Practice Parameter update: Management issues for women with epilepsy—Focus on pregnancy (an evidence-based review): Obstetrical complications and change in seizure frequency: Report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society

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SPECIAL ARTICLE

Practice Parameter update: Management issues for women with epilepsy—Focus on pregnancy (an evidence-based review): Obstetrical complications and change in seizure frequency

Report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society

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ABSTRACT

Objective: To reassess the evidence for management issues related to the care of women with epilepsy (WWE) during pregnancy, including the risk of pregnancy complications or other medical problems during pregnancy in WWE compared to other women, change in seizure frequency, the risk of status epilepticus, and the rate of remaining seizure-free during pregnancy.

Methods: A 20-member committee including general neurologists, epileptologists, and doctors in pharmacy evaluated the available evidence based on a structured literature review and classification of relevant articles published between 1985 and February 2008.

Results: For WWE taking antiepileptic drugs, there is probably no substantially increased risk (greater than two times expected) of cesarean delivery or late pregnancy bleeding, and probably no moderately increased risk (greater than 1.5 times expected) of premature contractions or premature labor and delivery. There is possibly a substantially increased risk of premature contractions and premature labor and delivery during pregnancy for WWE who smoke. Seizure freedom for at least 9 months prior to pregnancy is probably associated with a high likelihood (84%–92%) of remaining seizure-free during pregnancy.

Recommendations: Women with epilepsy (WWE) should be counseled that seizure freedom for at least 9 months prior to pregnancy is probably associated with a high rate (84%–92%) of remaining seizure-free during pregnancy (Level B). However, WWE who smoke should be counseled that they possibly have a substantially increased risk of premature contractions and premature labor and delivery during pregnancy (Level C). ***Neurology*® 2009;73:126–132**

GLOSSARY

AAN = American Academy of Neurology; **CI** = confidence interval; **OR** = odds ratio; **RR** = relative risk; **WWE** = women with epilepsy.

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Recent estimates of the US population[1] and the prevalence of epilepsy[2] indicate that approximately one-half million women with epilepsy (WWE) are of childbearing age. It has also been estimated that three to five births per thousand will be to WWE.[3] Epilepsy is defined by the presence of recurrent, unprovoked seizures, and the treatment is typically a daily, long-term antiepileptic drug (AED) regimen. The majority of people with epilepsy have well-controlled seizures, are otherwise healthy, and therefore expect to participate fully in life experiences, including childbearing.

This parameter and the two companion parameters are updates of the previous practice parameter from 1998.[4] They employ improved methodology for the development of practice parameters to analyze a large number of new studies informing the clinical management of WWE who are pregnant or plan pregnancy.

Supplemental data at www.neurology.org

See pages 133 and 142

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The Mission Statements of the Quality Standards Subcommittee (QSS) and Therapeutics and Technology Assessment (TTA) Subcommittee, Conflict of Interest Statement, QSS members, TTA members, AAN classification of evidence, Classification of recommendations (appendices e-1 through e-5), as well as tables e-1 through e-4, are available as supplemental data on the *Neurology*® Web site at www.neurology.org.

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This parameter summarizes evidence for two broad clinical questions:

1. Compared to women without epilepsy, are WWE at increased risk for pregnancy-related complications, including a) Cesarean delivery; b) preeclampsia; c) pregnancy-induced hypertension; d) premature contractions or premature labor and delivery; e) bleeding complications; and f) spontaneous abortion?
2. For WWE who become pregnant, what is the risk of epilepsy-related complications during pregnancy, including a) change in seizure frequency; b) risk of status epilepticus; and c) chance of recurrent seizures if WWE are seizure-free for 9 months prior to pregnancy?

DESCRIPTION OF THE ANALYTIC PROCESS

Panel formation. The American Academy of Neurology (AAN) assembled a panel of experts including epileptologists, general neurologists, and doctors in pharmacy with expertise in AEDs. Panel members with expertise in obstetrics, obstetrical nursing, and teratology were also included. This effort was supported by a grant from the Milken Family Foundation.

Literature review and article selection. A literature search was performed using MEDLINE, MEDLINE-In-Process, Current Contents, Biologic Abstracts, and BIOSIS previews for relevant articles published between 1985 and December 2005. An updated search was performed from December 2005 through June 2007, with manual searches on some topics through February 2008. The arbitrary cutoff date of 1985 was chosen because these relatively recent articles were thought to reflect current practice and AED usage patterns and therefore be more applicable and reliable for this assessment than earlier reports. The search terms used were seizures/epilepsy, catamenial epilepsy, pregnancy, anticonvulsants, antiepileptic drugs, teratogenesis, birth defects, pregnancy registry, cognitive outcome, vitamin K, folate/folic acid, breastfeeding, oral contraceptives, polycystic ovary syndrome, hormone replacement therapy, menopause, perimenopause, and fertility. The search was confined to articles using human subjects and included all languages for which there was an abstract in English. A secondary search for missed references was done by reviewing the bibliographies of review articles and meta-analyses identified in the primary search.

The literature search yielded a total of 876 abstracts. To find relevant articles, two panel members screened each of the abstracts. If either panel member thought the article was potentially relevant, the full text was obtained for review. In general, abstracts were excluded from further analysis if they related to eclampsia rather than seizures due to epilepsy, related to basic mechanisms such as teratogenesis or placental AED metabolism, or were unrelated to the questions posed by the panel.

From the abstracts, a total of 285 were selected for complete review. Four panel members reviewed the full text of the articles and identified those that were relevant to each clinical question. Articles were included in the analysis of this article if they determined the frequency of pregnancy-related or epilepsy-related complications in a cohort of pregnant WWE. Articles relevant to the clinical questions of the companion articles were included in the appropriate article and are described there.

Study classification and measures of effect. With the exception of the question pertaining to recurrent seizures in seizure-free WWE, articles were classified according to the AAN prognostic classification of evidence scheme (appendix e-4A on the *Neurology*® Web site at www.neurology.org). Articles regarding recurrent seizures in seizure-free WWE were classified according to the AAN screening classification of evidence scheme (appendix e-4B). This scheme was chosen because the absolute risk of seizure recurrence, rather than the relative risk, was deemed most clinically relevant to this question. Articles were classified separately by four panel members. Disagreements on categorization of the articles were resolved by discussion and consensus.

For pregnancy-related complications, studies were given a lower class of evidence when they did not compare complication frequencies in pregnant WWE to pregnant women without epilepsy. For epilepsy-related complications, studies were given a lower class of evidence when they did not compare complication frequencies in pregnant WWE to nonpregnant WWE.

Additionally, studies were downgraded for a lack of masked outcome assessment or if they provided insufficient information to determine relative risk (RR) or odds ratios (ORs). The requirement for masked outcome assessment was waived for obviously objective outcomes such as cesarean delivery, preeclampsia, pregnancy-induced hypertension, spontaneous abortion, and status epilepticus. Meta-analyses were not performed due to heterogeneity of the studies.

When possible, the associations between epilepsy and pregnancy-related complications or pregnancy and epilepsy-related complications were determined using ORs. If not reported in the article, the writing panel attempted to calculate the appropriate ORs. For the only Class I article,[5] the authors were personally contacted to provide further detail on data reported in the article. To allow calculation of the OR

when one of the cells of the two by two table was zero, 0.5 was added to each cell.[6]

For the purposes of this parameter, a moderately increased risk is defined by an OR of greater than 1.5 and less than 2.0 and a substantially increased risk by an OR of 2.0 or greater.

The 95% confidence intervals (CIs) of the ORs were used as the measure of precision. Negative studies were judged to be sufficiently sensitive to exclude an increased risk based on the upper limit of the 95% CIs. Thus, a study failing to show a significant increased risk of a complication based on an OR of 1.2 with 95% CIs of 0.6 to 1.7 would be judged to be too insensitive to exclude a moderately increased risk of the complication.

The strength of the practice recommendations was directly linked to the class of evidence using the scheme described in appendix e-5.

ANALYSIS OF EVIDENCE Do WWE have an increased risk of pregnancy-related complications? Twenty-five articles met inclusion criteria for pregnancy-related complications in WWE. Several articles included information pertinent to more than one question. Of these 25 articles, 9 were graded Class III or higher (table e-1).

Cesarean delivery. One Class I study[5] did not show a significant increased risk of cesarean delivery in WWE taking AEDs compared to women without epilepsy (OR 1.04, 95% CI 0.71–1.52). A Class II study[7] did not show a significant increased risk of cesarean delivery in WWE compared to women without epilepsy (OR 1.24, 95% CI 0.99–1.55). However, both studies were insufficiently sensitive to exclude a moderately increased risk.

Three Class III studies (OR 17.88, 95% CI 4.73–67.58[8]; OR 1.58, 95% CI 1.10–2.25[9]; and OR 2.2, 95% CI 1.42–3.41[10]) demonstrated a significant substantial increased risk.

Other than the increased risk of bias and statistical imprecision of some studies, there is little information to explain the increased cesarean delivery rate observed in the Class III studies compared to the Class I and II studies.

Conclusion. Based on evidence from one Class I and one Class II study, it is probable that WWE taking AEDs do not have a substantially increased risk of cesarean delivery. Because of the lack of statistical precision in the Class I and Class II studies and the evidence from multiple Class III studies, a moderately increased risk of cesarean delivery is possible.

Preeclampsia. One Class I study[5] did not show a significant increased risk of preeclampsia in WWE taking AEDs compared to women without epilepsy (OR 1.4, 95% CI 0.66–3.15). However, this study was insufficiently sensitive to exclude an increased risk.

Two Class II studies (RR = 0.8, 95% CI 0.2–2.9[11] and OR 1.24, 95% CI 0.77–1.99[7]) did not observe a significant increase in the risk of preeclampsia in WWE compared to women without epilepsy. These studies were insufficiently sensitive to exclude an increased risk.

Conclusion. There is insufficient evidence to support or refute an increased risk of preeclampsia in WWE taking AEDs.

Pregnancy-induced hypertension. One Class II study (OR 1.4, 95% CI 1.1–1.9)[7] showed an increased risk of pregnancy-induced hypertension in WWE as compared to women without epilepsy. Another Class II study (OR 0.7, 95% CI 0.3–1.6)[11] showed no significant increased risk but was insufficiently sensitive to exclude a moderately increased risk.

Two Class III studies (OR 7.8, 95% CI 0.8–76.9[8] and OR 1.2, 95% CI 0.7–2.1[10]) demonstrated no significant increased risk. These studies were insufficiently sensitive to exclude a substantially increased risk.

Conclusion. Based on results from two conflicting Class II studies, there is insufficient evidence to support or refute an increased risk of pregnancy-induced hypertension in WWE.

Premature contractions and premature labor and delivery. One Class I study[5] showed no substantially increased risk of premature contractions or premature labor and delivery in WWE taking AEDs compared to control women without epilepsy (OR 0.51, 95% CI 0.19–1.36).

One Class II study[12] showed an increased risk for WWE who were smokers compared to control women who were also smokers (OR 3.4, 95% CI 1.8–6.5) (data not given for all WWE compared to controls). One Class III study[13] also showed an increased risk ($p < 0.05$). Another Class III study[8] demonstrated no significant increased risk but was insufficiently sensitive to exclude a substantially increased risk (OR 8.24, 95% CI 0.92–70.32). A Class III study[11] showed no significant increased risk but was not sufficiently sensitive to exclude an increased risk (RR 0.7, 95% CI 0.3–1.4). In a categorical, χ^2 statistic, it was reported that the rates of premature births were not different than controls ($p = 0.3$),[9] and another study found no differences in gestational ages in the offspring of WWE compared to controls (WWE = 38.06, SD 1.42 vs controls = 38.17, SD 3.58 weeks).[10]

Conclusions. Based on evidence from one Class I study, it is probable that WWE taking AEDs do not have a moderately increased risk of premature contractions and premature labor and delivery during pregnancy. However, based on evidence from one

Class II study, it is possible that WWE who smoke do have a substantially increased risk of premature contractions and premature labor and delivery during pregnancy compared to women without epilepsy who smoke.

Pregnancy-related bleeding complications. One Class I study[5] did not show a significant increased risk of late pregnancy bleeding in WWE taking AEDs compared to women without epilepsy (OR 1.18, 95% CI 0.70–1.97). One Class III study[11] also demonstrated no increased risk (RR 0.9, 95% CI 0.4–2.0). However, neither study was sufficiently sensitive to exclude a moderately increased risk.

Conclusion. Based on evidence from one Class I and one Class III study, it is probable that WWE taking AEDs do not have a substantially increased risk of late pregnancy-related bleeding complications. However, because of a lack of statistical precision in these studies, a moderately increased risk cannot be excluded.

Spontaneous abortion. One Class III study[14] showed a decreased risk of spontaneous abortion in WWE compared to controls (6.9% vs 7.5%). No denominator is provided for the control group to allow calculation of ORs.

Conclusion. The data are inadequate to support or refute an increased risk of spontaneous abortion in WWE.

Do WWE have an increased risk of epilepsy-related complications during pregnancy? Twenty-five articles met inclusion criteria for epilepsy-related complications in pregnant WWE.

Change in seizure frequency. No study compared the change in seizure frequency in pregnant WWE to nonpregnant WWE; therefore an appropriate gold standard comparator group was not available. Hence, all studies were graded Class IV (table e-2). Three articles[15-17] used each patient's nonpregnant seizure frequency (per pregnancy) as its own control. In one study, which evaluated 154 pregnancies,[15] seizure frequency was unchanged in 54% (95% CI 0.46–0.62) (including 48 [31%] seizure-free patients), decreased in 14% (95% CI 0.10–0.21), and increased in 32% (95% CI 0.25–0.40) compared to prepregnancy seizure frequency. In this study, AED doses were increased when seizure frequency increased.

In another study, which evaluated 78 pregnancies,[16] seizure frequency was unchanged in 72% (95% CI 0.61–0.81) for major seizures (Wilcoxon test $p > 0.50$ for significant differences), decreased in 14% (95% CI 0.08–0.24), and increased in 14% (95% CI 0.08–0.24) compared to prepregnancy baseline. AED doses were increased when seizure frequency increased in this study as well.

In a third Class IV study, which evaluated 93 pregnancies,[17] seizure frequency as a whole was not different in pregnancy compared to baseline ($p = 0.42$). The exact numbers were not provided, but the percent change was reported as the following: 61% unchanged, 24% decreased, 15% increased. Seizure increase was more likely in partial epilepsy (29%) than idiopathic epilepsy (7%). AED doses were unchanged in this study.

Another Class IV study[18] used both retrospective recall and postpartum prospective seizure frequency as comparators. In this study of 74 AED-compliant patients, seizure frequency was unchanged in 80% (95% CI 0.69–0.87), decreased in 4% (95% CI 0.01–0.11), and increased in 16% (95% CI 0.01–0.26). AED doses were unchanged in this study.

Another article[19] used postpartum seizure frequency as a comparator. In this study of 138 pregnancies, seizure frequency was unchanged in 80% (95% CI 0.72–0.86), decreased in 3% (95% CI 0.01–0.07), and increased in 17% (95% CI 0.12–0.25). The AED management was not stated in this study.

The percentage of patients with unchanged seizure frequency in these studies ranged from 54% to 80%. The highest rate of unchanged seizure frequency was the 80% reported in AED-compliant patients, documented by serum levels.[18] The rate of seizure decrease ranged from 3% to 24%. The rate of seizure increase ranged from 14% to 32%.

Unfortunately, none of these studies included an appropriate nonpregnant WWE comparator group to provide information on the natural stability of seizure frequency among WWE. Without this information, it is impossible to determine if the changes in seizure frequency observed were related to the pregnancy itself.

Conclusion. There is insufficient evidence to determine the change in seizure frequency in pregnant WWE.

Status epilepticus. No studies compared the risk of status epilepticus in nonpregnant WWE to pregnant WWE. Hence, all studies were graded Class IV (table e-3). Three population-based studies reported a frequency of status epilepticus in WWE during pregnancy of 0%–1.3% (0/154, 0%, 95% CI 0.00–0.3[15]; 1/78 convulsive status epilepticus, 1.3%, 95% CI 0.00–0.07[16]; and 0/89, 0%, 95% CI 0.00–0.04[17]). Similarly, a large prospective, but not population-based, study of nearly 2,000 pregnancies[20] found status epilepticus in 36/1,956 (1.8%, 95% CI 0.01–0.03) pregnancies. Twelve of these 36 episodes of status epilepticus were convulsive and 24 were nonconvulsive.

Although there is no accurate information in a similar population of persons with epilepsy to use as

a historical comparator, these estimates closely approximate an annual frequency of 1.6% for status epilepticus reported in a large series of patients with varied epilepsy types.[21] This comparison suggests that status epilepticus does not occur more frequently during pregnancy. However, the absence of a comparison group of nonpregnant WWE within these studies makes it impossible to determine the relative risk of status epilepticus during pregnancy.

Conclusion. There is insufficient evidence to support or refute an increased risk of status epilepticus in pregnant WWE.

Seizure recurrence in previously seizure-free WWE. Two Class II articles[16,17] showed that for WWE who were seizure-free for 9 months prior to pregnancy, 84%–92% remained seizure-free during pregnancy (table e-4). In one study, 38 of 45 (84%; CI 0.71–0.92) pregnant WWE remained seizure-free,[16] and in the other study, 47 of 51 (92%; CI 0.82–0.97) pregnant WWE remained seizure-free.[17]

One larger Class III article[22] showed that 80% of a group of WWE (n = 450) who were seizure-free at least 1 year prior to pregnancy remained seizure-free during pregnancy (exact number not provided). One Class III article showed that of 72 WWE who were seizure-free for 10 months, 74% (95% CI 0.62–0.82) remained seizure-free during pregnancy.[18] A second Class III article showed that of 54 WWE who were seizure-free for 9 months, 94% (95% CI 0.85–0.98) remained seizure-free during pregnancy, and of 48 WWE who were seizure-free for 1 year, 92% (95% CI 0.80–0.98) remained seizure-free during pregnancy.[19] These results are all fairly consistent across the class of evidence and sample size of the studies.

Conclusion. Two Class II articles show the rate of remaining seizure-free during pregnancy if WWE are seizure-free for at least 9 months to 1 year prior to pregnancy is probably 84%–92%.

RECOMMENDATIONS Counseling of WWE who are pregnant or are contemplating pregnancy should reflect the following:

- There is probably no substantially increased risk (greater than two times expected) of cesarean delivery for WWE taking AEDs (Level B). However, there is possibly a moderately increased risk (up to 1.5 times expected) of cesarean delivery for WWE taking AEDs (Level C).
- There is probably no substantially increased risk (greater than two times expected) of late pregnancy bleeding for WWE taking AEDs (Level B).
- There is probably no moderately increased risk (greater than 1.5 times expected) of premature contractions or premature labor and delivery for WWE taking AEDs (Level B).
- There is possibly a substantially increased risk of premature contractions and premature labor and delivery during pregnancy for WWE who smoke (Level C).
- Seizure freedom for at least 9 months prior to pregnancy is probably associated with a high likelihood (84%–92%) of remaining seizure-free during pregnancy (Level B).
- There is insufficient evidence to support or refute an increased risk of preeclampsia, pregnancy-related hypertension, spontaneous abortion, a change in seizure frequency, or status epilepticus (Level U).

CLINICAL CONTEXT Some of the most important findings of this practice parameter are what they do not demonstrate. There was no conclusive evidence of an increased risk of many obstetrical complications often discussed as associated with WWE during pregnancy. This raises the possibility that there is no true difference in the rates of obstetrical complications in WWE compared to the general population.

Further, the findings do not suggest high rates of seizure increase or status epilepticus during pregnancy or an increased risk of seizure relapse during pregnancy for WWE who are seizure-free. The data available to determine how seizure-free WWE fare during pregnancy indicate it is likely that they will remain seizure-free, providing practitioners with another reason to strive for seizure freedom in their patients planning pregnancy.

It is hoped that this information will herald a new outlook about how high (or low) the actual risk is for health complications in WWE who become pregnant, and may serve to decrease the anxiety and perhaps the stigma produced by this clinical situation for both patient and practitioner.

RECOMMENDATIONS FOR FUTURE RESEARCH Stronger evidence is needed to determine if there are increased risks of preeclampsia, pregnancy-induced hypertension, and spontaneous abortion for WWE. These risks should be evaluated in large, prospective studies using well-matched control groups. The effect of specific AEDs on obstetrical outcomes also remains unexplored and deserves further study. The existing databases for evaluating the outcomes of pregnancies exposed to AEDs could potentially provide a source for such information. Further evaluation for the risks of seizure increase during pregnancy should be done, using prospective baseline information when possible. This type of analysis would help to reveal more information about the causes of seizure increase during pregnancy, which may be more complicated than AED noncom-

pliance, decreased levels due to pregnancy metabolism, or lack of sleep. For example, the effect of the hormonal changes during pregnancy on seizure frequency could be evaluated in a careful, prospective study.

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DISCLOSURE

The authors report the following conflicts of interest: Dr. Harden has served on the scientific advisory board of Cyberonics, GlaxoSmithKline, UCB Pharma, Valeant, and SK Pharmaceuticals and on the speakers' bureau of GlaxoSmithKline, Pfizer, UCB Pharma, and Abbott. She serves as an editor of *Epilepsy Currents* and receives publishing royalties from Elsevier. Dr. Harden has received research funding from Forest, UCB Pharma, Ortho McNeil, and NIH/NINDS. Dr. Harden sees women with epilepsy in her office practice. Dr. Hopp receives royalties from UpToDate.com electronic medical journal. She has been on the speakers' bureau of UCB Pharma and GlaxoSmithKline. Dr. Hopp has given testimony in a medico-legal case. Dr. Ting served on the scientific advisory board of UCB Pharma and has received honoraria from the Epilepsy Foundation of America. Dr. Pennell has served on the Expert Panel for the Keppra Pregnancy Registry sponsored by UCB Pharma. She has received funding for travel from the Northeast Regional Epilepsy Group for speaking at their 2008 Epilepsy Symposium, by the UK Research Council for speaking at the Epilepsy Research UK International Expert Workshop, by UCB Pharma for attending the Executive Panel meeting for the Pregnancy Registry, by the American Epilepsy Society for attending the Board of Directors' Meeting, by the Epilepsy Foundation for attending the Board of Directors' and orientation meetings, by the Long Island Jewish Hospital for lecturing at Neurology Grand Rounds, by Duke University for lecturing at Neurology Grand Rounds, by Brigham and Women's Hospital for lecturing at the Epilepsy Research Conference, by the Milken foundation for attending Pregnancy Registry meetings, and by Massachusetts General Hospital for speaking at the Annual Teratogens Course. She has received honoraria from Journal Watch Neurology for a contributing article, paid for by Massachusetts Medical Society, *NEJM*, for review for the *Lancet Neurology*, the Northeast Regional Epilepsy group for speaking at 2008 Epilepsy Symposium, North Shore Long Island Jewish Health system, Duke University, University of Maryland, the Massachusetts General Hospital for speaking at the postgraduate course in Human Teratogens, and the AAN for speaking and directing annual courses. Dr. Pennell has served as a contributing editor for *Epilepsy Currents* and is on the editorial board of *Epilepsia*. Dr. Pennell has received research support from UCB Pharma, Marinus Pharmaceuticals, NIH, NINDS, NIMH, CDC, and Emory University Research Council. Dr. French has served on the scientific advisory board of UCB Pharma, Johnson and Johnson, Eisai, Novartis, Valeant, Icagen, Intranasal, Sepracor, and Marinus. She has received funding for travel to present findings or give lectures from UCB Pharma, Kyowa, Eisai, Johnson and Johnson, Valeant, and GlaxoSmithKline. She has served as an associate editor for *Epilepsy Currents* and supplement editor for *Epileptic Disorders*. Dr. French is the president of the Epilepsy Study Consortium, which receives money from multiple pharmaceutical companies (including GlaxoSmithKline, UCB Pharma, Johnson and Johnson, Cyberonics, Schwarz Pharma, Ortho McNeil, Eisai, Jazz Pharmaceuticals, Ovation Pharmaceuticals, Endo Pharmaceuticals, Bial Pharmaceuticals, Neurovista, Valeant Pharmaceuticals, Icagen, Supernus, Intranasal, SK Pharmaceuticals, Taro Pharmaceuticals, Neurotherapeutics, Sepracor, and Novartis) and she consults on behalf of the consortium. Dr. French has received research funding from Johnson and Johnson, Eisai, UCB Pharma, SK Pharmaceuticals, Valeant, Pfizer, NIH, and Epilepsy Research Foundation. Dr. Hauser has served on the scientific advisory board of Ovation and Valeant. He has served on the editorial board of *Acta Neurologica Scandinavia, Neuroepidemiology*, and *Epilepsy Research*. He has received honoraria from Cornell University Symposium on epilepsy and acted as a consultant to Pfizer. Dr. Hauser has received research support from AAMC/CDC, NIH/NINDS, FAA, Mayo Clinic, and Hotchkiss Neurological Institute, and has given expert testimony in his role as an FAA consultant. Dr. Wiebe serves on the editorial board of *Neurology*, *Epilepsia*, *Epilepsy & Behavior*, and *Canadian Journal of Neurological Sciences*. Dr. Gronseth serves as an editor of *Neurology Now* and on the speakers' bureau of Boehringer-Ingelheim. He receives compensation from the AAN for consulting work. Dr. Thurman is an employee of the CDC. 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He has received speaker honoraria from Medical College of South Carolina, Duke University, and Medical College of Virginia, has received research funding from NIH, Schwarz, Ortho McNeil, and Pfizer, and has acted as a consultant for Schering-Plough and Infinite Biological Technologies. Dr. Robinson reports no disclosures. Dr. Gidal has served on the scientific advisory board for GlaxoSmithKline, UCB Pharma, and Abbott Labs and served as an editor for *Epilepsy & Behavior, The Annals of Pharmacotherapy*, and *Pharmacist's Letter*. Dr. Gidal has received research support from UCB Pharma. Dr. Hovinga estimates less than 10% of his clinical effort is spent on pharmacology consults. Dr. Wilner has served on the scientific advisory board of and received funding for travel from GlaxoSmithKline. He receives royalties from Demos Publications for *Epilepsy: 199 Answers* and *Epilepsy in Clinical Practice*. He receives board of directors compensation from GlaxoSmithKline. 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He has received funding for travel from Fundacion BBVA, NIEHS National Advisory Environmental Health Sciences Council, IKMC Steering Committee, European Epilepsy Meeting, NIH, and AES. Dr. Finnell has served as a journal editor for *Birth Defects Research Part A* and holds a patent on folate receptor autoantibody assay. He has received honoraria from McGill University-Montreal Neurological Institute and has received research funding from the Centers for Disease Control and Prevention for the National Birth Defects Prevention Study and the Methodist Hospital Research Institute. Dr. Finnell has given expert testimony, prepared affadavits, and acted as a witness regarding legal proceedings related to the topic of this manuscript. Ms. Le Guen reports no disclosures.

DISCLAIMER

This statement is provided as an educational service of theAmerican Academy of Neurology. It is based on an assessmentof current scientific and clinical information. It is not intended to include all possible proper methods of care for a particular neurologic problem or all legitimate criteria for choosing to use a specific procedure. Neither is it intended to exclude any reasonable alternative methodologies. The AAN recognizes that specific patient care decisions are the prerogative of the patient and the physician caring for the patient, based on all of the circumstances involved. The clinical context section is made available in order to place the evidence-based guideline(s) into perspective with current practice habits and challenges. No formal practice recommendations should be inferred. The findings and conclusions in the report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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The Child Neurology Society has endorsed the following guidelines:

- Management issues for women with epilepsy—Focus on pregnancy (an evidence-based review): Obstetrical complications and change in seizure frequency
- Management issues for women with epilepsy—Focus on pregnancy (an evidence-based review): Teratogenesis and perinatal outcomes
- Management issues for women with epilepsy—Focus on pregnancy (an evidence-based review): Vitamin K, folic acid, blood levels, and breastfeeding

Practice Parameter update: Management issues for women with epilepsy—Focus on pregnancy (an evidence-based review): Obstetrical complications and change in seizure frequency: Report of the Quality Standards Subcommittee and Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and American Epilepsy Society

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