IVF-Worldwide Survey

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RESULTS-Oocyte Donation

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Oocyte Donation Survey - Results

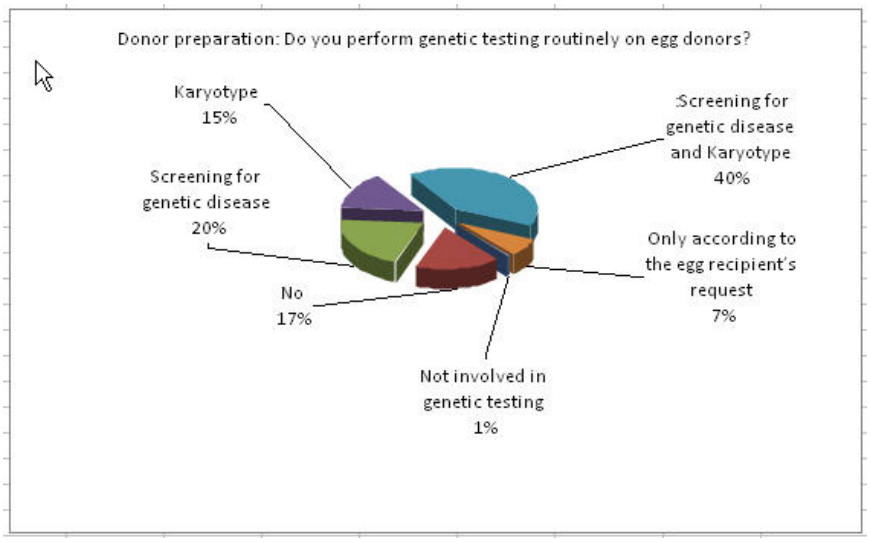
The purpose of the this survey is to explore current trends, practices, and issues related to donor and recipient evaluation and treatment.

Oocyte donation is widely practiced worldwide, and since its introduction almost 30 years ago, has become an extremely efficient therapeutic approach for both pre- and postmenopausal women who are in need of donor eggs. Like any other field in medicine, and in particular, reproductive medicine, many of the current practices associated with donor and recipient preparation and treatment have not been standardized. The purpose of the this survey is to explore current trends, practices, and issues related to donor and recipient evaluation and treatment.

The survey is conducted by Dr. Ariel Weissman, Wolfson Institute, IVF Center, Israel

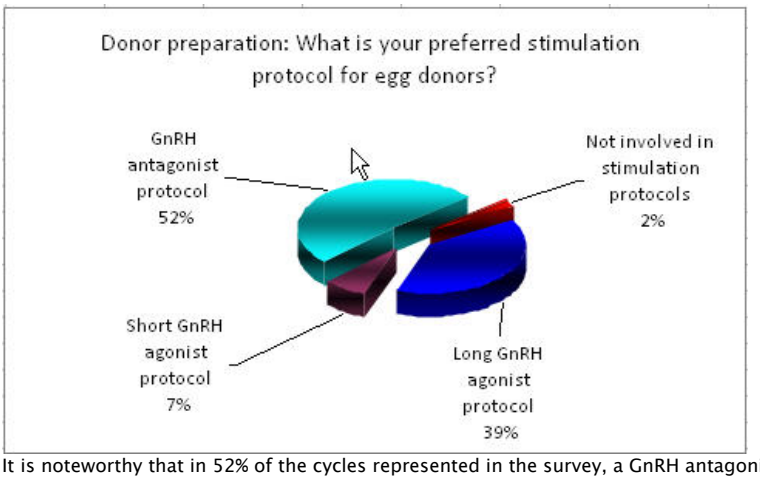
Continent	IVF Cycels	%	Egg donation cycles	%
USA & Canada	22900	22.3	2530	16.9
South America	7800	7.6	1840	12.3
Australia & New Zeland	9000	8.8	590	3.9
Asia	19900	19.4	2510	16.8
Europe	37300	36.4	5950	39.7
Africa	5700	5.6	1560	10.4
Total	102600		14980	14.6

Since the Monash IVF team's announcement of the birth of the first healthy baby conceived by oocyte donation in 1983 (Trounson et al., Br Med J 1983), the use of oocyte donation has spread exponentially. Today, oocyte donation is widely used throughout the world, except in countries where it is legally prohibited (Italy, for example). It is impossible to give a true estimate of the number of oocyte donation cycles performed annually worldwide. In the US alone, the latest CDC data (from 2009) reveals that 17,697 oocyte donation cycles (frozen oocytes: 6,659 cycles, fresh oocytes: 11,038 cycles) were performed (http://www.cdc.gov/art/ART2009/section4.htm), representing approximately 12% of all ART cycles performed in 2009. While the success rates of oocyte donation cycles have been consistently high, usually higher than those of non-donor cycles, practices regarding the evaluation and preparation of both donors and recipients vary considerably among countries and clinics. Very few interventions related to oocyte donation are evidence-based. The purpose of the oocyte donation survey was to analyze clinical and laboratory practices, as reflected by clinicians from five continents.

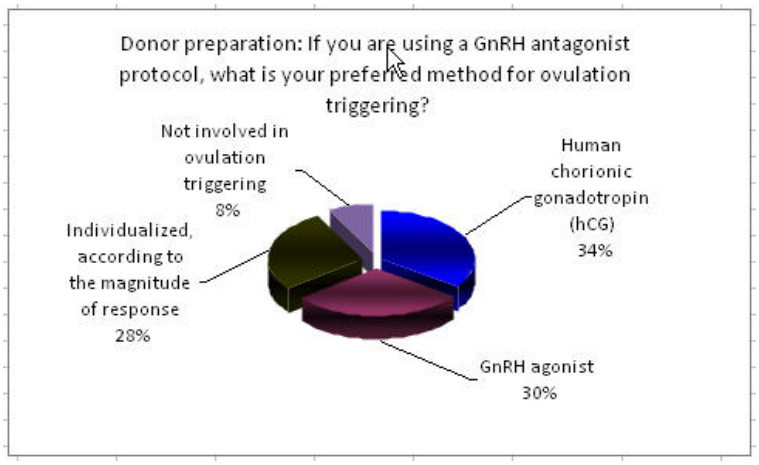


One of the most important aspects of a safe and successful oocyte donation program is the screening for genetic disease. As there are no uniform guidelines available, there is great variability in genetic testing requirements, as reflected by the survey. In 18% of the cycles represented in the survey, no genetic testing was performed, and 60% performed genetic testing regularly, of which 40% performed both karyotyping and testing for genetic disease.

In the US, new ASRM Practice Committee guidelines for oocyte donation suggest that cystic fibrosis testing should be performed on all donors. Consideration should be given to performing chromosome analysis and fragile X testing on donors, but is not required.

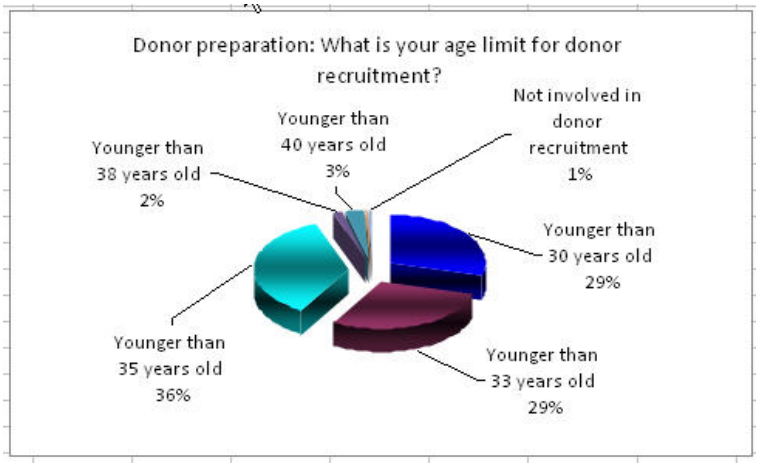


It is noteworthy that in 52% of the cycles represented in the survey, a GnRH antagonist protocol was used for donor stimulation. Most likely, this had not been the case until several years ago. Clinicians and scientists now recognize that compared to GnRH agonist-based protocols, there is a lower statistically significant incidence of ovarian hyperstimulation syndrome (OHSS) in GnRH antagonist cycles (Al Inany et al., Cochrane Database Syst Rev 2011). In a recent meta-analysis, no significant differences were observed in pregnancy rates or in the number of retrieved oocytes after donor stimulation with GnRH agonist or antagonist protocols (Dodri et al., Fertil Steril 2011).

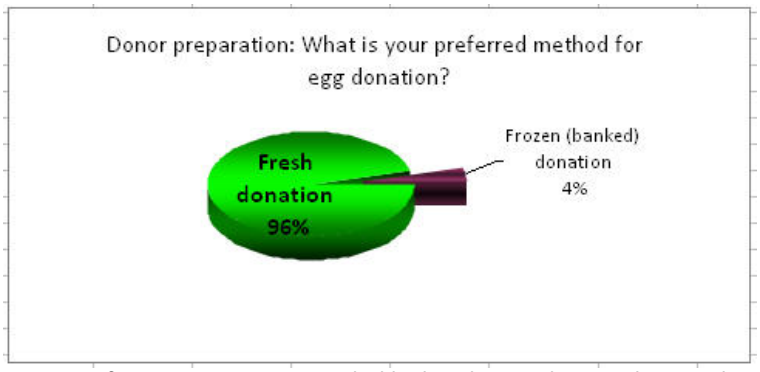


The use of GnRH antagonist stimulation regimens for oocyte donors has not only directly reduced the risk for OHSS, but it also gives the clinician a choice between hCG and a GnRH agonist as the ovulatory trigger. Using a GnRH agonist to trigger final oocyte maturation has shown to reduce significantly the occurrence of OHSS compared to using hCG, and represents a valid

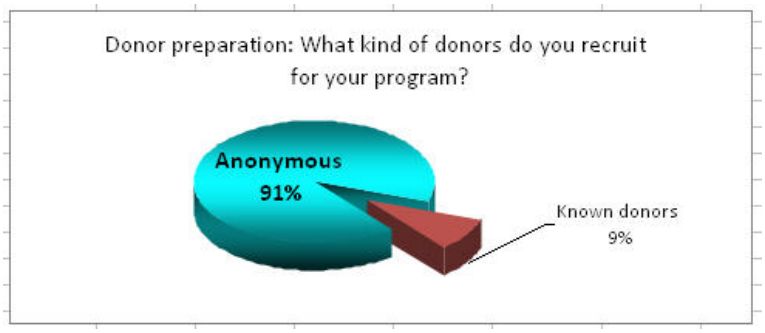
alternative for hyperstimulated oocyte donors to further reduce fetal morbidity. In terms of efficacy, a recent Cochrane Review showed that in contrast to fresh non-donor cycles, in donor recipient cycles, there was no evidence of a statistical difference in the live birth rate per randomized woman (Youssef et al., Cochrane Database Syst Rev 2011).



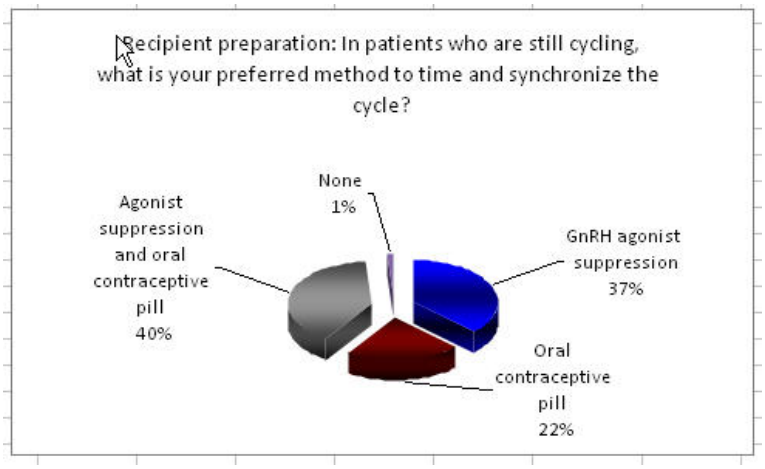
No uniform inclusion criteria exist. New ASRM Practice Committee guidelines suggest that donors should preferably be between the ages of 21 and 34 years. Generally, it is preferable that oocyte donors be under 30 years old, as younger donors appear to have higher pregnancy rates (Balmaceda et al., Hum Reprod 1994; Cohen MA et al., Hum Reprod 1999). The oocyte donation survey reveals that in 94% of the cycles reported, donors are younger than 35 years.



Oocyte vitrification is emerging as a valuable clinical ART technique. The equivalence in outcomes for frozen-thawed and fresh oocytes was demonstrated recently in a randomized controlled trial (RCT) (Cobo A et al., Hum Reprod 2010). While frozen (banked) oocytes represented only a small proportion (4%) of the cycles reported in the oocyte donation survey, this percentage is expected to rise in the near future.

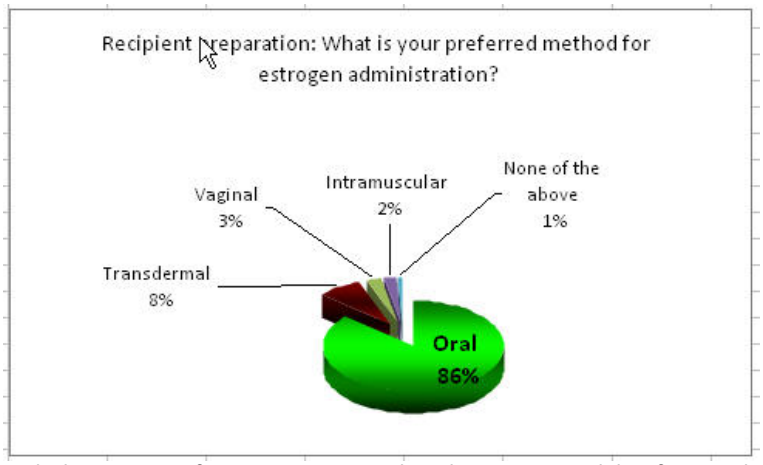


In the vast majority of countries, only anonymous donations are allowed, and there has been a long-standing debate as to whether it is ethical to use known donors. In programs that responded to the survey, 91% of the treatment cycles were conducted using only anonymous donors, probably reflecting worldwide donor recruitment percentages.

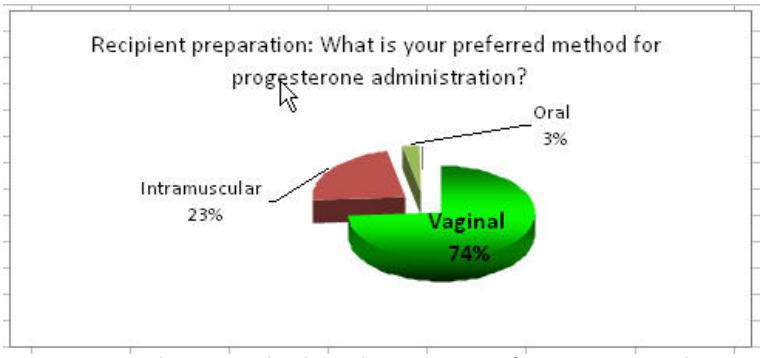


Although oocyte donation cycles have been used clinically for many years, there is no agreement about the optimal way to prepare the endometrium prior to embryo transfer and to care for the endometrium following transfer. Surprisingly, very few RCTs have been conducted to assess the various methods for endometrial preparation, and of those that have been published, very few report the live birth rate, which is without a doubt, the most important parameter for the critical assessment of the intervention studied.

Endometrial preparation and synchronization in amenorrheic recipients is straightforward. Ovulating recipients may be at risk of premature ovulation and cycle cancellation. In many patients, pretreatment with an oral contraceptive pill followed by high-dose estrogen is sufficient to prevent ovulation. Nevertheless, because of the fear of cancellation, GnRH agonist suppression is used in many clinics, as evidenced by the high figure of 77% agonist suppression use in cycles reported in the survey. In a recent Cochrane Review, (Glujovsky et al., Cochrane Database Syst Rev 2010), looking at both artificial preparation for frozen-thawed embryo transfer and oocyte donation cycles, no significant benefit was demonstrated for using GnRH agonists. Of course, the use of banked oocytes makes the use of GnRH agonist suppression unnecessary.

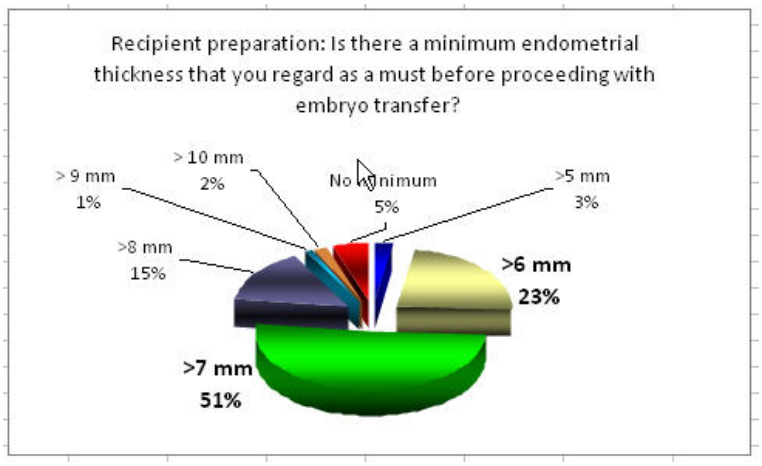


Oral administration of estrogen is very simple and convenient, and therefore it is the method of choice in most oocyte donation programs (86% in the oocyte donor survey). Transdermal estrogen adequately prepares the endometrium with overall lower serum estrogen concentrations because there is no hepatic first-pass effect. The supraphysiologic serum E2 levels associated with oral micronized E2 (10-fold higher than transdermal) may have a deleterious impact on endometrial receptivity (Krasnow et al., Fertil Steril 1996). In cases with lack of or slow endometrial response, vaginal or IM estradiol may be added.

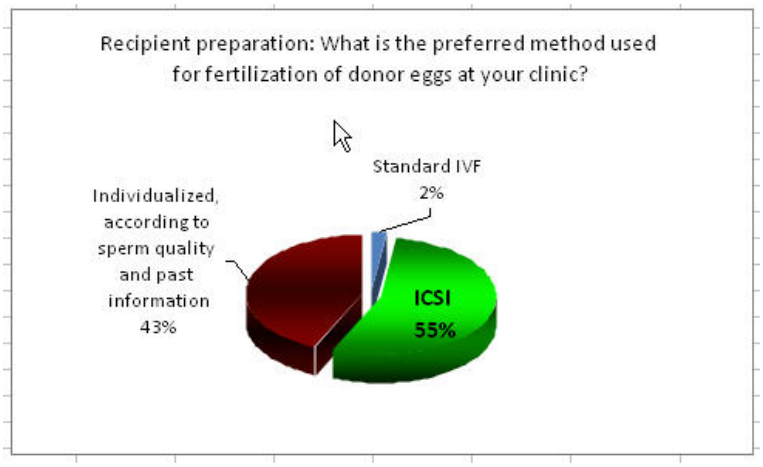


For many years, the IM route has been the sine qua non for progesterone administration in oocyte donation programs. For an unknown reason, many clinicians that have switched to vaginal progesterone for luteal support in fresh ART cycles, are still concerned and unwilling to adopt the vaginal route as a first-line treatment. It appears, however, that this trend is now changing, as reflected by the fact that in 74% of the cycles reported in the survey, the vaginal route was the preferred method for progesterone administration, versus only 23% for the IM route. A recent retrospective study in the US (Berger and Phillips, J Assist Reprod Genet 2012) showed that the switch from IM to vaginal progesterone administration did not have a negative

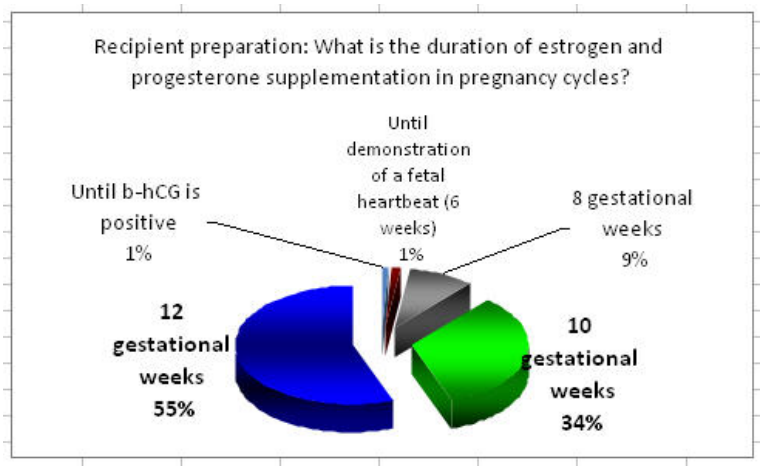
effect on the outcome.



Despite the lack of firm evidence, endometrial thickness is considered an important surrogate marker to assess endometrial receptivity and predict cycle outcome in oocyte donation cycles. Many studies have suggested a correlation between endometrial thickness and uterine receptivity, with significantly higher pregnancy rates the greater the endometrial thickness (Zenke et al., Fertil Steril 2004; Noyes et al., Fertil Steril 2001). In contrast, others have failed to demonstrate such a relationship among endometrial thickness, pattern, pregnancy, and implantation rates (Garcia-Velasco et al., Fertil Steril 2003; Remohi et al., Hum Reprod 1997; Barker et al., J Assist Reprod Genet 2009). There is probably no endometrial thickness limit below which implantation is impossible, and successful pregnancies have been reported with an endometrial thickness of 3-4 mm. Thus, in 5% of cycles reflected in the survey, no minimum of endometrial thickness was required, 3% required a minimum of 5 mm, and the majority (51%) required a minimum of ≥7 mm.



Oocyte donation per se is not considered an indication for the use of intracytoplasmic sperm injection (ICSI), and in many programs, ICSI is used only when indicated, for example, with co-existing male factor infertility. Nevertheless, in order to maximize the outcome and to avoid unexpected low fertilization rates with standard IVF, in many programs, ICSI is routinely used for all patients in all cycles. This trend was well reflected in the survey, in which 55% of cycles reported that ICSI was used.



In the majority of cycles reported in the survey, hormone replacement was continued until proof that the utero-placental shift had occurred. This shift is believed to occur at eight gestational weeks. In only 8% of the cycles reported, clinicians felt safe to withdraw hormonal support at eight weeks. Most preferred to continue a bit longer, and in 34% of the cycles, hormone

replacement was discontinued at 10 gestational weeks. In 55% of the cycles hormonal support was discontinued at 12 gestational weeks.

Do you routinely include the following adjunct in the recipient's protocol?		
	Yes	No
Low dose aspirin	31%	69%
Steroids	17%	83%
hCG	7%	93%

Recipient preparation: adjuvant use of low dose aspirin and steroids

There is insufficient data to support the routine use of either low dose aspirin or steroids in oocyte donation programs (Glujovsky et al., Cochrane Database Syst Rev 2010). This is in agreement with previous findings on the lack of benefit from the use of peri-implantation steroids in fresh ART cycles (Boomsma et al., Cochrane Database Syst Rev. However, these conclusions are based on very few studies, and there is a lack of large RCTs on oocyte recipients. This might be a partial explanation for the survey finding that despite the lack of evidence, low dose aspirin (31%) and steroids (17%) are prescribed to oocyte recipients.**Recipient** 2007)

preparation: adjuvant use of hCG

Tesarik et al. (Reprod Biomed Online 2003) demonstrated an increased implantation rate after the administration of hCG during the early secretory phase of patients undergoing egg donation cycles combined with pituitary down-regulation. No subsequent RCTs are available on oocyte recipients. In a RCT on patients undergoing artificial endometrial preparation for frozen-thawed embryo transfer without pituitary suppression, Ben-Meir et al. (Fertil Steril 2010) found no advantage concerning pregnancy and implantation rate by supplementing the secretory phase with hCG. Some clinicians, however, have adopted this intervention, as reflected in 7% of the cycles reported in the survey.

|Introduction|Patients' investigation and evaluation|IVF - Drugs in use|IVF - Stimulation protocols|IVF - Monitoring|IVF - Egg collection|IVF - Sperm collection|IVF - Fertilization & embryo growth|Embryo transfer|IVF - Luteal support|IVF - Due Date Calculator|Pregnancy following IVF|IVF - Complications|Up to date|Israel lawyers|IVF - New terminology|IVF regulation around the world|IVF - costs (Worldwide)|IVF - Global Perspective (environnants)|IVF - Global Perspective (religious)|Age related infertility|Female investigation|Male investigation|IVF - Guideline for drug administration|IVF - Culture media|In-Vitro Maturation (IVM)|IVF - Cryopreservartion|IVF - Cryopreservartion|Preimplantation Genetic Diagnosis (PGD)|Intracytoplasmic Sperm Injection (ICSI)|Blastocysts|Assisted Hatching Partial Zona Dissection (PZS)|Embryo freezing|Embryo Bank|IVF - Quality control of the process|Birth defects|Ovarian Hyperstimulation Syndrome (OHSS)|Bleeding|Infections|Ectopic pregnancy|Egg donation|Surrogacy|Clomiphene Citrate|Human menopausal gonadotropins (hMG)|Instructions how to inject the drug|Recombinant gonadotropins|Instruction to inject of Gonal-F|Instructions to inject of Puregon|Recombinant LH|Gonadotropin Releasing Hormone (GnRH)|Human chorionic gonadotropin (hCG)|Progesterone|Egg bank|Sperm bank|IVF treatment and procedures|IVF - Eggs for assisted reproduction|IVF - Eggs for research|IVF - Preimplantation genetic diagnosis|IVF - Research cloning|IVF - Sex selection|IVF - Surrogacy (worldwide)|Number of cycles performed around the world|The costs of IVF in different countries|Literature summary of the costs of IVF|Policy of reimbursement|IVF - Islam|IVF - Christianity|IVF - Judaism|IVF - Hindu|IVF - Buddhism

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