CHAPTER 1
The history and examination

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Introduction
The focus of this chapter will be on the information most helpful to understand, counsel, and treat female neurology patients in their reproductive years. The key elements of the neurologic history and examination will be systematically reviewed with emphasis on gender differences. It will conclude with a few clinical cases. The goal is to enable neurologists to develop the knowledge and skills to maximize care for their female patients with regard to family planning and pregnancy. The objective of this chapter is to help physicians to perform a history and examination that focuses on and identifies the specific family planning concerns of the female patient and how these concerns relate to their neurologic disease.

Many common neurological diseases preferentially affect young women. How we, as neurologists, approach treatment depends on our patients’ needs at that point in her life cycle. This is different for each disease process.

Migraine is a very common disorder with lifetime prevalence in women of up to 25%. Because of hormonal influences, the ratio of affected women over men is 3:1 [1]. The history should include usual triggers, of which menses and ovulation are common. Birth control pills (BCPs) have a variable influence on migraine frequency and in some women may aggravate the disorder [2]. However, many women with menstrual headaches report that cycle suppression (which can be obtained using the subdermal implant, injectable contraception, a pill, patch, or ring) improves their symptoms. The type of migraine is important when discussing contraception. Women with classic migraines should be counseled to avoid estrogen-containing contraceptives (e.g., the pill, patch, or ring), given the increased risk of ischemic stroke. However, common migraine does not preclude use of estrogen-containing contraceptives unless associated with other cerebrovascular risk factors such as an underlying hypercoagulable state. [3] Furthermore, when choosing medications (abortive or prophylactic), you should take into account, whether the woman are trying to get pregnant, or, if not trying to conceive, what birth control they are utilizing. For instance, topiramate in doses above 200 mg/day may reduce the effectiveness of oral contraceptives [4]. Does the patient have regular menses? Could she have polycystic ovarian syndrome? If so, Valproate would not be a good choice as a prophylactic medication [5]. Another concern with patients already predisposed to obesity is that many prophylactic medications can contribute to weight gain.

Multiple sclerosis is another example of a neurologic disease that affects women in their childbearing years [6]. Many of these patients are on an immunomodulatory medication. Interferons are pregnancy class C, copaxone pregnancy class B, and methotrexate a pregnancy class D medication. Because immunomodulatory
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medications are not recommended during pregnancy, birth control should be discussed if the woman is not planning pregnancy. What should we recommend to our patients who would like to become pregnant? They should discontinue their immunomodulatory medication when they discontinue their hormonal or intrauterine contraceptive, as the only contraceptive that typically delays return to fertility is depot medroxyprogesterone acetate. They should be counseled that pregnancy does not worsen overall MS disability. Treatment needs to be appropriately adjusted to best address our patient’s needs at each particular point in her life cycle.

Past medical history

Patients’ medical background allows us to frame a more accurate diagnosis for their current complaints. The disorders from which women suffer are different from those that affect men. A woman’s reproductive desire adds an additional layer of complexity. The medical illnesses more common in women influence which is the most probable neurologic disorder. The following is a brief snapshot of some of the disorders that are more prevalent or occur exclusively in women and how that shapes their care.

The psychiatric problems of depression, anxiety, and borderline personality disorder are more frequent in women. Thus, their neurological problems may be a consequence of somatization, conversion, or have an overlay due to these conditions. These women are at risk for over testing and noncompliance, as well as poor maternal weight gain, poor infant bonding, substance abuse, and postpartum depression. The medications we choose need to take these factors into account.

Autoimmune disorders also affect women more frequently. They may have neurologic complications directly due to their rheumatologic problem, like lupus flares. In addition, their neurologic problem may be due to a result of an underlying hypercoaguable state or as a consequence of their immunosuppressant medications. The recommendations and concerns for these women during pregnancy are highly specialized.

Cardiovascular concerns are important though they are uncommon in premenopausal women. Although estrogen before the menopausal transition is likely protective against cardiovascular disease, we cannot ignore women with a strong family history of vascular disease especially if associated with other risk factors such as tobacco use and migraines. These women do suffer from cardiovascular complications and need advice about risk factor modification. Women with congenital or acquired cardiac disease will need specialized care to appropriately manage the physiologic changes that occur during pregnancy and labor.

An obstetrical and lactation history is extraordinarily important. The number of pregnancies, the gestational stage of the current pregnancy, and the history of either planned or spontaneous abortions predict which obstetrical and neurological diseases are most likely. These factors also determine how, if necessary, to image and what medications are appropriate. For instance, the association with antiphospholipid antibody syndrome and spontaneous miscarriages is well established. A history of eclampsia should be sought. There is good evidence that prior eclampsia predicts eclampsia in future pregnancies as well as increases risk of future maternal hypertension. Other obstetrical issues such as preterm premature rupture of membranes and placenta previa should be asked about directly as these patients are predisposed for recurrence in future pregnancies. A woman with a history of recurrent fetal loss needs an obstetrical referral to help planning/monitoring in future pregnancies.

Bone health is often neglected. The medications we choose should reflect this concern. In addition, many neurologic patients’ disability may limit weight bearing. It is
Table 1.1 Drugs that may have adverse effects on bone metabolism

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<td>Warfarin</td>
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<td>Medroxyprogesterone acetate</td>
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<td>Thiazolidinediones</td>
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<td>Antiretroviral therapy</td>
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important to be aware of the effects of medication on bone health; as the long-term use of many medications increase the risk of osteoporosis [22] (see Table 1.1). Examples of commonly used medications that promote bone loss include the anticonvulsants, phenytoin, and carbamazepine. Counseling about the benefits of exercise as well as recommending daily calcium and vitamin D intake is helpful to avoid these complications.

A history of an underlying hypercoaguable disorder is an extremely important historical data in pregnancy planning. During pregnancy there is an increase in factors I, II, VII, VIII, IX, and X as well as a decrease in protein S. The net result is that normal pregnancy is a hypercoaguable state. If a woman has a preexisting hypercoaguable disorder, her chance of having a clotting complication is high and anticoagulation during her pregnancy should be recommended [23].

Surgeries such as those involving the lower spine may make epidural anesthesia more challenging or complicated. For example, a lumbar peritoneal shunt depending on the location may preclude an epidural. Other patients with severe scoliosis, obesity, or lumbar fusion may make neuroaxial anesthesia challenging. A personal or family history of anesthetic complications is an additional historical piece to be obtained. A prior history of postdural headache should be inquired about as this increases a patient risk for recurrence [24]. Anything that would make the patient at risk for anesthesia should warrant an early consult to an obstetrical anesthesiologist.

**Medication considerations**

Contraception is a topic that neurologists tend to neglect. It is important to provide patients with recommendations on which contraception options are most appropriate. The most effective contraceptives are the subdermal implant and intrauterine contraceptives, which have been estimated to be 20 times as effective as oral contraceptives and surgical sterilization. There is a myriad of contraceptive choices and they are generally chosen due to personal preference, efficacy, and safety. In our patients, efficacy may be affected by medication interactions (e.g., topiramate) or at times disability. For instance, young women whose disability involves the spinal cord may not be good candidates for certain barrier methods of contraception due to difficulty in positioning or with peroneal sensory loss. In other women, certain types of contraception are contraindicated by safety concerns. For women who have had a stroke, significant cardiovascular risk factors, an underlying hypercoaguable state, and migraine with aura, combined estrogen-containing pills, patch, or ring are not recommended [3]. However, progestin-only methods including the subdermal implant, intrauterine contraceptive, the injectable contraceptive,
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or progestin-only pills (e.g., Micronor) are safe.

When choosing to prescribe medications to women of childbearing age, it is important counsel the patient on risks and benefits of treatment. We are prescribing medications to young women who may or may not be planning on pregnancy at the time of consultation. Knowledge of the pregnancy class of the medication prescribed and what that means to your patient is essential in order to counsel them on the risks of taking that medication during pregnancy and what to do with the medication if they get pregnant. The Mother to Baby website (www.mothertobaby.org) and hotline is a useful source for information on medication use during pregnancy; free information on medication use during lactation is available from Lactmed (http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?LACT). Is there any influence of the medication on their method of birth control? Should they be taking higher doses of folate (e.g., 5 mg/day)? The potential effect of in vitro fertilization on the underlying neurological disease may need to be discussed especially for women with migraines [25]. The effects of medication on the long-term gender-specific health issues such as weight and bone health should also be considered.

The issues around fertility are complex. What are the potential risks of fertility treatment? Are there alternatives? The available options for these women require discussion, planning, and individualization for best care. A number of medications may affect fertility. The mechanisms are diverse, but weight gain is the most common. Additional weight contributes to the metabolic syndrome and polycystic ovarian syndrome. In addition, to weight gain, valproate may also influence androgen levels making contraception more problematic [26]. It has also been associated with neural tube defects. Therefore, if there is a reasonable alternative medication that controls the neurological disorder in women of childbearing age that would be preferred.

**Family history and genetics**

Family history is a critical component to the history. It tells us which disease processes are likely, so we can appropriately screen and counsel patients to minimize risk. Women with a strong family history of coronary artery disease, hypertension, or diabetes need to be made aware of increased risk of vascular disease associated with obesity, sedentary life style, smoking, and estrogen. Pregnancy may add to risk factors.

Do they have a genetic disorder? What is the mode of inheritance? Is there a reliable genetic test? These are important factors to help women make informed decisions about pregnancy. The more information the patients have the better equipped they are to make appropriate choices. It is a mistake to assume a patient understands the disease, simply because it runs in their family. For example, a young woman presented to clinic with a family history of maternal Huntington’s disease. Her mother had tested negative. She did not understand that she was not at risk for inheriting the disorder. Knowledge is a powerful tool.

**Habits**

The habits (good and bad) that women employ before and during pregnancy affect their cardiovascular risk. During pregnancy, these risks are magnified. Moreover, it is hard to over emphasize the benefits of exercise on managing stress, weight, depression, and sleep. The effects on heart and brain health are well documented. Barriers for routine monitoring including health screening like mammograms and Pap smears need to be recognized. These may be cultural, socioeconomic, or driven by the patient’s disability. For example, consider a patient with multiple sclerosis who attempted to obtain a gynecologic examination. If she is paraplegic, she may be unable to transfer onto her internist’s examination table.
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Review of systems

A review of systems there should include special attention to a number of issues for female patients. Are they at their ideal weight? Has there been weight loss or gain? Their weight influences their risks, as well as what medications should be chosen or avoided. Obesity increases the risk for gestational diabetes, hypertension, and eclampsia [27–29]. Irregular menses may indicate an underlying hormonal imbalance, influence fertility, and determine which medications are most appropriately employed. Menorrhagia and iron deficiency are common problems in young women that can be effectively treated with use of the levonorgestrel-containing intrauterine system. Iron deficiency is often compounded during pregnancy exacerbating conditions such as restless leg syndrome. Breast masses or discharge are key elements/components that deserve to direct query of our female patients.

Examination

Gender does not affect the neurologic examination. The areas on which to focus are determined by the patient’s history. The history of the present illness, medical background, and physiologic state of the woman allows the physician to generate a list of the most likely possibilities. The findings on examination help to narrow and/or confirm this differential. The most important elements of the medical examination include blood pressure and weight. The other necessary pieces of the medical examination are patient-specific and dependent on the history.

Cases studies

Below are vignettes that demonstrate the importance of a gender-based history and how this will guide a therapeutic approach. These cases are based on actual patients.

Case 1

A 24-year-old woman comes in for evaluation of her headaches. She has two kinds of headaches. The first is a daily constant aching headache worst at the end of the day. It is aggravated by stress and is associated with bilateral neck pain. This headache has been present for past 1 year, but worse over the last several months. She takes acetaminophen or ibuprofen about six tablets of either everyday for this headache.

The second headache is hemicranial throbbing and much more severe. She has nausea, rare vomiting, and light sensitivity with this headache. She denies any other symptoms. During this headache she has to lie down. The frequency varies from one to three times a month. It occurs always 1–2 days prior to her menses. She has noted that red wine can trigger it. The headache lasts usually 1 day. These headaches began in her teens. Her mother and sister have similar headaches. She has never been treated for her headaches.

Her past medical and surgical history is unremarkable.

Medications include: acetaminophen prn, ibuprofen prn

She drinks four to six caffeinated beverages a day.

She recently stopped her oral contraceptives as she wants to become pregnant.

Pertinent social history is that she is engaged to be married in 2 months. They are planning on starting a family as soon as possible. She has no history of tobacco use, alcohol use, or illicit drugs, but she does not exercise on a regular basis.

Her family history is positive for migraine in mother and sister. In addition, her mother and an aunt had breast cancer.

On review of systems she endorses the following: She has lost ten pounds over the last 2 months. She has regular menses and normal breasts; she has not had an obstetrics and gynecology (OB/GYN) examination for 2 years. Her sleep is poor with difficulty falling asleep. She says she has been quite anxious about her upcoming wedding.
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The history is consistent with a diagnosis of chronic daily headaches of the tension type and common migraine. Her triggers, factors that are provoking her headaches, and her desire to conceive all frame the therapeutic approach. In this case, education about analgesic rebound, overuse of caffeine, and poor sleep will need to be addressed. Stress management including a regular exercise program and its importance and relation to headache and sleep. She needs education on which medications are considered safe in pregnancy and the importance for women with a family history of breast cancer to have regular examinations. Prophylactic medication is less appropriate as she is actively trying to conceive. Abortive therapy may be an option, providing the medication is not contraindicated during pregnancy, it is also important to avoid the potential pitfall of analgesic rebound.

Case 2

A 28-year-old woman gravida 7 para 3, 24 weeks pregnant with chronic hypertension comes in for evaluation of headaches. The headache began 3 weeks ago. They were initially intermittent, but over the last 10 days they have become constant. They are worse in the morning or if she coughs. She has no clear relieving factors. Her blood pressure has not been well controlled with systolic pressures recorded as high as 220. Her labetalol was increased and her blood pressures have improved. They have been running around 140–150/90. Over the last week, she has been having blurred vision and worsening headache. Over the last 2 days, she has noted some double vision with the images side by side. The diplopia is worse when she looks far away and while watching television. She denies any other neurologic problems. She does not usually suffer from headaches. She underwent a 24-hour urine protein which was normal, suggesting that preeclampsia was not the source of her headache. CBC including platelet count was normal. Liver enzymes were also normal. She had a brain MRI and MR venogram 10 days ago which were normal.

Her past medical history is remarkable for hypertension, renal stone, history of requiring a nephrostomy tube during her last pregnancy, and a history of herpes simplex virus

She is taking multivitamins and labetalol only.

Her review of systems is notable for weight gain of 30 pounds since the start of the pregnancy. She has no diabetes and no sleep problems.

The history is concerning for elevated intracranial pressure causing a sixth nerve palsy in the second trimester of pregnancy with a 30 lb. weight gain. Of note is that she had recent normal imaging. She had gained a significant amount of weight which makes idiopathic intracranial hypertension (IIH) a concern. The hypercoagulability associated with pregnancy causing cerebral venous thrombosis is also in this differential, but less likely given her normal venogram. Neurologic consequences of hypertension such as stroke (ischemic or hemorrhagic) are unlikely given her history and normal imaging studies. Posterior reversible encephalopathy syndrome would also be less likely given her history of worsening headache with improved blood pressure control. On examination, her blood pressure was 120/90. Her weight was 205 lbs. and height 61 inches. The neurological examination confirmed a left sixth nerve palsy and papilledema. A repeat brain MRI and MR venogram was done. The MR venogram was normal. The repeat brain MRI showed dilatation of the subarachnoid space around the optic nerve sheath a finding seen in IIH (Figure 1.1) Her CSF opening pressure was 550 mm. The testing confirms a diagnosis of IIH.

These cases illustrate how to individualize the history in order to consider gender differences and allow us to better treat our female patients. It is important to anticipate our patient’s risks for disease based on their genetic makeup, lifestyle choices, and preexisting medical conditions. In this setting, clinicians must also be aware of the patient’s desires for conception present and future. This will allow our patients to achieve their life goals with minimal health risk.
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Figure 1.1 The axial $T_2$ image on the left shows dilatation of the subarachnoid space around the optic nerves. On the right is a sagittal $T_1$ image depicting an empty sella.

References

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