies • Presents with hypotonia, poor sucking, or even respiratory muscle weakness. Treatment is usually supportive, but some may need pyridostigmine or even intravenous immunoglobulin • Its presentation does not correlate with the onset of myasthenia gravis later in life Fig. 14.12.1 Large right middle cerebral artery infarction on a computed tomography (CT) brain scan. Fig. 14.12.2 Magnetic resonance imaging (MRI) of the brain showing symmetrical bilateral hyperintense lesions in the posterior cerebral hemispheres, typically seen in posterior reversible vasoconstriction syndrome.

Section 14 Medical disorders in pregnancy 2646 Cerebral venous thrombosis Cerebral venous thrombosis accounts for approximately 20% of all strokes occurring in pregnancy and puerperium. It com- monly presents with headaches (can be thunderclap), focal neuro- logical deficit, low Glasgow Coma Scale, and seizures. Cerebral venous thrombosis can be diagnosed with an unenhanced CT (see Fig. 14.12.4), but MRI with magnetic resonance venography is the modality of choice during pregnancy as it can provide a detailed view of the cerebral venous system without any X-ray exposure and does not require administration of contrast. The treatment of cere- bral venous thrombosis involves anticoagulation, even if there is evidence of haemorrhage on the scan. Anticoagulation should be continued for a minimum of six months. Vascular malformations There are conflicting opinions as to whether pregnancy or delivery increases the risk of cerebral aneurysm or arteriovenous malforma- tion rupture. This is primarily due to paucity of evidence. Cerebral aneurysm In patients diagnosed with a ruptured aneurysm during preg- nancy, acute treatment should be offered during pregnancy as this leads to better outcomes. In pregnant patients with an unruptured aneurysm, the evidence suggests that there is not an increased risk of rupture during pregnancy or delivery. Recommendations re- garding delivery are difficult and decisions should be made on an individual patient basis. A caesarean section is not mandatory in patients with unruptured aneurysm. In our clinical practice, we would routinely avoid a prolonged second stage of labour in this group of patients and recommend assisted delivery, should the need arise. Similarly, pregnant women with treated cerebral an- eurysms should be encouraged to deliver vaginally without any specific considerations. Fig. 14.12.3 MRI brain and magnetic resonance angiogram (MRA) showing changes compatible with reversible cerebral vasoconstriction syndrome. Top row (left to right) shows MRI brain scan (coronal section) with hyperintensity in the sulci of the frontal lobes compatible with subarachnoid haemorrhage (solid arrow) and MRA reveals multifocal beading of the cerebral arteries (dashed arrows). The bottom row shows resolution of both these changes. (a) (b) Fig. 14.12.4 (a) Unenhanced CT head scan showing a hyperdensity in the superior sagittal sinus, suggestive of a thrombosis (solid arrow) with fragmented parenchymal haemorrhage seen in the left posterior temporal lobe (dashed line). (b) CT venogram showing a filling defect in the superior sagittal sinus, known as the ‘empty delta sign’ (arrow).

14.12 Neurological conditions in pregnancy 2647 Arteriovenous malformations Intracranial arteriovenous malformations are relatively uncommon but a recognized cause of catastrophic intracerebral haemorrhages. The evidence suggests that the risk of rupture in pregnancy is not increased. Furthermore, there are identified predictors of haemor- rhage, such as age, location, and deep venous drainage, and these can be useful for evaluating risk. Treatment of unruptured arteriovenous malformations should largely be restricted to outside of pregnancy. Treatment options include endovascular embolization, surgery, or stereotactic radiotherapy. In terms of the

issues surrounding labour, these are similar to those mentioned in the management of cere- bral aneurysms, and decisions should be made on an individual patient basis. Peripheral nerve disorders The most frequent examples of peripheral nerve disorders encoun- tered during pregnancy, labour, and the post-partum period are listed in Table 14.12.4. FURTHER READING Bove R, et al. (2014). Management of multiple sclerosis during preg- nancy and the reproductive years. Obstet Gynecol, 124, 1157–68. Bove RM, Kleim JP (2014). Neuroradiology in women of childbearing age. Continuum, 20, 23–41. Knight M, et al. on behalf of MBRRACE-UK (2017). Saving lives, improving mothers' care - lessons learned to inform maternity care from the UK and Ireland confidential enquiries into maternal deaths and morbidity 2013–15. National Perinatal Epidemiology Unit, University of Oxford, Oxford. Harden CL (2014). Pregnancy and epilepsy. Continuum, 20, 60–79. Macgregor EA (2014). Headaches in pregnancy. Continuum, 20, 128–47. Marsh MS, Nashef LAM, Brex PA (2012). Neurology and pregnancy. Informa Healthcare, London. Norwood F, et al. (2014). Myasthenia in pregnancy: best practice guide- lines from a UK multispecialty working group. J Neurol Neurosurg Psychiatry, 85, 538–43. Powrie RO, Greene MF, Camman W (2010). De Swiet's medical disor- ders in obstetric practice. Blackwell Publishing, Chichester. Wiles KS, et al. (2015). Reversible cerebral vasoconstriction syndrome: a rare cause of postpartum headaches. Pract Neurol, 15, 141–4. Table 14.12.4 Common peripheral nerve disorders associated with pregnancy Neuropathy Clinical presentation Treatment Bell's palsy (facial nerve) Asymmetrical facial droop (lower motor neurone) Short course prednisolone treatment, eye protection, and artificial tears Carpal tunnel syndrome (median nerve) Paraesthesia and pain in lateral side of hand and wrist, especially at night Overnight wrist splints. Some require local steroid injections or even decompression Meralgia parasthetica (lateral cutaneous nerve of the thigh) Numbness and pain over anterior, lateral aspect of the thigh. Improves with sitting and lying down Usually improves spontaneously but treatment options can include lidocaine patch or capsaicin cream Femoral neuropathy Weakness of the quadriceps (i.e. knee extension) and sensory loss anterior thigh and medial calf. Common mechanism of injury is excessive flexion of hip in lithotomy position Conservative management with physiotherapy and analgesia Recovery usually within three to four months Common peroneal nerve Foot drop, foot eversion weakness compared with inversion and sensory loss over the dorsum of foot and lateral aspect of shin. Can be precipitated by prolonged squatting or stirrups See treatment of femoral neuropathy Obturator nerve Weakness of hip adduction and sensory loss medial aspect of thigh. Usually precipitated during assisted delivery See treatment of femoral neuropathy

---

Revision #1
Created 2026-01-22 16:38:07 UTC by Omar Ayman
Updated 2026-01-22 16:38:07 UTC by Omar Ayman