FDA rankings of drugs’ teratogenic potential are guided by the lowest tier of evidence-based medicine.
FDA classification of medications’ teratogenic potential

<table>
<thead>
<tr>
<th>Category</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>A:</td>
<td>Controlled studies in pregnant women demonstrate no fetal risk</td>
</tr>
<tr>
<td>B:</td>
<td>Controlled animal studies have not shown a fetal risk, but there are no studies done on women OR controlled studies in animals have shown a fetal risk that was not reproduced in controlled human studies</td>
</tr>
<tr>
<td>C:</td>
<td>Controlled animal studies have demonstrated adverse fetal effects and there are no human studies OR there are no controlled studies in humans or animals</td>
</tr>
<tr>
<td>D:</td>
<td>Controlled studies in humans demonstrate adverse fetal effects but the benefits of using the drug may be greater than the risks</td>
</tr>
<tr>
<td>X:</td>
<td>Controlled studies in animals and humans have demonstrated adverse fetal effects OR there is evidence of fetal risk based on human experience. The risk of using these drugs outweighs any possible benefit. The drug is absolutely contraindicated in pregnancy</td>
</tr>
</tbody>
</table>


Because of teratogenicity concerns, pregnant women are excluded from clinical trials of investigational drugs. Thus, new drugs are not approved for use in these patients, and FDA rankings of drugs’ teratogenic potential (Table) are guided by nonblinded, noncontrolled, naturalistic, after-the-fact observations—the lowest tier of evidence-based medicine.

Proceed with caution. Against this background, I follow these principles when treating pregnant patients:

- **Counsel all mentally ill women** about the potential risks of conceiving while receiving a psychotropic before they consider pregnancy. Counseling should include all prescription and nonprescription drugs.
- **Obtain a family history** of psychiatric disorders from all pregnant patients.
- **Make an accurate psychiatric diagnosis** in pregnant patients, and assess the risks of providing vs withholding needed pharmacotherapy.

- **Use nondrug treatments** (if evidence-based) before medications. Options include behavioral therapies, interperonal therapy, supportive therapy, and somatic treatments such as electroconvulsive therapy, repetitive transcranial magnetic stimulation, and light therapy.

  - **When using psychotropics**, select the lowest-risk agents (Category A) first, and use the lowest efficacious dose.
  
  - **Collaborate with** the patient’s obstetrician. I coined the term “psychiatric dystocia” to describe the complicating potential of mental illness on pregnancy.
  
  - **Completely avoid drugs** with established teratogenicity, and educate the patient not to take these drugs if another physician prescribes them to her.
  
  - **Prescribe high-dose folate** (4 to 5 mg/d) for psychotropic, bipolar, or depressed pregnant patients to protect against neural tube defects and enhance fetal CNS development.
  
  - **Regularly check** the patient’s nutrition, sleep hygiene, substance use (smoking, alcohol, coffee, illicit drugs), and use of over-the-counter supplements.

  - **Use stress-reduction techniques** to reduce potential deleterious effects of stress-induced hypercortisolemia on the fetus, and involve the patient’s partner.

  - **See the mentally ill pregnant patient frequently** for check-ups on response and/or side effects.

  - **Arrange for a child psychiatrist** to examine the infant of a seriously mentally ill patient shortly after birth. A newborn’s irritability, crankiness, or insomnia may be perceived as withdrawal symptoms or behavioral teratogenesis, whereas it could very well be a genetically inherited temperament instability from a mother suffering from anxiety, depression, or psychosis.

  Helping the mother without harming the child is like walking a tightrope: it calls upon all our skills, experience, and sound judgment.

Henry A. Nasrallah, MD
Editor-in-Chief

P.S. To help you manage potential medico-legal issues such as prescribing during pregnancy, CURRENT PSYCHIATRY welcomes Douglas Mossman, MD, as editor of Malpractice Rx. This month, Dr. Mossman discusses documentation and invites you to submit questions about liability.

Reference