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Every three years the singular event of our organization occurs – the IFFS Congress, now our 21st. Always a scientific cornucopia, this triennial congress will be especially exciting this year. Our traditional IFFS trilogies (21 in number) are the product of a diligent Scientific Committee, chaired by Past President Basil Tarlatzis. IFFS Trilogies, four key note talks, and the IFFS Surveillance report will be intercalated with the traditionally excellent program of our member society ASRM.

But IFFS is not just an organization whose purpose is a triennial congress. As a Non-Governmental Organization (NGO) for the World Health Organization (WHO), IFFS is very much in synchrony with the WHO mission that provides educational and clinical services in reproductive medicine throughout the globe. Pivotal in this effort are workshops under guidance of Educational Director Paul Devroey. In 2013, workshops will or have been held either as a unique event (February in Peru; Algiers in December) or as a focused component of meetings of regional or national significance (REDLARA, Panama in May; Russian Association Human Reproduction in Volgograd in September). See elsewhere in this Newsletter for details. Through these workshops IFFS extends its educational mission from clinical reproductive medicine to state-of-the-art science. These workshops are now supported by a generous grant from Ferring Pharmaceuticals that has enabled establishment of the IFFS/UIT (Update in Infertility Treatment) partnership. Enduring educational material from workshops, as well as timely scientific articles, can be accessed online at the Elsevier/UIT Resource Center.

Some reading this newsletter may come from venues in which their organizations are not among the 53 official IFFS member societies. We welcome new member societies, most recently the Malaysian Society of Obstetrics and Gynecology. I was privileged to participate in the formal signing ceremony April, 2013. Requirements for a member society include a formal organizational framework, democratically elected officers, and at least 40 members. Member societies vote and participate in the two IFFS General Assemblies, which elect not only individual officers, but member societies that designate representatives to the Board of Directors, Scientific Committee and Educational Committee. The Board is charged with working together with officers on all matters of concern, in identifying and forging new directions (e.g., the UIT/IFFS partnership), and in recommending sites for future triennial congresses and regional international symposia held other years. The Scientific Committee chooses trilogy and keynote topics and then speakers. This process will be followed for the next IFFS World Congress (India 2016). The Educational Committee identifies sites, topics and speakers for the workshops alluded to above. Both Committees are charged with identifying speakers from around the globe.

The IFFS Officers and Board of Directors welcome all to Boston, for what surely will be one of the most exciting congresses of reproductive medicine any of us have attended.
Environmental Contributors to Reproductive and Developmental Health

A growing body of scientific evidence suggests that our reproductive health and ultimately our reproductive capacity are under strain (1). Across the globe, indicators of reproductive adversity include increased rates of poor birth outcomes (preterm birth, small for gestational age), developmental disorders and chronic childhood diseases (e.g., autism, asthma, diabetes), certain cancers, obesity, earlier onset of puberty, and, in specific populations, altered sex ratios and longer time to pregnancy (1, 2). As these changes have occurred in a relatively short timeframe, they are unlikely to be explained solely by genetic mutations, warranting consideration of other causes, including the environment – social, built, nutritional environment, and physical and chemical agents.

In developed and developing countries, air pollution, stress, nutrition, and chemicals in personal care and household cleaning products, and in industrial waste, pesticides, and nearly ubiquitous plastics are of concern. Since 1950, there has been a dramatic increase in human exposure to natural and synthetic chemicals, Figure 1 with over 80,000 chemicals registered for use in the U.S. and Europe (3, 4) with 3,000-4,000 each manufactured or imported in excess of 1 million pounds and 700 new industrial chemicals introduced into commerce/year (4). Most chemicals in commerce have had little regulatory oversight for their introduction, use/re-use, disposal or their effects on chronic toxicities or reproductive capacity, other than teratogenicity in animal models (5, 6). Toxicity testing varies from country to country, and while in Europe, the Registration, Evaluation, Authorisation and Restriction of Chemical substances (REACH) regulation has been the most progressive approach, the majority of chemicals in commerce known to have health impacts have been tested after a health problem is recognized or potentially associated. This is in marked contrast with pharmaceuticals that undergo extensive pre-clinical in vitro and in vivo testing before widespread use is permitted.

Environmental Chemical Exposures in the Pre/Periconception/Prenatal Periods

Critical Windows of Susceptibility

Pre/peri-conceptual and prenatal exposure to environmental chemicals and subsequent effects on fecundity, pregnancy and developmental outcomes and long-term health of exposed individuals (parents and fetus/neonate) and trans-generationally comprise a growing area of inquiry (7). Toxic chemicals are currently widely distributed in homes, workplaces and communities, and contaminate food, water, air and consumer products. Human gametogenesis, embryogenesis, the developing fetus, neonate and adolescent periods are particularly vulnerable developmental “windows” to biological perturbations (Figure 2) caused by ambient levels of environmental contaminants (8-10). This is because cellular processes (meiosis, imprinting, mitosis, cell migration, proliferation, and differentiation) are occurring uniquely or more rapidly in these periods (7). While precise mechanisms of toxic chemical alterations in cellular and macromolecule functions have yet to be conclusively determined, some reflect their properties as endocrine disrupters, mimicking or inhibiting steroid hormone action (see below), or promoting epigenetic changes in key genes for development and cell cycle control or altering neurodevelopmental or other tissue/organ patterning (7). Also, most exposures are to multiple chemicals simultaneously at different levels, which can have different mechanisms of actions together than singly (8).
For couples contemplating pregnancy, pre-conception exposures to chemicals can affect reproductive capacity (8). A variety of chemicals are associated with shortening or lengthening menstrual cyclicity, endometriosis, polycystic ovarian syndrome, uterine fibroids, male infertility, male reproductive tract dysfunction, and oocyte nondisjunction (9). The most striking are cigarette smoking that affects a woman’s ovarian reserve (10), and the effect of paternal obesity on IVF outcomes (12). In addition, a variety of chemical exposures, i.e., parental exposure to DDE or PCBs and agent orange, are associated with altered sex ratios in offspring subsequently conceived (16). There is still much to be learned about pre-/peri-conceptual exposures and reproductive capacity.

Virtually all pregnant women in the U.S. have at least 43 toxic exogenous chemicals in their bodies—many at levels associated with adverse health outcomes, including harm to human reproduction and/or development (11). These include lead, mercury, tolue, perchlorate, bisphenol A (BPA), and some phthalates, pesticides, perfluorochemicals (PFCs), polychlorinated biphenyls (PCBs) and polybrominated diphenol ethers (PBDEs) (13). Many of these chemicals are found in consumer products and in the home. In some cases, such as mercury, fetal exposures to environmental contaminants may be higher than maternal exposures, and it has been observed that “to a disturbing extent babies are born ‘pre-polluted’” (14). Postnatally, maternal exposure to environmental contaminants can continue to expose a newborn through breast-feeding, although this is not a reason to discontinue breast-feeding per se.

Endocrine Disrupting Chemicals (EDCs)

Of importance to reproductive capacity is exposure to “endocrine disrupting chemicals” (EDCs), defined as compounds that “interfere with the synthesis, secretion, transport, binding, action, or elimination of natural hormones in the body that are responsible for the maintenance of homeostasis (normal cell metabolism), reproduction, development, and/or behavior” (15). Examples of EDCs commonly found in food, water, air, house dust, and/or personal care products include phthalates, BPA, PBDEs, perchlorate and some pesticides (16). Because hormonal regulation is critical to human reproduction, chemicals that perturb the system can cause permanent effects. The most well-known EDC to physicians is diethylstilbestrol (DES) and its delayed effects of benign and reproductive tract abnormalities and increased risk of female breast cancer (17). DES remains one of the most scientifically robust illustrations of the link between developmental exposure to a hormonally active exogenous chemical and adult disease (17).

Implications of the New Science for Reproductive Health Professionals

Our understanding of the nature and extent of the relationship between reproductive health and environmental chemicals is rapidly evolving. The current strength of the evidence linking ubiquitous exposure to environmental contaminants to adverse reproductive and developmental health outcomes is sufficiently robust that leading scientists and health care professionals have called for timely action to prevent harm (18). Among physicians, OB/GYNs and reproductive health professionals are uniquely poised to intervene in critical stages of human development (i.e., pre-/peri-conception and during pregnancy) to prevent harm. In 2009, the Endocrine Society reviewed the evidence of health impacts from EDCs and concluded that “the evidence for adverse reproductive outcomes (infertility, cancers, malformations) from exposure to endocrine disrupting chemicals is strong, and there is mounting evidence for effects on other endocrine systems, including thyroid, neuroendocrine, obesity and metabolism, and insulin and glucose homeostasis” and advised that “Until such time as conclusive scientific evidence exists to either prove or disprove harmful effects of substances, a precautionary approach should be taken in the formulation of EDC policy” (19). The recent report from the World Health Organization and the United Nations on Endocrine Disrupting Chemicals came to virtually the same conclusions (20).

Summary and Conclusions

It is increasingly of concern that environmental chemicals are affecting human health, including reproductive health. We are at a unique time in history, as reproductive health professionals and scientists, to assure that the state of the science and quality of the evidence are critically evaluated and that sound scientific principles are followed to guide us in minimizing environmental chemical exposures in our patients, the population at large, and generations to come. This is a global challenge best approached by global collaboration to minimize harm and maximize health and well being for all citizens of the world.

Address for correspondence:
Linda C. Giudice, MD, PhD
Distinguished Professor & Chair
Department of Obstetrics, Gynecology & Reproductive Sciences
University of California, San Francisco
505 Parnassus Avenue, M1496
San Francisco, CA 94143-0132
Giudice@obgyn.ucsf.edu

References
10. Woodruff TJ, Janson SJ, Guillet LJ, J, Giudice LC. Environmental impacts on reproductive health and...
On May 02-04 2013 a general meeting on ART and Latin America was organized in Panama by Doctor Maria do Carmo. This meeting was structured by RED-LARA, in collaboration with IFFS-UIT. Preceding this meeting, on May 1, a pre-congress course was held in response to the interest in bio-ethics. During the meeting, a very important tribute to Sir Robert Edwards was given by Ian D. Cooke. The case of Costa Rica has been analyzed in depth. A panel discussion with experts covered several aspects of the final implementation of IVF in Costa Rica. A lively discussion was held by F. Zegers, S. Munné, J. O’Brian, I. Cooke and M.T. Urbina. A session was also devoted to the state of the ART of Pre-implantation Genetics. A round table discussion was held on ovarian stimulation in 2013. Special interest was given to the use of GnRH antagonist. An additional round table dealt with controversies related to andrology.

During the opening ceremony the subject of 20 years of ICSI was addressed by P. Devroey. On Friday topics related to non-invasive imaging through parturition were discussed in a lecture given by G. Schatten. Also the black-box of implantation was analyzed. Special interest was given to the competent embryo.

A special session was devoted to oncofertility, related to the preservation of female fertility in patients with cancer: Do we freeze ovarian tissue or do we perform oocyte banking? Different topics were proposed such as in vitro maturation, trophoblast biopsy and highlights of research in Latin America.

In a special IFFS-UIT session, presentations were given on the following topics:

- How to do a study?
- How to write an abstract?
- How to write a scientific article?
- How to present a lecture?

Approximately 500 participants were present, engaging in lively discussions.
Consensus on Birth Defects in Children Born Following Assisted Reproduction

Richard Kennedy, MD
for the International Consensus in Safety in ART Group

Since the introduction of Assisted Reproductive Technology (ART) there have been a series of publications which have shown a small but significant increase in the likelihood of birth defects in children born following ART. The data however is at times inconsistent and open to interpretation due to a number of confounding factors.

In order to reach a consensus on this important issue, several leading international organisations in the field of ART have come together under the auspices of a Collaborative on Safety in ART. The participating organisations are American Society for Reproductive Medicine (ASRM), European Society of Human Reproduction and Embryology (ES-HRE), International Committee Monitoring Assisted Reproductive Technologies (ICMART), International Federation of Fertility Societies (IFFS) (Chair) and Society for Assisted Reproductive Technologies (SART).

Confounding data

One of the key areas of concern in interpreting outcome studies reporting on birth defects following ART are the confounders of this data. Inclusion in birth defect registries may vary according to the timing of diagnosis and whether there is inclusion of pre-implantation losses and termination following prenatal diagnosis of birth defects. Furthermore data are weakened by several confounding factors such as the underlying impact of infertility, multiple pregnancy and the demographic characteristics of the infertile population and may be biased through ascertainment, lack of proper controls and conclusions based on extrapolation as a result of insufficient sample size, especially when considering rare abnormalities. For the purposes of ART surveillance, we call for consistency in the application of these criteria as well as the definitions applicable so as to enable valid investigation of these and other reported associations. In constructing this consensus the definition of infertility described in the 2009 ICMART WHO revised glossary of ART terminology and the definition of birth defect was used by the CDC and WHO.

Evidence base for this consensus

The increased risk of a baby being born with a birth defect following ART has been reported in several systematic reviews which have produced broadly similar results. However it is also evident from a number of studies that the underlying infertility itself plays a significant role in the increased risk. Whilst it appears that the association with birth defects is stronger with ICSI than with IVF, the evidence is inconsistent. In addition there is no convincing data to relate an increased risk to any other procedure involved in ART with the possible exception of blastocyst culture. In this latter case, the association is more likely to be related to an increased risk of monozygosity although further evidence is required. Readers are directed to the reference list of evidence used in this consensus.

Consensus statements

1. Overall, ART has produced approximately five million children and can be regarded as safe technology for the vast majority of children resulting from treatment.
2. Couples who have infertility and then conceive naturally, compared to fertile couples, have a slightly increased chance of conceiving a child with a birth defect.
3. Overall, there is a modest but significant increase in the possibility of a baby born following ART suffering from a birth defect compared to a fertile population, but not compared to infertile women who give birth without ART.
4. There are insufficient data to demonstrate a proven relationship with a particular anomaly, possibly excepting hypospadias in ICSI offspring.
5. There is no proven or consistent relationship to a specific assisted conception procedure. Studies comparing outcomes from IVF and ICSI are inconsistent. Some have reported similar increases in the risk of a birth defect with both IVF and ICSI whereas other publications indicate a significant risk with ICSI but not with IVF irrespective of giving birth naturally or following ART.
6. Multiple pregnancy is known to be associated with an increased incidence in birth defects. This increase is most marked in monozygotic compared to dizygotic pregnancies. Some studies suggest that blastocyst transfer increases the risk of monozygotic twin pregnancy, although the overall incidence of monozygotic twins in the ART population is less than in the general population.
7. Available evidence shows that cryopreservation of gametes and embryos is not associated with an additional risk of birth defects.
8. Patients planning to undergo IVF / ICSI should be provided written information about the treatment which should include the above information.
9. There is a need for international agreement of the scope of surveillance of birth defects so that it includes: birth defects identified antenatally, at birth to 42 days post-delivery and within the first year of life. For birth defects that are identified antenatally information about termination of pregnancy is critical to determining the incidence of birth defects. For lethal congenital abnormalities, cause of perinatal (fetal and neonatal) death data is essential information for the birth defect registers for monitoring safety and quality of infants born following assisted reproduction.
10. There is a continuing need for international surveillance of birth defects in children born following assisted reproduction. This is particularly important following new techniques. These statements are made in July, 2013. New evidence will be reviewed as it becomes available and used to update this document.
History of the International Federation of Fertility Societies

Roger D. Kempers, MD
Professor of Obstetrics and Gynecology, Emeritus
Mayo Clinic School of Medicine

The 21st Triennial IFFS World Congress caps a long and outstanding history of important scientific conferences bringing the latest advances and knowledge in fertility research and practice to a global audience. IFFS is honored that its 2013 World Congress is a conjoint meeting with the American Society for Reproductive Medicine (ASRM), repeating the success of the 1998 World Congress also sponsored jointly by these two organizations.

The first World Congress was held in New York City in 1953 and served to launch a grand tradition of signature World Congresses. Since its inception, IFFS has held 20 triennial congresses across the globe and looks forward to continuing this practice.

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Roger D. Kempers, MD
Professor of Obstetrics and Gynecology, Emeritus
Mayo Clinic School of Medicine

Welcome to the land of rich heritage

NEW DELHI

22nd IFFS World Congress
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Hosted by:
Indian Fertility Society &
Indian Society for Assisted Reproduction

Contact Information for IFFS Secretariat

INTERNATIONAL FEDERATION OF FERTILITY SOCIETIES
IFFS SECRETARIAT OFFICE
19 MANTUA ROAD, MT. ROYAL, NJ. 08061
TEL.: 1 856 423 7222; FAX.: 1 856 423 3420
E-MAIL: SECRETARIAT@IFFS-REPRODUCTION.ORG
WEBSITE: WWW.IFFS-REPRODUCTION.ORG