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Over the last 15 years, IFFS has undergone an important transformation from a Federation planning a Congress every 3 years to a modern organization with proper structures and a strong commitment to science and education.

However, as these changes are still evolving, it was felt that it would indeed be very interesting to look back into the history of IFFS: how and when the Federation started, who were the pioneers and what was their vision, which were the difficulties and the long path leading from the early days to today’s structure.

Hence, the Executive Committee decided to ask Roger Kempers, who has been involved with IFFS for a long time and has personally known some of the founders, to undertake this ambitious project. Undoubtedly, this was not an easy task, since the available sources were not abundant, but, fortunately, Roger accepted gladly.

Using a review by Kurt Semm, the minutes of the different Board Meetings, but also his personal recollections as well as those of other IFFS officers, he managed to put together a detailed chronicle about the foundation and evolution of IFFS, which appears in this issue of the Newsletter.

The Executive Committee and all the members of IFFS are most indebted to Roger Kempers for his great effort to provide us with this exciting information, a great part of which is not widely known, especially to our younger colleagues. Moreover, this historical perspective is extremely valuable because it gives us the opportunity, when setting our goals for the Federation, to bridge the past with the future.
It was my extraordinary privilege to have served the IFFS in several capacities for over 20 years. With this background I have attempted to provide a brief history of the Federation. I have not attempted to review all the amazing scientific advances that occurred during the life of the federation but have rather attempted to record some of the details of the evolution of the organization and provide important tabular records such of those who have been awarded Honorary Membership. For history of the first three decades I am deeply indebted to the late Kurt Semm, Kiel, Germany for the historical review he published in 1989 from which I have quoted liberally. He had served as Secretary General of the Federation since its inception in 1968 until 1983 when he became President-elect. This gave him ready access to the historical records for his report. Information following his historical review is taken from the minutes of board meetings and personal recollections, both mine and of my colleagues in the IFFS leadership.

Beginning of the International Fertility Association (IFA)

There was no international organization devoted to problems of human infertility existing prior to late 1951. In fact, at that time, there were only a few recently formed national fertility organizations such as those in the United Kingdom, the United States and Brazil. The first major congress of the fledgling Brazilian Society for Sterility was organized by Arthur Campos da Paz in Rio de Janeiro, Brazil October 14-18, 1951. The program was centered around a number of invited international speakers. It was during a casual dinner conversation among six of them late on the evening of October 16, 1951, in the Gloria Hotel that the idea arose to form a new society to be called the “International Fertility Association”. In attendance were the following:

Campos da Paz, Arthur, Rio de Janeiro, Brazil
Guerrero, Carlos D., Mexico D.F., Mexico
Murray, Edmundo, Buenos Aires, Argentina
Weisman, Abner I., New York City, USA
Weinstein, Bernard B., New Orleans, USA
Williams, Walter W., Boston, USA

Minutes were kept. A document outlining the needs and purposes for such a society was drafted. Campos de Paz was appointed Provisional Chairman and was instructed to invite a larger group of medical leaders in attendance at that congress to meet the following day to more formally found the new society.

The document read as follows:

Whereas:
I. There is a need for promoting the study and investigation in the field of human fertility all over the world;
II. There is a need for coordinating the work and disseminating of studies being carried out in various parts of the world;
III. Our utmost effort and knowledge should be the purpose of satisfying the desire of married couples to bear children, through the holding of International Fertility Congresses to permit the exchange and coordination of ideas from all over the world;
IV. The causal factors and psychological and medi-co-social repercussions of human sterility are almost the same in all parts of the world;
V. For proper organization and for the achievement of the objectives mentioned there is a need for an international agency capable of satisfying the goals mentioned;

There is therefore felt to be justification for the founding of the “International Fertility Association” (IFA)

Purposes of the Association:

a. To sponsor the holding of international congresses in the specialty at regular intervals and in different parts of the world.
b. To standardize and orient processes for the studying and classifying of sterility all over the world.
c. To encourage scientific and social research in the field of infertility without limitation of national frontiers.
The successes of cancer therapy led those in the field to envision fecundity after cancer. The successes of assisted reproductive therapies usually described as Technologies (ART) offered new efficacious options for optimizing the chances of pregnancy after cancer. These therapeutic measures include notably, emergency or immediate ART prior to chemotherapy with freezing of embryos or oocytes and the freezing of ovarian fragments. Furthermore, donor-egg IVF forces us to reconsider certain surgical options, as in the case of ovarian cancer for preserving the uterus even when both ovaries need to be removed.

Breast cancer: the most frequent cancer in young women.
The most frequent of all cancers in women, breast cancer, is also the most frequent in women <40 years of age. Surveys indicate that questions regarding fecundity and ways to preserve it are most commonly not discussed. Delays in seeking help prevent women from properly considering all the possible options without risking disruption of the cancer treatment. First amongst questions regarding pregnancies after breast cancer is whether this may increase the risk of cancer recurrence. Fortunately, the literature unanimously reports reassuring information with all but one publication actually showing a decrease in recurrence risk following pregnancy. This remained true irrespective of when (25 years after cancer) and how (spontaneous or through ART) the pregnancy took place and whether the tumor was hormone receptor positive or negative.

Emergency or immediate ART in case of breast cancer: banking potential pregnancies, just in case.
Treatment for breast cancer typically includes surgical removal of the tumor, which is most often followed by adjuvant chemotherapy 3-6 weeks later. This leaves ample time for one cycle of emergency or immediate ART, provided that there is forward planning. An alternate reverse sequence or neo-adjuvant regimen uses chemotherapy before surgery. Experience indicates that the neo-adjuvant protocol is solely superior in case of inflammatory cancers.

Aromatase inhibitors (AI): COH with low E2 levels.
The fear that the high E2 levels of COH could impact on breast cancer recurrence have led to choosing stimulation regimens that minimize plasma E2 elevation. Oktay et al. demonstrated that the continuous use of the AI, letrozole (Femara®), allowed stimulation of a normal crop of follicles while maintaining E2 below menstrual cycle levels. In the case of breast cancer, immediate ART keeps the chances of spontaneous pregnancy unaltered.

Freezing oocytes rather than zygotes in the single woman.
In the case of immediate ART, embryos are frozen at the zygote stage. In the absence of a stable relationship however, it is now possible to freeze mature oocytes with slow freezing or vitrification techniques. Recent progress has been made in these fields because of 2 distinct factors. 1. Vitrification has gained credence based on positive results reported at all stages of development, from oocytes to zygotes and blastocysts. 2. Slow freezing techniques have been adjusted and refined for oocyte freezing under pressure from a new Italian law that precludes the insemination of more >3 oocytes in ART.

Bimodal follicular decay determines when ovarian freezing can be considered.
Women’s personal endowment with primordial oocytes decreases with time, from 2 millions at birth to approximately 400,000 at menarche and barely 1,000 at menopause. Gougeon’s team undertook the behemoth task of charting the number of primordial follicles present throughout life, based on histological analyses of ovarian specimens obtained from women of all ages. Their data revealed that follicles disappear following a bimodal pattern (Fig. 1) with first a slow depletion phase and later, a rapid depletion phase starting around the age of 37, when the total number of remaining follicles falls below a critical value of 25,000. The authors determined that it is the number of remaining oocytes (<25,000 oocytes) rather than chronological age that determines when the second or rapid depletion phase starts. Theoretical calculations have concluded that if the second or rapid depletion phase did not exist, menopause would occur at the age of 71. In view of the above, it is possible to predict the consequences of the abrupt loss of 50% of the remaining oocytes that result from removal of a single ovary (Fig. 1). If the loss of 50% of primordial oocytes leaves >25,000 oocytes, as it would be the case at the age of 20, follicular decay will remain in the slow depletion phase after oophorectomy, with minimal impact on ovarian ageing. Conversely, if oophorectomy is performed later, when the net loss of 50% of primordial follicles will bring the remaining value to <25,000, it will accelerate ovarian ageing and reduce...
the chances of spontaneous pregnancies. From Waddy’s chart we see that this would be the case as early as at the age of 27, when oophorectomy would lead to the fast depletion phase, which is normally encountered around the age of 37. Consequently, we believe that ovarian cryopreservation is not indicated in case of breast cancer, which usually strikes after the age of 27.

Conservative surgery in case of borderline and early stage ovarian cancer
Borderline tumors of the ovary, commonly diagnosed at FIGO stage I, have an excellent prognosis. In spite of this, textbooks still recommend extensive surgery with total hysterectomy and bilateral slingo-oophorectomy (TAH-BSO). Yet overwhelming evidence today supports more conservative approaches that preserve the uterus with all or part of an ovary. Likewise, women with FIGO stage IA, grade 1-2 ovarian cancer, who have a 5-year survival rate of 90-95%, may be eligible for conservative surgery with preservation of the uterus and possibly the contralateral ovary. Women however need to be fully informed, nulliparous and have explicitly expressed their eagerness to preserve their chances of pregnancy.

Pregnancies after cancer: Fear the great Turner syndrome dread.
During its heyday, donor egg-IVF was offered to young women with Turner’s syndrome without many afterthoughts. Yet cardiovascular risks loomed large when Turner patients who presented anatomical anomalies of the aortic arch and/or with bicuspid variants of the left cardiac valve became pregnant. Today, appropriate screening is mandatory before considering pregnancy in a Turner patient. Lessons learned the hard way in the Turner syndrome context should serve to stress the need for appropriate screening in women with a past history of cancer and chemotherapy before they become pregnant. Regarding chemotherapy, the primary concerns are about the use adriamycin derivatives, which may affect cardiac function. Likewise, exposure of the aortic arch to radiation therapy, as in the case of left breast cancer, may increase the cardiovascular risk associated with pregnancy. Hence, we strongly recommend preconception cardiac screening when pregnancy is considered after cancer.

Assessing the ovarian reserve for predicting fecundity after cancer
The state of the ovarian reserve prior to surgery and/or chemotherapy-radiation therapy will impact heavily on the chances of pregnancy after treatment. It is therefore important to determine the state of the ovarian reserve before starting cancer treatment. This is now practical with the measurement of serum anti Mullerian hormone (AMH) level and the total count of ovarian follicles present in both ovaries (total AFC), which can be done at any particular time in the menstrual cycle. In ovarian cancer patients, baseline AMH and total AFC values will help determine the possible benefit from attempting to preserve an ovarian fragment. In case of insufficient AMH and total AFC values, it is not warranted to retain ovaries from which one could not benefit.

Conclusion
Long term survival after cancer has led to consideration of fecundity after cancer. Breast cancer is the most frequent cancer encountered in women of reproductive age whereas the majority of lymphomas and hematological cancers affect individuals <40 years of age. It is estimated that approximately 50-70 women per million inhabitants are concerned yearly by post-cancer fecundity preserving measures. The need for specialized care must therefore be scaled accordingly.

Guidelines need to be agreed through multidisciplinary validation processes in each community so that fecundity needs of cancer patients can be appropriately catered for. It is necessary to emphasize that fecundity-preserving measures are to be undertaken in full agreement with the cancer team.
From 6-8 August, 2007 Prof. Johan Smitz, of Brussels and Prof. Martha Valdivia Cuya, ran the third International Symposium on Reproductive Sciences at the San Marcos University in Lima, Peru. This was supported by IFFS, who additionally provided four scholarships for local participants and the Colombian Association of Fertility and Sterility provided two more. Lecturers came from Argentina, Chile, Peru and Belgium and the 27 participants came from Colombia, Chile, Bolivia and Peru. The topics discussed were in vitro technologies in reproductive management, gonadotropins as drugs and reproductive hormones as therapeutic tools. It is important to spread skills across the continent.

IFFS continued its programme of Workshops, this time in Sri Lanka, holding one in Colombo on 24-5 September, 2007 after WHO invited us to deliver it. The activity, with 60 participants, concentrated on ethical issues in ART as clinics were increasing in number and there was a need for the profession to advise the government about regulation. WHO had been asked for help by the National Co-ordinating Committee on Reproductive Health Research, The University of Colombo, The Institute of Biochemistry, Molecular Biology and Biotechnology and the College of Obstetricians and Gynaecologists and had turned to IFFS to deliver that information and support. The Secretary-General, Dr. Richard Kennedy and I contributed to discussions of representative clinical situations. Later, small groups discussed and made recommendations for ethical practice in Sri Lanka, so that representations could subsequently be made to government about the nature of future regulation. A more formal basis for ethical review was given to another group of 30 younger participants. Complex cases were presented for lively general discussion. It was clear that recommended practice differs in every place, and local attitudes need to be taken into account. Although Western philosophical ideas underpin much dialogue on ethics, it was fascinating to appreciate that the Eastern origins of Buddhism also have a significant impact in such countries. It would be informative to encourage greater exchanges between cultures. We have much to learn from each other.

A further Workshop was held by Prof. Smitz on behalf of IFFS with Dr Soledad Sepulveda from Peru in Baranquilla, immediately prior to the Colombian National Congress on 9-10 October. The topics were in vitro maturation and cryopreservation and the Workshop was held in the Procrear Clinic with 10 embryologists attending to extend their experience. This was a valuable opportunity to use the facilities of an established clinic for educational purposes, an example which should be encouraged.

One of the elements of the educational programme of IFFS is the development of a Low Cost IVF programme in conjunction with the Low Cost IVF Foundation of Switzerland. Discussions with a Special Task Force of ESHRE, “Developing countries and infertility” lead to a recognition of mutual interest and participation in a meeting in Arusha, Tanzania on 15-17 December organised by Willem Ombelet of Ghent, Belgium. The intensive interactions of the 37 participants resulted in a plan to co-ordinate activities to promote skills and training. Publications will follow and collaboration in efforts to provide skills
and services will be augmented. There is a need to recruit donors for these programmes and scientists and clinicians who would be prepared to devote time and energy to creating these new programmes. Please make contact if you think you could help.

Plans are well advanced for Workshops in 2008. These are to be in Iran from 8-10 May, Tunisia on 18 May, and in China on 20-22 June, others are at earlier stages. The plans for 2009 have already begun for Malaysia, Ivory Coast and Chile. An interest in developing ethical workshops is growing, an idea initially propounded by the late Jean Cohen, a member of our Education Committee and a Past President of IFFS.

A third arm of our educational programme is e-learning. The current idea is to identify websites around the world which have high quality content in reproductive biology and medicine and negotiate access to some of their material, which can be co-ordinated through the IFFS website. The IFFS portal could be entered by identified members of national Societies. A good deal of material has already been identified, but if you know of websites which have such material, please let me know at i.d.cooke@sheffield.ac.uk. It is hoped to facilitate availability of highly rated information to those who currently find it difficult to identify and use.

The Education Committee has been expanded and now includes representatives from more countries. Different perspectives on education are being presented and corresponding opportunities will develop. If you have ideas or requests please make contact. We have been fortunate to have had substantial support from Casmed, IBSA, Organon and Schering Plough (recent donor) and Serono in the form of unrestricted educational grants. These allow IFFS to develop a programme with a national Society on subjects that the local Society wishes to have. The IFFS speakers contribute as well as local speakers and the exchanges are valuable for all concerned. It is hoped that these experiences will continue to be shared with many societies, promoting international standards, and creating new networks for future expansion.

Since the first successful pregnancy and birth following IVF-ET by Edwards and Steptoe in 1978, the results of the assisted reproductive technology (ART) have been dramatically advanced by the improvement of basic techniques and the development of new techniques. In Japan, ART also has been remarkably developed and generalized.

Although there were only 27 ART institutions in Japan in 1986, the number has risen to 641 in 2005. The number of cases treated has also rapidly increased since the 1990s, and the number of cases of standard IVF-ET increased to 42,822 in 2005. The number of cases of ICSI dramatically increased after 1999 and it has further increased to 47,579 cycles in 2005. If the cases of frozen embryo transfer (35,013 cycles) are included, then ART treatments of approximately 125,000 cycles are conducted each year in Japan. Since 1999, in particular, the number of the cases of ICSI has increased remarkably compared with that of standard IVF. As a result, it means that 1.6% of children have been born by ART. One half of them were born by ICSI and one quarter of them by frozen embryo transfer.

However, at the same time, there are problems involved in the progress of reproduction medicine in Japan.

Late marriage may well be the cause of infertility. There has been a continuing trend to marry later in Japan. Already, approximately half of the women in Japan become pregnant and give birth for the first time in their thirties. Therefore, the number of infertility patients has increased and their treatment window is shortened. As a result, the patients needing of ART have increased.

Medically, the infertility treatment results have been dramatically improved with ART and the treatment of ovulation induction with gonadotropin. However, the cases of multiple pregnancies and the side-effects caused by OHSS have increased substantially. From recent data concerning multiple pregnancies, 3/4 of those caused by fertility treatment were associated with ART

Some ethical and legal problems including surrogate mother and parent-child relationships occur at the social level. Medical expenses for receiving ART are quite high, so that the economics of fertility treatment should also be investigated. Because it is predicted that the number of patients in need of ART will increase more and more, these problems should be resolved as soon as possible.
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