

Teratology Primer, 3rd Edition

www.teratology.org/primer

What Sources of Information Are Available on Developmental Risks and Pregnancy Safety?

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Concern about birth defects sends many people planning to have children to health care professionals with questions about how their exposures to drugs and environmental agents might affect their pregnancies. The number of published teratology and developmental toxicology studies continues to increase and communicating accurate and up-to-date information is challenging.

Prospective parents need help in understanding that there is a background rate of adverse pregnancy outcome in the general population. Approximately 15–20% of recognized pregnancies end in spontaneous abortion (miscarriage), and with the use of sensitive early pregnancy testing, that rate is even higher. The higher rate with sensitive testing is due to most miscarriages occurring early in the pregnancy, before some women know they are pregnant. In a woman who is paying close attention to her menstrual cycles and who uses a sensitive test soon after a cycle is missed, these early pregnancy losses can be detected. About 2–4% of pregnancies result in a child with a major birth defect or cognitive impairment. Add to that the other illnesses that might be diagnosed in childhood—attention deficit/hyperactivity disorder, autism, leukemia—and there is a large burden of outcomes for which parents might be inclined to blame themselves if they have been exposed to a medication, virus, radiation, or chemical. Even exposures that don't cause adverse outcomes can cause guilt.

In women being treated with medications, it is not fair to emphasize risks associated with drug therapy without balancing the discussion with the benefits to the mother and baby of treating an illness in the pregnant woman. The best place to grow a healthy fetus is in a healthy mother, and discontinuing medication therapy during pregnancy may not be in the best interest of the mother or the fetus. A patient's family or medical history may indicate more risk for the pregnancy than the drug(s) in question. Occupational history can also be helpful when [evaluating teratogenic risk](#). What sources of information are best? When health care practitioners have questions about medications during pregnancy, they usually consult the product labeling. For drugs, product labeling is developed at the time a new product is approved by regulatory agencies such as the Food and Drug Administration (FDA) in the U.S, European Medicines Agency (EMA) in the European Union, and national regulatory authorities in other locations. The labeling describes the chemistry, pharmacology, and toxicology of the drug. It provides information on which uses (indications) and for which patient populations the drug has been approved and what the recommended doses are. The labeling includes results from both experimental animal and clinical studies to describe the safety and effectiveness of the drug. The pregnancy section of the label for a new drug is based almost entirely on laboratory animal data. It is a challenge to practitioners and pregnant patients to understand the information in the labeling and determine the risk for an individual patient. Experimental animal studies are discussed in [another chapter](#) and [global product labeling](#). Drug labeling may not provide all the information that might be helpful in making treatment decisions for reproductive couples, and environmental/occupational chemicals have little useful labeling information. Physical and biological exposures (X-rays, heat, ultrasound, viruses) can also be of

concern to couples and do not come with labels. Resources include textbooks, computerized databases, and teratology information services. Textbooks that provide information regarding the reproductive effects of environmental agents can be found in the Suggested Reading section that follows; however, textbooks quickly become outdated. A few textbooks now are sold with access to an updatable online version. One such textbook is *Drugs in Pregnancy and Lactation* by Gerald Briggs and colleagues. Peer-reviewed journals publish original studies, review articles, editorials, and information on upcoming conferences, but the sheer volume and complexity of these studies put them beyond the reach of some clinicians and most patients. Computerized databases contain information on thousands of agents, including medications, and summarize information from scientific studies. We will discuss the two databases with which we are involved.

TERIS is a computerized database designed to assist healthcare providers in assessing and counseling pregnant women regarding possible risks of teratogenic exposures. TERIS includes information on teratogenicity, transplacental carcinogenesis, embryonic or fetal death, and fetal and perinatal pharmacologic effects of drugs and other environmental agents. The database consists of a series of agent summaries, each of which synthesizes and evaluates data obtained from a thorough review of the primary literature. Every TERIS summary includes a risk assessment derived by consensus of 10 internationally-recognized authorities in clinical teratology. TERIS was developed and is maintained through user subscriptions and royalties.

REPROTOX® (www.reprottox.org) is written and maintained by the Reproductive Toxicology Center, A Non-Profit Foundation in Washington, D.C. The database contains several thousand summaries on medications, environment and occupational chemicals, physical agents, and biologics. Database entries are updated on a continual basis with the entire database updated on average every 6–7 months. New summaries are added on request. Unlimited access to the database is available to members online and on handheld devices. Students at any level of training are given memberships without charge. Other members pay a monthly or yearly fee that supports the professional staff in the updating of existing summaries and the writing of new summaries.

Teratology Information Services (TIS) are comprehensive, multidisciplinary resources that provide free, up-to-date information about the developmental and reproductive effects of environmental agents to health care providers and the public. Most TIS have at least one full time teratogen information specialist and are directed by individuals with a medical or doctoral degree and expertise in clinical teratology. TIS are usually located at major medical universities or state health departments and access a variety of resources, including medical libraries, online reproductive databases, and consultants in teratology-related fields, including toxicology, pharmacology, occupational medicine, genetics, radiation biology, infectious diseases, perinatology, and epidemiology. Although TIS operate independently, the Organization of Teratology Information Specialists (OTIS) was formed in 1987 to facilitate education and training in this area and to establish quality-assurance criteria. Public outreach is conducted through a public-facing service called MotherToBaby. Teratology information specialists are in a unique position to quickly respond to public concerns that may be raised when research findings reach the popular press before health care providers can critically evaluate them. Take a look at <https://MotherToBaby.org> where you will find more information, dozens of fact sheets, information about research projects and more.

Suggested Reading

Briggs GG, Freeman RK, Towers CV, Forinash AB: *Drugs in Pregnancy and Lactation: A Reference Guide to Fetal and Neonatal Risk*, 11th ed. Philadelphia, Pa.: Wolters Kluwer Health, 2017.
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