

LABCC100 Lesson 22

1.1 Embryo Transfer



Notes:

Welcome to the American Society for Reproductive Medicine's eLearning modules. The subject of this presentation is Embryo Transfer.

1.2 Learning Objectives

Learning Objectives

At the conclusion of this presentation, participants should be able to:

- Define embryo transfer (ET).
- Describe how the embryo transfer process is performed.
- Assess the factors that may affect the success of ET.
- Analyze the benefits and limitations of utilizing embryo transfer techniques.

Notes:

At the conclusion of this presentation, participants should be able to:

Define embryo transfer (ET).

Describe how the embryo transfer process is performed.

Assess the factors that may affect the success of ET.

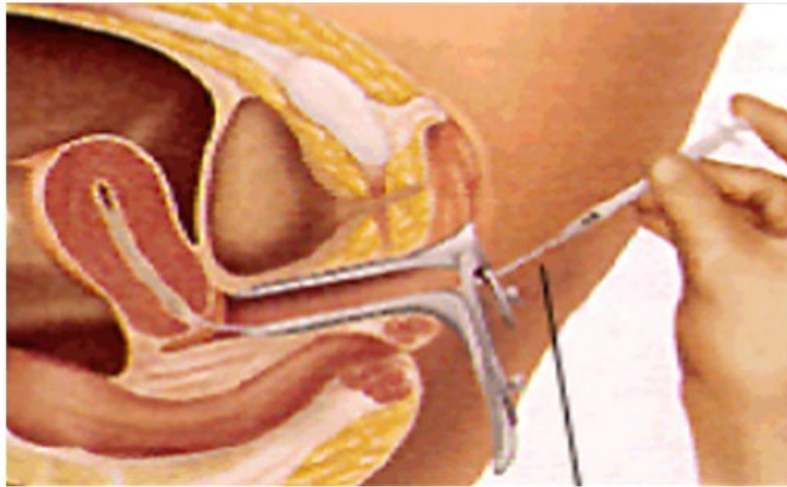
Analyze the benefits and limitations of utilizing embryo transfer techniques.

1.3 Definition

Definition

Simple but critical procedure

- Embryo(s) produced with in vitro fertilization (IVF) are placed into the uterus of the woman



With permission from *Fertility and Sterility* 2013;99:1093-1099

Notes:

One of the most critical steps in the process of in vitro fertilization (IVF) is the embryo transfer. Embryo(s) produced with in vitro fertilization (IVF) are placed into the uterus of the woman.

1.4 Historical Perspective

Historical Perspective

- **1890 W. Heape:** first successful mammalian pregnancy by embryo transfer
- **1978 Steptoe and Edwards:** first successful embryo transfer in humans
- **1984 Asch et al.:** GIFT (gamete intrafallopian transfer)
- **1986 Devroey et al.:** ZIFT (translaparoscopic zygote intrafallopian transfer) on a patient with sperm antibodies

- GIFT and ZIFT rarely used today

Notes:

In 1890, Walter Heape established the first successful mammalian pregnancy by transferring rabbit embryos from one uterine cavity to another. Nearly 90 years later, Steptoe and Edwards performed the first successful embryo transfer in humans. A variation of transferring embryos into the uterus is gamete intrafallopian transfer (GIFT), a procedure for transferring eggs and sperm into the recipient woman's fallopian tubes. Asch and colleagues reported the first pregnancy using GIFT in 1984. Two years later, Devroey and colleagues described zygote intrafallopian transfer (ZIFT), in which fertilized eggs were transferred into the fallopian tubes. GIFT and ZIFT have gradually disappeared with the improvement of the laboratory environment.

1.5 Success Rates

Success Rates

2014 ART SUCCESS RATES ^c		Total number of cycles ^d : 208,604 (includes 3,596 cycle[s] using frozen eggs)					
Type of Cycle	Age of Woman						
	<35	35-37	38-40	41-42	43-44	>44	
Fresh Embryos from Nondonor Eggs							
Number of cycles	39,573	19,376	17,617	9,114	5,131	2,051	
Percentage of cancellations before retrieval (%)	6.1	9.7	13.4	17.4	19.4	25.1	
Average number of embryos transferred	1.7	1.9	2.2	2.6	2.8	2.5	
Percentage of embryos transferred resulting in implantation (%)	41.1	32.3	21.1	10.8	5.0	2.3	
Percentage of elective single embryo transfers (eSET) (%)	28.5	16.7	6.9	2.1	1.2	0.4	
Outcomes per Cycle							
Percentage of cycles resulting in term, normal weight & singleton live births ^e (%)	23.2	19.2	13.0	7.1	2.8	0.8	
Percentage of cycles resulting in singleton live births (%)	27.4	22.8	15.6	8.3	3.4	1.0	
Percentage of cycles resulting in twin live births (%)	9.4	6.8	3.7	1.3	0.3	0.2	
Percentage of cycles resulting in live births (%)	37.1	30.0	19.5	9.7	3.8	1.2	
Percentage of cycles resulting in pregnancies (%)	42.6	36.4	26.9	16.4	8.8	2.7	
Outcomes per Transfer							
Number of transfers	30,902	14,654	12,257	5,629	2,807	821	
Percentage of transfers resulting in term, normal weight & singleton live births ^e (%)	29.7	25.4	18.6	11.5	5.2	1.9	
Percentage of transfers resulting in singleton live births (%)	35.0	30.1	22.4	13.5	6.3	2.4	
Percentage of transfers resulting in twin live births (%)	12.1	9.1	5.3	2.0	0.5	0.5	
Percentage of transfers resulting in live births (%)	47.5	39.6	28.0	15.7	6.9	3.0	
Percentage of transfers resulting in pregnancies (%)	54.6	48.1	38.6	26.5	16.0	6.7	

CDC 2016; ASRM Guideline 2017

^c Births are defined as term if at least 37 full weeks gestation and normal birth weight if at least 2,500 grams (approximately 5 pounds, 8 ounces).

Notes:

Many factors have been proposed to explain the disparity between embryonic development and pregnancy rates. In young women, approximately half of embryo transfers result in live births, whereas the success rate drops steadily with a woman's age. Studies have consistently demonstrated that embryo transfer pregnancy rates differ depending upon the clinician performing the procedure. In addition, there is limited training in fellowship programs and for practitioners who may have embryo transfer success rates consistently below the mean.

1.6 Factors that May Affect the Success of ET

Factors that May Affect the Success of ET

- The ease of the procedure
- Ultrasound (US) guidance
- Transfer catheter type
- Catheter-loading and -unloading technique
 - Retained embryos
- Catheter tip placement
- Trial/“mock” transfer
- Number of embryo(s) transferred

Notes:

Past studies have attempted to characterize variables associated with embryo transfer success and failure. Such variables have included: ease of the procedure, presence of blood or mucus on the tip of the transfer catheter, ultrasound guidance, the type of transfer catheter, techniques of catheter-loading and –unloading, catheter tip placement in the uterine cavity, trial or “mock” transfer, and the number of embryos transferred.

1.7 Guidelines

Guidelines

ASRM PAGES

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Performing the embryo transfer: a guideline

Practice Committee of the American Society for Reproductive Medicine
American Society for Reproductive Medicine, Birmingham, Alabama

A systematic review of the literature was conducted which examined each of the major steps of embryo transfer. Recommendations made for improving pregnancy rates are based on interventions demonstrated to be either beneficial or not beneficial. (Fertil Steril® 2017;107:882–96. ©2017 by American Society for Reproductive Medicine.)

Discuss: You can discuss this article with its authors and with other ASRM members at <https://www.fertsterdialog.com/users/16110-fertility-and-sterility/posts/14713-23759>

Notes:

ASRM's 2017 Guideline "Performing the embryo transfer" provides a systematic review of the literature to determine which steps in the procedure are supported by sufficient data. In this Guideline, recommendations are made for improving pregnancy rates based on interventions demonstrated to be either beneficial or not beneficial.

1.8 ASRM Protocol

ASRM Protocol



ASRM standard embryo transfer protocol template: a committee opinion

Practice Committee of the American Society for Reproductive Medicine
American Society for Reproductive Medicine, Birmingham, Alabama

Standardization improves performance and safety. A template for standardizing the embryo transfer procedure is presented here with 12 basic steps supported by published scientific literature and a survey of common practice of SART programs; it can be used by ART practices to model their own standard protocol. (Fertil Steril® 2017;107:897-900. ©2017 by American Society for Reproductive Medicine.)

Discuss: You can discuss this article with its authors and with other ASRM members at <https://www.fertstertdialog.com/users/16110-fertility-and-sterility/posts/15158-23913>

Notes:

Standardization improves performance and safety. ASRM's template for standardizing the embryo transfer procedure provides the basic steps supported by published scientific literature and a survey of common practice of SART programs. These steps will be addressed in the following slides.

1.9 The Embryo Transfer Procedure

The Embryo Transfer Procedure



1. Reviewing prior mock or transfer patient notes
2. Patient preparation
3. Time-out with identification and matching of patient and embryo(s)
4. Use of transabdominal ultrasound
5. Practitioner preparation for the procedure
6. Cervical/vaginal preparation
7. Removal of mucus from endocervical canal
8. Loading of the catheter and embryo transfer
9. Catheter tip placement
10. Embryo expulsion and catheter removal
11. Checking catheter for retained embryo(s)
12. Patient discharge

ASRM ET Protocol 2017

Notes:

Prepare for the embryo transfer procedure by the following steps.

Review of prior mock or transfer patient notes.

Time-out process with identification and matching of patient and embryo(s).

Transabdominal ultrasound to assess the endometrial cavity and other pelvic structures and for guidance of the embryo transfer procedure.

Practitioner preparation for the procedure should include some form of hand washing and sterile latex-free gloves.

Speculum placement and cleansing/flush of cervix or vagina.

Mucus removed from the endocervical canal.

Loading of the embryo transfer catheter with the embryos and transfer across the cervix.

Catheter tip placed at the ideal location.

Embryo(s) are expelled and the catheter is removed.

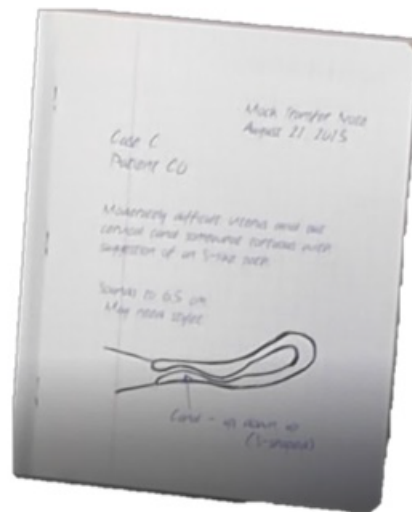
Catheter is checked for retained embryo(s).

The patient is discharged.

1.10 1. Reviewing Prior Mock or Transfer Patient Notes

1. Reviewing Prior Mock or Transfer Patient Notes

- Prepare for the embryo transfer procedure by reviewing prior mock or transfer patient notes for the level of difficulty and tips for guiding the procedure.
- Literature unclear on trial transfer before an actual ET
- Mock ET before actual ET may increase chance of easy transfer



Moossavifar et al., 2005; ASRM ET Protocol 2017

Notes:

Reviewing any prior mock or transfer patient notes is the first step. This can provide insight for the anticipated level of difficulty and tips for guiding the procedure. For example, notes may reveal a severely anteflexed uterus or a tortuous path through the cervix.

It should be noted that the literature is conflicting regarding a trial transfer before an actual embryo transfer and whether a mock embryo transfer could allow better management and preparation for “difficult” transfer.

It has been suggested that a mock procedure before the beginning of a treatment cycle is highly consistent with the subsequent actual embryo transfer and provides each patient with the highest chance of having an easy transfer.

1.11 2. Patient Preparation

2. Patient Preparation

- Transfer in clinic or operating room – but near embryology laboratory
- Analgesics and other techniques for patient comfort
- Acupuncture not shown to improve pregnancy rates
- Insufficient evidence for other interventions specifically to improve pregnancy rates (massage, transcutaneous electrical acupoint stimulation [TEAS], whole-systems traditional Chinese medicine)
- Routine anesthesia not recommended
- Routine prophylactic antibiotics not recommended
- Dorsal lithotomy position
- Full bladder for ultrasound visualization

Mains & Van Voorhis, 2010; ASRM Guideline 2017; Derks et al., 2010

Notes:

As the transfer procedure is not necessarily a sterile one, it may be performed in a clinic or an operating room, but the room should be in close proximity to the embryology laboratory.

Analgesics and other patient preparation techniques can be used as needed for patient comfort but not for improving pregnancy rates.

There is fair evidence that acupuncture performed around the time of the transfer does not improve pregnancy rates. There is insufficient evidence to recommend for or against use of the other techniques specifically to improve pregnancy rates (analgesics, massage, transcutaneous electrical acupoint stimulation [TEAS], whole-systems traditional Chinese medicine). One randomized controlled trial (RCT) demonstrated that TEAS improves embryo transfer outcomes. However, there are no other studies.

There is insufficient evidence that anesthesia during embryo transfer improves pregnancy rates. Given that there is no clear benefit and that there are inherent risks associated with anesthesia, routine anesthesia is not recommended to improve IVF-embryo transfer outcomes.

The use of routine prophylactic antibiotics is not recommended.

In the past, the knee-chest position was used in women with an anteverted uterus, and the dorsal position for a retroverted uterus. At present, all patients are generally placed in the dorsal lithotomy position regardless of uterine position. There is no difference in pregnancy outcomes for ET with the patient's bladder full or empty.

1.12 3. Time-out

3. Time-out

- Use a time-out process with identification and matching of patient and embryo(s) (Standard Expected Practice)



ASRM Guideline 2017

Notes:

Using a time-out process with identification and matching of patient and embryo(s) is part of Standard Expected Practice. This time-out matching process should occur with the patient, physician, and the embryologist all present in the transfer room. At this time, there can also be one final statement of the number of embryos to be loaded by the embryologist for transfer.

1.13 4. Ultrasound-guided Embryo Transfer

4. Ultrasound-guided Embryo Transfer

- Facilitates placement of soft catheters
- Avoids touching the fundus
- Ensures the proper placement of embryos in the uterine cavity
- Avoids any pathological situation contraindicated to ET (hydrometra, hematometra, presence of excessive peritoneal fluid, etc.)
- Determines endometrial thickness
- Avoids disruption of the endometrium
- Determines utero-cervical angle to aid in bending the tip of the catheter accordingly
- Visualize orientation/straightening of the uterus, ensures full bladder

Kovacs et al., 2003

Notes:

Advantages of ultrasound-guided embryo transfer include: facilitates placement of soft catheters, avoids touching the fundus, and ensures the proper placement of embryos in the ideal location in the uterine cavity.

Additionally, ultrasound provides the ability to examine and avoid any pathological situation that is contraindicated with ET (hydrometra, hematometra, or presence of excessive peritoneal fluid, etc.). It also helps determine endometrial thickness. Although increased endometrial thickness is associated with higher pregnancy rates, endometrial thickness alone does not predict attainment of pregnancy or pregnancy outcome.

During the transfer, ultrasound helps avoid disruption of the endometrium. Determination of the uterocervical angle allows the tip of the catheter to be bent accordingly. Another advantage is the ability to visualize the orientation/straightening of the uterus, and ensure that the bladder is sufficiently filled.

1.14 4. Ultrasound-guided Embryo Transfer

4. Ultrasound-guided Embryo Transfer

- Transabdominal ultrasound-guided ET recommended to improve pregnancy and live-birth rates
- Limited centers have utilized transvaginal ultrasound for embryo transfer

ASRM Guideline 2017

Notes:

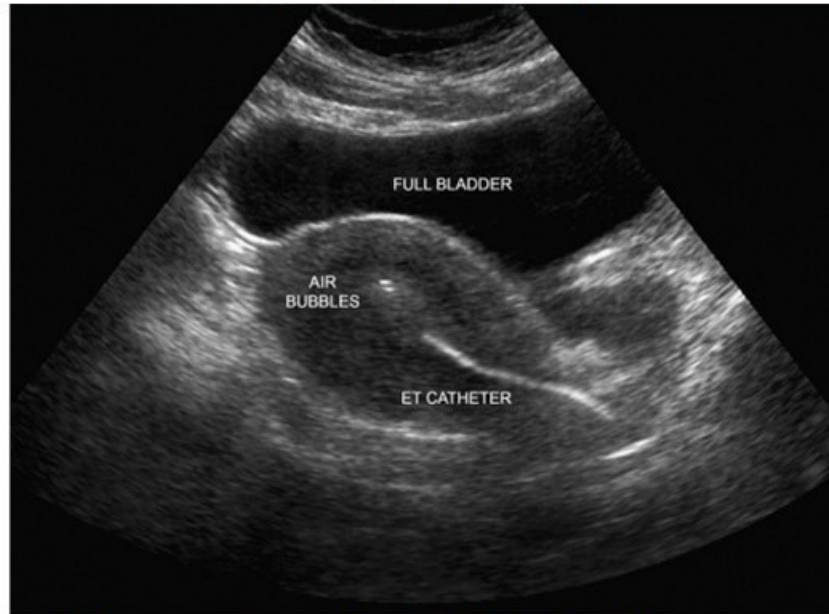
There is good evidence based on 10 randomized controlled trials (RCTs) to recommend transabdominal ultrasound guidance during embryo transfer to improve clinical pregnancy rate and live-birth rate. While selected ultrasound guidance for an anticipated difficult embryo transfer may be an alternative to routine ultrasound guidance, there is insufficient evidence to recommend for or against this practice.

A few centers have utilized transvaginal ultrasound for embryo transfer but there are few data for this approach.

1.15 4. Ultrasound-guided Embryo Transfer

4. Ultrasound-guided Embryo Transfer

Ultrasound image showing echogenic flash post-ET



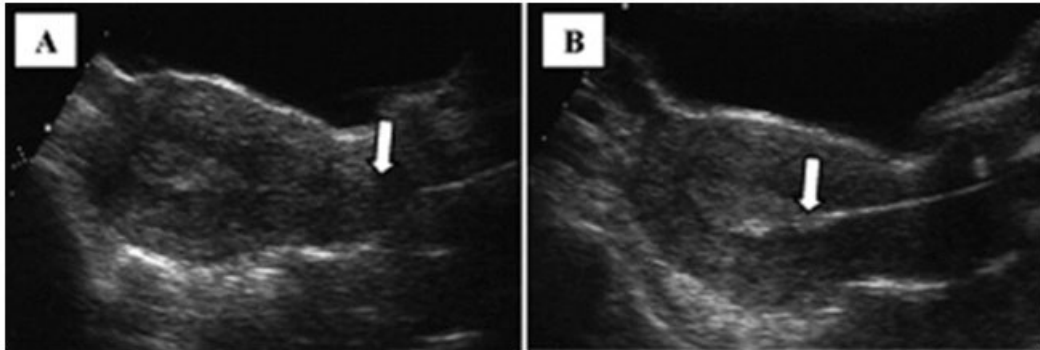
With permission from *Fertility and Sterility* 2010;94:785-90

Notes:

Cavity length is measured from the fundal endometrium to the external cervical os adjacent to the vaginal stripe. This is the measurement used for comparison to the transfer depth. Direct visualization of the embryo transfer catheter at the cervico-uterine angle can facilitate its insertion, allowing the physician to place an appropriate curve on the catheter, which can be particularly helpful in severely flexed uteri. The full bladder required for abdominal ultrasound also helps to straighten the cervico-uterine angle and facilitate entry of the catheter, particularly for the strongly anteverted uterus. Patients seem to take great comfort in visualizing this final step of an often long and difficult process.

1.16 4. Ultrasound-guided Embryo Transfer

4. Ultrasound-guided Embryo Transfer



Approaching the internal os

Tip is past the internal os

With permission from *Fertility and Sterility* 2007; 88:499-503

Notes:

These images show an ultrasound-monitored embryo transfer with the catheter approaching the internal os and then as it has passed the internal os. Arrows indicate the tip of the catheter.

1.17 5. Practitioner Preparation for the Procedure

5. Practitioner Preparation for the Procedure

- Handwashing
- 62% of surveyed practitioners wear a surgical mask.
- No specific type of glove is recommended for embryo transfer.
- Powdered gloves worn during embryo transfer do not have an adverse effect on pregnancy rates.
- No studies assessing glove use and live-birth rates.
- Avoid touching tip of catheter with gloves.



ASRM Guideline 2017
ASRM ET Protocol 2017

Notes:

Handwashing is expected standard practice. More than half of surveyed practitioners wear a surgical mask. Although some physicians may opt to avoid non-sterile, latex, or powdered gloves in hopes of minimizing embryo toxicity, no data support the usage of a particular type of glove to optimize pregnancy rates. There is fair evidence based on one, single-center RCT that powdered gloves worn during embryo transfer do not have an adverse effect on pregnancy rates. There are no studies assessing glove use and live-birth rates. Since there are studies that show some brand of gloves are embryotoxic, the tip of the embryo catheter should not be touched by the physician or the embryologist.

1.18 6. Cervical/Vaginal Preparation

6. Cervical/Vaginal Preparation

- Speculum placement
- Flushing/cleansing of cervix/vagina with cotton swab or gauze sponge using media or saline

ASRM ET Protocol 2017

Notes:

Once the speculum is placed, common protocol is to cleanse the vagina and external cervix with saline or culture media. The vast majority of practitioners use media.

1.19 7. Removal of Mucus from Endocervical Canal

7. Removal of Mucus from Endocervical Canal

- Removing cervical mucus at the time of embryo transfer may improve clinical pregnancy and live-birth rates.



ASRM Guideline 2017
ASRM ET Protocol 2017

Notes:

Some studies have indicated that cervical mucus interferes with embryo transfer by blocking the passage of embryos through the tip of the catheter, pulling embryos back from the site of expulsion, or contaminating the intrauterine environment with cervical flora. While it has been suggested that removing cervical mucus might stimulate uterine contractility or cervical bleeding, with a possible negative impact on pregnancy outcomes, there is fair evidence based on one RCT and one prospective cohort study that there is a benefit to removing cervical mucus at the time of embryo transfer to improve clinical pregnancy and live-birth rates.

1.20 Type of Catheter for Embryo Transfer

Type of Catheter for Embryo Transfer

- Much data on role of transfer catheter
- Catheter type
 - Tip characteristics: rounded instead of squared
 - Flexibility and malleability important
 - Memory of the material used for catheter: sleeve must keep angle desired until placed through the cervix
 - Length of the catheter (12 cm, 18 cm, 23 cm)
 - Non-embryotoxic
 - Clearly visible on ultrasound
 - Soft catheter

Notes:

The data assessing the influence of embryo transfer catheter type and IVF outcomes span almost three decades. A number of controlled trials provide insight into the role that the transfer catheter plays in IVF outcomes.

Commercially available embryo-transfer catheters can be classified by their material (i.e., metal, hard plastics, or soft plastics) and whether they are equipped with or without an introducing cannula that facilitates the transfer procedure. The catheter types are classified by their tip characteristics, flexibility and malleability, memory of the material used for catheter, and length of the catheter. The catheter must be non-embryotoxic and clearly visible on ultrasound.

Due to anatomical variation in patients, the flexibility and the malleability of the catheter and its sleeve are important. The length of the catheter is mostly a physician's choice. However, due to anatomical variation, a 23 cm catheter may occasionally be necessary. A supply of the longer catheters should be kept in stock in case they are needed.

On rare occasions the embryo transfer cannot be accomplished with a soft catheter. Because a firm catheter may be needed at these times, a supply should be kept in stock.

1.21 Commercially Available ET Catheters

Commercially Available ET Catheters

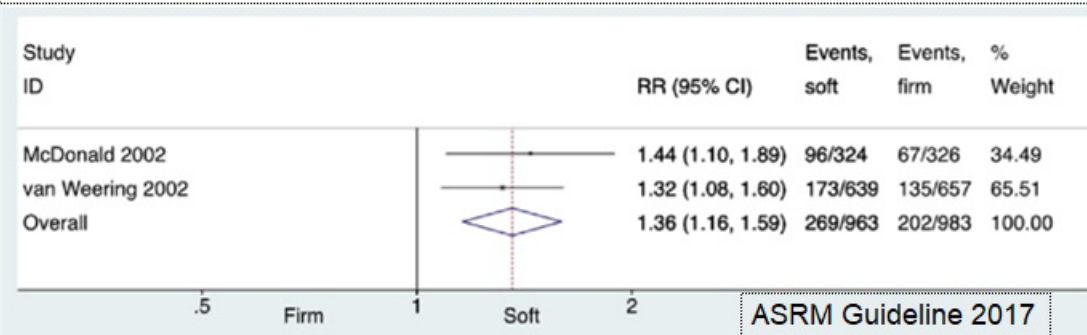
Soft ET catheters

- Frydman[®] catheter
- Edwards–Wallace[®] system
- Cook[®] Soft-Pass system
- Cook[®] Soft-Trans system
- Cook[®] Sydney IVF[®] system
- Gynetics[®] Delphin catheter
- Gynetics[®] Emtrac-A transfer

Firm ET catheters

- Erlangen[®] catheter
- Tom Cat[®] catheter
- TDT (Tight Difficult Transfer) catheter
- Rocket[®] Embryon catheter
- Gynetics[®] Emtrac-A catheter

Comparison of pregnancy rates with the use of soft and firm embryo transfer catheters



Notes:

While there are many brands and types of embryo transfer catheters commercially available, there is good evidence to recommend the use of a soft embryo transfer catheter to improve IVF-embryo transfer pregnancy rates. It also appears that no soft embryo transfer catheter is clearly superior and that commercially available soft catheters perform similarly. Personal choice and cost can guide differential use of one soft catheter over the other.

1.22 Lab Equipment for ET Catheter Loading

Lab Equipment for ET Catheter Loading

- Sterile conditions should be used under hood
- Gloves worn
- Embryo handling temperature 37°C
- Stereo microscope



© ASRM 2014

Notes:

The catheter-loading procedure should be performed using sterile conditions under a biological hood or a portable incubator at 37°C using a stereomicroscope.

Gloves should be used by the embryologist during the embryo transfer procedure. The purpose is to protect the embryologist from patient tissue fluids while the embryologist receives the catheter from the physician post transfer and then flushes it.

Since many glove brands have been shown to be embryotoxic, it is important to prevent contact of the gloves with the catheter tip or on the portion of the sleeve that enters the cervix.

Since there may be difficulty or delay in preparing the cervix for the passage of the embryo catheter, the embryos should be kept in culture conditions until the physician is ready to pass the catheter. At that point, the embryo(s) may be loaded into the prepared transfer catheter.

1.23 Choosing and Preparing Embryo(s) for ET

Choosing and Preparing Embryo(s) for ET

Embryo development can change rapidly on ET day



Choice of embryo(s)

- If based on embryo development: choose just before ET
- May be based on genetic testing results, if applicable
- Number to transfer
 - SART recommendations
 - Before day of transfer
 - In writing
- Cryopreservation should wait until after fresh ET

Notes:

When transferring fresh cleavage-stage embryos, the number of cells and symmetry of cells can change rapidly on the day of transfer. If there are several embryos from which to choose and the choice is based on development, the decision of which embryo(s) to transfer should be made by the embryologist as close to the time of transfer as possible.

When transferring fresh Day 5 blastocysts, the expansion and degree of hatching can change rapidly on the day of transfer. If there are several blastocysts from which to choose and the choice is based on development, the decision of which blastocyst(s) to transfer should be made by the embryologist as close to the time of transfer as possible.

If genetic testing has been performed and the result is known, this information should also be factored in once the physician, the patient and the embryologist are aware of this result.

The decision of the number of embryos to transfer should be based on SART recommendations, made prior to the day of transfer and in writing, and should be

confirmed at the time-out immediately before embryo transfer. Cryopreservation of embryos during a fresh cycle should wait until after the embryo transfer is completed.

1.24 Number of Embryos Transferred

Number of Embryos Transferred

- Optimal number of embryos for transfer depends on
 - Quality of embryos, age of women, presence of good-quality spare embryos
- Individual program data and monitoring
- ASRM 2017 recommendations

Prognosis	<35 years	35-37 years	38-40 years	41-42 years
Cleavage-stage embryos				
Euploid	1	1	1	1
*Other favorable	1	1	≤3	≤4
All others	≤2	≤3	≤4	≤5
Blastocysts				
Euploid	1	1	1	1
*Other favorable	1	1	≤2	≤3
All others	≤2	≤2	≤3	≤3

*Any ONE of these criteria: Fresh cycle: expectation of 1 or more high-quality embryos available for cryopreservation, or previous live birth after an IVF cycle; FET cycle: availability of vitrified day-5 or day-6 blastocysts, euploid embryos, 1st FET cycle, or previous live birth after an IVF cycle.

Notes:

An important component of individualized patient care during embryo transfer is consideration for the optimal number of embryos to transfer. This is determined by several factors: quality of embryos, a woman's age, and the presence of good-quality spare embryos.

The ASRM and SART published their first set of recommendations for the number of embryos transferred in 1998. The introduction of these voluntary guidelines coincided with a national decrease in high-order multiple gestations resulting from IVF, although there was little impact on the incidence of IVF twins. Recommendations continue to be revised, with increased emphasis on consideration of single-embryo transfer for women under the age of 35 years—a technique that reduces the number of twin gestations but may also reduce pregnancy rates if used indiscriminately.

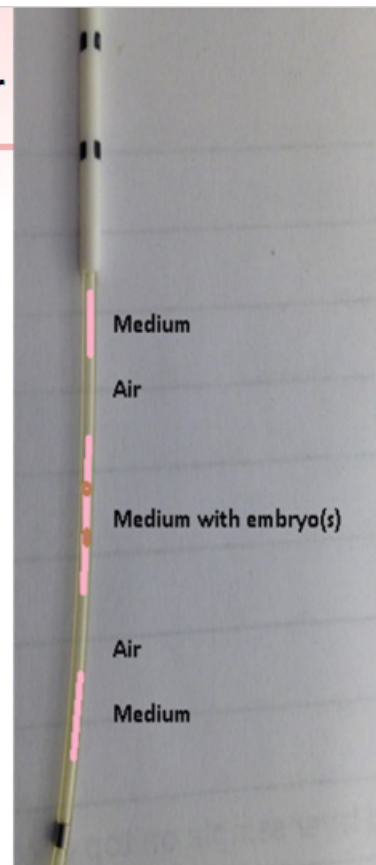
Individual programs are encouraged to follow SART recommendations for patient characteristics and the number of embryos to be transferred. Accordingly, programs should monitor their results continually and adjust the number of embryos transferred to minimize undesirable outcomes. Programs that have a high-order multiple pregnancy rate that is >2 standard deviations above the mean rate for all SART-reporting clinics for 2 consecutive years may be audited by SART.

1.25 Loading the Embryo Transfer Catheter

Loading the Embryo Transfer Catheter

- Catheter flush/rinse
- Fill catheter with media; expel all air
- Aspirate 5 μ L of air
- Aspirate ~ 20 μ L fluid with embryo(s)
- Aspirate another 5 μ L of air
- Avoid inappropriate transfer volumes
 - Excessive >60 μ L
 - Insufficient <10 μ L
- Air bubbles in catheter have not been shown to affect PR or IR
- Careful loading of hatching and hatched blastocysts

PR = pregnancy rate
IR = implantation rate



Notes:

The catheter should be examined with the stereomicroscope for sharp edges and thoroughly flushed with equilibrated and warm culture media to remove any debris from the catheter manufacturing process.

After rinsing, the catheter should be completely filled with transfer media from the syringe plunger to the catheter tip. All air bubbles should be expelled from this initial

column. This column of fluid is not as compressible as air so it will better transfer the plunger movement to the column of fluid containing the embryo(s) during embryo transfer.

Be sure that the syringe plunger is pushed all the way down and is now ready to pick up the first air bubble.

A 5 μL bubble of air is aspirated into the catheter.

Next, a column of fluid totaling about 20 μL , which contains the embryo(s) for transfer, is aspirated into the catheter. Most of this fluid is proximal to the embryo(s) to increase the chance of embryo expulsion during transfer.

If more than one embryo is to be transferred, the embryos should be placed in as close proximity to each other within the catheter as possible. This decreases the total volume of the fluid aspirated into this column and lessens the possibility of a retained embryo. When embryos vary in their degree of expansion, the more expanded embryos will travel in and out of the catheter faster. Attention to their position within the catheter should be noted and caution should be taken to prevent them from traveling too far from other embryos in the catheter. Total medium volume in this fluid column should be approximately 20 μL .

Next, a 5 μL bubble of air is aspirated to bracket the column of fluid containing the embryos. This has two purposes; it prevents the embryos in their fluid column from traveling farther up the catheter or prematurely out of the catheter, and it makes the column of fluid containing the embryos more easily visualized on ultrasound-guided transfer.

At this point, the catheter is loaded and ready for transfer. Some prefer to aspirate an additional 5 μL column of fluid followed by a final 5 μL bubble of air. This is a matter of preference. In either case, the final air bubble is also important in that it prevents the wicking of fluid out of the catheter as it comes into contact with the walls of the cervix and uterus during transfer.

Transfer volumes of more than 60 μL may result in expulsion of the embryos into the vagina, whereas volumes less than 10 μL may also negatively affect implantation rates. The use of air bubbles in the catheter has not been shown to affect pregnancy rates or implantation rates.

Due to the fragile nature of hatching and hatched blastocysts, great care should be taken during loading these embryos into the transfer catheter. They are particularly susceptible to breaking apart if they are aspirated too quickly. Also, they should never be exposed to a fluid-air interface because this will most likely cause them to completely break apart.

1.26 Transfer Techniques

Transfer Techniques	
Direct	• Catheter is loaded with embryo(s) and transfer performed without immediate prior trial
Trial followed by transfer	• Immediately before actual transfer, catheter passed to and just through internal os; catheter loaded and transfer performed
Afterload	• Only 1 cm only of inner catheter tip extends through outer sheath; outer sheath positioned at top of cervical canal, and left in place while withdrawing inner catheter • Inner catheter then loaded with embryos and threaded through outer sheath into the endometrial cavity for expulsion
Conversion	• If difficult trial transfer, once inner catheter has passed internal cervical os, outer sheath moved forward to top of cervical canal while withdrawing inner catheter • Inner catheter then loaded with embryo(s) and threaded through outer sheath into the endometrial cavity for expulsion

Notes:

Prepare the embryo transfer catheter and traverse the cervix using one of the following techniques. Common and acceptable variations exist and the names given to them may vary locally.

Direct Transfer: The catheter is loaded with embryo(s) and the transfer is performed without a prior trial immediately preceding the transfer.

Trial Followed by Transfer: A trial or regular embryo transfer catheter (both the inner catheter and outer sheath connected together in standard configuration) is used immediately before the actual transfer. It is passed up to and just through the internal os. When it appears that the actual transfer will be possible without great difficulty, an embryo transfer catheter is loaded and the transfer is performed.

Afterload Transfer: The outer sheath of an embryo transfer catheter is separated from the inner catheter. The inner catheter is pulled back so that approximately 1 cm only of its tip is extending through the outer sheath. The two catheters are held together while traversing the cervical canal. Once the inner catheter has just passed through the internal cervical os and the outer sheath is positioned at the top of the cervical canal, the outer sheath is left in place while

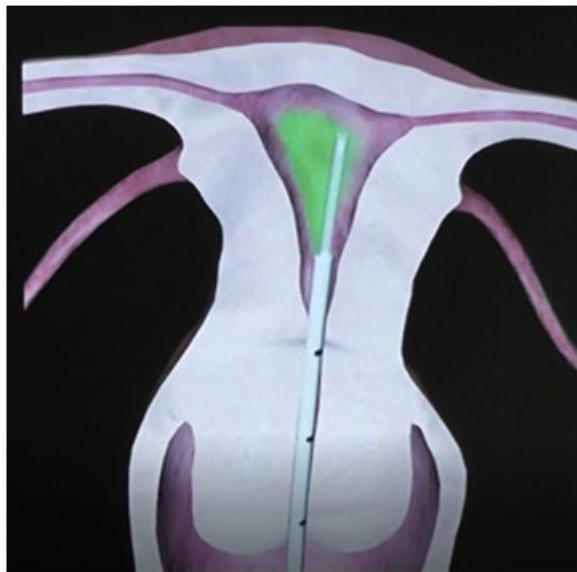
withdrawing the inner catheter. The inner catheter is loaded with embryos and threaded through the outer sheath into the endometrial cavity for expulsion.

Trial Transfer Converted into an Afterload Transfer: If a Trial Transfer is difficult, once the inner catheter has passed the internal cervical os, the outer sheath is separated from the inner catheter and moved forward to the top of the cervical canal while withdrawing the inner catheter. As with the Afterload Transfer, the inner catheter is then loaded with embryo(s) and threaded through the outer sheath into the endometrial cavity for expulsion.

1.27 9. Catheter Tip Placement

9. Catheter Tip Placement

- Precise location of the catheter tip and site of transfer
 - Upper or middle (central) third of the uterine cavity
 - >1 cm from the fundus
- Echogenic catheter may improve ET technique



Allahbadia et al., 2010

ASRM ET Protocol 2017

Notes:

Atraumatic passage of the catheter into the uterine cavity and the precise location of the catheter tip and site of transfer of the embryos are considered essential for successful implantation.

Using ultrasound guidance, the catheter is gently inserted through the cervical canal. The ultrasonographer helps guide the physician in positioning the tip of the catheter to a suitable point near the cavity fundus. This is done using care to avoid contact with the

fundal endometrium.

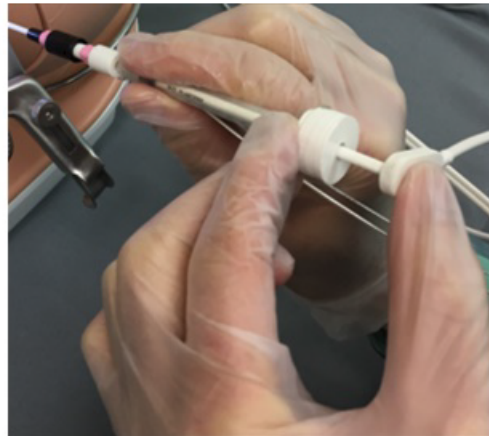
There is fair evidence that placement of the catheter tip in the upper or middle third of the uterine cavity, greater than 1 cm from the fundus for embryo expulsion, optimizes pregnancy rates.

At least one prospective, randomized study found that using an echogenic catheter may help to refine the transfer technique by tracking the position of the cannula and placement of the catheter in relation to the endometrial surface and uterine fundus, thus avoiding even minimal endometrial damage.

1.28 10. Embryo Expulsion and Catheter Removal

10. Embryo Expulsion and Catheter Removal

- Complete transfer within 1–2 minutes after loading
- Embryos deposited into the uterine cavity
 - Optimum embryo injection speed not known
 - Caution with hatching or hatched blastocysts
- Catheter withdrawal
 - Immediate or brief pause
 - Delay in catheter removal not shown to increase pregnancy rates



Grygoruk et al., 2011; ASRM Guideline 2017

Notes:

The embryo transfer should be completed as efficiently as possible within 1–2 minutes after loading.

Once the catheter tip is in place, the embryos are deposited into the uterine cavity. The pressure generated in the working chamber of a syringe is passed into the catheter, where it causes the ejection of the transferred load. The disproportion between the diameters of the syringe plunger and the catheter lumen creates favorable conditions for the fast fluid flow inside the catheter.

Some practitioners recommend using minimal injection speed to transfer embryos to minimize potential increases in shear stress and the pressure changes with the injection speed. Also, some studies have suggested that the injection velocity of the embryo could impact the trajectory of the placement, and therefore potentially impact implantation rate and the risk of ectopic pregnancy if a fast speed was used too near the fundus. However, at this time there is insufficient evidence to recommend any specific injection speed of the catheter at the time of embryo transfer.

Due to the fragile nature of hatching or hatched blastocysts, greater care should be taken by the physician during the expulsion of the embryos from the transfer catheter.

Once the embryo(s) is discharged from the embryo catheter the physician has the option of immediately withdrawing the transfer catheter or pausing briefly before withdrawal of the catheter. There is fair evidence that a delay in catheter withdrawal after embryo placement does not lead to improved pregnancy rates.

1.29 11. Checking Catheter for Retained Embryo(s)

11. Checking Catheter for Retained Embryo(s)

- Check catheter after embryo transfer
- Retained embryos in the transfer catheter and immediate re-transfer do not affect implantation, clinical pregnancy, or spontaneous abortion rates
- If retained embryos present
 - Wash embryo(s) if needed
 - Reload into new catheter
 - Re-check cervix for presence of mucus
 - Repeat transfer

ASRM Guideline 2017

Notes:

Once the catheter is removed, it is checked under the microscope for retained embryos. Retained embryo(s) after the initial transfer attempt is an uncommon, but clinically worrisome event, creating anxiety for patients and practitioners. The majority of studies addressing this question report an incidence of retained embryo(s) of <3%; however, three studies reported rates of 5%, 7.5%, and 10%, respectively. There is fair evidence that retained embryos in the transfer catheter and immediate re-transfer do not affect implantation, clinical pregnancy, or spontaneous abortion rates.

If retained embryos are present, common practice is to wash embryo(s) if needed, reload into a new transfer catheter, and repeat the transfer.

1.30 11. Checking Catheter for Retained Embryo(s)

11. Checking Catheter for Retained Embryo(s)

Mucus on catheter

- Does not appear to affect clinical pregnancy or live-birth rates

Blood on catheter
after embryo
transfer

- Unknown if affects implantation or pregnancy rates

ASRM Guideline 2017

Notes:

Clinicians have debated whether the presence of mucus on the catheter after the embryo transfer has adverse effects; however, it does not appear to be associated with a lower clinical pregnancy rate or live-birth rate. The presence of blood on the catheter after embryo transfer and its possible implications have been studied often with mixed results. Evidence is insufficient to state conclusively that the presence of blood on the catheter, once it is withdrawn, is associated with implantation or pregnancy rates.

1.31 12. Patient Discharge

12. Patient Discharge

- Bed rest after embryo transfer not recommended
- Immediate ambulation once the embryo transfer procedure is completed

Notes:

The practice of bed rest post-embryo transfer has been studied extensively. During the early years of IVF, patients were kept supine in hopes of avoiding uterine contractions and “premature expulsion” of embryos from the uterus. Anecdotal reports included durations of bed rest that extended up to 24 hours and some as long as 2 weeks. However, recent studies have demonstrated that not only does bed rest after embryo transfer not improve pregnancy rates, but even short bed rest durations of 10 minutes are associated with lower success rates. Patients should ambulate immediately once the embryo transfer procedure is completed.

1.32 The Human Factor

The Human Factor

- Clinician effect
- Experience
- Working in harmony
- Standardized ET protocol



Hearns-Stokes et al., 2000; ASRM ET Protocol 2017

Notes:

The human factor must always be considered. Studies have demonstrated a significant difference in pregnancy rates attributable to clinician transfer variations. Experience and skill across the team is needed to perform efficient embryo transfer. There should be clear understanding and a precise approach to embryo transfer on the part of both embryologists and clinicians. Standardizing the embryo transfer protocol and methods to improve an individual practitioner's embryo transfer success rate should be considered.

1.33 Troubleshooting ET: Fluid in the Uterus

Troubleshooting ET: Fluid in the Uterus

- **Reasons**
 - Uterine pathology
 - Improper washing of cervical os
- **Recourse**
 - If there is uterine pathology, cancel transfer
 - If the fluid is present because of technical reasons, consider waiting 20 minutes and re-evaluate cervix

Notes:

Fluid in the uterus is caused either by uterine pathology or improper techniques used for washing the external cervical os or canal. If there is a uterine pathology, the transfer should be cancelled and treatment should be sought. However, if the fluid present is due to technical reasons, then ET should be delayed for 20 minutes and the cervix re-evaluated.

1.34 Troubleshooting ET:

Troubleshooting ET: Excessive Myometrial Contraction

- **Reasons**
 - Physiological differences in women
 - ET technique
- **Recourse**
 - Mock transfer (easy vs. difficult ET)
 - Training for ET

Notes:

There are physiologic differences among women; some women could feel cramping during embryo transfer while others do so specifically when certain instruments, such as a tenaculum, are used. Avoiding tenaculum use and waiting a few seconds until cramping ends can help. Again, a mock transfer can provide information on the best recourse for the patient.

1.35 Conclusions

Conclusions

The following interventions for embryo transfer are supported by the literature for improving pregnancy rates:

- Abdominal ultrasound guidance for embryo transfer
- Removal of cervical mucus
- Use of soft embryo transfer catheters
- Placement of embryo transfer tip in the upper or middle (central) area of the uterine cavity, greater than 1 cm from the fundus, for embryo expulsion
- Immediate ambulation once the embryo transfer procedure is completed

ASRM Guideline 2017

Notes:

Attention to the many details of embryo transfer technique appears to be important for IVF success. A holistic approach to IVF-ET on the part of both embryologists and clinicians will serve to maximize pregnancy rates.

Embryo transfer is considered a critical step in the IVF process. Extensive literature exists regarding all aspects of embryo transfer, which supports its importance to overall IVF success. While there are insufficient data to provide guidance on a number of techniques used during embryo transfer, the literature does provide guidance for many aspects of this critical component of IVF.

The following interventions are supported by the literature for improving pregnancy rates:

- Abdominal ultrasound guidance for embryo transfer
- Removal of cervical mucus
- Use of soft embryo transfer catheters
- Placement of embryo transfer tip in the upper or middle (central) area of the uterine cavity, greater than 1 cm from the fundus, for embryo expulsion
- Immediate ambulation once the embryo transfer procedure is completed

1.36 Thank you!



Notes:

Thank you for participating in this educational activity.