



<b>Title</b>	<b>Neurological disorders in pregnancy</b>
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<b>Citation</b>	<b>Hong Kong Medical Journal, 1997, v. 3 n. 4, p. 400-408</b>
<b>Issued Date</b>	<b>1997</b>
<b>URL</b>	<b><a href="http://hdl.handle.net/10722/53402">http://hdl.handle.net/10722/53402</a></b>
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# Neurological disorders in pregnancy

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**Pregnant women can present with a wide variety of neurological conditions. Patient data from 1 January 1985 through 31 December 1994 for all deliveries at the Tsan Yuk and Queen Mary hospitals were reviewed to determine the local frequency of various neurological conditions during pregnancy. Conditions including epilepsy, eclampsia, facial nerve palsy, pituitary tumour, cerebrovascular disorders, myasthenia gravis, multiple sclerosis, and non-pituitary intracranial tumours were encountered, in descending order of frequency. The limitations of this retrospective analysis are acknowledged. This paper reviews the current concepts of these conditions and outlines appropriate management.**

*HKMJ 1997;3:400-8*

*Key words: Cerebrovascular disorders; Eclampsia; Epilepsy/drug therapy; Facial paralysis; Pituitary neoplasms*

## Introduction

Neurological and neurosurgical conditions are encountered occasionally during pregnancy, but serious neurological complications of pregnancy are rare. Nevertheless, the range of neurological conditions affecting women of reproductive age is extremely broad.<sup>1,2</sup> In this article, we present data on the incidence of various neurological conditions in a local obstetric population; the data were obtained by a retrospective review of all deliveries in the Tsan Yuk Hospital and the Queen Mary Hospital from 1 January 1985 through 31 December 1994. In addition, important concepts and recent advances in the treatment of these conditions are discussed.

## Subjects and methods

Patients were identified from the obstetric audit database of the Department of Obstetrics and Gynaecology, The University of Hong Kong, over the 10-year period, and the original records and/or microfilm were retrieved to confirm diagnoses and to extract information. Only conditions requiring medication or active intervention during pregnancy were included, whereas a past history of a neurological diagnosis per se and conditions not requiring treatment were excluded from further analysis. Statistical comparisons

were made using the Chi squared test with a probability level of 0.05 or below used to indicate significance.

## Results

The total number of deliveries during the study period was 49 368. One hundred and sixty-one patients had various neurological diagnoses, giving an incidence of 326 per 100 000 pregnancies. Table 1 summarises the various conditions and their incidence.

Epilepsy was the most common neurological condition encountered, affecting 102 patients (Table 1). These patients were maintained on antiepileptic medications throughout their pregnancies. Patients who had a past history of seizure or epilepsy and were

**Table 1. Incidence of various neurological conditions found in pregnant women attending the Tsan Yuk and Queen Mary hospitals from 1 January 1985 through 31 December 1994**

Condition	No.	Incidence per 100 000 pregnancies
Epilepsy	102	207
Eclampsia	19	39
Facial nerve palsy	12	24
Pituitary tumour	10	20
Cerebrovascular disorders	7	14
Myasthenia gravis	5	10
Multiple sclerosis	4	8
Non-pituitary intracranial tumour	2	4
<b>Total</b>	<b>161</b>	<b>326</b>

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**Table 2. Maternal and foetal complications found in epileptic and non-epileptic patients**

Maternal and foetal complications	Epileptic patients, n=102 No. (%)	Non-epileptic patients, n=49 266 No. (%)	P value
Antepartum haemorrhage	4 (3.92)	1566 (3.18)	ns
Gestational hypertension	5 (4.90)	2964 (6.02)	ns
Preterm delivery (<37 weeks)	12 (11.76)	6638 (13.47)	ns
Congenital malformations:			
- cardiovascular	3 (2.94)	430 (0.87)	
- cleft lip/palate	2 (1.96)	212 (0.43)	
- chromosomal abnormalities	1 (0.98)	87 (0.18)	
- multiple abnormalities	1 (0.98)	73 (0.15)	
- other*	0	759 (1.88) <sup>†</sup>	
Total	7 (6.86)	1561 (3.17)	ns
Neonatal death	1 (0.98)	252 (0.51)	ns

ns not significant

\*More than one other congenital malformation, not classifiable as 'multiple abnormalities'

<sup>†</sup>An additional 169 (0.34%) patients had more than one of the listed congenital malformations

not taking any medication were excluded. The anti-epileptic medications included phenobarbital, carbamazepine, sodium valproate, and phenytoin. It is impossible to interpret the quality of seizure control during pregnancy, because the frequency of seizures and drug compliance were not recorded systematically before pregnancy and because this group could represent a biased sample of epileptic patients who decided to become pregnant after achieving good control of their seizures. About 80% of these patients were seizure-free during pregnancy, and the rest had infrequent minor attacks in the antepartum period. One patient, who was not taking any antiepileptic medication during pregnancy, and two other patients with poor drug compliance had a seizure on the second day post-partum; antiepileptic medications were re-started and no further seizures occurred. Maternal and foetal complications occurred in 28% of these patients, but there was no significant difference between the incidences of various complications compared with those for non-epileptic women of the same cohort (Table 2). Congenital malformations were documented in 6.86% of deliveries by epileptic patients; there was no preponderance for cleft lip and/or palate (Table 2).

Eclampsia was the second most common neurological condition, affecting 19 patients (Table 1). During the study period, 2969 patients were diagnosed with gestational hypertension, and eclampsia developed in 0.64% of these patients. In 11 eclamptic patients, seizures developed before delivery, and the remainder had eclamptic seizures within 24 hours of delivery. Eclampsia was associated with one perinatal

and one neonatal death. Twelve patients had idiopathic facial nerve palsy. The nerve palsy occurred during the third trimester in five patients and in the early post-partum period in another five. There was no predilection for any particular side of the face; bilateral facial nerve palsy was not reported. All 10 patients with pituitary tumours had prolactinomas. Bromocriptine was given to these patients because two had a macroadenoma. The remainder were re-started on bromocriptine because of progressive symptoms such as headache, recurrent vomiting, and deteriorating visual fields. One patient had progressive enlargement of her tumour during the third trimester despite medical therapy, and required a simultaneous transphenoidal resection of tumour and caesarean section near term. None of the babies born to these mothers had congenital anomalies.

Table 3 shows the history and results for seven patients who had cerebrovascular disorders while pregnant. The first two patients received special attention during pregnancy and intensive monitoring during delivery because of a prior history of subarachnoid haemorrhage; they both had a good outcome. The remaining five patients had an intracranial haemorrhage during pregnancy and had variable outcomes. Causes of these intracranial haemorrhages included a vascular malformation, an aneurysm, or the use of anticoagulant medication.

Five patients with myasthenia gravis were pregnant in this series. All were carefully monitored throughout their pregnancies with continuation of pyridostigmine bromide, and their pregnancies, labour, and

**Table 3. Cerebrovascular disorders complicating pregnancy**

Patient	Condition	Treatment	Outcome
1	Past history of SAH* due to an arteriovenous malformation; post-SAH epilepsy	Antiepileptic medications; elective caesarean section at term	Good
2	Past history of SAH due to a frontal parasagittal arteriovenous malformation	Regular neurological surveillance; cranial MRI†; elective caesarean section at term	Good
3	IVH‡ due to corpus callosal arteriovenous malformation at 15 weeks' gestation	Right parietal craniotomy; external ventricular drainage; right frontal ventriculostomy at 15 weeks' gestation; antiepileptic medication; elective caesarean section at term	Good; minimal residual neurological deficits
4	SAH at 24 weeks' gestation	Prolonged mechanical ventilation	Preterm labour at 30 weeks' gestation with stillbirth; vegetative state postpartum
5	SAH due to a cerebral aneurysm at 18 weeks' gestation	Craniotomy with clipping of the aneurysm at 19 weeks' gestation; elective caesarean section at 36 weeks for breech and previous cerebrovascular haemorrhage	Good; minimal residual deficit
6	Left occipito-parietal haemorrhage after caesarean section under general anaesthesia; mitral valvular replacement with heparin in the peripartum period	Conservative; temporary cessation of anticoagulation	Complete recovery
7	Chronic rheumatic heart disease with mitral valvular replacement; subcutaneous heparin in first trimester; spontaneous subdural haematoma at 11 weeks' gestation	Craniotomy and drainage of subdural haematoma	Prolonged vegetative state on artificial ventilation; succumbed at 18 weeks' gestation with pregnancy in situ

\*SAH subarachnoid haemorrhage

†MRI magnetic resonance imaging

‡IVH intraventricular haemorrhage

deliveries were uneventful. None of the babies had neonatal myasthenia gravis. Three patients who were known to have multiple sclerosis became pregnant, and a fourth patient developed right-sided optic neuritis as the presenting symptom of multiple sclerosis at 30 weeks' gestation. Table 4 summarises the salient features of these four patients, including the presenting symptoms, symptoms in the antenatal and post-partum periods, and outcomes of the neonates. Two of the three patients who were known to have multiple sclerosis experienced a relapse during the third trimester, but their symptoms improved in the post-partum period. Two patients with non-pituitary intracranial tumours were seen. One patient, who presented with

sudden collapse, had a craniotomy and resection of her left frontal glioma at 29 weeks' gestation. Subsequently, she had an uneventful lower segment caesarean section at 34 weeks' gestation. Another patient, who had a left optic nerve meningioma and visual loss, had a tumour resection after the labour and delivery had been completed.

## Discussion

The data reflect the experience in a major district obstetric hospital (the Tsan Yuk Hospital) and a related tertiary referral unit for high-risk pregnancies (the Queen Mary Hospital). Retrospective analyses of

**Table 4. Multiple sclerosis complicating pregnancy**

Patient	Presenting symptom	Symptoms in antenatal period	Symptoms in post-partum period	Neonatal outcome
1	Bilateral lower limb weakness	Bilateral blurring of vision in third trimester	Visual symptoms improved	Good
2	Bilateral lower limb weakness	Bilateral optic neuritis and urinary retention in third trimester	Visual and urinary symptoms improved with increased steroid dosage	Good
3	Bilateral lower limb weakness	Stationary during pregnancy, otherwise ambulatory	Stationary	Prelabour ROM* at 34 weeks' gestation; LSCS† for foetal distress; mild IUGR‡
4	Right optic neuritis at 30 weeks' gestation	Condition improved with steroids	Neuropathic bladder requiring prolonged catheterisation	Good

\*ROM rupture of membranes

†LSCS lower segment caesarean section

‡IUGR intrauterine growth retardation

the data and the selection bias of the obstetric cases seen at these two hospitals did not permit an accurate determination of the local incidence of various neurological conditions at pregnancy.

### **Epilepsy**

Epilepsy is a common neurological disorder characterised by a tendency to develop recurrent seizures.<sup>3</sup> Epidemiological studies have suggested that about 7% of epileptic females become pregnant during their lifetime and that approximately 0.5% of all pregnancies are complicated by epilepsy<sup>4</sup>; 0.2% of patients had epilepsy in this report. Our figure is low because patients who had a previous history of epilepsy but were not on any antiepileptic medication were not included in our analysis. As patients may not volunteer a remote history of epilepsy, a prospective study is needed to provide an accurate figure. Knight and Rhind report that the control of epilepsy during pregnancy becomes worse in 45% of patients, is unchanged in 50%, and improves in 5%.<sup>5</sup> Four recent studies show that a majority (60% to 83%) of pregnant epileptic patients experience no significant change in seizure frequency, but changes in seizure frequency are unpredictable in individual patients.<sup>6</sup> Poor seizure control prior to pregnancy is associated with an increased seizure frequency during pregnancy.<sup>5,6</sup> The pathophysiological factors responsible for increased seizure frequency during pregnancy include hormonal changes, pharmacokinetic alterations, use of folate supplementation, metabolic changes, sleep deprivation,

non-compliance with antiepileptic medications, and stress and anxiety.

Oestrogens have been shown to be epileptogenic in both animal and human studies while gonadotropins reduce the seizure threshold in animals. Conversely, progesterone has antiepileptic effects in both animals and humans.<sup>6</sup> Thus, elevated in plasma oestrogen, a high plasma oestrogen to progesterone ratio, and increased serum chorionic gonadotropin levels may account for the increased seizure frequency seen in the first trimester.<sup>7</sup> In addition, the natural alterations in the ratio between oestrogen and progesterone that occur during the menstrual cycle are responsible for catamenial epilepsy i.e. affected epileptic women have increased seizure frequency prior to and during menstruation and at ovulation, but have infrequent attacks in the mid-luteal phase.<sup>8</sup>

Pharmacokinetic changes arise during pregnancy that result in a steady decline in both the total and free serum levels of all anticonvulsants, except for free valproic acid which may increase.<sup>9</sup> This decline in serum levels is caused by many factors, including a larger volume for drug distribution, reduced plasma protein binding, decreased albumin concentration, increased renal clearance, hepatic microsomal enzyme induction, and impaired intestinal absorption. The total, and preferably, the free serum levels of anticonvulsants should thus be monitored throughout pregnancy and the puerperium.

Folate supplementation before and during pregnancy is becoming a routine practice to reduce the risk of major congenital malformations. In theory, folate supplementation may lower the serum phenobarbital and phenytoin levels, but supportive evidence for this is lacking.<sup>6</sup> Pregnancy is associated with weight gain, water and sodium retention, hypomagnesaemia, and other metabolic changes. The contribution of these changes to increased seizure frequency during pregnancy remains unresolved.

Sleep deprivation reduces the seizure threshold and is occasionally used before electroencephalographic recording to provoke epileptiform discharges.<sup>6</sup> Insomnia from physical and psychological causes is common during pregnancy. Drug compliance is a common problem of all chronic diseases. Schmidt and colleagues report that sleep deprivation or non-compliance was temporally associated with seizures in 34 of 50 women during their pregnancies and in five of six women in the puerperium.<sup>10</sup> Well-intentioned non-compliance is common, because of the fear of teratogenicity.<sup>11</sup> Stress and anxiety also increase the risk of seizures and may contribute to poor seizure control during pregnancy.

Epilepsy is associated with mental retardation, lower socioeconomic status, unemployment, lower marital rates, and reduced fertility.<sup>6</sup> Oral contraceptives interact with antiepileptic medication so that rates of contraceptive failure are higher, and a larger dose of antiepileptic medication may be required. Offspring of epileptic mothers have an approximately three times greater risk of developing seizures, whereas offspring of epileptic fathers have no greater risk.<sup>12</sup> Although genetic counselling is advisable, the genetic transmission of epilepsy should not be overstated. Uncontrolled seizures during pregnancy are dangerous to both the mother and foetus. Tonic-clonic seizures can cause physical injury and abruptio placentae in the mother and hypoxia, acidosis, intracranial haemorrhage, and death in the foetus.<sup>6</sup> Thus, a balance should be achieved between maternal seizure control and potential foetal teratogenicity. There seems to be a residual effect from antiepileptic medication, as studies have revealed a higher risk of teratogenicity in epileptic women taking antiepileptic medication when compared with untreated epileptic pregnant women.<sup>13</sup> The highest incidence of congenital abnormalities has been found in babies exposed to multiple antiepileptic medications in utero.<sup>4,14</sup> In addition, babies of epileptic fathers are at risk of congenital malformations.<sup>13,15</sup> The relative teratogenicity of many commonly prescribed antiepileptic medications has not been resolved with

certainty, and no antiepileptic medication is free of this side effect.<sup>6,16</sup> Although some authors report a low teratogenic risk for phenytoin,<sup>17</sup> the foetal hydantoin syndrome is well recognised. Trimethadione should be avoided in pregnancy and in women of reproductive age, as the incidence of spontaneous abortion and congenital malformations is as high as 37%.<sup>18</sup> A prospective study reports that carbamazepine is associated with developmental delay, craniofacial defects, and fingernail hypoplasia in 20% of exposed children.<sup>19</sup> Spina bifida was found in 1.5% of foetuses exposed to sodium valproate during the first trimester;<sup>20</sup> and this drug should be avoided in those with a family history of neural tube defects. Although phenobarbital crosses the placenta and may cause foetal sedation and neonatal withdrawal syndrome, it probably has the least teratogenicity potential.<sup>6</sup> In general, major congenital malformations occur in 4% to 6% of children born from epileptic mothers,<sup>14,16</sup> which is similar to the results of this review (6.86%) [Table 2].

The principles of management are as follows<sup>6,21,22</sup>: (1) female epileptic patients of reproductive age should be educated on the risks associated with pregnancy; (2) the diagnosis of epilepsy should be definite, and the need for continued antiepileptic therapy should be evaluated before conception occurs; (3) mono-therapy is preferred, the least number of drugs at the lowest effective dose should be used, and new anti-epileptic medications should be avoided. After conception, adjustments in medication offer no benefit but may increase the risk of seizure; (4) the pre-conceptual use of multivitamins and folate is beneficial. During pregnancy, attention should be directed to factors that reduce seizure control and the monitoring of anticonvulsant levels is needed. Free drug levels are preferred in difficult cases; and (5) following delivery, dosage adjustment is needed especially in lactating mothers. The assessment of infants and children of epileptic mothers for long-term complications and developmental delay is advisable.

### ***Eclampsia***

Pre-eclampsia or toxæmia gravidarum is a complex disorder with pregnancy-induced hypertension, proteinuria, and oedema developing after 20 weeks of gestation. Eclampsia, a life-threatening complication of gestational hypertension with high maternal and perinatal mortality, is diagnosed when seizure or coma occurs in a pre-eclamptic patient.<sup>23</sup> Eclamptic seizures, which may be focal motor or generalised tonic-clonic, usually appear within the first 24 hours postpartum. The underlying causes for pre-eclampsia and eclampsia remain unknown, but abnormal immu-

nological interactions between foetal and maternal tissues are involved.<sup>24</sup> The neuropathological changes in eclampsia include diffuse cerebral oedema, subarachnoid haemorrhage, subcortical haemorrhage, small haemorrhages, and microinfarctions at several levels of the neuraxis.<sup>23</sup> Many eclamptic patients have visual symptoms secondary to pathophysiological changes in the eye or visual cortex, and cerebral vasospasm may be responsible.<sup>25</sup> Metabolic or hypertensive encephalopathy may also contribute to the pathogenesis of eclampsia.

In severe pre-eclampsia and eclampsia, immediate delivery of a viable baby and maintenance of maternal health are the therapeutic goals.<sup>23</sup> Thus, treatment strategies include control of arterial blood pressure within the range of cerebral autoregulation, reduction of cerebral oedema, and rapid control and prevention of seizures. Use of magnesium sulphate is popular in pre-eclampsia and eclampsia, even though this salt has no proven anticonvulsant effect. Ongoing seizures should be aborted with intravenous diazepam, and phenytoin or chlormethiazole may prevent recurrent seizures. An intravenous loading dose of phenytoin at 20 mg/kg may be followed with daily maintenance. Neurological referral is advisable for the management of seizures and cerebrovascular events.

#### ***Cranial and peripheral neuropathies***

Idiopathic facial nerve palsy or Bell's palsy is common at all ages. The annual incidence is 17 per 100 000 in women of reproductive age and 38 to 45 per 100 000 during pregnancy and the post-partum period.<sup>26,27</sup> When facial nerve palsy is associated with pregnancy, 75% of the cases are seen in the third trimester and early post-partum period,<sup>28</sup> which is in accordance with the present results. Bell's palsy is rarely bilateral or recurrent in non-pregnant patients, but recurrence during successive pregnancies and bilateral facial nerve palsy in pregnant women have been described. The prognosis for recovery is excellent, and a 10-day course of steroids at 40 mg to 60 mg daily is safe during pregnancy.<sup>26</sup>

Lumbosacral radiculopathy or plexopathy and femoral, tibial, lateral femoral cutaneous, obturator, and peroneal neuropathies may occur during pregnancy and delivery.<sup>27</sup> Abdominal neuropathies, carpal tunnel syndrome, neuralgic amyotrophy, and chronic inflammatory demyelinating polyneuropathy are associated with pregnancy, whereas Guillain-Barré syndrome occurs randomly, irrespective of pregnancy. These neurological disorders were not seen in this review. Diagnosis is based on clinical assessment plus

appropriate neuroelectrophysiological tests. The management varies according to the diagnosis.

#### ***Pituitary tumours***

The most common type of pituitary tumour in women of reproductive age is the prolactinoma, which typically causes amenorrhoea, galactorrhoea, and infertility.<sup>29</sup> Most prolactinomas are microadenomas confined within the sella turcica, but occasionally they become macroadenomas and compress the optic chiasma and other neighbouring structures. Magnetic resonance imaging (MRI) of the head is preferred to computed tomography (CT) to visualise pituitary tumours. As hyperprolactinaemia suppresses ovulation, pregnancy is associated with prolactinomas that have responded to ergoline drugs such as bromocriptine or pergolide. Empirical data do not suggest any increased risk for abortion or congenital malformations after using these ergoline drugs during pregnancy.<sup>30</sup> The common practice is to stop these drugs when pregnancy is confirmed in patients with microadenomas. Most patients have an uneventful pregnancy while not taking any medication.<sup>31</sup> Unfortunately, a few patients have a recurrence of symptoms or new complaints during their pregnancies. In fact, the normal pituitary gland enlarges in pregnancy and hyperplasia of prolactin-secreting cells occurs.<sup>32</sup> This latter group is represented in this report by eight of the 10 patients with prolactinoma. Under these circumstances, ergoline treatment should be continued with regular monitoring of visual fields, visual acuity, and other neurological signs during pregnancy. Surgical resection is reserved for those with severe or progressive clinical features despite adequate medical treatment having been given.<sup>29</sup> Our results overemphasise the need to continue ergoline treatment during pregnancy because patients who had a past history of prolactinoma but did not require treatment during pregnancy were excluded. This exclusion was necessary because of the inconsistent entry of such histories in the database.

#### ***Cerebrovascular disorders***

Pregnancy increases the risk of a cerebrovascular event.<sup>33,34</sup> The risk of bleeding from arterial aneurysms and arteriovenous malformations is increased during pregnancy. Haemodynamic, haematological, and cardiovascular changes of pregnancy are associated with arterial and venous thrombosis, arterial embolism, and intracerebral haemorrhage. As indicated above, eclampsia carries an additional risk of cerebral infarctions and haemorrhage.<sup>23</sup> Subarachnoid haemorrhage predominated in this study, and cerebral infarction and cerebral venous thrombosis were not observed. In general, a neurological consultation is indicated, CT

or MRI of the head is needed, and appropriate management should be offered depending on the diagnosis and assessment.<sup>33,34</sup>

Non-traumatic subarachnoid haemorrhage is caused by the rupture of berry aneurysms and arteriovenous malformations in most cases.<sup>34</sup> Rarely, haematological disorders, bacterial endocarditis, and metastatic choriocarcinoma are responsible. The risk of aneurysmal bleeding increases with the duration of pregnancy and so most haemorrhages occur in the third trimester; re-bleeding is a risk during labour.<sup>34-36</sup> In contrast, arteriovenous malformations bleed more often during the second trimester or during labour. Patients with subarachnoid haemorrhage who are comatose on presentation are likely to die, and patients surviving an initial bleed may succumb to re-bleeding.<sup>34</sup> Computed tomography of the head or lumbar puncture is diagnostic, and four-vessel cerebral angiography is indicated.<sup>33</sup> Nimodipine may be used despite a lack of scientific data supporting its use in pregnant women. Neurosurgical referral and definitive treatment of the underlying cause are crucial. An elective caesarean section is often used to deliver the baby near term.

Intracerebral haemorrhage is a rare but serious disorder in pregnancy with an associated mortality rate of 40% to 50%.<sup>37</sup> The differential diagnoses are venous infarction or haemorrhagic transformation of arterial infarction. The causes are the same as in non-pregnant patients, and include hypertension, arteriovenous malformations, anticoagulation treatment, bleeding disorders, and brain tumours. Management depends on the underlying cause and size of the haematoma.

Both transient ischaemic attacks and ischaemic stroke occur five to 10 times more commonly during pregnancy and the puerperium than they do in non-pregnant women of the same age.<sup>33,34</sup> The risk is probably highest in the first week post partum. Atherothrombosis, cardioembolism, artery-to-artery embolism, hypercoagulability, haemodynamic disturbances, and other rare causes are responsible. Specific treatment should be offered to deal with any underlying cause and associated stroke risk factors. Low-dose aspirin is safe during pregnancy. Coumadin is teratogenic and should be avoided before conception and during the first trimester; heparin is the anti-coagulant of choice during pregnancy despite being inconvenient.

Cerebral venous thrombosis is a rare type of stroke associated with the puerperium<sup>33,34,38</sup>; the cause is unknown in most cases. Magnetic resonance imaging and angiography are the preferred diagnostic tests. The

clinical presentations depend on the site and severity of the bleed, but headache, focal neurological signs, and focal seizures are common. Anticoagulation for 2 to 3 months is the popular treatment despite the absence of any supporting evidence.

### ***Myasthenia gravis***

Myasthenia gravis is a rare disorder with fluctuating fatiguability of skeletal muscles and unpredictable exacerbations and is occasionally seen in pregnancy because this chronic disease is twice as common in females and has a peak incidence in the reproductive years.<sup>27</sup> The neuromuscular block is caused by an autoimmune mechanism, and anti-acetylcholine receptor antibody is detectable in 90% of affected patients.<sup>39</sup> Antistriated muscle antibody is associated with an underlying thymoma. In the pre-thymectomy era, one third of myasthenic patients deteriorated during their pregnancies, one third had their health unchanged, and one third improved.<sup>27</sup> In addition, the disease course for any one pregnancy does not predict the course during subsequent pregnancies. Exacerbations are common in the first few weeks post partum.

Thymectomy is indicated for thymoma and is recommended in all young myasthenic patients who have a deteriorating response to an anticholinesterase drug.<sup>27,39</sup> The thymoma should be resected prior to a planned pregnancy; otherwise the tumour becomes more aggressive or develops metastases during pregnancy. Steroid-sparing immunosuppressants such as azathioprine should be discontinued prior to pregnancy owing to the risk of teratogenicity.<sup>27</sup> Corticosteroid therapy also poses a risk to both the mother and the foetus. The oral or intramuscular administration of quaternary ammonium compounds such as pyridostigmine and neostigmine is safe as there is little passage through the placenta. Magnesium sulphate, aminoglycosides, and muscle relaxants may cause a myasthenic crisis and should be avoided. Although myasthenia gravis can present initially in pregnant patients and the control may become poor during pregnancy, early termination of the pregnancy is neither necessary nor beneficial.<sup>27</sup> Aggressive treatment with plasmapheresis throughout pregnancy and thymectomy in the second trimester can result in favourable outcomes.<sup>40</sup> As the IgG type anti-acetylcholine receptor antibodies can cross the placenta, all neonates born of myasthenic mothers should be evaluated for transient symptoms and signs of neonatal myasthenia and respiratory distress.<sup>27</sup>

### ***Multiple sclerosis***

Multiple sclerosis is a multifocal demyelinating dis-



ease of the central nervous system characterised by remissions and relapses, resulting in white-matter lesions that are disseminated in space and time.<sup>29,41</sup> The incidence of multiple sclerosis is 8.8 per 100 000 in the Hong Kong Chinese population<sup>42</sup>; this incidence is low when compared with western populations or other Asian populations.<sup>43</sup> At onset, 65% of patients have a relapsing/remitting course, 15% have relapsing/progressive disease, and 20% have a chronic progressive form.<sup>41</sup> The underlying cause remains unknown, but immunological factors are involved.<sup>44</sup> A short course of steroids may shorten the acute relapse but this has no effect on the relapse rate nor the prognosis. Otherwise treatment is largely supportive; use of immunosuppressants is empirical.<sup>41,45-47</sup> Recent data indicate that long-term use of  $\beta$ -interferon can reduce the clinical relapse rate and the disease activity as seen by MRI.<sup>46,47</sup>

Multiple sclerosis does not affect fertility or the course and outcome of pregnancy, labour, and delivery.<sup>29,48</sup> In addition, carefully designed studies have failed to show that pregnancy can cause multiple sclerosis or precipitate its onset. On the other hand, the disease activity is modified during pregnancy. Most studies report an antepartum decrease in disease activity and an increase in relapse rates post partum.<sup>49</sup> The latter also applies to myasthenia gravis and other autoimmune diseases. Thus, the overall relapse rate remains unchanged.<sup>29,48</sup> If a relapse is encountered during pregnancy, a course of corticosteroids may be given. The safety of  $\beta$ -interferon during pregnancy has not been established.

### ***Non-pituitary intracranial tumour***

Apart from pituitary tumours, all other types of intracranial tumour have been reported during pregnancy. Gliomas, meningiomas, and acoustic neuromas predominate in descending order of frequency, but only choriocarcinomas are specifically associated with pregnancy.<sup>29</sup> In general, intracranial tumours enlarge during pregnancy owing to the associated physiological changes, and regression may follow delivery. Receptors for sex steroids are found in meningiomas, neurofibromas, and some gliomas. Diagnosis is based on the clinical features and the characteristic findings on CT or MRI of the head. Management varies according to the type of intracranial tumour.<sup>29</sup> A neurosurgical consultation is indicated. Therapeutic or prophylactic anti-epileptic medications are useful. Corticosteroids improve the vasogenic oedema. Regular monitoring of symptoms, signs, and tumour size is crucial in planning treatment such as surgery, chemotherapy, and radiotherapy.

### ***Other neurological conditions***

Other neurological conditions that may be seen during pregnancy were not observed in our local obstetric population during the period of review. Headaches are extremely common in women, irrespective of pregnancy.<sup>50</sup> Common benign causes include migraine, tension headache, and acute sinusitis. Symptomatic headache occurs in subarachnoid haemorrhage, intracerebral haemorrhage, cerebral venous thrombosis, benign intracranial hypertension, and intracranial tumour.

Movement disorders occur infrequently during pregnancy.<sup>51</sup> Restless leg syndrome is the most common movement disorder and is characterised by a crawling, burning, or aching sensation in the calves, with an irresistible urge to move the legs. In general, this syndrome presents during the second or third trimester and resolves following delivery. Benzodiazepam, clonazepam, levodopa/carbidopa, and codeine are often used to relieve symptoms. Chorea gravidarum is not a distinct condition but refers to chorea of any cause starting in pregnancy. Major causes are Sydenham's chorea, systemic lupus erythematosus, and neuroleptic-induced chorea. Less common causes include hyperthyroidism, Wilson's disease, cerebrovascular disorders, and meningovascular syphilis.<sup>51</sup>

Many connective tissue disorders preferentially affect young women of reproductive age.<sup>52</sup> Although neurological manifestations are seen in these disorders, there is no increased frequency during pregnancy. Management depends on the underlying diagnosis and the neurological manifestation.

### **Conclusion**

Many different neurological conditions may be encountered during pregnancy, whereas only eight types were seen in our review of a local database. Epilepsy is the most predominant condition. Effects of the condition and its treatment on pregnancy and the effects of pregnancy on the condition and its treatment should be kept in mind when dealing with these conditions in pregnancy. Appropriate management, preferably under the joint care of obstetricians, neurologists, neurosurgeons, and paediatricians in established centres, will ensure successful foetal and maternal outcomes.

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