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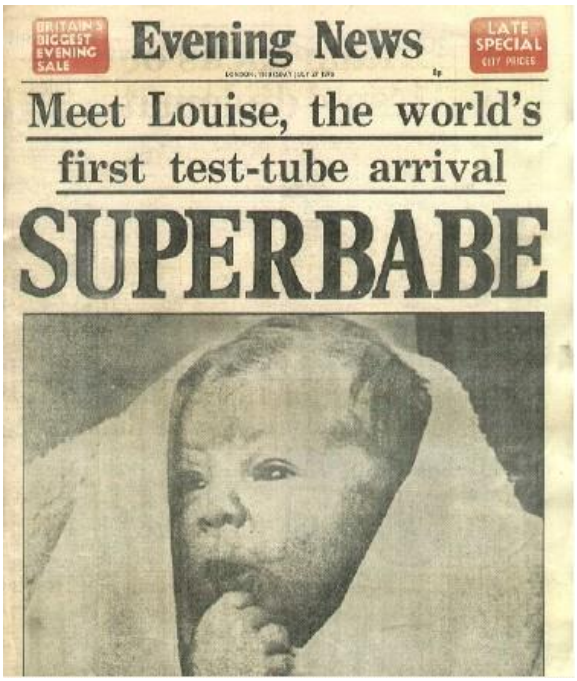
To the Distinguished Chair, Ranking Member and Honored Members of the Committee.

I am a cell biologist, currently working for a think tank in Washington, D.C. and as an adjunct professor at a local university. Previously I spent 20 years as Professor of Life Sciences at Indiana State University and Adjunct Professor of Medical & Molecular Genetics at Indiana University School of Medicine. Prior to that I was a faculty member in the Department of Obstetrics, Gynecology and Reproductive Sciences, University of Texas Medical School at Houston. I have done federally-funded laboratory research, lectured, and advised on these subjects extensively, in the U.S. and internationally. I've taught embryology, developmental biology, molecular biology and biochemistry for over 30 years to undergraduate and graduate students, as well as medical and nursing students.

Thank you for the opportunity to provide information in this Assisted Reproduction Educational Hearing, on this important and poorly understood public health topic.



On July 25, 1978, the world met Louise Brown, the very first "test tube baby". Louise, born on that date in the U.K., was the first baby born using "In Vitro Fertilization", IVF. The initial method was developed by Drs. Robert Edwards and Patrick Steptoe; Edwards had tried various aspects of IVF for years before finally getting a normal embryo, a pregnancy, and a baby that made it to birth.[1,2] The first United States IVF baby was born in 1981. It is estimated that there are now over 5 million babies who have been born via IVF and similar techniques.[3]

Assisted Reproductive Technology (ART) has been controversial from the beginning. It involves conception and manipulation of human embryos in the laboratory. While the technique has helped some infertile couples to have children, the practice of manipulating human embryos has also opened the way to areas of ethical concern and to cavalier views of nascent human life and of women, including stockpiling of "excess" human embryos, and instrumental use of women

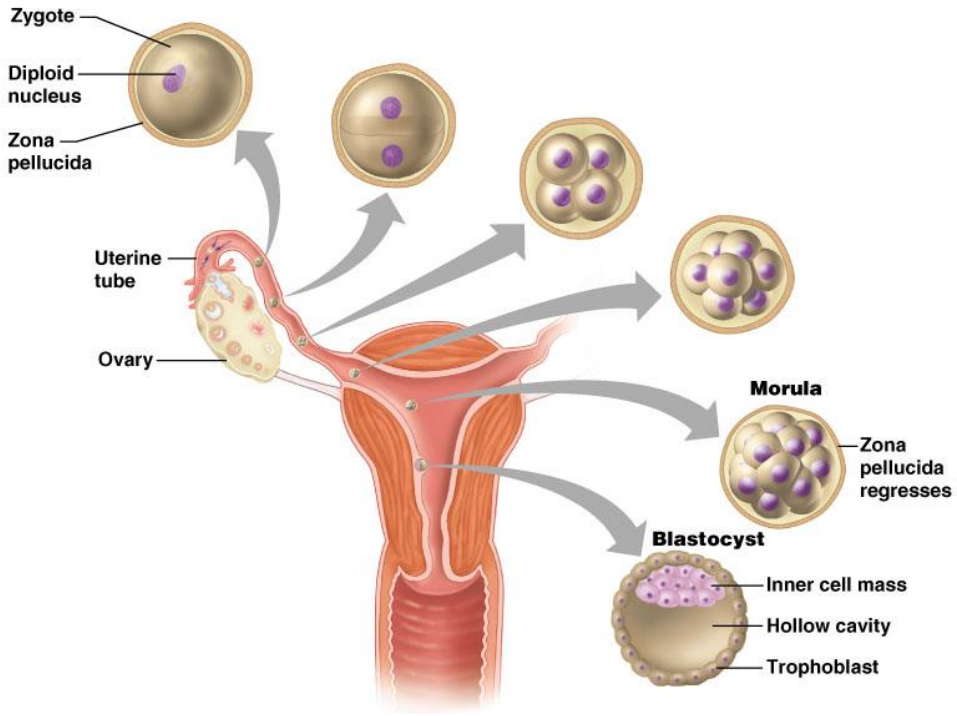
1 Edwards RG, Ethics and moral philosophy in the initiation of IVF, preimplantation diagnosis and stem cells, Reproductive BioMedicine Online 10, Supp 1, 1, 2005

2 Biggers JD, IVF and embryo transfer: historical origin and development, Reproductive BioMedicine Online 25, 118, 2012

3 "The world's number of IVF and ICSI babies has now reached a calculated total of 5 million", European Society of Human Reproduction and Embryology, 2 July 2012, http://www.eshre.eu/ESHRE/English/Press-Room/Press-Releases/Press-releases-2012/5-million-babies/page.aspx/1606

for buying of their eggs or use of their wombs as surrogates. The controversy was not lessened, and actually intensified, when Edwards received Nobel Prize recognition in 2010 for his work in this area (Steptoe died in 1988).

NORMAL FERTILIZATION and EMBRYO DEVELOPMENT



Normal fertilization and commencement of human development begins in the fallopian tube, or oviduct. Usually only one egg (oocyte) is ovulated each month, from only one ovary. The egg is swept into the fallopian tube and travels toward the uterus. If fertilized by sperm that have swum into the fallopian tube, the embryo will undergo several rounds of cell division before it reaches the uterus. Implantation into the uterine wall takes place about 7-8 days after fertilization/conception.

The standard definition of infertility means not being able to get pregnant after one year of trying. Some estimates suggest that as many as 10% of women (roughly 6 million) in the United States ages 15–44 years have difficulty getting pregnant or staying pregnant.

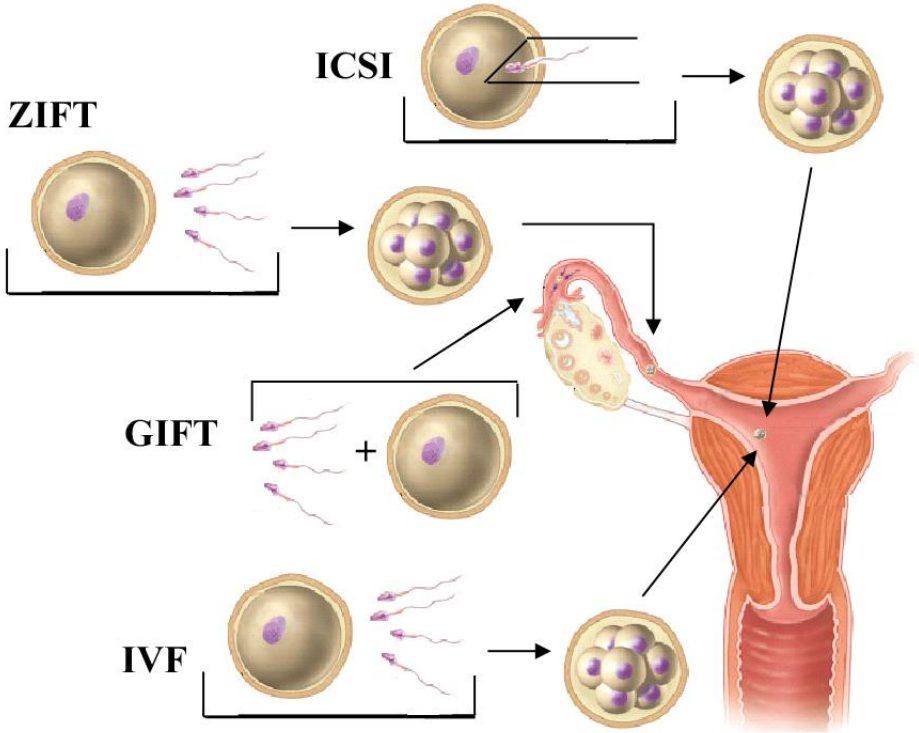
Assisted Reproductive Technology (ART) works by removing eggs from a woman's body. In the vast majority of cases, the woman's ovaries are first stimulated with high doses of hormones, to "superovulate" the ovaries and produce large numbers of eggs. The eggs are then mixed with sperm to create embryos, and some or all of the embryos are transferred to the woman's body. In most cases, the embryos that are not transferred to the womb are frozen in liquid nitrogen for future use. In some cases donor eggs are used, in which a young healthy woman receives the high hormone dose injections to harvest young, healthy eggs, often for compensation.

In ART, various methods are used regarding conception of embryos in the laboratory (in vitro, literally "in glass") and placement of embryos transferred to the woman's body.

VARIATIONS OF ASSISTED REPRODUCTIVE TECHNOLOGY

Differences in where fertilization or embryo transfer occurs

IVF—In Vitro Fertilization. Fertilization and maturation in lab, transfer to uterus
ZIFT—Zygote Intra-Follopian Transfer. Fertilization & maturation in lab, transfer to fallopian tube
GIFT—Gamete Intra-Fallopian Transfer. Fertilization & maturation in fallopian tube, after transfer there
ICSI—IntraCytoplasmic Sperm Injection. Artificial fertilization, maturation in lab, transfer to uterus



Most fertility clinics use IVF for their patients, but there is increasing use of some of the other techniques, including use of ICSI. One concern has been that there have been few detailed studies of health problems of children conceived via ART. While most of the over 5 million IVF babies seem healthy, there are several studies that indicate potential problems are increased in IVF children[4] and concerns that more problems may crop up in the future.[5]

[4] Wen J et al., Birth defects in children conceived by in vitro fertilization and intracytoplasmic sperm injection: a meta-analysis, Fertility and Sterility 97, 1331, 2012

[5] Grace KS and Sinclair KD, Assisted reproductive technology, epigenetics and long-term health: a developmental time bomb still ticking, Seminars in Reproductive Medicine 27, 409, 2009

In addition, ART often is categorized according to whether the procedure used a woman's own eggs (nondonor) or eggs from another woman (donor) and according to whether the embryos used were newly fertilized (fresh) or previously fertilized, frozen, and then thawed (frozen).

There is currently almost no regulation of the fertility industry (IVF, ART) in the United States. The sole federal regulation is a reporting requirement on success rates to the Centers for Disease Control and Prevention (CDC). Congress enacted the Fertility Clinic Success Rate and Certification Act (FCSRCA, or Public Law 102-493, 42 U.S.C. 263a–1 et seq) in 1992, mandating that all ART clinics report success rate data to the federal government in a standardized manner
Below are the latest data from the CDC for the reporting numbers. Even a brief glance shows the complexity of techniques, diagnoses, and options used in the fertility industry.

Centers for Disease Control and Prevention

Assisted Reproductive Technology (ART) Report

National ART Success Rates

2010 NATIONAL SUMMARY

A Comparison of clinic success rates may not be meaningful because patient medical characteristics and treatment approaches vary from clinic to clinic. For more details about this, along with information on how to interpret the statistics in this table, see Introduction To Fertility Clinic Success Rates.

ART CYCLE PROFILE

Type of ART[a]				Patient Diagnosis			
IVF	>99%	**Procedural Factors:**		Tubal factor	7%	Other factor	7%
GIFT	<1%	With ICSI	66%	Ovulatory dysfunction	7%	Unknown factor	12%
ZIFT	<1%	Unstimulated	<1%	Diminished ovarian reserve	15%	*Multiple Factors:*	
Combination	<1%	Used gestational carrier	<1%	Endometriosis	4%	Female factors only	11%
		Use of PGD	4%	Uterine factor	1%	Female & Male factors	18%
		With eSET	6%	Male factor	17%		

PREGNANCY SUCCESS RATES

Type of Cycle	Age of Women					
	<35	35-37	38-40	41-42	43-44	>44
Fresh Embryos From Nondonor Eggs						
Number of cycles	41744	21369	21741	10122	4501	1347
Percentage of embryos transferred resulting in implantation	36.5	26.9	17.7	9.6	4.2	1.7
Percentage of cycles resulting in pregnancies	47.6	38.8	29.9	19.9	10.6	3.2
Percentage of cycles resulting in live births[b]	41.5	31.9	22.1	12.4	5.0	1.0
Percentage of retrievals resulting in live births[b]	44.4	35.4	25.3	14.8	6.3	1.4
Percentage of transfers resulting in live births[b]	47.6	38.3	28.1	16.7	7.4	1.8
Percentage of transfers resulting in singleton live births[b]	31.4	27.3	21.5	13.7	6.6	1.6
Percentage of cancellations	6.6	9.9	12.8	16.4	20.6	25.5
Average number of embryos transferred	2.0	2.2	2.6	3.0	3.2	2.7
Percentage of pregnancies with twins	32.9	27.3	21.6	15.0	8.1	2.3
Percentage of pregnancies with triplets or more	2.6	3.1	3.7	3.0	0.6	2.3
Percentage of live births having multiple infants[b]	34.0	28.7	23.3	18.0	10.2	2 /14
Frozen Embryos From Nondonor Eggs						
Number of transfers	12631	6195	4682	1591	710	432
Percentage of transfers Resulting in live births[b]	38.4	34.7	28.4	21.5	16.8	13.0
Average number embryos transferred	2.0	1.9	2.1	2.2	2.2	2.0

	All Ages Combined[c]	
Donor Eggs	**Fresh Embryos**	**Frozen Embryos**
Number of transfers	9866	6665
Percentage of transfers resulting in live births[b]	55.8	34.9
Average number of embryos transferred	2.0	2.0

CURRENT CLINIC SERVICES AND PROFILE

Total Number of reporting clinics: 443

Percentage of Clinics that offer the following services:

Donor egg	93	Gestational Carriers	84
Donor embryo	69	Cryopreservation	99
Single women	95		

Clinic Profile:

SART Member	85
Verified lab accreditation[d]	
Yes	93
No	6
Pending	2

a Reflects patient and treatment characteristics of ART cycles performed using fresh nondonor egges or embryos.
b When fewer than 20 cycles are reported in a age category, rates are shown as a fraction and confidence intervals are not given. Calculating percentages from fractions may be misleading and is not encouraged.
c A multiple-infant birth is counted as one live birth.
d Clinic-specific outcome rates for women older than 42 or 44, depending on reporting year, undergoing ART cycles using fresh or frozen embryos with nondonor eggs are not included because of small numbers. Readers are urged to review national outcomes for these age groups.
e All ages (including ages >42 or >44 depending on reporting year) are reported together because previous data show that patient age does not materially affect success with donor eggs.

Beyond the Fertility Clinic Success Rate and Certification Act, there are essentially no regulations in the United States regarding the ART industry. While fertility groups in the U.S. have guidelines for clinics to follow, the CDC notes that 80% of clinics do not follow these guidelines.[6] Moreover, the only penalty for violating the guidelines is expulsion from some of the industry's professional organizations.

There are currently no limits on the number of human embryos created by fertilization each cycle for purposes of attempting to achieve a pregnancy, nor on the number of embryos that can be transferred to the womb. No limits, in the United States or in any individual state. We saw the abuse of this practice with the 2009 "Octamom" case in California, where six embryos were implanted in the womb, resulting in a multiple birth of 8 babies. And as the CDC's own data have shown, the majority of fertility clinics also abuse the guidelines (which some consider simply suggestions) put forward by the professional organizations. There are also no regulations regarding tracking gamete donors, disposition of embryos, nor even a standard on informed consent for infertile couples who come to a fertility clinic.

In fact, even one of the most vocal supporters of IVF in the U.K. has noted:[7]

> "The United States… has no nationwide prohibitions on keeping embryos for more than 14 days, no databases of donors and treatments, no uniform safety standards and no control on the sale and advertising of gametes."
> "It will be hard to form rules that might encumber what is now a big business in assisted reproduction."

Numerous other countries including the U.K., Germany, and Italy have addressed this issue legislatively, but not the U.S.

Germany, since 1990, has in place what it calls its Embryo Protection Law that makes it against the law to destroy any human embryos, and limits the practice of embryo freezing for storage. While some have claimed that the German law is overly restrictive regarding handling of embryos, a recent 10-year study found that the German success rate for live births showed "internationally comparable levels."[8] Thus, the German experience has shown as good a level of success at live birth of babies as countries such as the U.S. where multiple embryos are created and destroyed in a quality-control manufacturing process.

The German experience as well as that of other countries also shows that transferring low numbers of embryos, including single-embryo transfer, rather than mass production of embryos and transfer of multiple embryos to the woman, is healthier for both mothers and babies.[9,10,11]

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[6] Reported at, e.g., "Most fertility clinics break rules", USA Today, 2/21/2009, http://usatoday30.usatoday.com/news/health/2009-02-21-fertility-clinics_N.htm; Data from Fertility Clinic Success Rates Report, Centers for Disease Control and Prevention (CDC), http://www.cdc.gov/art/

[7] Deech R, 30 years: from IVF to stem cells, Nature 454, 280-281, 2008

[8] Gnoth C et al., Final ART success rates: a 10 years survey, Hum. Reprod. 26, 2239-2246, 2011

[9] Ludwig M et al., Experience with the elective transfer of two embryos under the conditions of the German embryo protection law: results of a retrospective data analysis of 2573 transfer cycles, Hum. Rep. 15, 319-324, 2000

[10] Sunderam S et al, Assisted Reproductive Technology Surveillance — United States, 2009, Morbidity and Mortality Weekly Surveillance Summaries Vol. 61, No. 7, Nov 2, 2012

[11] Engmann L et al., Outcome of in vitro fertilization treatment in patients who electively inseminate a limited number of oocytes to avoid creating surplus human embryos for cryopreservation, Fertil Steril 84, 1406-1410, 2005

The U.K., in fact, has begun to consider moving to even lower numbers of embryos transferred. Studies have indeed shown that using better techniques, implanting just one embryo can give just as good results for pregnancies as implanting more embryos. The lower numbers make it safer for the mother as well as for the children, and decrease the incidences of multiple births and attendant health risks.[12]

This is not to say that the U.K has a stellar record regarding its practice and policies for ART. In fact, in some ways the U.K. has become "Brave New Britain", because it has now gives legal sanction to mixed animal–human embryos, preimplantation genetic diagnosis (PGD, in which embryos are screened genetically for diseases or genetic traits, and then kept or discarded based on the results)[13] and savior siblings (wherein a genetically-screened embryo that meets certain criteria is brought to birth, to provide a transplant for an already-born sibling.) The U.K. has also considered the possibility of using artificial gametes,[14] and most recently the creation of 3-parent embryos.[15,16]

Inducements for egg donation or trafficking in eggs or embryos is also a concern in the ART industry. Egg donation is a practice that provides incentives for young women to risk their health, and even their lives, to donate eggs for payment. The practice, often undertaken by "egg brokers", solicits young fertile women to undergo injection with high doses of hormones in order to produce large numbers of eggs for compensation.[17] This practice has significant health risks from Ovarian Hyperstimulation Syndrome (OHSS). As many as 10-20% of women in some studies have reported health complications, which in some cases has led to hospitalization, kidney failure, infertility, and even death.[18,19,20,21]

Thus, use of no-stimulation (natural cycle) or low-stimulation cycles, as well as single-embryo transfer, would significantly improve health of mothers as well as babies.[22] The advantages usually noted for no-stimulation or low-stimulation IVF include eliminating the risk of OHSS, significant cost savings (about half that of standard IVF), no painful and expensive hormonal injections, fewer office visits, generally a higher-quality egg, and use of one egg to eliminate the risks from multiple pregnancies.

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12 Klemetti R et al., Health of Children Born as a Result of In Vitro Fertilization, Pediatrics 118, 1819-1827, 2006

13 Goldman B, The first cut, Nature 445, 479, 2007

14 Nagy ZP et al., Development of artificial gametes, Reproductive BioMedicine Online 16, 539, 2008

15 James Gallagher, BBC, 'Three people, one baby' public consultation begins, 16 September 2012, http://www.bbc.co.uk/news/health-19597856

16 HFEA, debating mitochondrial replacement, http://mitochondria.hfea.gov.uk/mitochondria/

17 Blake Ellis, "Broke college students turn to fertility clinics, sugar daddies", CNN Money, October 3, 2012, http://money.cnn.com/2012/09/18/pf/college/paying-for-college/index.html

18 Magnus D and Cho M, "Issues in Oocyte Donation for Stem Cell Research," Science 308, 1747-1748, 17 June 2005

19 Shmorgun D et al., The Diagnosis and Management of Ovarian Hyperstimulation Syndrome, J OB Gyn Canada 268, 1156, 2011

20 Pecks U et al., Oocyte Donation: A Risk Factor for Pregnancy-Induced Hypertension, Deutsches Ärzteblatt International 108, 23, 2011

21 van Leeuwen FE et al., Risk of borderline and invasive ovarian tumours after ovarian stimulation for in vitro fertilization in a large Dutch cohort, Hum. Reprod. 26, 3456, 2011

22 Pelinck MJ et al., Cumulative pregnancy rates after three cycles of minimal stimulation IVF and results according to subfertility diagnosis: a multicentre cohort study, Hum. Rep. 21, 2375–2383, 2006

The IVF industry in this case would be going back to its roots, as the very first IVF baby, Louis Brown in 1978, was a result of one egg obtained without hormonal stimulation, one egg fertilized, and one embryo transferred (single-embryo transfer), resulting in one baby born.

Another area of concern with ART include the transfer of multiple embryos followed by use of "selective reduction" if too many embryos implant and begin gestation. In this little-known but all-too-common procedure, some of the developing babies are selectively destroyed in the womb.[23]

Embryo freezing (cryopreservation) has also been a concern. Many question the ethics of freezing embryos, putting them in a sort of suspended animation, which some consider a form of stockpiling. In the U.S., there are over 400,000 human embryos frozen at fertility clinics.[24] Long-term freezing can also lead to some interesting societal and familial questions, including thawing and birth of siblings decades apart in their birth age.[25]

One false statement has been that any limits or regulations on embryo freezing would mean young female cancer patients would no longer be able to preserve their fertility. The statement suggests that the only way to address future fertility is by superovulating the woman with massive doses of hormones to obtain large numbers of eggs, then fertilizing all of these eggs to create large numbers of embryos, which can be frozen for future transfer to the uterus.

The statement is blatantly false. Fertility can be preserved by freezing eggs rather than embryos. This has been done for many years now, and over 2,000 babies around the world have been born using this technology, especially in cases of young women preserving their fertility before cancer treatment.[26] The success of freezing eggs rather than embryos has been documented, including in a recent review by Dr. Jeffrey Boldt, with whom I worked in the past. Dr. Boldt is Scientific Director of Assisted Fertility Services in Indianapolis, clinical associate professor of Medical and Molecular Genetics at Indiana University School of Medicine, and Scientific Director for The World Egg Bank. He notes in his review paper that use of freezing eggs has produced:

"pregnancy rates that rival those obtained with either frozen-embryo transfer or fresh IVF."[27]

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[23] Ruth Padawer, "The Two-Minus-One Pregnancy", New York Times, August 20, 2011, http://www.nytimes.com/2011/08/14/magazine/the-two-minus-one-pregnancy.html

[24] Hoffman DI et al., Cryopreserved embryos in the United States and their availability for research, Fertility and Sterility 79, 1063, 2003

[25] Dowling-Lacey D et al, Live birth from a frozen–thawed pronuclear stage embryo almost 20 years after its cryopreservation, Fertility and Sterility 95, 1120.31, 2011

[26] E.g., Porcu E. *et al.*, Healthy twins delivered after oocyte cryopreservation and bilateral ovariectomy for ovarian cancer, Reproductive Biomedicine Online 17, 265, 2008.

[27] Boldt J, Current results with slow freezing and vitrification of the human oocyte, Reproductive BioMedicine Online 23, 314, 2011

At some points the ART industry has even attempted to re-define basic biological terms to promote incorrect perceptions about basic human development, and thereby alter attitudes of patients and the public.

For example, in previous years the term "pre-embryo" was coined for very early embryos, prior to the stage of implantation in the uterus. Lee Silver, a Princeton biologist, wrote about this in his book, noting:

> "I'll let you in on a secret. The term pre-embryo has been embraced wholeheartedly by IVF [in-vitro fertilization] practitioners for reasons that are political, not scientific. The new term is used to provide the illusion that there is something profoundly different between what we nonmedical biologists still call a six-day-old embryo and what we and everyone else call a sixteen-day-old embryo.
> "The term pre-embryo is useful in the political arena where decisions are made about whether to allow early embryo (now called pre-embryo) experimentation..."[28]

One of the leading embryology texts notes this inappropriate use of the term as well:

> "The term 'pre-embryo' is not used here for the following reasons: (1) it is ill-defined because it is said to end with the appearance of the primitive streak or to include neurulation; (2) it is inaccurate because purely embryonic cells can already be distinguished after a few days, as can also the embryonic (not pre-embryonic!) disc; (3) it is unjustified because the accepted meaning of the word embryo includes all of the first 8 weeks; (4) it is equivocal because it may convey the erroneous idea that a new human organism is formed at only some considerable time after fertilization; and (5) it was introduced in 1986 'largely for public policy reasons' (Biggers). ... Just as postnatal age begins at birth, prenatal age begins at fertilization."[29]

In the end, there are numerous concerns with the ART industry which need to be addressed, with straightforward and accurate terminology and with facts.

Thank you for the opportunity to discuss the information on this important issue.

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[28] Lee Silver, Remaking Eden: Cloning and Beyond in a Brave New World (New York: Avon Books, 1997), p. 39

[29] Ronan O'Rahilly and Faiola Muller, Human Embryology & Teratology (3rd ed.)(New York: Wiley-Liss, 2001), p.88