

Mini-Review: History of Organized Teratology Information Services in North America

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ABSTRACT A history of the Organization of Teratology Information Services (OTIS) is presented in context of the history of teratology information services. During the late 1970s, teratology information services grew out of the need for current and accurate information about fetal effects of environmental exposures in pregnancy. Over the next decade, teratology information services networked and collaborated, developing their own professional organization. A description of the activities of OTIS is described. *Teratology* 61: 314–317, 2000. © 2000 Wiley-Liss, Inc.

INTRODUCTION

Before the twentieth century, congenital malformations were believed to be the result of factors that we now call genetic. In the early part of the twentieth century, animal researchers were observing congenital anomalies that had resulted from environmental exposures. For example, in 1922, Bragg described the offspring of irradiated rats with eye defects; 11 years later, Hale reported cyclopic pigs as a result of vitamin A deficiency in the sows (Beck, '76). During the 1940s, extensive research was initiated regarding the effects of certain maternal nutritional deficiencies in rats (Beck, '76).

Human evidence for environmental causation was suggested in 1941 by Gregg, when he reported that rubella during pregnancy was the etiology of certain malformations (Beck, '76). In 1951, aminopterin became available for the treatment of acute leukemia in children. The drug was known to cause abnormalities in animals and was labeled with a warning against the use in pregnancy. A report of fetal malformations appeared in 1952, after the use of aminopterin as an abortifacient in clinical trials (Thiersch, '52). Most noted, however, is the thalidomide incident during the late 1950s and early 1960s (Kelsey, '82). The idea that a maternal exposure to environmental agents could cause congenital malformations was confirmed; these agents became known as "teratogens."

As a result of this new knowledge, questions regarding the effects of maternal exposures in pregnancy became common place. These questions were often addressed by various health care providers of diverse

backgrounds and training, including pharmacists, physicians, genetic counselors, poison control centers, and drug information centers (Buitendijk et al., '91). Buitendijk and colleagues ('91) documented that about 66% of women were exposed to prescription or over-the-counter medications during the first trimester, demonstrating how commonly these questions can arise. Resources available to practitioners regarding pregnancy exposures were often inaccessible, inadequate, difficult to interpret, and outdated (Elefant et al., '92; Ludowese et al., '93). Information resources for the general public were even more distorted: an analysis of 10 popular science, health, family, and "women's" magazines over a 1-year period indicated that the information presented had a tendency to be alarming as well as inaccurate, misleading, and not supported by the scientific literature when discussing fetal effects of maternal exposures (Gunderson et al., '90).

Best exemplified by the Bendectin episode, a climate of litigation had developed regarding exposures in pregnancy (Brent, '95). Although documented teratogens are only responsible for about 5% of the birth defects that occur, many lawsuits were initiated under the assumption that an agent is the cause of the problem (Nelson and Holmes, '89). It is thought that the rise in malpractice litigation is a result of attitudes in our society regarding events in the medical and legal systems and the lay public (Brent, '95). Such factors as limited information, complexity of data, and the issues of litigation created a need for teratology information services.

DEVELOPMENT OF TIS

In developing a teratology information services, the necessity to evaluate and interpret medical literature regarding pregnancy exposures became apparent. Familiarity with the disciplines of teratology, dysmorphology, toxicology, pharmacology, epidemiology, clinical genetics, infectious disease, obstetric/maternal fetal medicine, radiation biology, and occupational health

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was thought to be necessary (Elefant et al., '92; Ludowese et al., '93). Not only was it important to have knowledge of various medical disciplines, but it was, and continues to be, imperative to keep current with medications and other products available on the market. Moreover, in 1961, 656 drugs were available for use in the United States, as compared with 1989, where it was estimated that more than 8,000 drugs were on the market (Manasse, '89).

In 1979, the California Teratology Registry, based in San Diego, became the first formalized teratology information service established in North America. Initially this service was developed to follow pregnancies for prospective assessment of fetal outcomes. However, it became apparent that the public was more interested in an information service than in a research project, making the center as much a teratology information service as a registry (Chernoff et al., '85; Hanson, '87). During the 1980s, there was an increase in the number of teratology information services in the United States and Canada (Koren et al., '86), including the development of reproductive information databases such as *Reprotox* (Scialli et al., '95) at the Reproductive Toxicology Center in Washington, DC, and the Teratology Information System (*TERIS*) (Friedman et al., '94) in Seattle, Washington.

Teratology information services vary in size, population served, delivery of service, and research goals. Some services have a staff of one or two, while others may have as many as five or six. Some programs provide information solely to health care practitioners, while others are available to both health care practitioners and the public. Some programs that provide information over the phone; others require an in-person visit; some provide information through letters to the caller's health care practitioner, and in other cases, needs are met by providing agent summaries through databases. Research may be an integral part of some programs, whereas others may choose not to conduct research projects.

As teratology information services emerged and developed, the need arose to meet and exchange ideas about program operations and to share information regarding current research. The first such networking meeting was convened by Dr. Barbara Vogt, in 1985, in Philadelphia, with several themes emerging from this meeting: determining whether a project was primarily research or service oriented was of great importance. The issues addressed with regard to research-oriented projects included sample bias and validity of collection over the telephone, consistency of the data collected, ability to obtain an appropriate control group for comparison, and measurement of the outcome. It was thought that these issues needed to be addressed before the initiation of a project, to ensure the validity of the research.

Another important discussion centered on whether a program provided information, consultation, counseling, recommendations, or risk evaluation. These categories represent a continuum with information at one end

and comprehensive risk evaluation at the other. Information-based services provide information in a generic manner. Risk evaluation-based services make a judgment regarding risk evaluation for a particular client during a particular pregnancy. Between the two extremes are gradations of service, which include consultation, counseling, and recommendations.

From this interaction of individuals and programs, a consensus was reached to continue to meet to foster communication, to provide quality assurance and to develop an identity as an association of participating centers, with the eventual goal of forming a professional society.

Individuals working in teratology information services met consistently over the next few years. These meetings examined operational issues, exposure updates, and risk assessments among teratology information services. At the 1988 Teratology Society Annual Meeting, a symposium addressed whether teratology information should be given over the phone or in person. Owing to the complexity of clinical teratology, some believed that education should not be attempted over the telephone (King, '86). Others noted the success of existing services, such as Poison Control Centers, rape crisis, and child abuse hotlines, which provide difficult information over the phone. This suggested that the telephone model was client oriented, supportive, interactive, and potentially anonymous and that it provided an opportunity for education and, in certain situations, an opportunity for prevention (Rayburn et al., '82; Elefant et al., '92; Ludowese et al., '93).

DEVELOPMENT OF OTIS

During the 1990 Third International Conference of Teratology Information Services in Park City, Utah, the Organization of Teratology Information Services (OTIS) was established. In this meeting, OTIS was defined as an international organization of individuals providing information and education regarding clinical teratology. The alliance of services functions to strengthen existing programs in their ability to provide accurate and timely information regarding pregnancy exposures, without interfering in the individual program philosophy or character of the individual program (O'Brien et al., '91).

Since its inception, OTIS has been instrumental in facilitating communication among teratology information programs, providing access to common database information, increasing visibility, and providing a means for using prospective pregnancy outcome data in a scientific manner. It has also collaborated with other organizations, such as the Council of Regional Networks for Genetic Services (CORN), to develop guidelines for teratology information services regarding program staffing, training and education, research, funding, internal legal and ethical issues, and access for all communities to a teratology information service. These guidelines serve as a mechanism for quality assurance, a goal of OTIS (Committee of CORN, '94). In addition,

OTIS has developed a liaison with the European Network of Teratology Information Services (ENTIS). This relationship is extremely beneficial providing a mechanism to share information as well as a means for additional collaboration (Garbis et al., '90; Scialli, '91).

Currently, OTIS is a network of more than 45 member organizations throughout the United States and Canada. The governing board of OTIS, a seven-member executive committee, is elected for a 2-year term by the membership. The Executive Committee includes a president, vice-president, secretary, and treasurer, as well as three counselors. With the exception of the elected Executive Committee, all OTIS committees are open to its members. The current OTIS committees include Bylaws, Education, Executive, Grievance, Legislative Action, Membership Review, Occupation/Environmental Exposures, Research and Quality Assurance, and Thalidomide Ad-hoc.

MEMBERSHIP

To become an OTIS member, a teratology information service must meet established criteria and pay yearly dues. There are four membership categories: teratology information services in the Large Service Membership category must complete a minimum of 520 consultations annually, based on a 5-year average, and are allowed two votes on policy issues, while those in the Small Service Membership category must complete a minimum of 250 consultations annually, based on a 5-year average, and are allowed one vote on policy issues. Individual Memberships and Honorary Memberships are also available. Members have the option of participating in collaborative registry-style research projects. Several studies have already been completed on maternal exposure to varicella infection (Pastuszak et al., '93), sumatriptan (Shuhaiber et al., '98), cisapride (Bailey et al., '97), claritromycin (Einarson et al., '98), fluoroquinolones (Loebstein et al., '98), and psychotropic drugs (Pastuszak et al., '93), as well as angiotensin-converting enzyme (ACE) inhibitor agents (Feldkamp et al., '97). Currently, OTIS members are participating in the Asthma Medications in Pregnancy Project and will begin a new registry on maternal exposure to Arava (leflunomide), a drug used for rheumatoid arthritis. In addition, OTIS members have created "fact sheets" for health care providers to distribute to their clients on such topics as Prozac (fluoxetine), toxoplasmosis, hyperthermia, chickenpox, and fifth disease. These fact sheets along with a list of OTIS member services and membership guidelines can be found on the OTIS Web page (www.ucsd.edu/otis), or by calling the toll-free referral line at 1-888-285-3410.

With all the inherent complexities of human teratogenic risk assessment, it is not surprising that the results of studies on a particular agent often conflict. Teratology information services have been established to assist health care practitioners, as well as pregnant women and their families with the difficult tasks of assigning risk of teratogenicity.

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