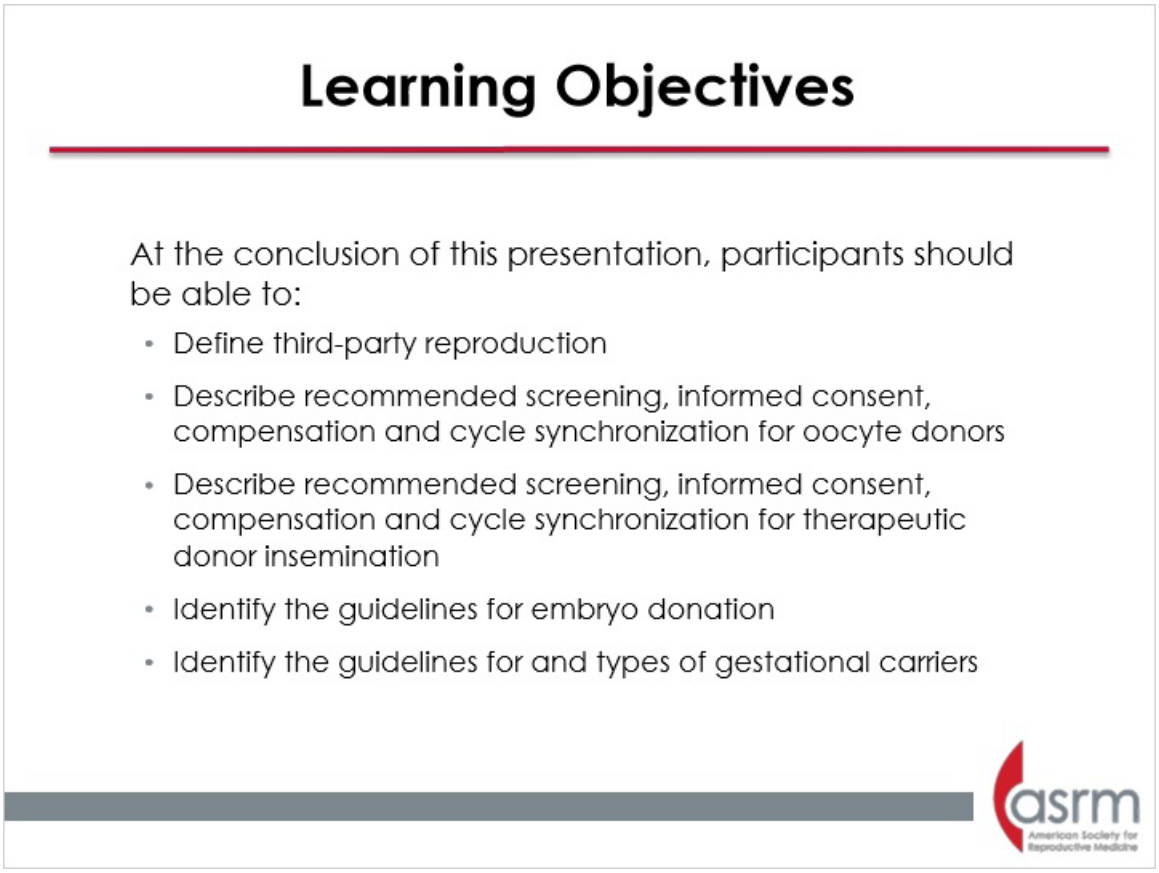
LABCC100 Lesson 23

1.1 Third-Party Reproduction: Gamete and Embryo Donation and Gestational Carrier Use

Notes:

Welcome to the American Society for Reproductive Medicine's eLearning modules. This presentation addresses Third-Party Reproduction - Gamete and Embryo Donation and Gestational Carrier Use.

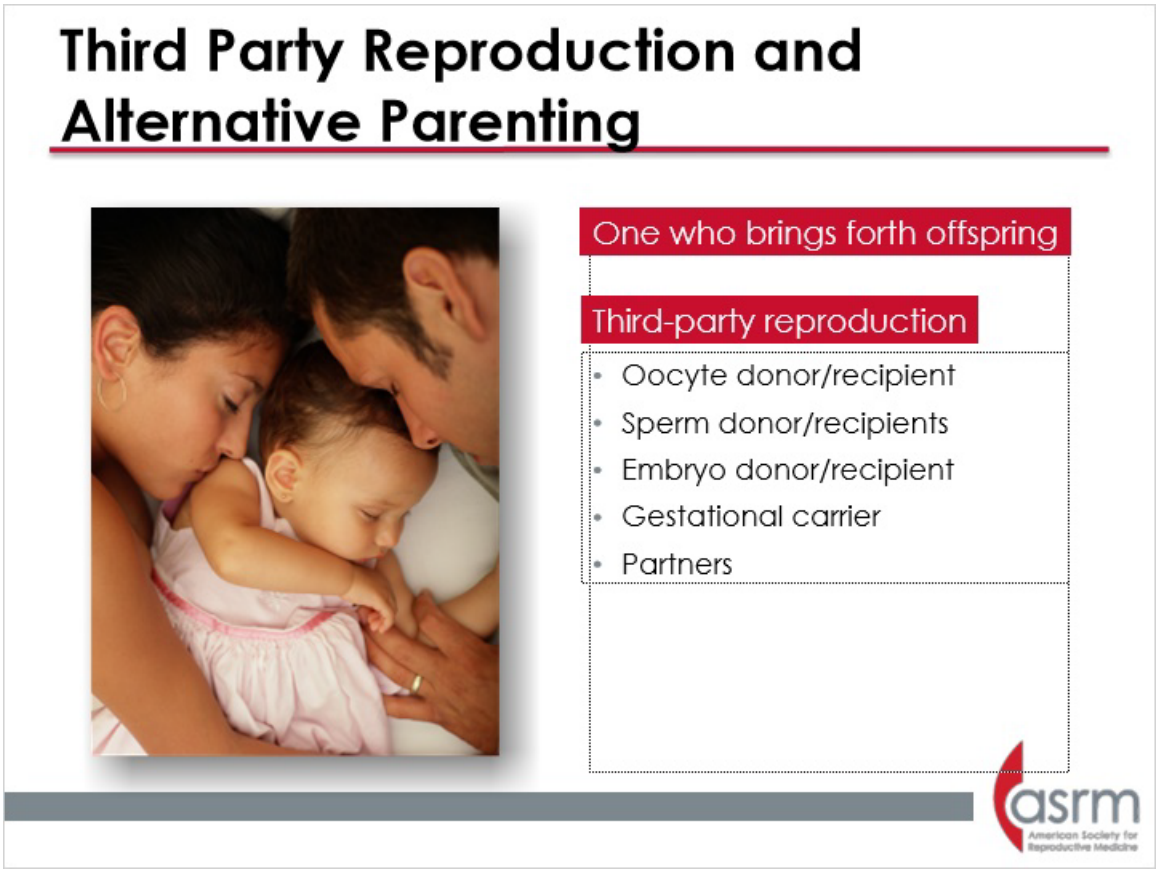
1.2 Learning Objectives



Notes:

At the conclusion of this presentation, participants should be able to:
Define third-party reproduction.
Describe recommended screening, informed consent, compensation and cycle synchronization for oocyte donors.
Describe recommended screening, informed consent, compensation and cycle synchronization for therapeutic donor insemination.
Identify the guidelines for embryo donation.
Identify the guidelines for and types of gestational carriers.

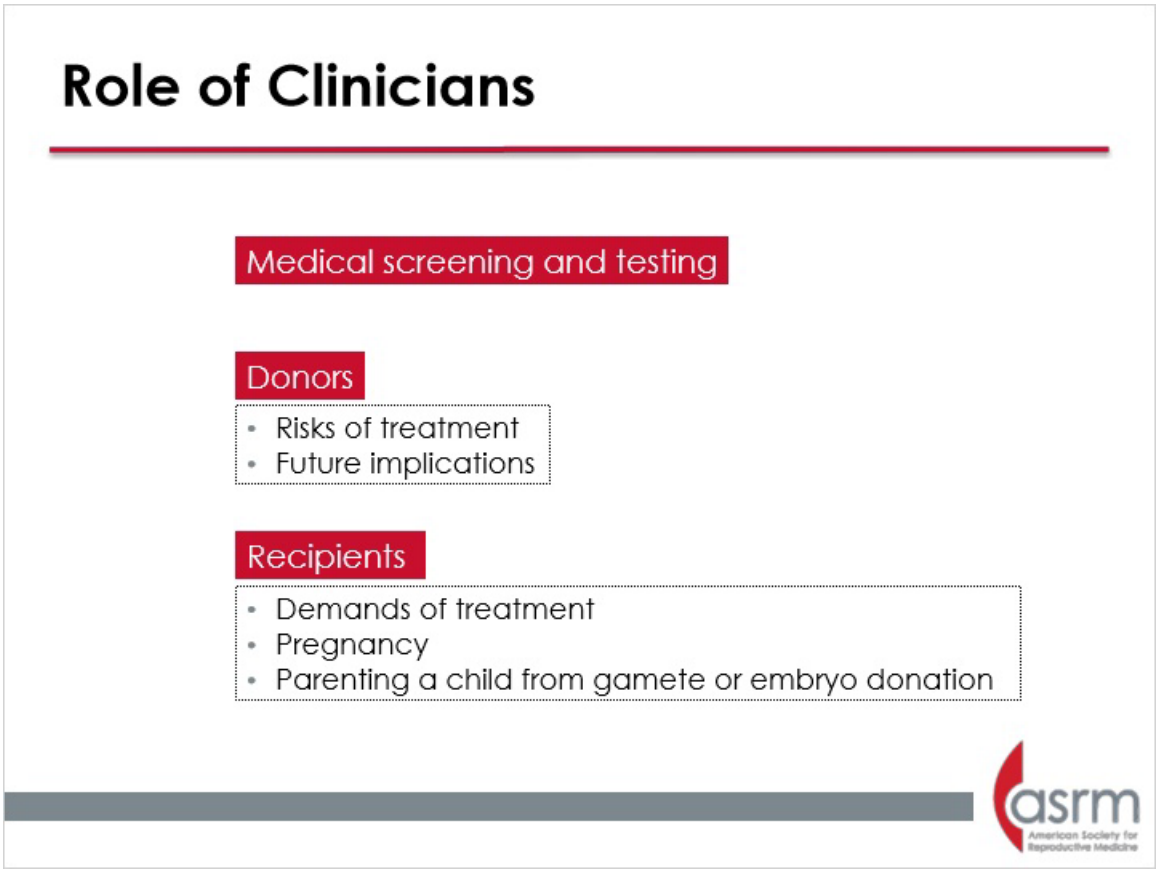
1.3 Third Party Reproduction and Alternative Parenting



Notes:

A parent is one who brings forth offspring. In most cases, offspring result from a man and woman producing gametes that lead to conception in the mother's uterus. However, the term parent may take on new meaning. Third-party reproduction has made it possible for infertile couples to have more choices in building a family. Third-party reproduction can involve one or more third parties including an oocyte donor and recipient, sperm donor and recipient, embryo donor or recipient, and gestational carrier, and the partners of these individuals. This presentation discusses the clinical aspects involved in providing alternative approaches to parenting through third-party reproduction. While some procedures are accomplished with little intervention, many approaches include the use of assisted reproductive technologies (ART), such as in vitro fertilization. Third-party reproduction is a complex process requiring consideration of psychological, social, ethical, and legal issues that will be discussed in this module. and in the module Psychological Counseling in Third-Party Reproduction.

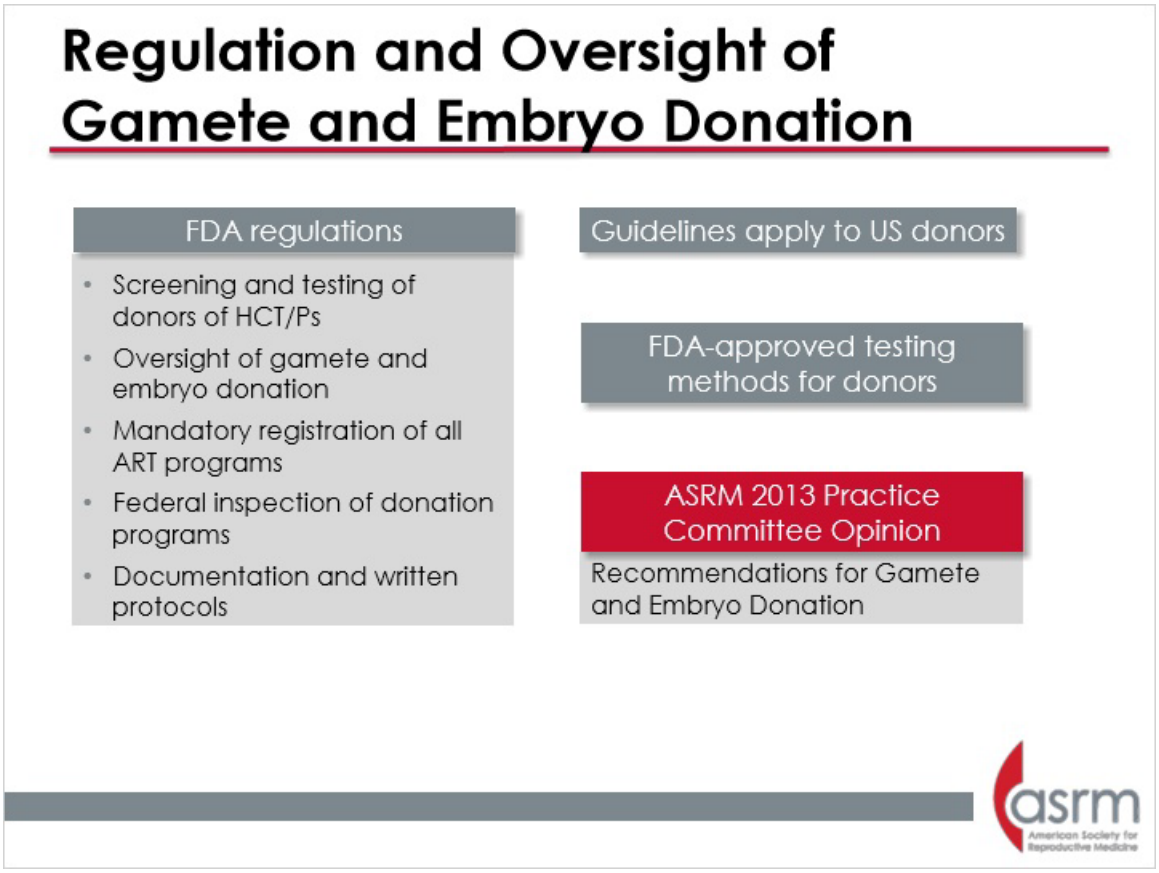
1.4 Role of Clinicians



Notes:

The role of reproductive clinicians in third-party reproduction is to provide appropriate medical screening and testing and to help inform both donors and recipients about the risks and implications of treatment. Roles include determining if donors are properly informed of the risks of treatment and are they prepared for how they might feel in the future, and whether recipients are able to tolerate the demands of treatment with its successes and failures, pregnancy with all its risks, and parenting a child from gamete or embryo donation.

1.5 Regulation and Oversight of



Notes:

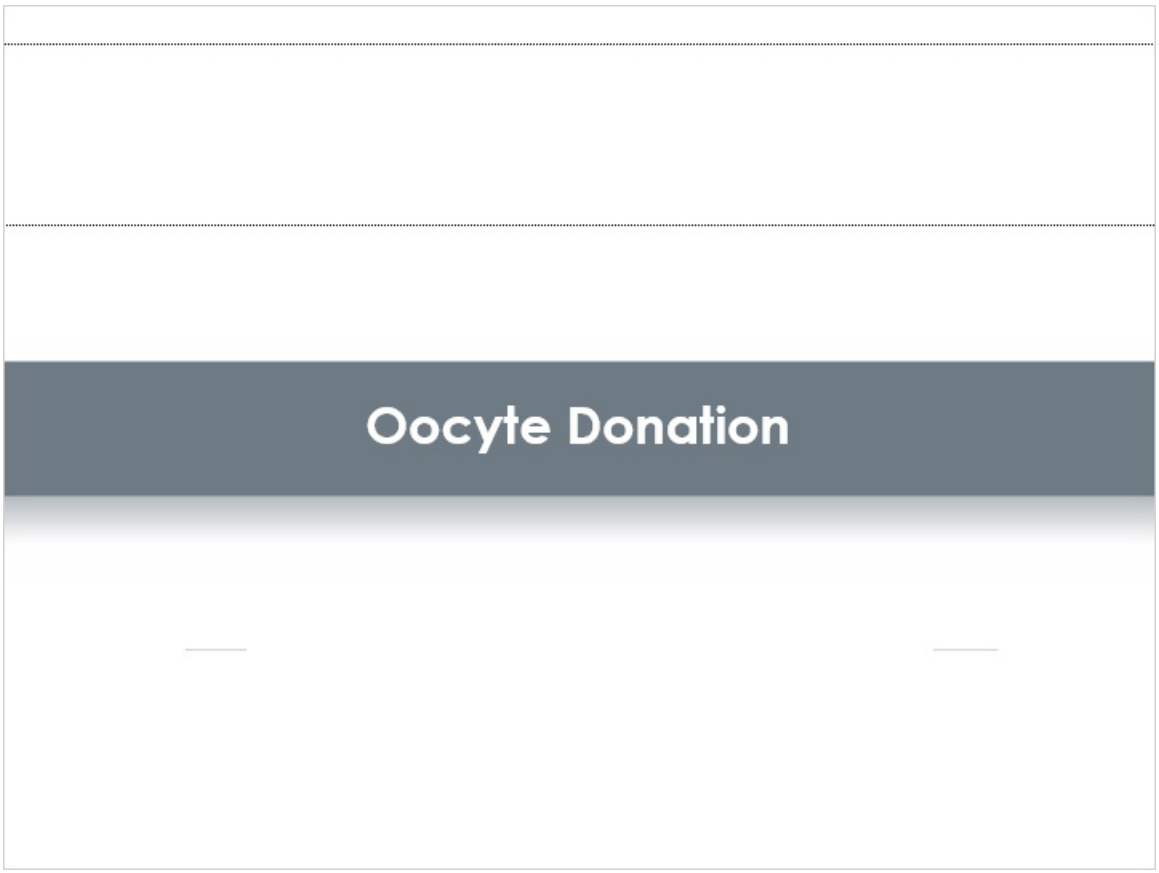
The FDA has published requirements for the screening and testing of donors of human cells, tissues, and cellular and tissue-based products (HCT/Ps). In many instances, the federal requirements may be less rigorous than those in the state in which an individual practice is located, or than those recommended by the American Society for Reproductive Medicine (ASRM) and the Society for Assisted Reproductive Technology (SART). It is the responsibility of all clinics to know the regulations of their individual states and local municipalities and to comply with those standards.

FDA regulations provide oversight to gamete and embryo donation, including mandatory registration of all ART programs with the federal government, federal inspections of programs that are performing donation, required documentation, and written protocols attendant to donor screening, testing, selection, rejection, and follow-up. Complete records of all donor cycles, including documentation of adherence to FDA regulations, must be made available to FDA inspectors at their request.

Guidelines for screening and testing of gamete and embryo donors in this module apply to donors in the United States. Because the prevalence of sexually transmitted infections (STIs) and genetic diseases vary in other locales, these guidelines may not be appropriate for donors from other countries.

Not all testing methods have been approved by the FDA for use in donors and it is the responsibility of each center to determine if their laboratory uses an approved method. The information regarding third-party reproductive care in this module is presented as an overview of the recommendations from the ASRM, which incorporate federal guidelines. However, it is not inclusive of all specific screening and testing requirements and should not be used for determining eligibility of specific donors or recipients.

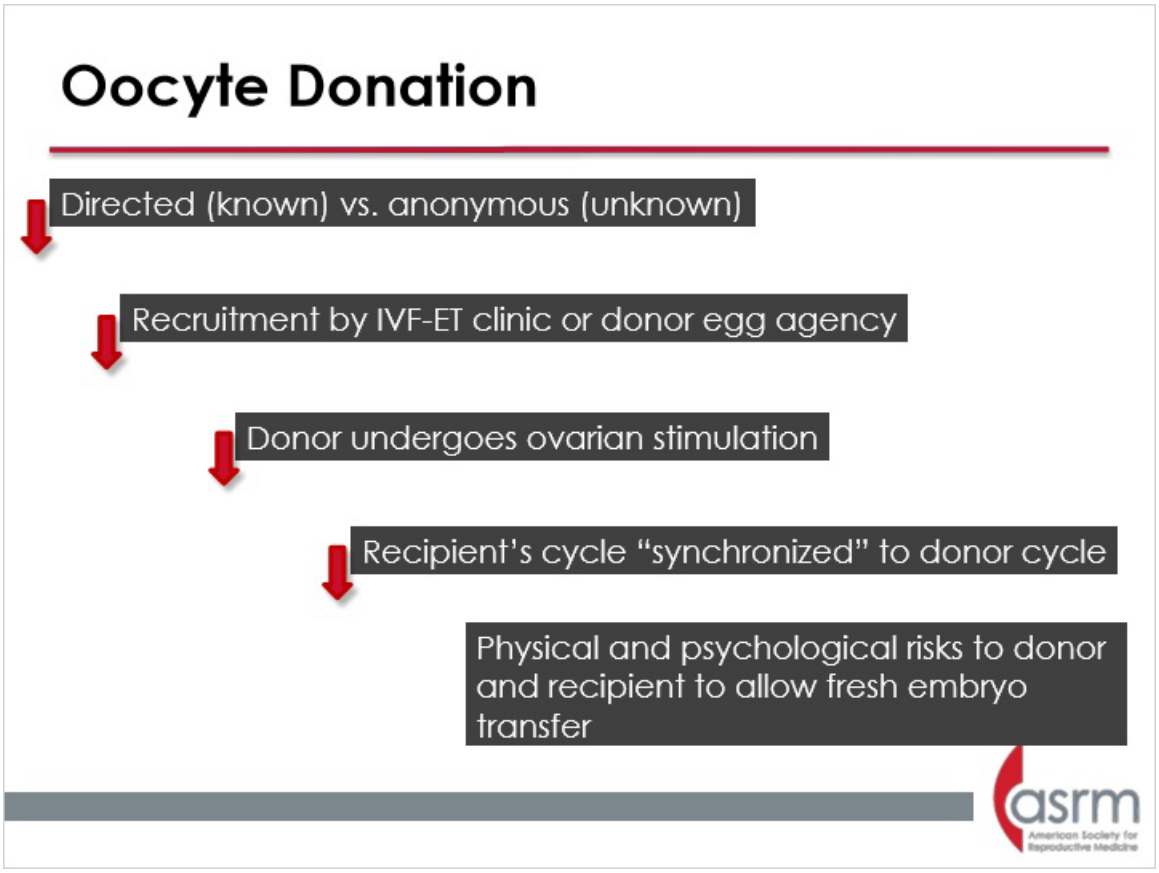
1.6 Oocyte Donation



Notes:

In an oocyte donation procedure, oocytes from a female donor are fertilized with the sperm of the recipient's partner, and the resultant embryos are placed in the recipient's uterus. Multiple oocytes are stimulated in the donor and the oocytes are retrieved using routine IVF-ET techniques.

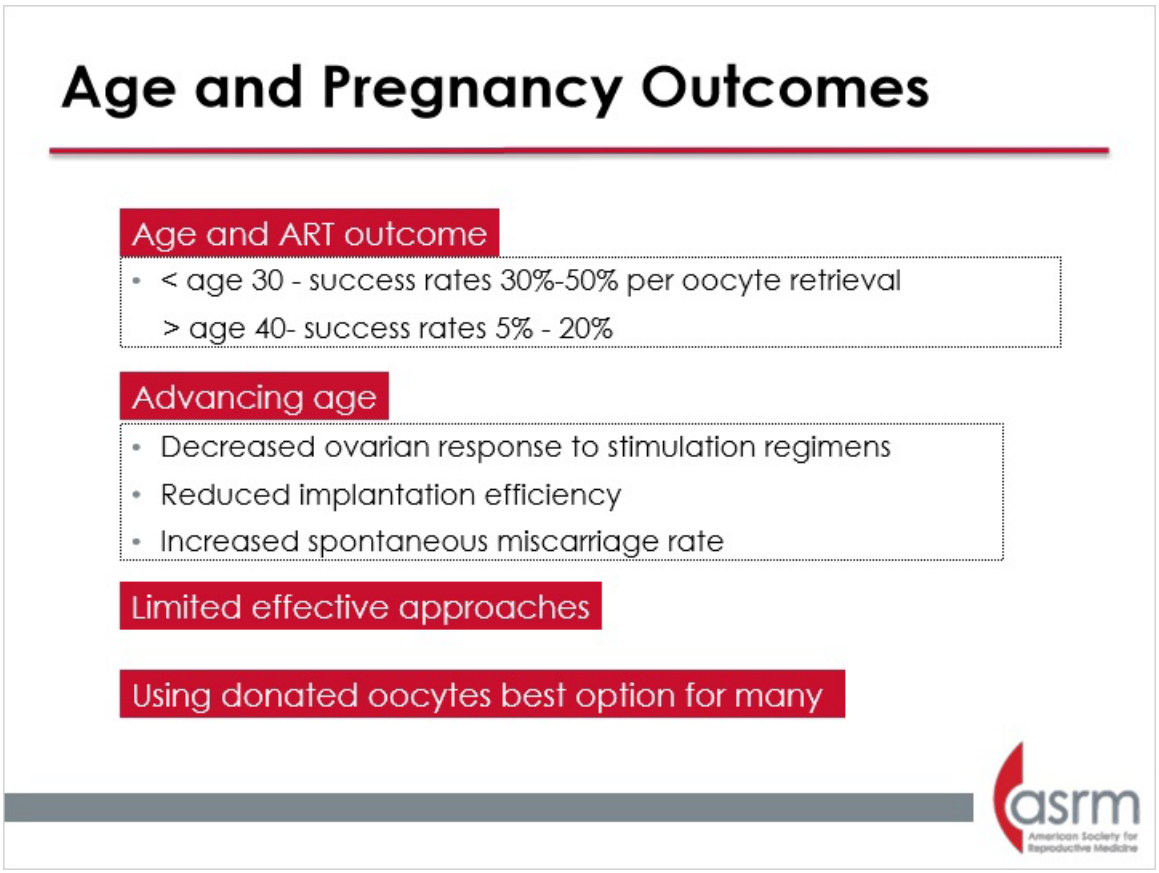
1.7 Oocyte Donation



Notes:

The donor may be known to and recruited by the recipient (directed donation), or instead may be unknown to the recipient, (anonymous donation) having been recruited by the IVF-ET program or by a donor egg agency. Anonymous oocyte donation usually occurs when a young, fertile woman donates all of her oocytes to a recipient during a particular cycle. This woman is not trying to achieve pregnancy and will therefore be reimbursed for her time and effort. In this case the recipient is responsible for all prerequisite costs for the oocyte donor as well as the cycle. Each recipient couple must decide the type of donor with whom they are most comfortable. In cases where a young donor is utilized, high success rates, comparable to those achieved in women of similar age using their own oocytes, can be expected. Oocyte donation requires ovarian stimulation with monitoring and oocyte retrieval, involving significant inconvenience, discomfort, and risks for the donor. The oocyte recipient's cycle is synchronized to the donor's cycle using various medications. There are physical and psychological implications for both the donor and the recipient to allow fresh embryo transfer. The use of the freeze-all technique is also common. This allows the patients to freeze all embryos during the first cycle of IVF then transfer can occur when the uterus has the time to recover from the effects of IVF medication.

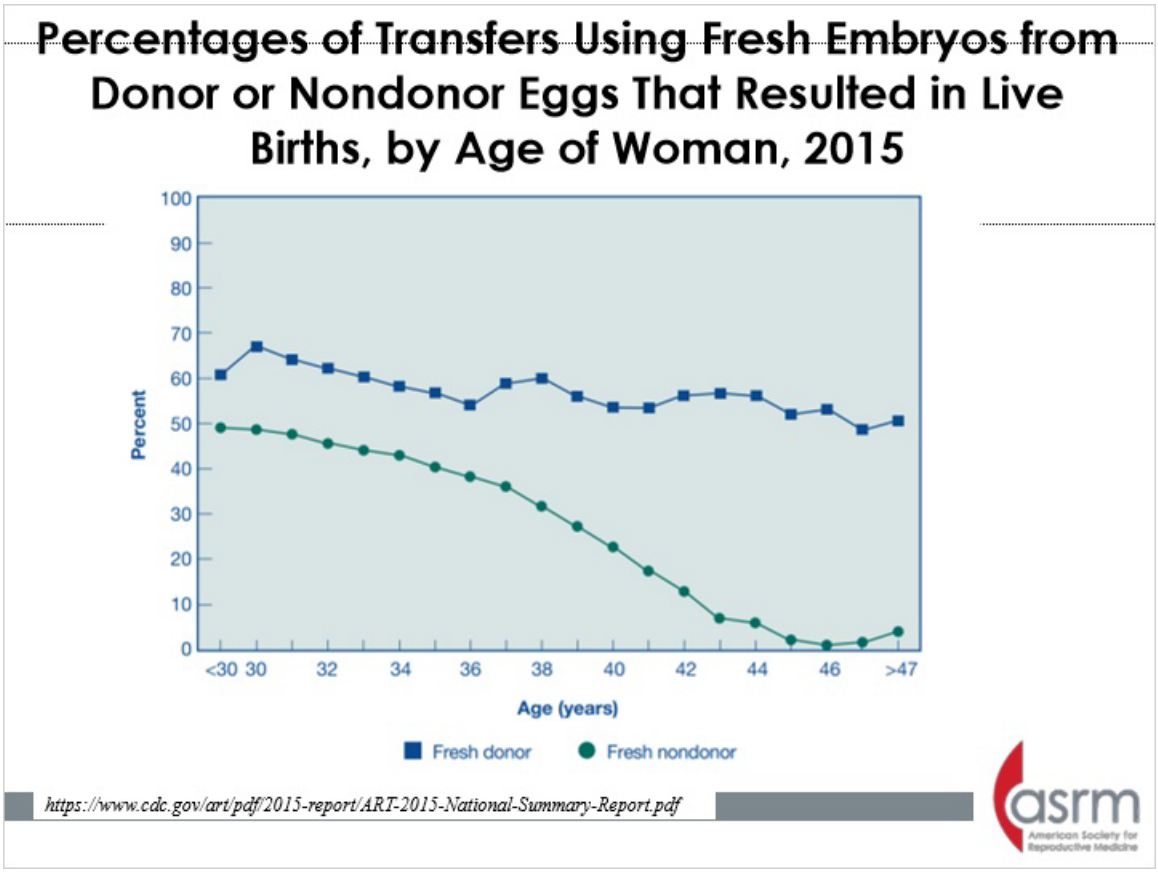
1.8 Age and Pregnancy Outcomes



Notes:

The use of donor oocytes by women is increasingly common, especially as women delay childbearing. A woman's age is the most important single variable influencing both ART and pregnancy outcomes as advancing age leads to decreases in the ovarian response to stimulation regimens, reduced implantation efficiency and increased spontaneous miscarriage rate. For patients under age 30 using their own oocytes in ART procedures, success rates in terms of live birth of 30-50% per oocyte retrieval can legitimately be expected; for patients over age 40, realistic success rates are only 5% to 20%. Oocytes from younger women possess greater fertility potential, and this potential is utilized in donor oocyte treatment. Because effective approaches are limited for the treatment of women of advanced reproductive age, for many of these women, using donated oocytes is the best option.

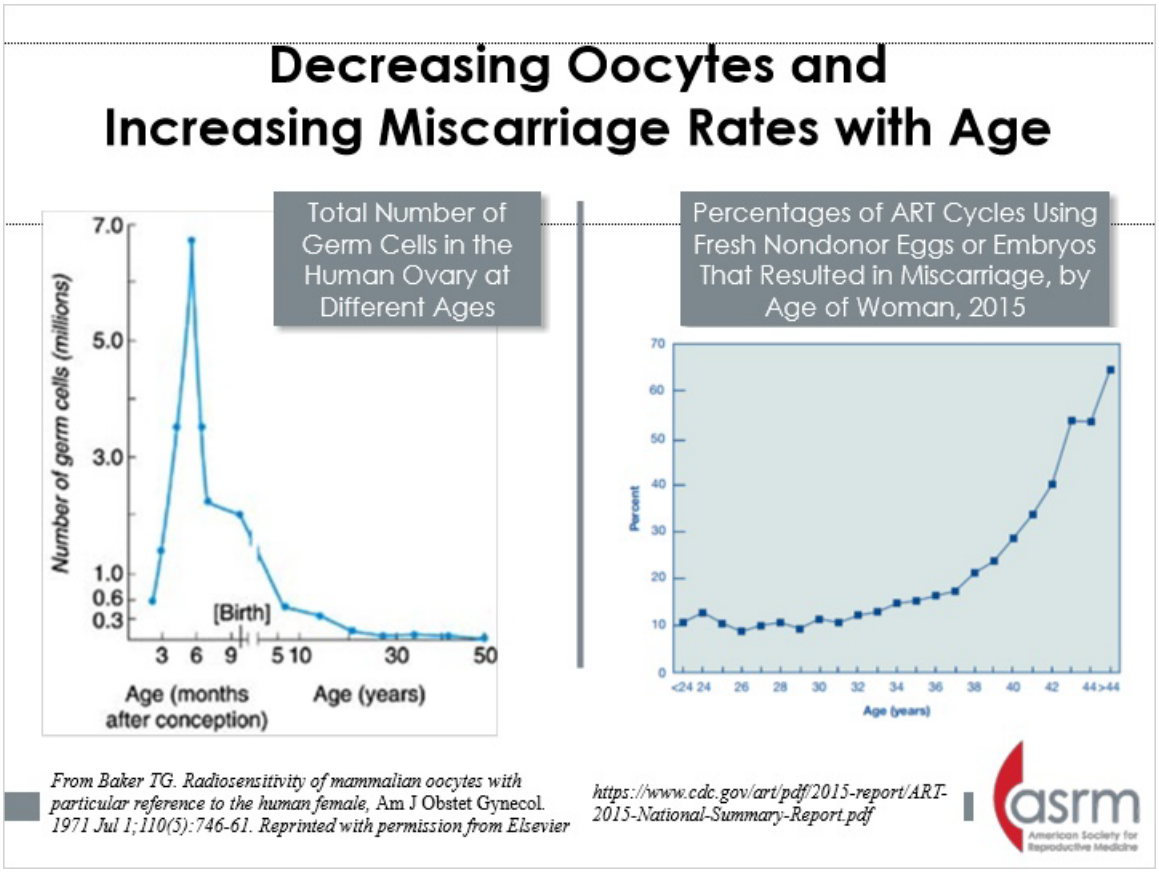
1.9 Percentages of Transfers Using Fresh Embryos from Donor or Nondonor Eggs That Resulted in Live Births, by Age of Woman, 2015



Notes:

The use of donor oocytes can help overcome the decline in pregnancy outcomes with advancing age due to decreased oocyte quality and quantity. In this graph from SART, live birth outcomes are compared among women using fresh embryos from their own and from donor oocytes. With the use of donor oocytes, live birth rates do not decline with age. This strongly suggests that the decline in female fertility with age is the result of ovarian aging with resulting poor oocyte quality.

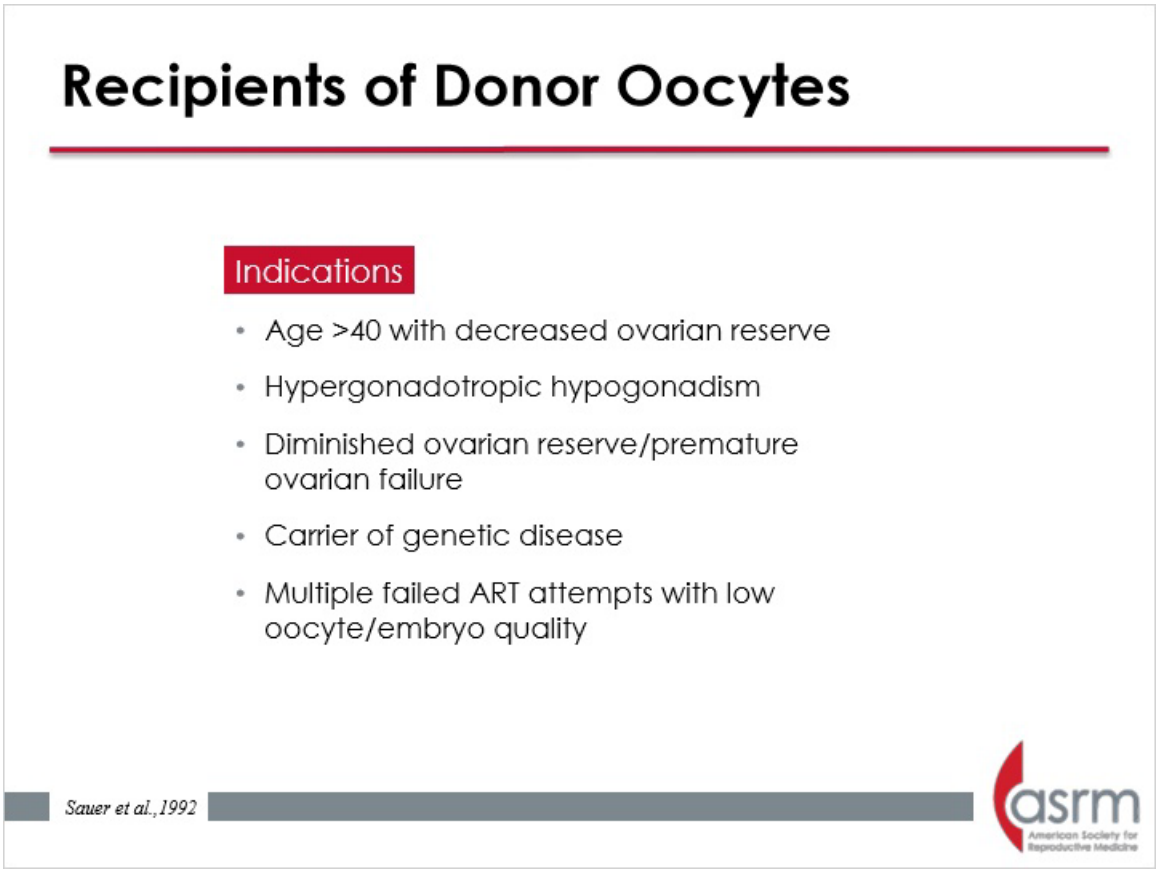
1.10 Decreasing Oocytes and



Notes:

Recall that women are born with a set number of oocytes which decreases with age due to atresia of the follicle/oocyte from the maximum number of 7 million at 7 months' fetal gestation, and decreasing to 300,000 by age 30. By menopause, the number is functionally zero. Miscarriages also increase as a function of age, as shown in the graph at the right. In women who had ART cycles using fresh, nondonor eggs or embryos, the rate of miscarriage was stable until about age 33, and then rose steadily beginning at about age 38.

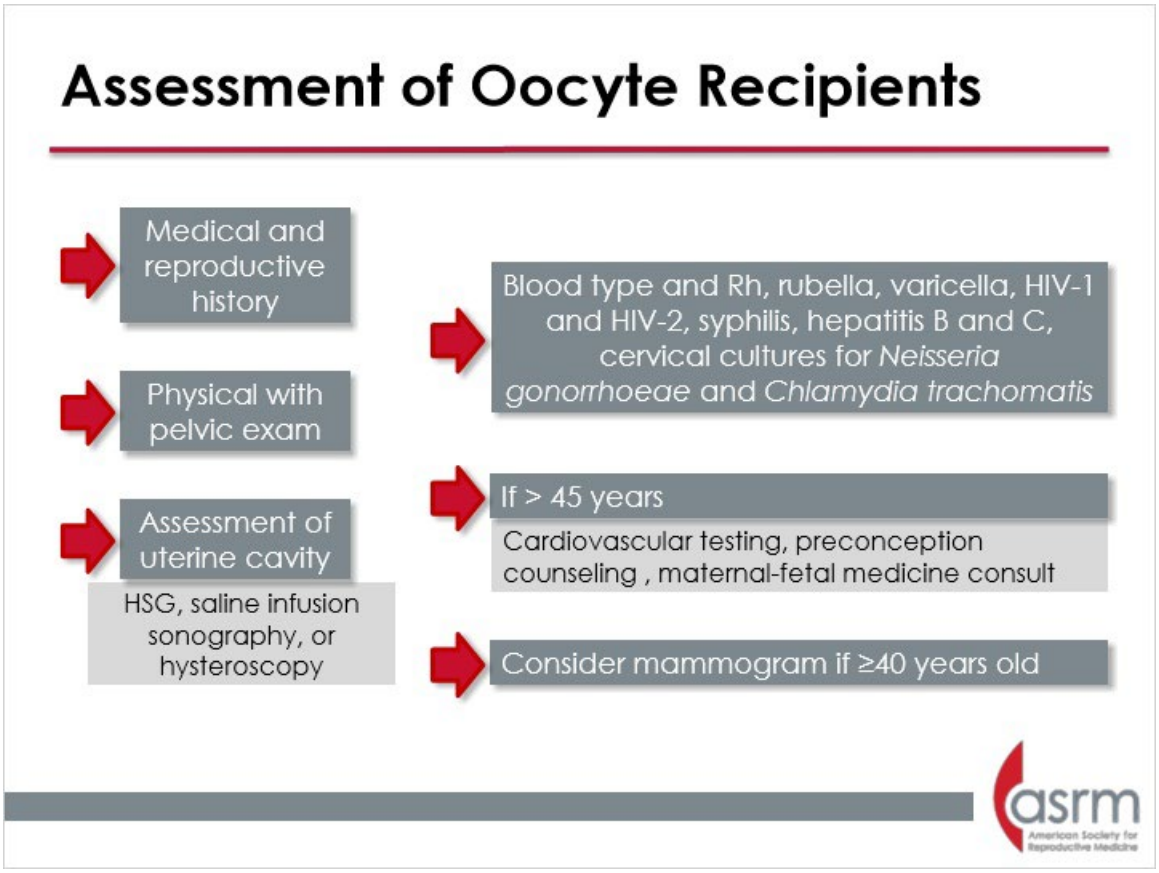
1.11 Recipients of Donor Oocytes



Notes:

The most common reason for the use of donor oocytes is maternal age greater than 40 years with decreased ovarian reserve**.** Other indications include hypergonadotropic hypogonadism, diminished ovarian reserve, premature ovarian failure, being a carrier of a genetic disease, and multiple failed ART attempts with low oocyte or embryo quality.

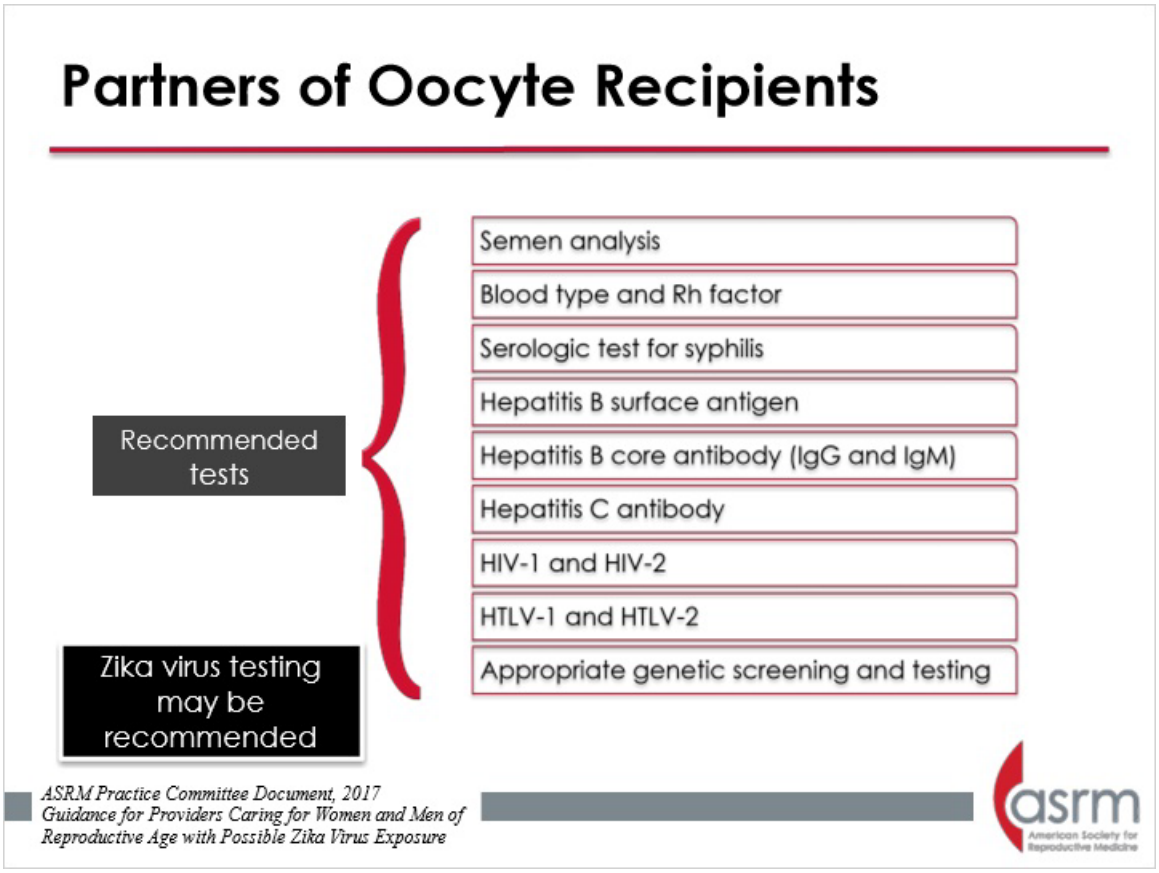
1.12 Assessment of Oocyte Recipients



Notes:

The FDA does not require screening or testing of the recipients of donated gametes; however ASRM recommends the following assessments of women who will be oocyte recipients: a complete medical and reproductive history, physical and pelvic examination, assessment of the uterine cavity using hysterosalpingogram, saline infusion sonography, or hysteroscopy**.** In addition, the tests shown here are recommended. If a woman is over 45 years of age, cardiovascular assessment, preconception counseling, and consultation with a maternal-fetal medicine specialist are also recommended. Mammogram should also be considered in women age 40 and older.

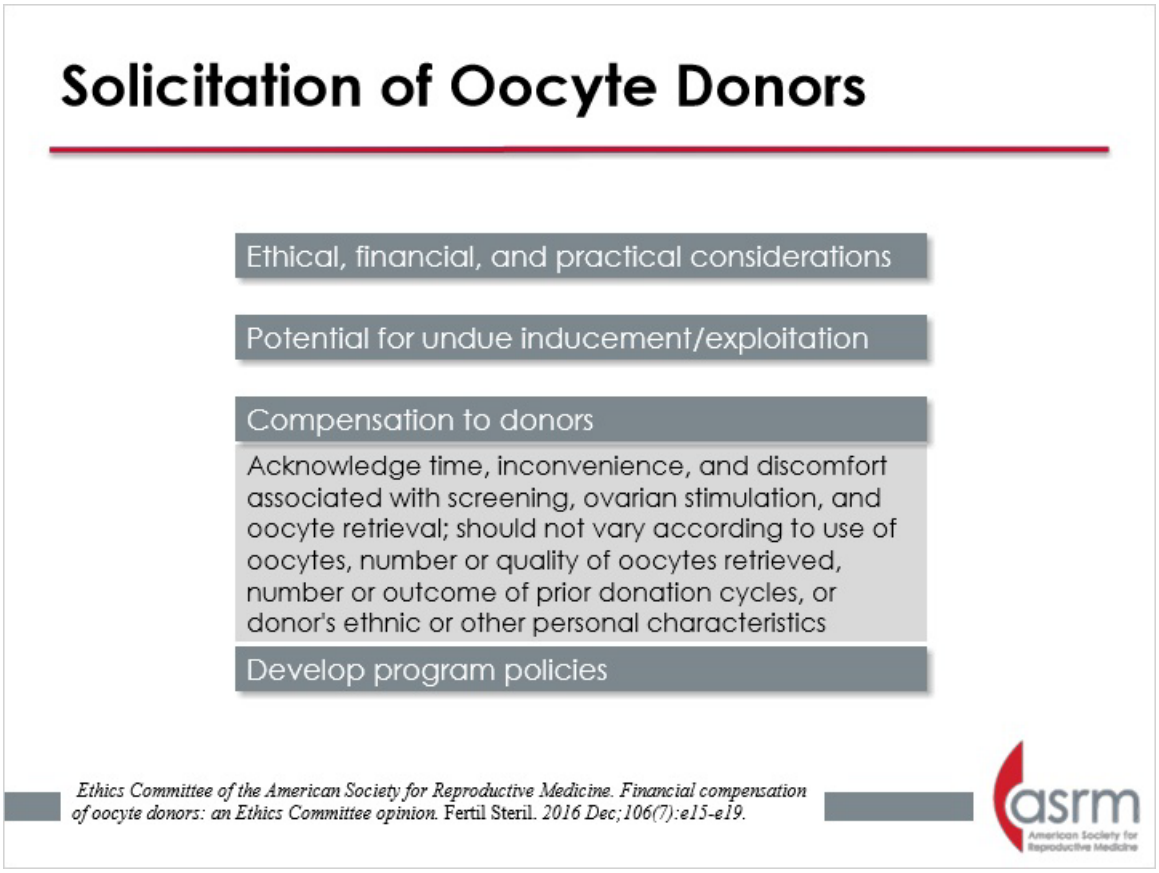
1.13 Partners of Oocyte Recipients



Notes:

Although no tests are required for the male partner of the oocyte recipient, these tests are recommended. Health care providers should elicit pertinent information from male partners about possible exposure to Zika virus. If partner has been exposed further testing will be required.

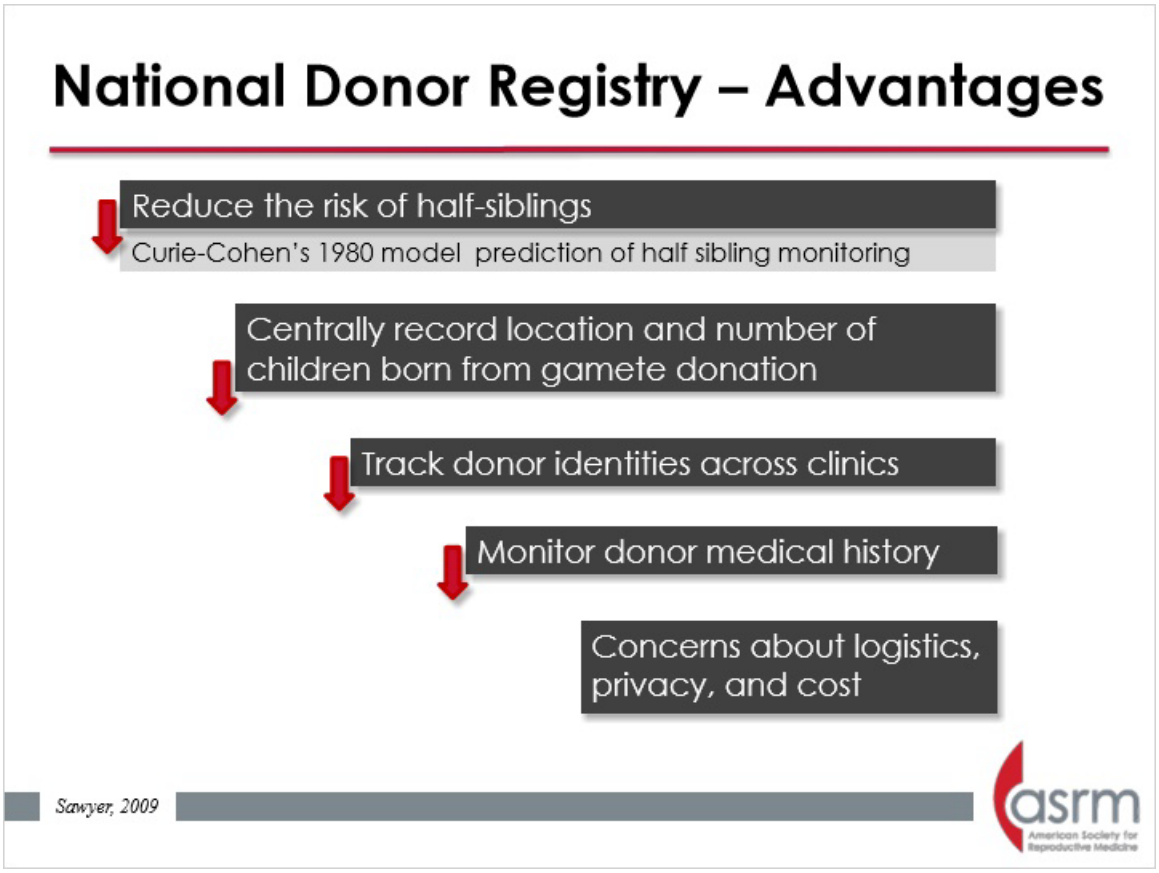
1.14 Solicitation of Oocyte Donors



Notes:

There are ethical, financial and practical considerations in the solicitation of oocyte donors. Due to the potential for undue inducement and exploitation in the oocyte donation process, a report from the Ethics Committee of ASRM provides guidance. Compensation should be structured to acknowledge the time, inconvenience, and discomfort associated with screening, ovarian stimulation, and oocyte retrieval. Compensation should not vary according to the planned use of the oocytes, the number or quality of oocytes retrieved, the number or outcome of prior donation cycles, or the donor's ethnic or other personal characteristics. Each oocyte donor program must develop policies in accordance with these guidelines to protect both donors and recipients.

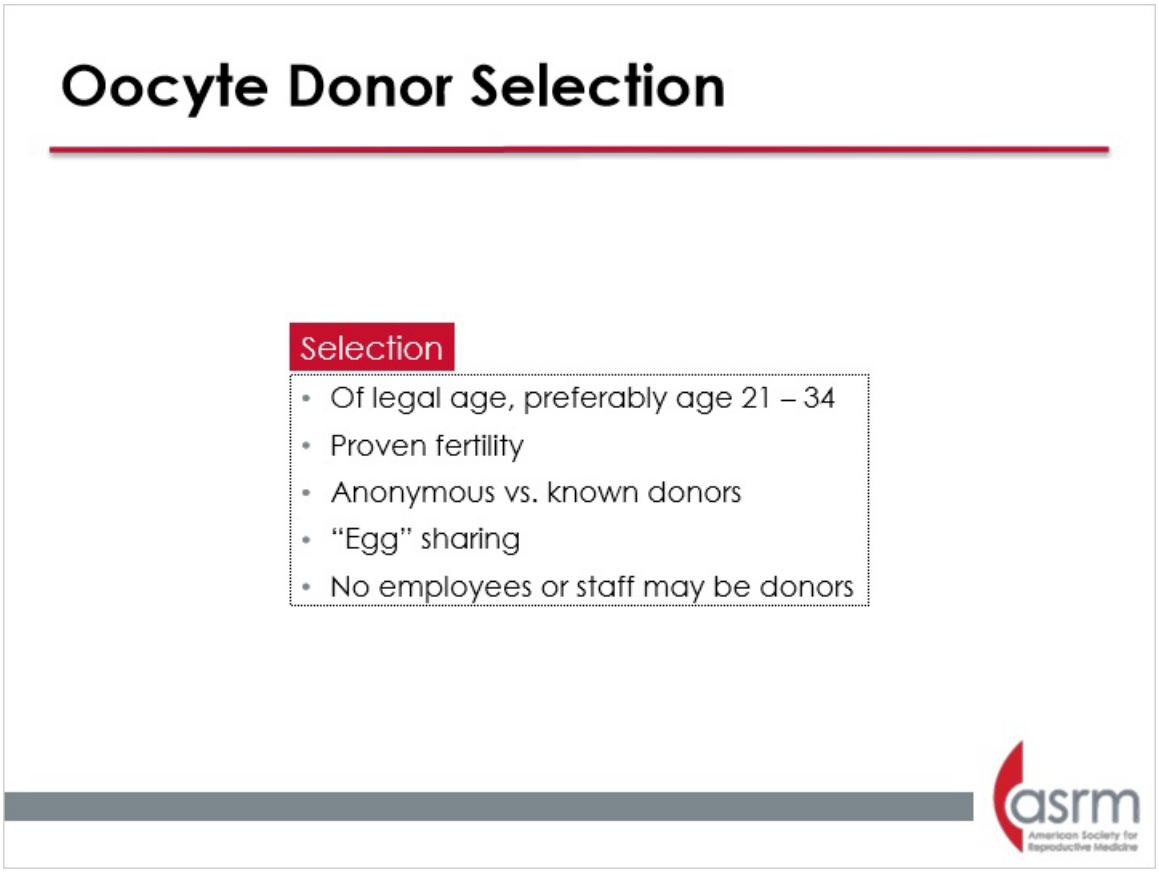
1.15 National Donor Registry – Advantages



Notes:

A national donor registry has been proposed in an effort to reduce the risk of half siblings from gamete donation. Exact numbers of offspring born as a result of gamete donation are unknown and thus it is difficult to estimate the potential number of half-sibling matings that could result from the multiple use of sperm donors. Curie-Cohen's 1980 model was developed to predict the number of half-sibling matings that would likely occur each year as a result of multiple use of sperm donors in the United States. The model is limited, however, in its usefulness because of changes in demographics and changes in the cohort of recipients and donors from the original data in the model. A national registry could centrally record the location and number of children born from use of donor oocytes and sperm, track donor identities across clinics, and monitor donor medical history. The national donor registry is a topic that ASRM has been exploring. Currently, the belief of ASRM is that a donor registry is conceptually a good idea; however, there are hurdles to overcome including what information should be included, who has access and who will be responsible for collecting, maintaining and protecting the privacy of the information. Cost is also a big issue.

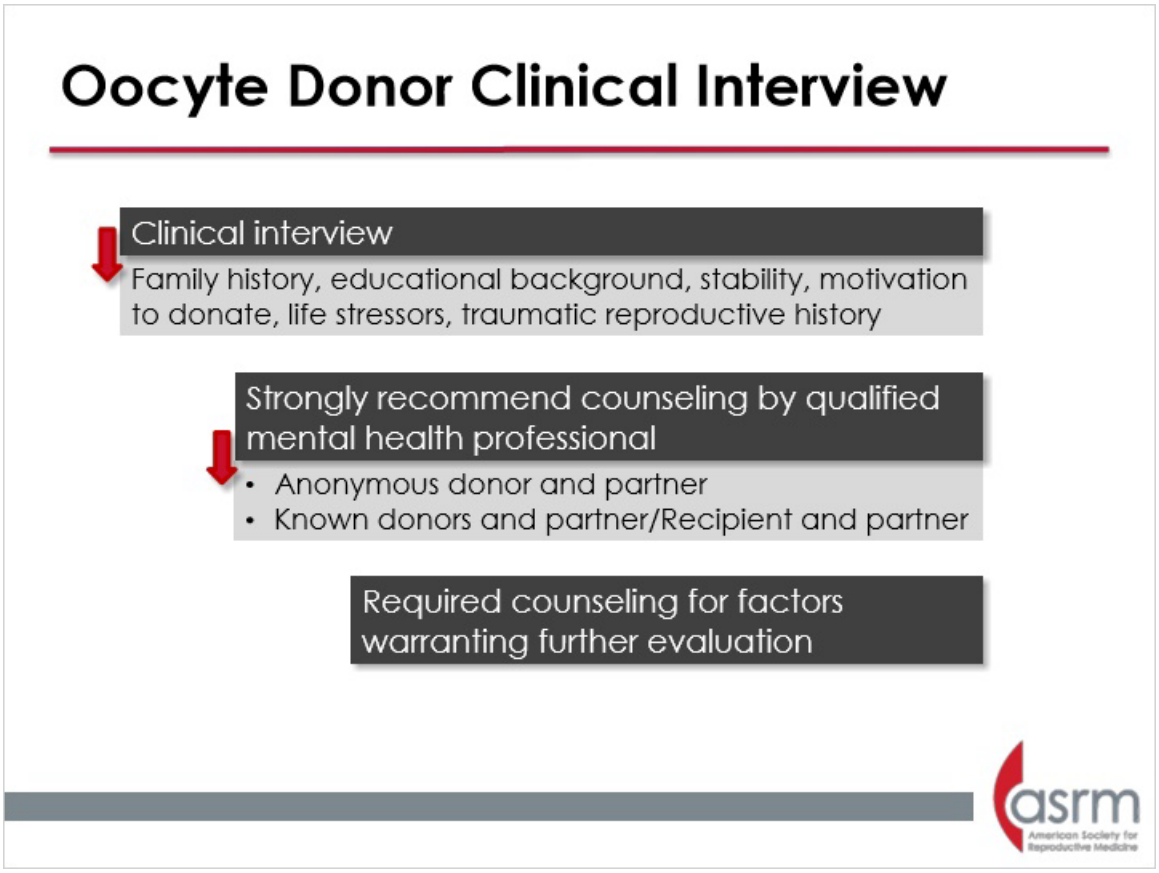
1.16 Oocyte Donor Selection



Notes:

Selection of oocyte donors involves several layers of evaluation and assessment. Donors must be of legal age, preferably between the ages of 21 and 34 years. Proven fertility in the donor is desirable but not required. Pragmatic considerations, such as the difficulty in recruiting suitable donors, support the use of known oocyte donors in the appropriate clinical situations. In certain situations, egg sharing may be considered. This is an arrangement that enables selected groups of infertile patients who cannot afford the cost of IVF treatment to receive IVF treatment in return for donating a proportion of their eggs to matching paying recipients. If sharing of oocytes is contemplated, informed consent must be obtained before the start of the cycle of retrieval. No owner, operator, laboratory director, or employee of a facility screening for, or performing oocyte donation, or of an agency used to recruit donors may serve as an oocyte donor.

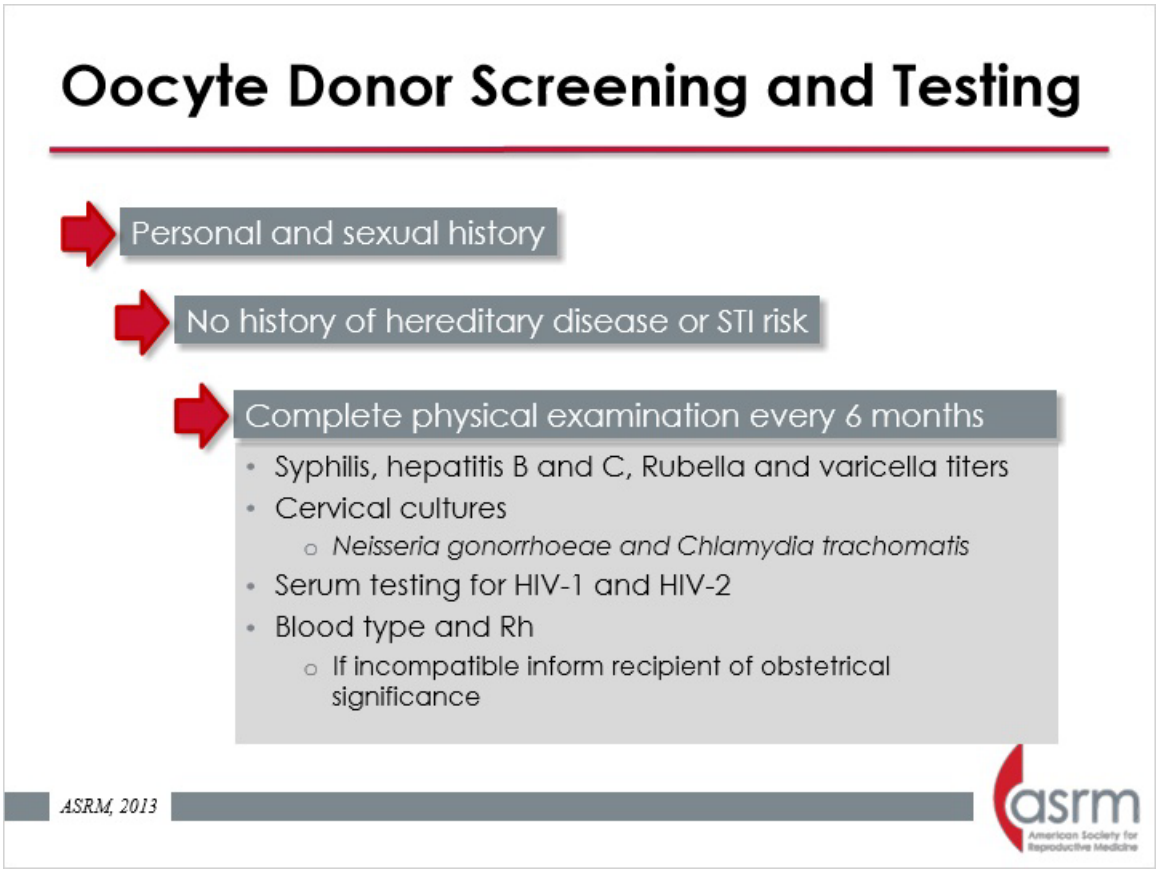
1.17 Oocyte Donor Clinical Interview



Notes:

The clinical interview should assess a donor's family history, educational background, assessment of stability, motivation to donate, life stressors and traumatic reproductive history. The decision to proceed with donated oocytes is complex, and psychological evaluation and counseling by a qualified mental health professional is recommended strongly for the oocyte donor and her partner. Psychological consultation should be required for individuals in whom there appear to be factors that warrant further evaluation. In circumstances involving known donors, psychological evaluation and counseling is recommended strongly for the donor and her partner, if applicable, as well as for the recipient and her partner, if applicable.

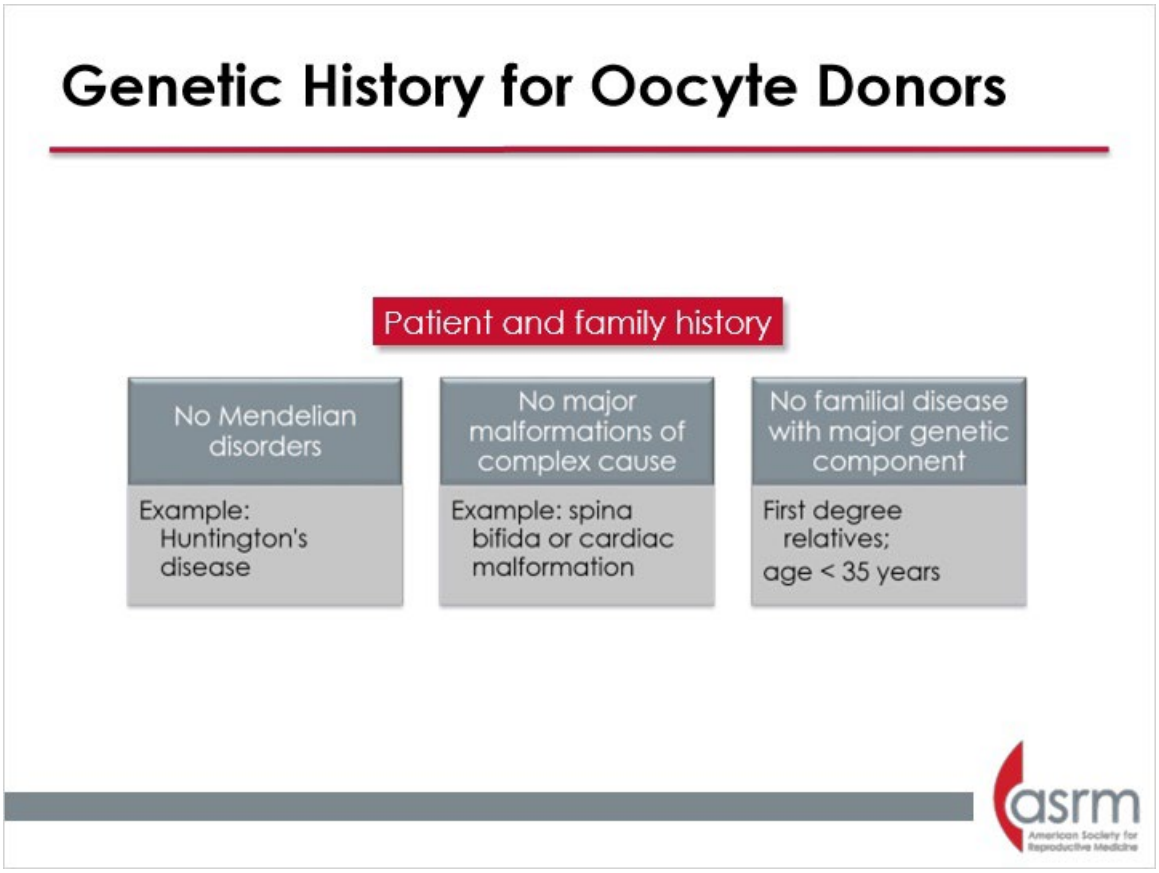
1.18 Oocyte Donor Screening and Testing



Notes:

Screening and testing are performed to minimize the chances that a disease will be passed from the donor to the recipient (and possible fetus) by the oocyte donation process. The following donor screening guidelines are from the ASRM. Donors should have a personal and sexual history to determine the risk of hereditary disease and sexually transmitted infections. A complete physical examination should be performed every 6 months for active donors. They should be tested as shown here. If the Rh of the donor is incompatible with recipient, the recipient should be informed about the obstetrical significance.

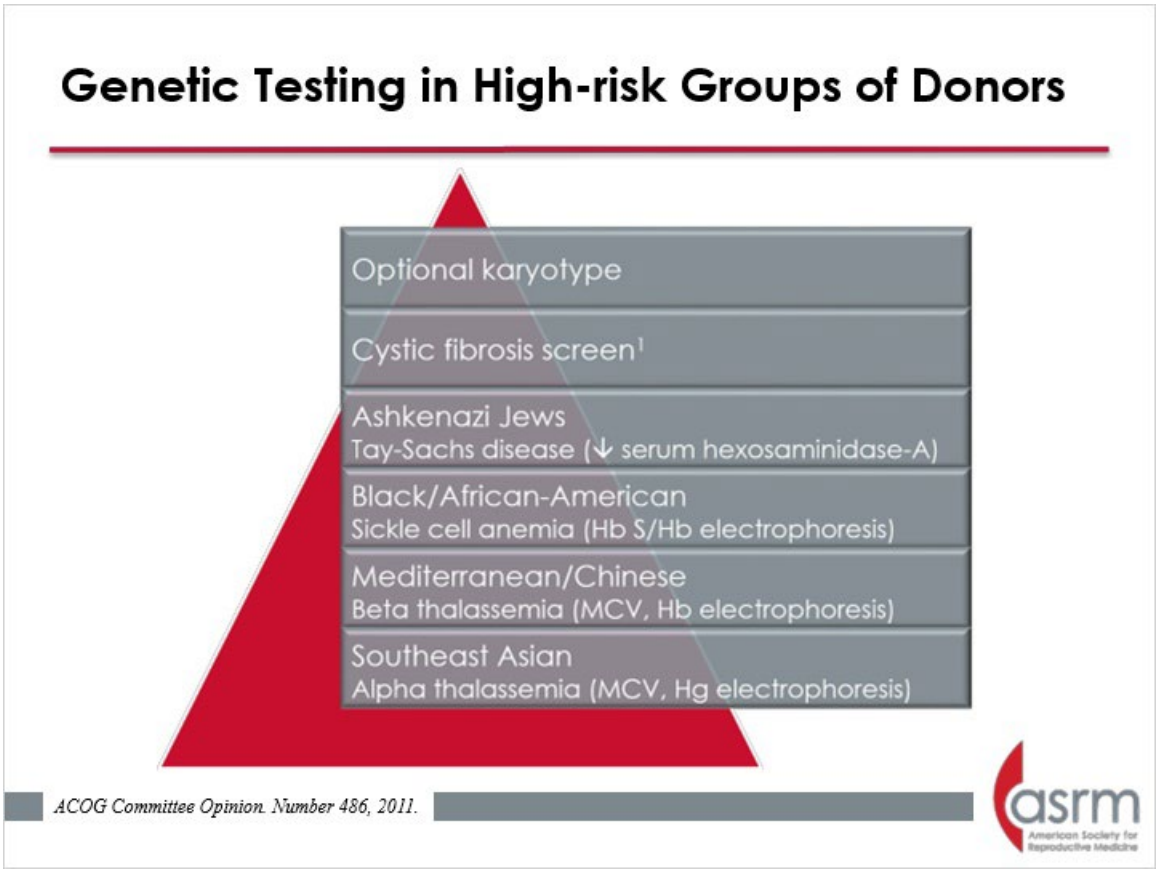
1.19 Genetic History for Oocyte Donors



Notes:

The donor's personal and family history should be assessed for the presence of Mendelian disorders, such as Huntington's disease; major malformations of complex cause, such as spina bifida or cardiac malformation; and familial disease with a major genetic component in first degree relatives and in individuals less than 35 years of age.

1.20 Genetic Testing in High-risk Groups of Donors

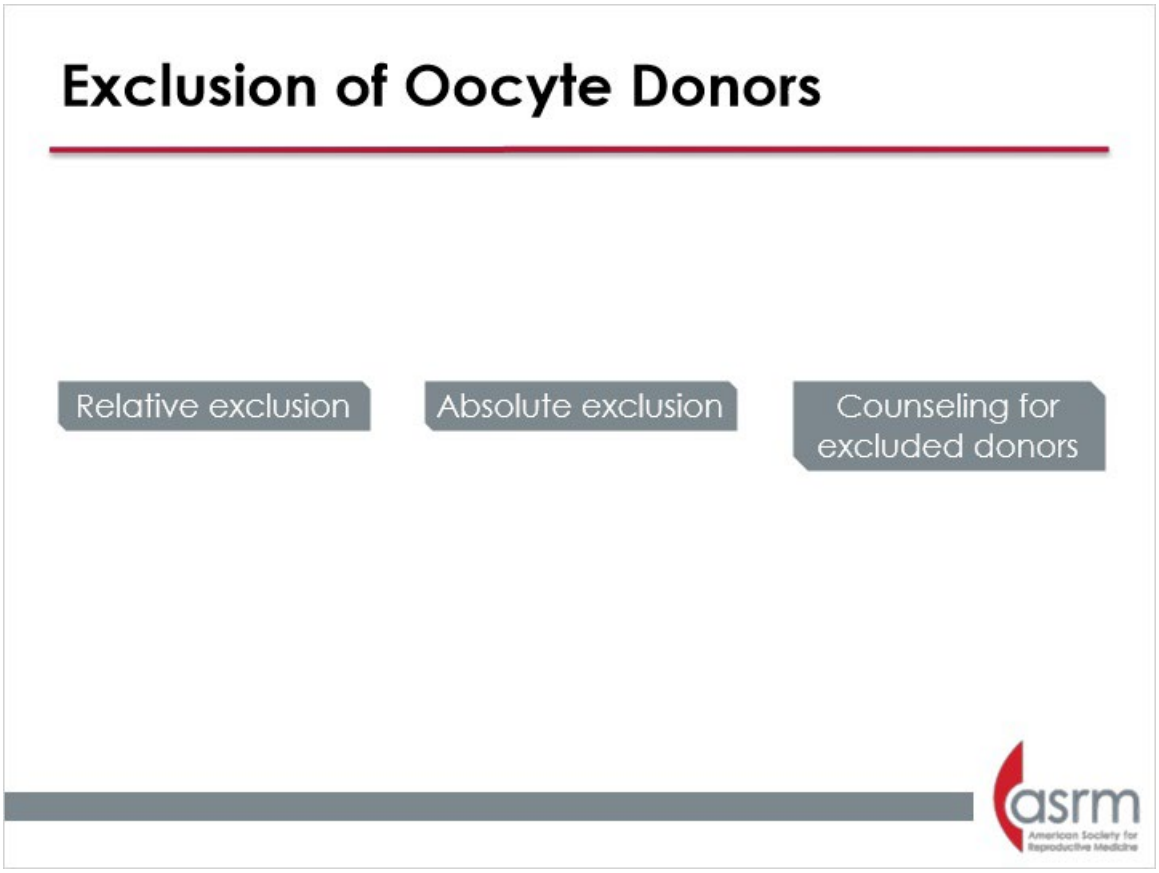


Notes:

Certain ethnic and racial groups are considered at high risk for inherited diseases. Karyotyping is optional for these donors. The American College of Obstetricians and Gynecologists recommends that cystic fibrosis carrier screening should be offered before conception or early in pregnancy to all women, and in particular when both partners are of non-Hispanic white or Ashkenazi Jewish ethnicity. Ashkenazi Jews are at risk for Tay-Sachs disease with decreased serum hexosaminidase-A. Blacks and African Americans are at risk for sickle cell anemia; screening is for hemoglobin S using electrophoresis. Individuals of Mediterranean and Chinese descent are at risk for beta-thalassemia; testing uses mean cell volume and hemoglobin electrophoresis. In Southeast Asians, testing for alpha thalassemia uses mean cell volume and hemoglobin electrophoresis. The cystic fibrosis gene in Caucasians is detected with DNA testing.

Some recipients may request a more thorough testing of a donor, such as for Huntington's disease or breast cancer. Identification of these conditions may have implications for the donor such as future insurance coverage problems or psychological effects.

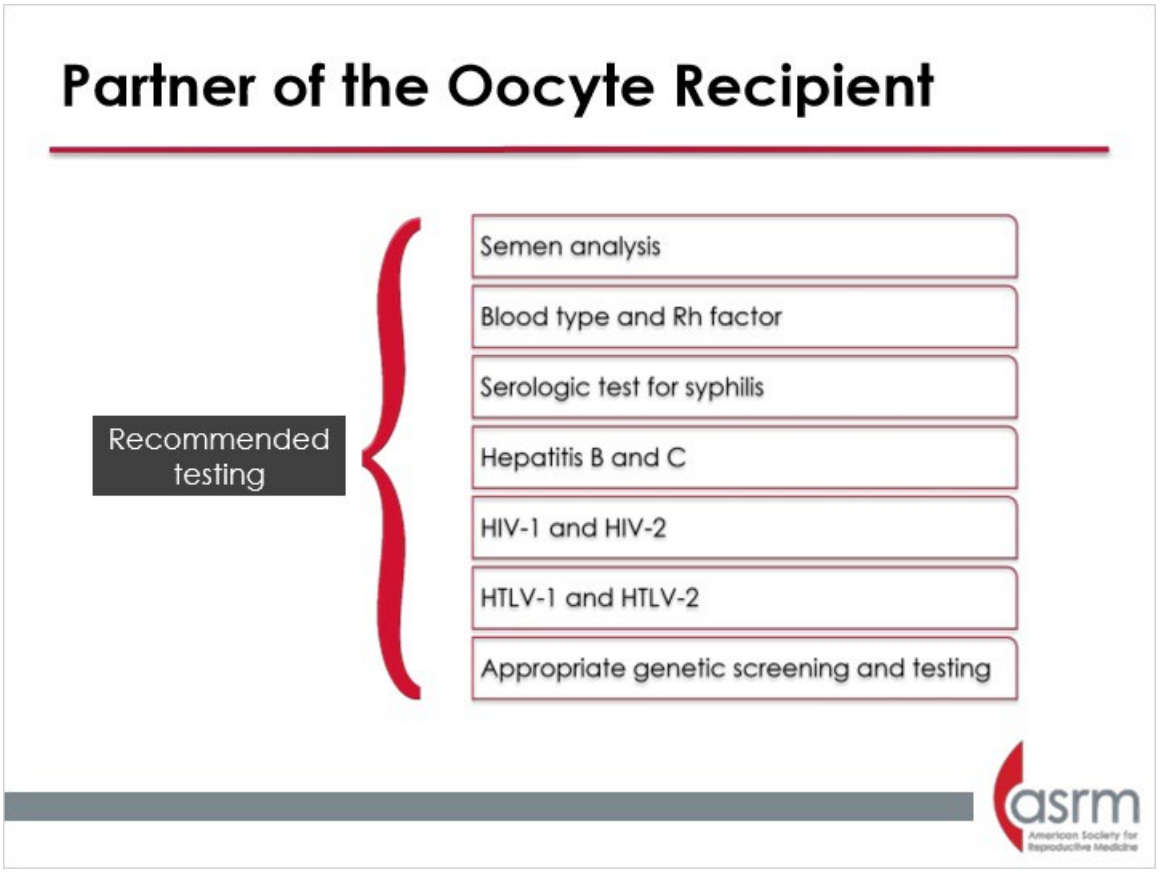
1.21 Exclusion of Oocyte Donors



Notes:

Criteria for exclusion of donors may be relative, which indicates further assessment is needed, or absolute, in which factors indicate that the donor is unacceptable because of significant psychopathology or medical reasons. Candidates who are excluded from the donor practice should be counseled regarding the reasons for their exclusion and, if appropriate, offered referral. In cases involving known donors, related issues such as the potential impact of the relationship between the donor and recipient should be explored. The impact on treatment failure should also be addressed.

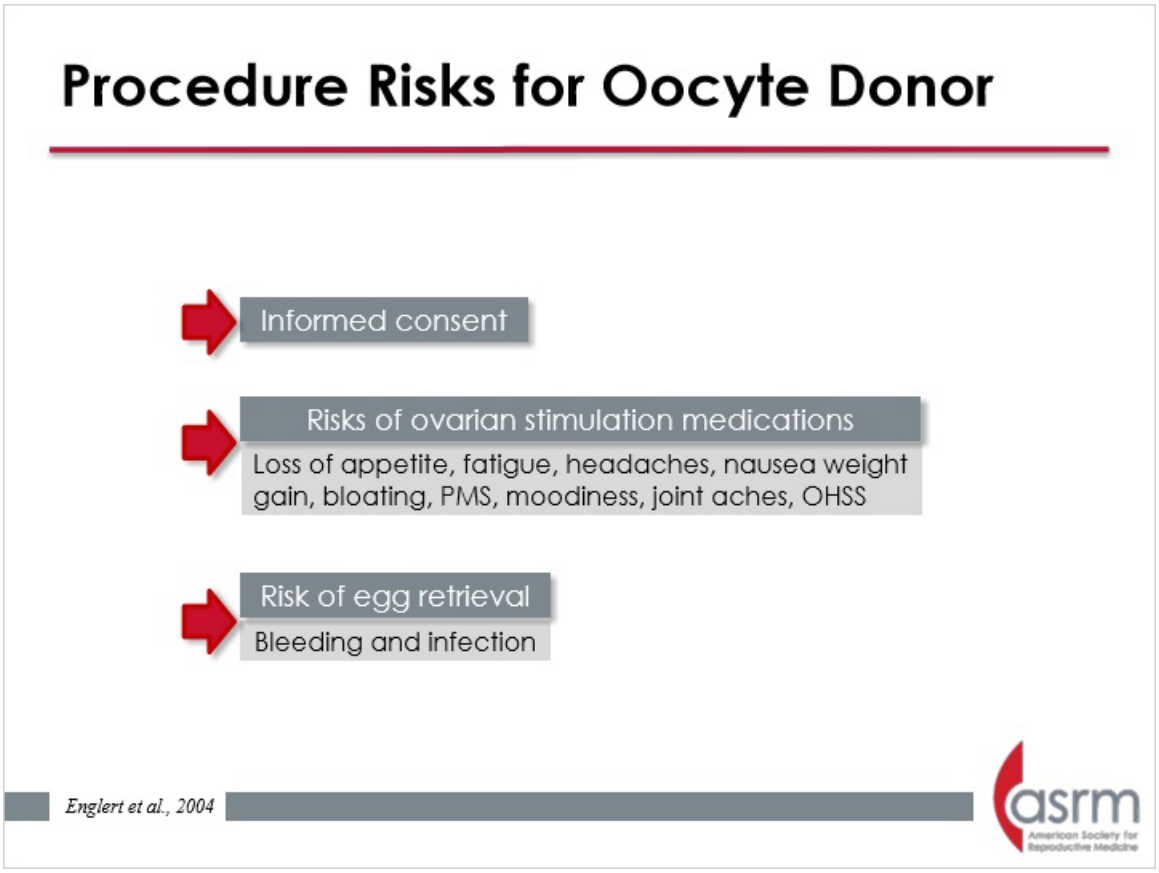
1.22 Partner of the Oocyte Recipient



Notes:

Recommended but not required testing for the oocyte donor's partner are shown here.

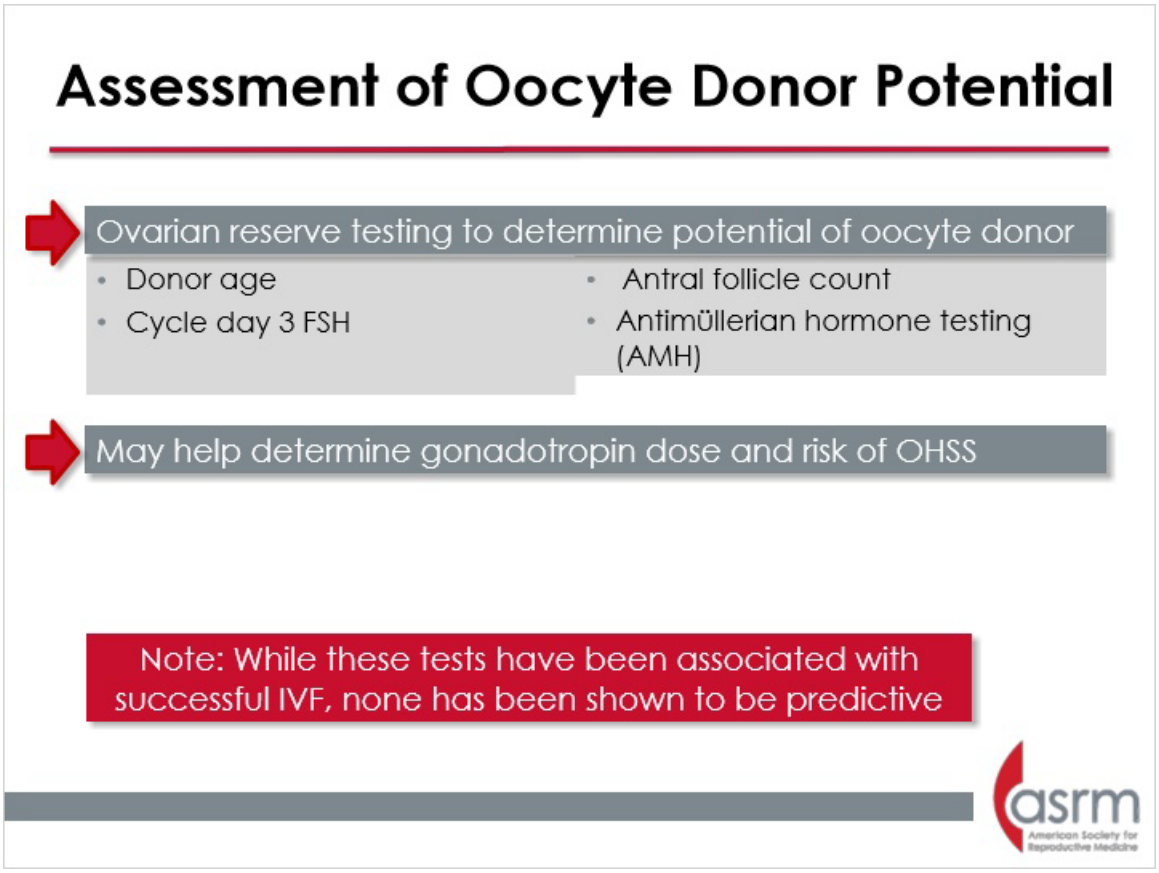
1.23 Procedure Risks for Oocyte Donor



Notes:

All individuals involved in oocyte donation should be advised explicitly of the risks and adverse effects of ovarian stimulation and retrieval, with such counseling documented by informed consent. Medications used for ovarian stimulation have multiple side effects including loss of appetite, fatigue, headaches, nausea, weight gain, bloating, premenstrual syndrome, moodiness, joint aches, and ovarian hyperstimulation syndrome (OHSS). Risks of the egg retrieval procedure include bleeding and infection. Post-procedure surveys found that oocyte donors have overall positive feelings about helping a couple as well as concerns about the recipients being fit parents. Half of respondents had second thoughts about costs to self, physical stress, concerns about the future of the offspring and concerns about their own future fertility. Respondents also indicated that side effects of fertility injections need to be discussed in depth as many found that the donation procedure was worse than expected.

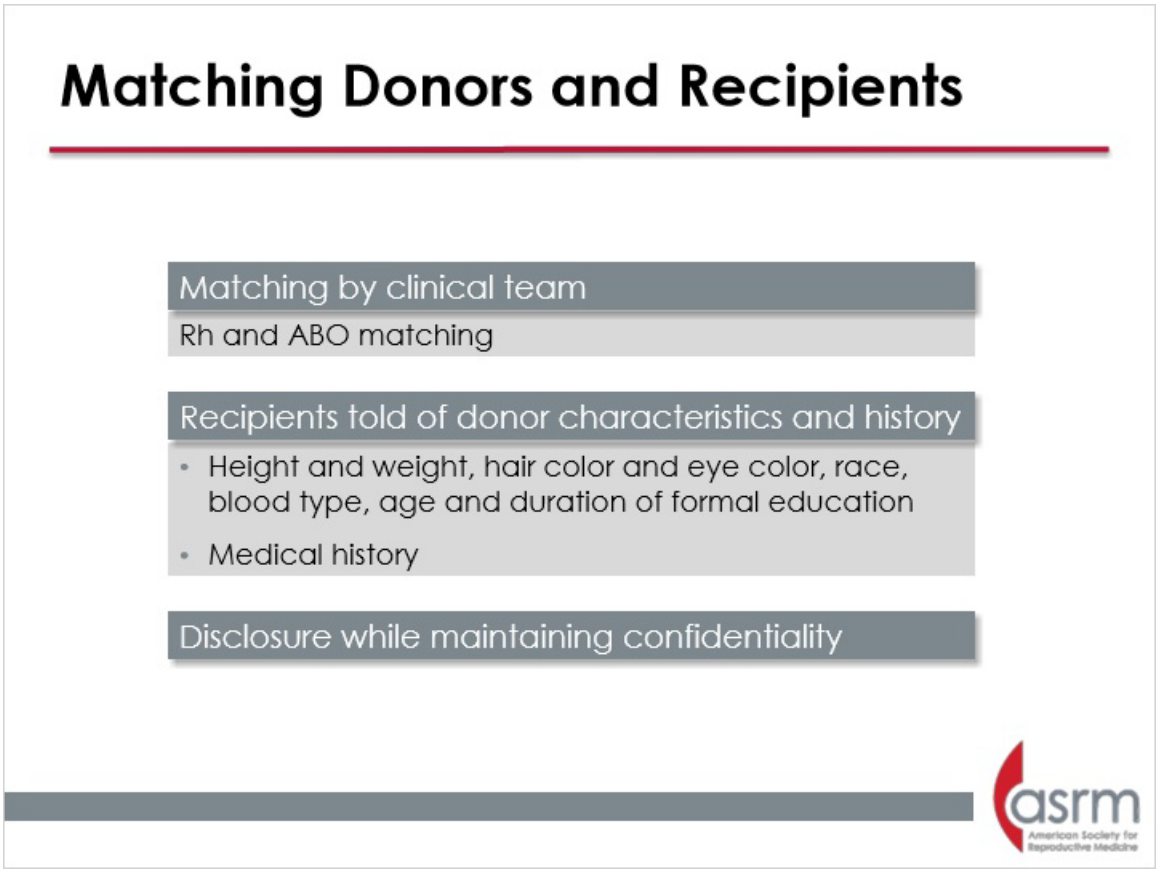
1.24 Assessment of Oocyte Donor Potential



Notes:

Various tests are available to help determine whether or not a donor has sufficient ovarian reserve, which may indicate her potential for optimal oocyte development and retrieval. These tests are shown here. Note that while these tests have been associated with successful IVF, none has been shown to be predictive. An assessment of ovarian reserve may be helpful in determining dose of gonadotropins and risk of ovarian hyperstimulation syndrome.

1.25 Matching Donors and Recipients



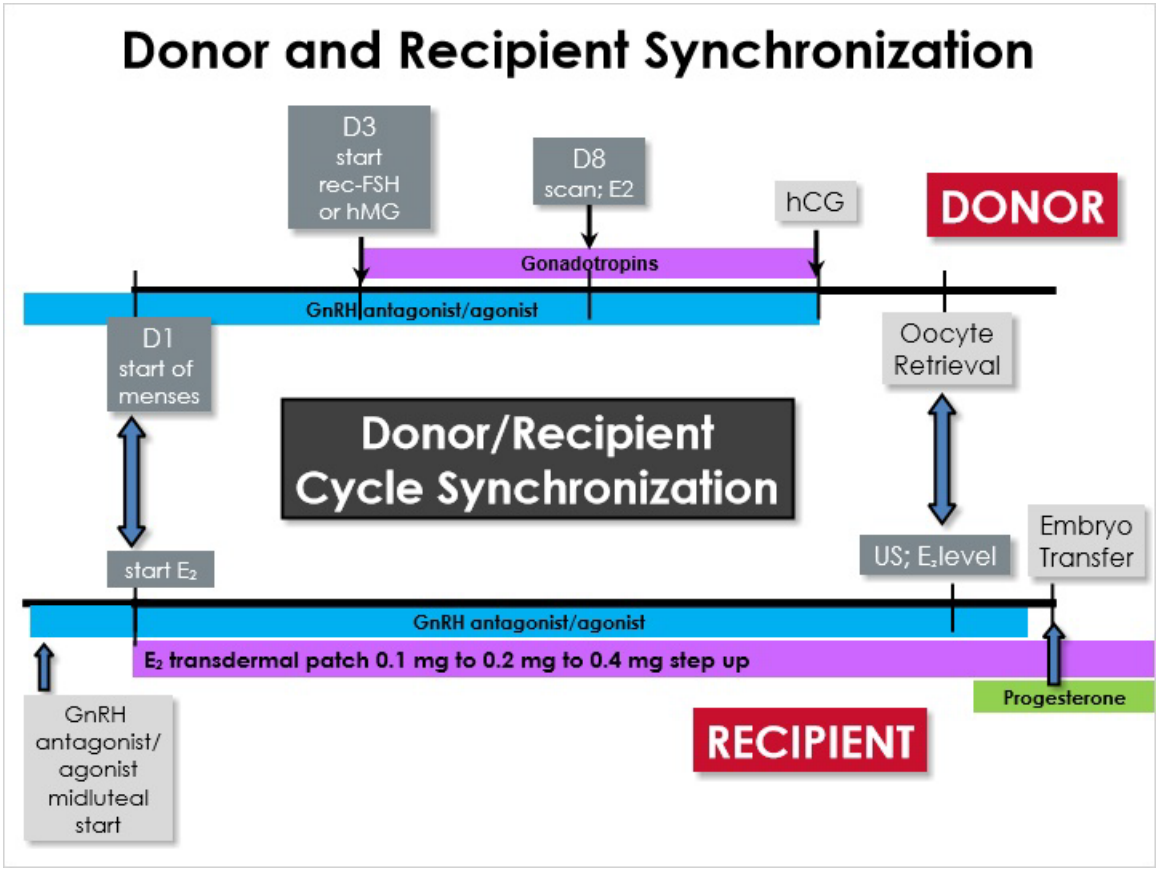
Notes:

In most donor oocyte programs, matches are made by the clinical team. Recipients have the right to be as specific as they like about donor characteristics, but this can delay the process of finding a donor match. The blood type and Rh of the recipient, donor and recipient's partner are factors that can play some role in the matching process. Primarily, when both the recipient and her partner are Rh negative, the donor should also be Rh negative. Using an Rh positive donor would expose the recipient's fetus to a risk of Rh incompatibility that would not have existed had the woman used her own eggs or received eggs from an Rh negative donor. Differences in ABO type between mother and fetus pose little risk to the health of the fetus. Therefore, use of an oocyte donor whose oocyte might produce a pregnancy, which is different from the ABO type of the recipient and husband, is not as great a medical concern. However, to some recipient couples it may still be an important factor to match, so that genetically impossible differences in ABO type between parents and child are not revealed later in life.

Generally, recipients are told of donors' characteristics, including height and weight, hair color and eye color, race, blood type, age and duration of formal education and the medical history. Disclosure of the maximum amount of information, while maintaining

confidentiality of the donor, is important to dispel any fears that information may be left out in the desire to make a match. **Some programs are moving toward the recipient choosing the donor.**

1.26 Donor and Recipient Synchronization



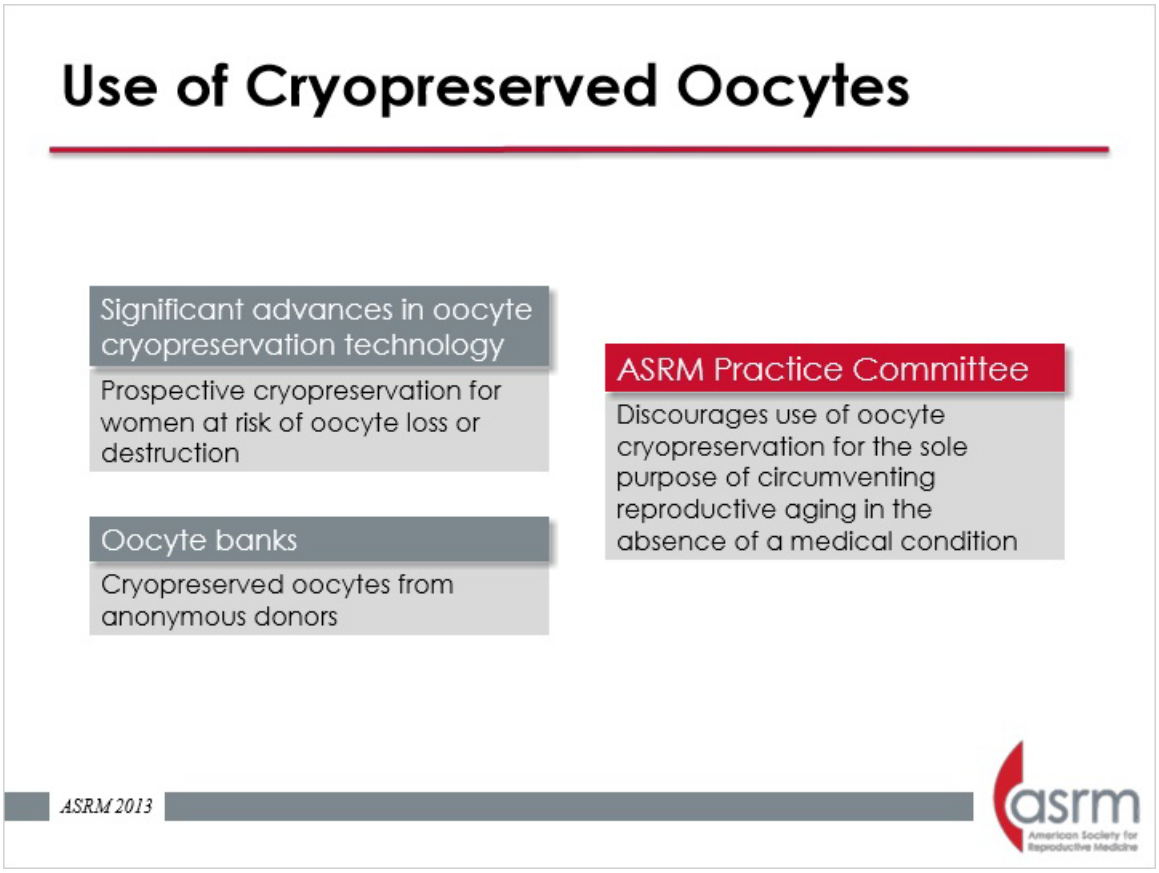
Notes:

The menstrual cycles of both the oocyte donor and recipient must be synchronized for optimal timing as shown in the chart here. In general, stimulation of the oocyte donor's cycle is similar to the protocol used for women using their own oocytes in an in vitro fertilization-embryo transfer cycle. Late in the cycle which precedes ovarian stimulation, the donor is started on daily injections of a gonadotropin-releasing hormone (GnRH) agonist such as leuprolide or an antagonist such as ganirelix to downregulate her own hormones. Oral contraceptives may also be used. Once her menses begin, she is given daily injections of a gonadotropin preparation, such as follicle stimulating hormone (FSH) or human menopausal gonadotropin (hMG), in addition to the daily GnRH antagonist injections, for about 7 to 12 days. After vaginal ultrasound examinations and serum estradiol levels determine optimal follicle development, the donor receives

human chorionic gonadotropin (hCG) as a trigger for oocyte release. Alternatively, if the donor is at risk for OHSS, a leuprolide trigger of 4 mg or GnRH agonist can be given. This has been associated with a reduction in OHSS symptoms. Approximately 36 hours after hCG injection, and before spontaneous ovulation, oocyte retrieval is performed.

Recipients who have regular menstrual cycles and bleeding on their own will receive a downregulation medication to suppress their own hormones several days prior to their expected start of menses. Sometimes oral contraceptives will be used to precede GnRH antagonist/agonist administration. A short time after her period starts the recipient will begin using either an estrogen transdermal patch, usually 0.1 mg dosage, or oral estradiol, in addition to the downregulation medication. The transdermal patch is applied to the abdomen or buttocks and changed every other day. The downregulation medication and estrogen patch or oral estradiol are continued while waiting for the donor's cycle to come into synchrony with hers. When the donor's cycle has "caught up" with the recipient's, a simulated (artificial) 28-day menstrual cycle will be created in the recipient with the hormonal medications. To do this, the recipient's estrogen patch dose is increased along with the donor's stimulation. Serum estradiol levels and/or an ultrasound for endometrial assessment are performed as oocyte retrieval approaches to ensure an appropriate response. Many centers perform a "mock cycle" prior to the donor's stimulation to make sure that the recipient can develop a sufficiently thick endometrium. Downregulation medications will continue throughout this time. On the morning after oocyte retrieval, the recipient begins progesterone treatment. Progesterone is given usually as a daily intramuscular injection of progesterone in oil. More recently, vaginal progesterone formulations have been found to also achieve appropriate endometrial response. The day before embryo transfer, the recipient's downregulation medication is discontinued. The recipient will continue taking the estrogen and progesterone at least until the day her pregnancy test is performed. Fresh embryo transfer will be performed 3 to 5 days after oocyte retrieval. A blood pregnancy test will be performed on the tenth day after embryo transfer. If the recipient is pregnant, patches and progesterone treatment will be continued through the 10^{th} to 12^{th} week of pregnancy. Recipients who have complete ovarian failure and have no spontaneous menstrual cycles will not be given downregulation medications, but otherwise will take the same regimen of medications just described.

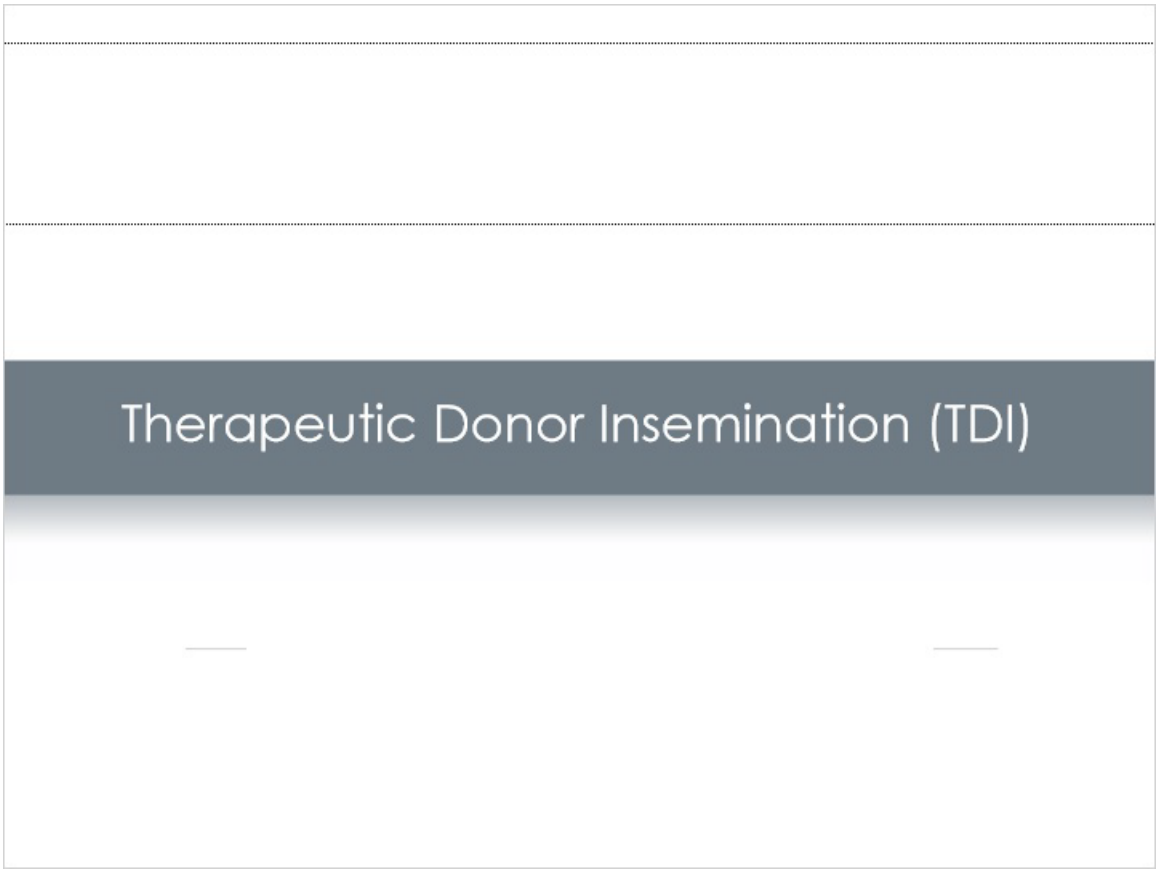
1.27 Use of Cryopreserved Oocytes



Notes:

Significant advances in oocyte cryopreservation technology make it possible for women at risk of oocyte loss or destruction to prospectively cryopreserve oocytes for later use. The establishment of oocyte banks makes it possible for women lacking viable oocytes to obtain cryopreserved oocytes from anonymous donors. However, the ASRM Practice Committee discourages the use of oocyte cryopreservation for the sole purpose of circumventing reproductive aging in the absence of a medical condition.

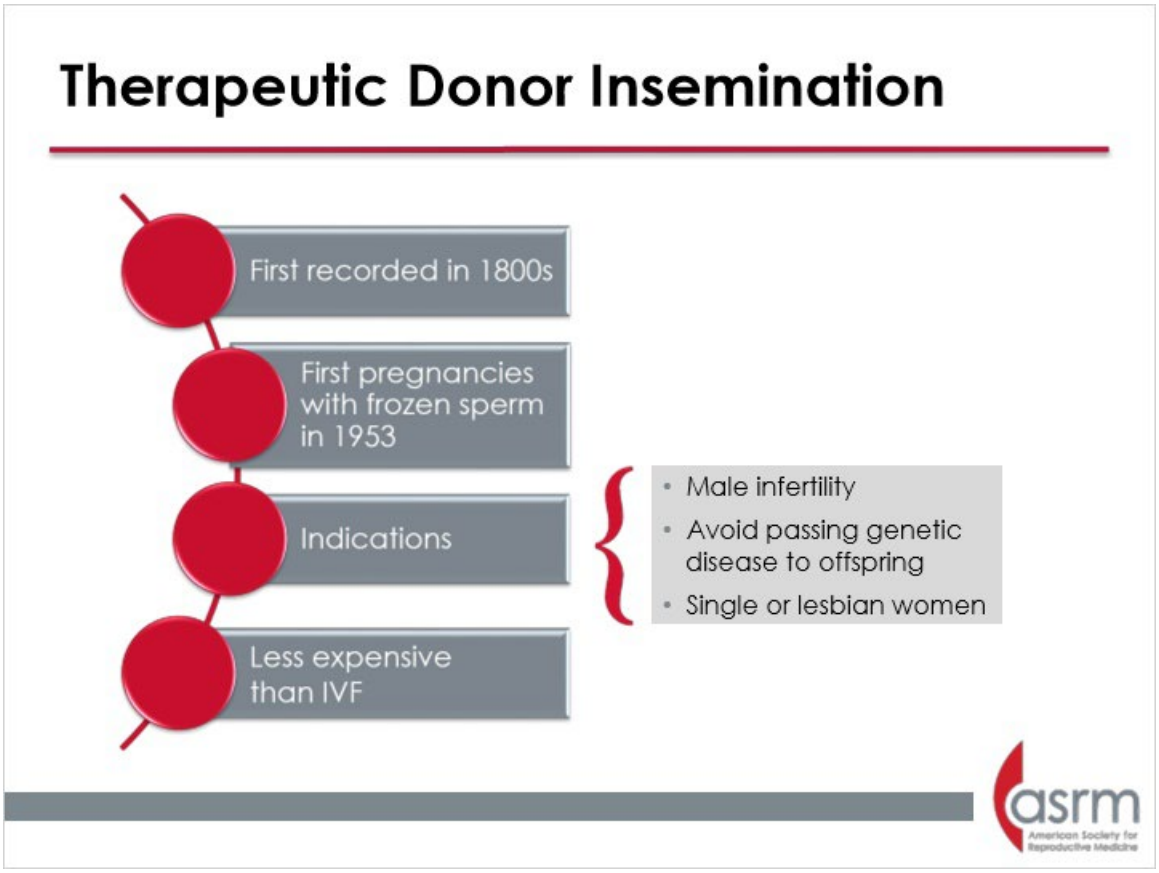
1.28 Therapeutic Donor Insemination (TDI)



Notes:

Therapeutic donor insemination (TDI) may be used to achieve pregnancy where appropriate indications exist. Sperm donors may be anonymous or directed, when they are known to the recipient.

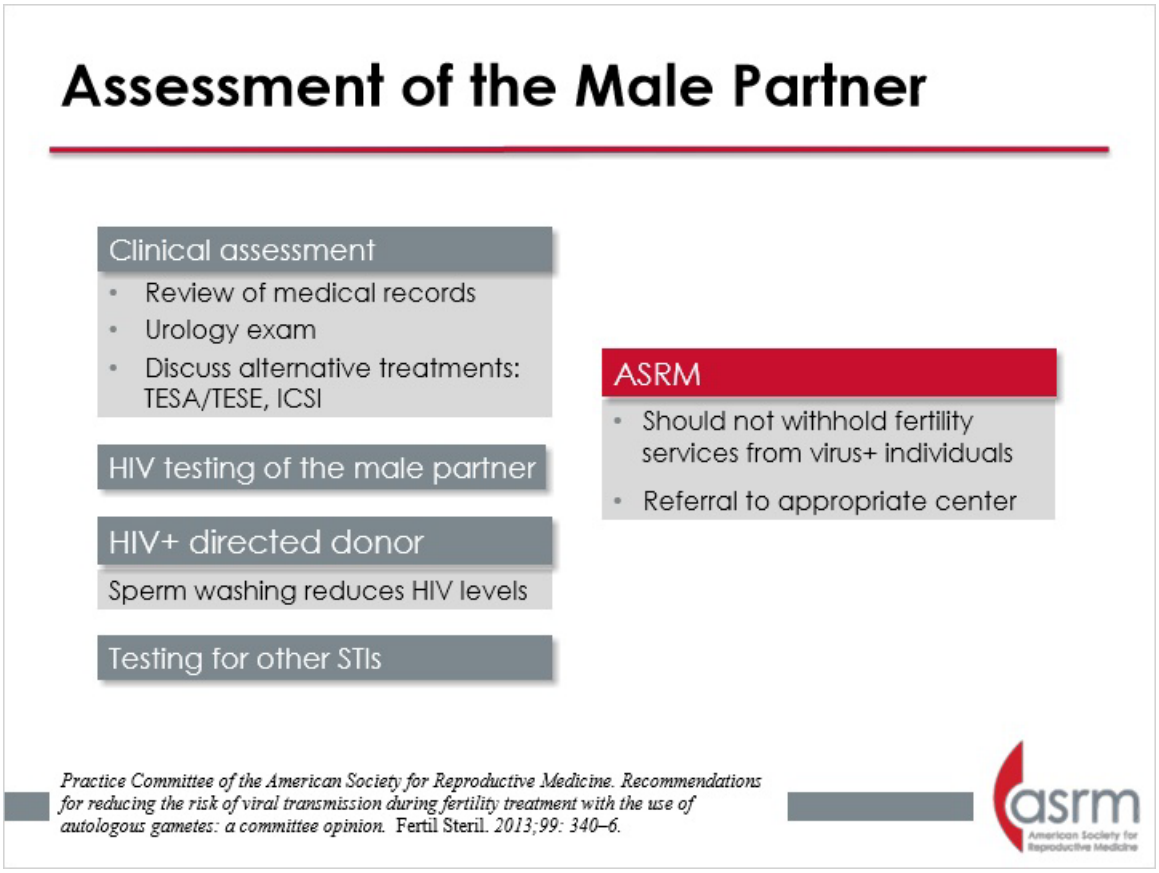
1.29 Therapeutic Donor Insemination



Notes:

Donor insemination is not new. The first record of therapeutic donor insemination was in the 1800s and the first pregnancies with frozen sperm were in 1953.
The primary indications for use of therapeutic donor insemination are for male infertility, such as when the male partner has azoospermia, severe oligospermia or other significant sperm or seminal fluid abnormalities; ejaculatory dysfunction; or prior failure to fertilize after in vitro insemination. In addition, it is indicated when the male partner has a significant genetic defect or the couple previously has produced an offspring affected by a condition for which carrier status cannot be determined. Other indications are when a male partner has a sexually transmissible infection that cannot be eradicated; the female partner is Rh-negative and severely Rh-isoimmunized with an Rh-positive male partner; and single or lesbian women. Therapeutic donor insemination is a much less expensive option than IVF for many couples.

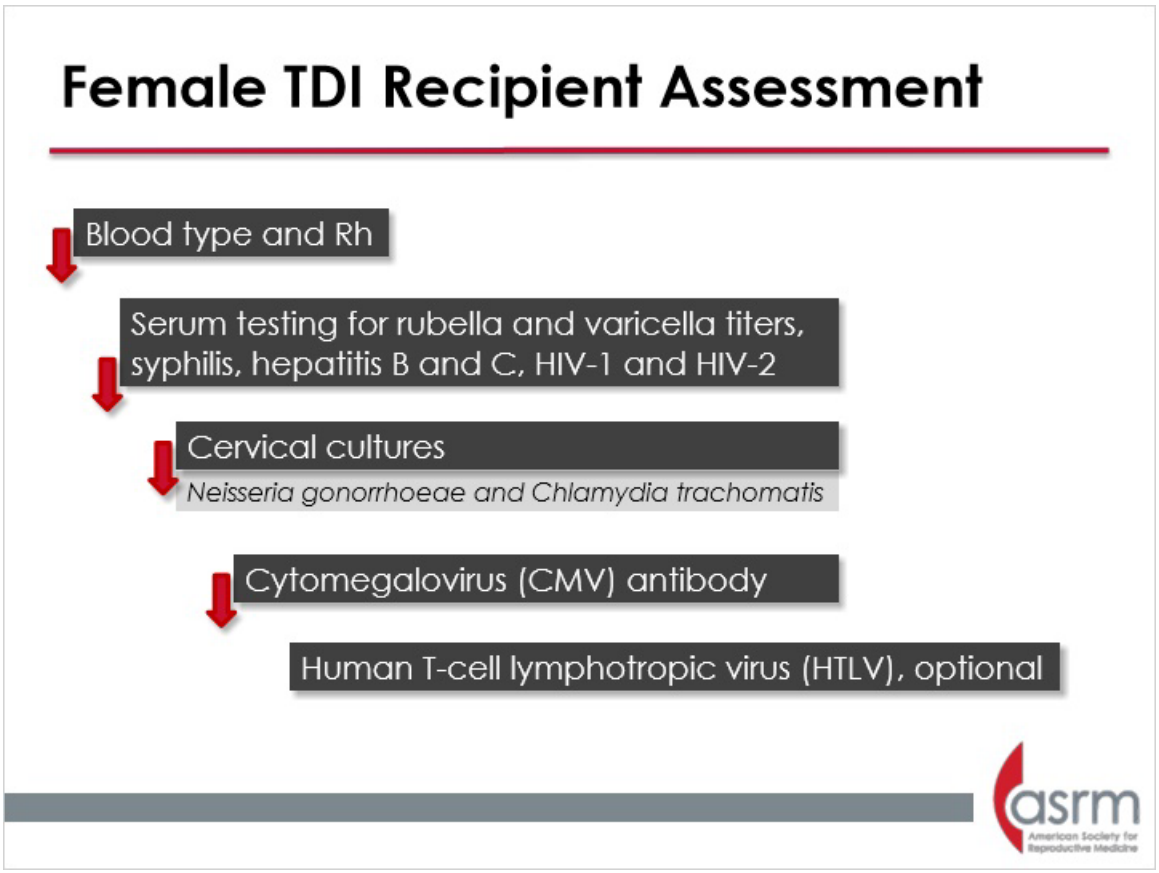
1.30 Assessment of the Male Partner



Notes:

The male partner in the couple requesting therapeutic donor insemination should have a thorough clinical assessment. Medical records should be reviewed before performing the insemination procedure. If appropriate, alternative treatments should be discussed with the couple, such as testicular sperm aspiration or extraction or intracytoplasmic sperm injection, known as ICSI. HIV testing should be done to address potential medical/legal issues that could arise if his partner seroconverts during or after the insemination. A positive HIV test result for the male partner should not be used as an exclusionary criterion for treatment of a couple using therapeutic donor insemination, provided that the semen to be used derives from an HIV-negative donor. Current FDA guidelines do not entirely preclude the use of an HIV-positive directed donor. Sperm-washing techniques have been shown to markedly reduce HIV levels prior to insemination. Testing for other STIs similar to that recommended for the female partner is encouraged. ASRM states that fertility services should not be withheld from individuals with chronic viral infections, including HIV, if the center has the necessary resources to provide care. Referral to a center having such capabilities is also appropriate.

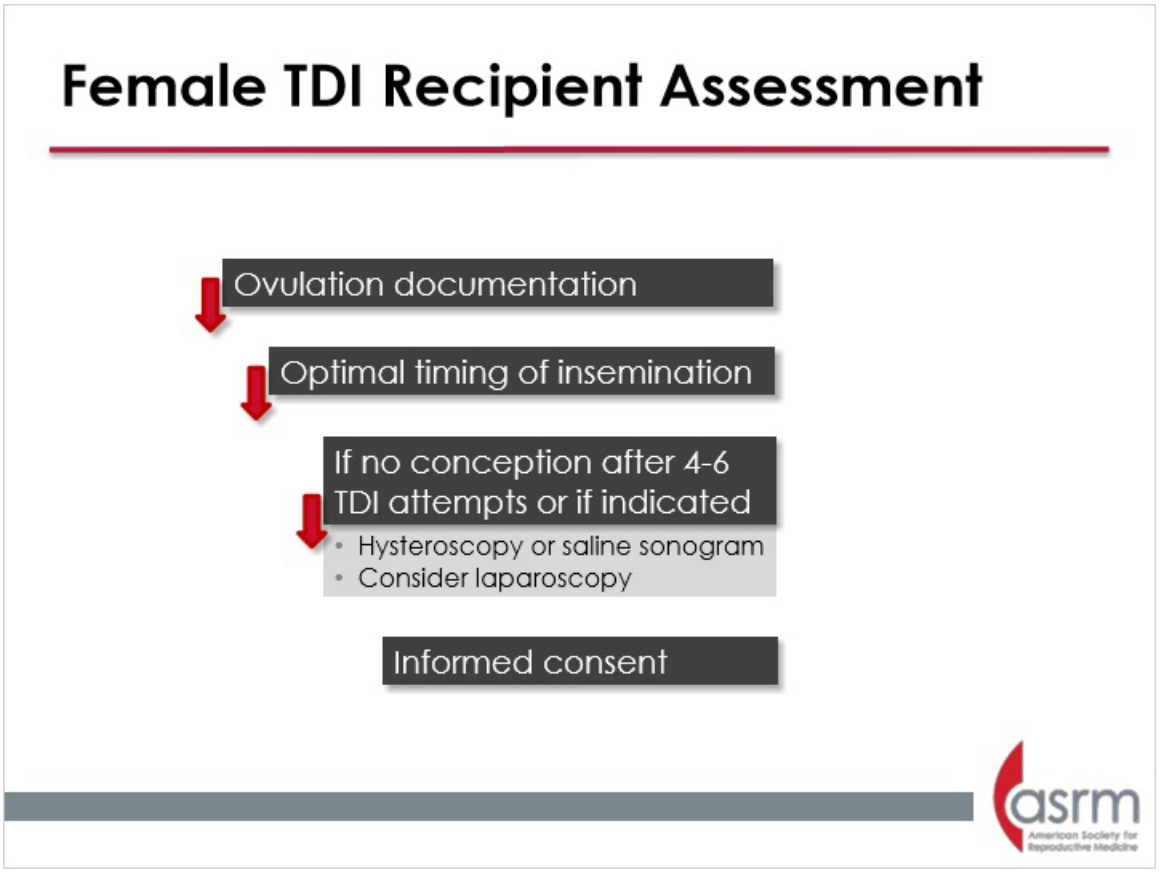
1.31 Female TDI Recipient Assessment



Notes:

In addition to a medical and reproductive history, a complete physical examination should be performed, including a pelvic examination for the female receiving the insemination. Abnormalities detected from history or physical examination may require more detailed evaluation and treatment before proceeding with insemination. Additional testing includes those tests shown here.

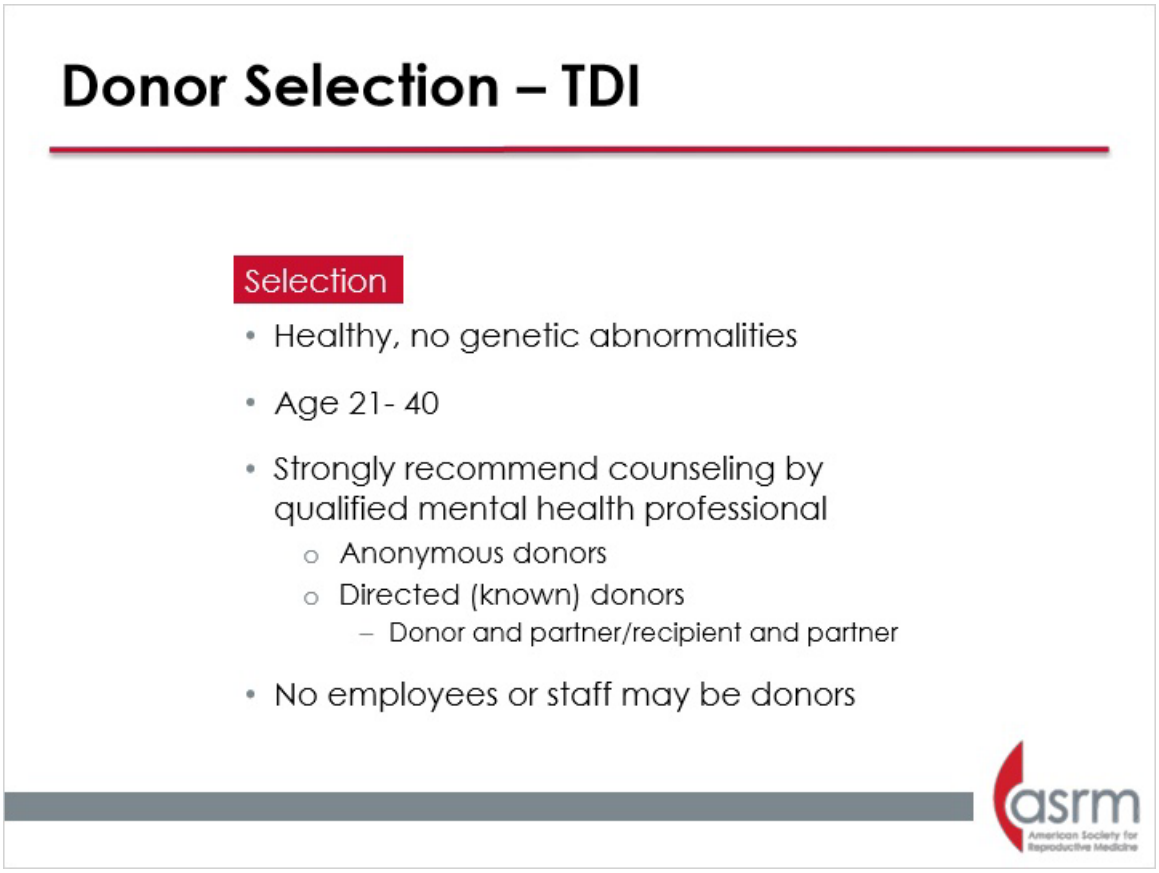
1.32 Female TDI Recipient Assessment



Notes:

It is also important to document ovulation in the female recipient. Women with regular menses and cycle-related symptoms are assumed to be ovulating. When doubt exists, an index of ovulation, such as a serum progesterone level, basal body temperature recordings, luteinizing hormone (LH) surge detection, and ultrasound monitoring of follicular maturation, may be used to document ovulation. Appropriate timing of the insemination procedure optimizes the chances for success. Evaluation for possible tubal or peritoneal abnormalities is also needed for recipients. Women who fail to conceive after four to six well-timed inseminations may be candidates for hysterosalpingography (HSG), laparoscopy, or other appropriate tests to detect possible causes for their failure to conceive. Pretreatment HSG or laparoscopy may be indicated by a woman's history and/or physical findings. Informed consent should be obtained from the patient (and her partner, if applicable).

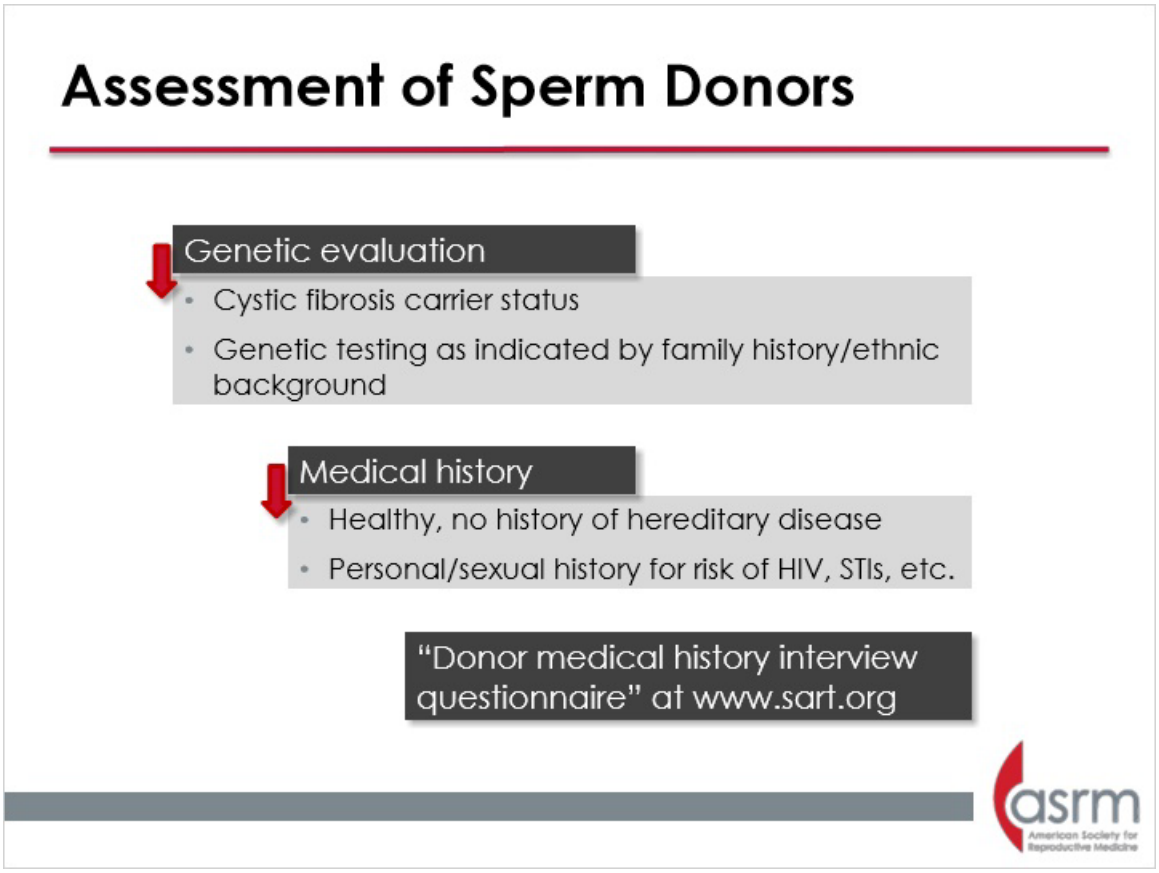
1.33 Donor Selection – TDI



Notes:

The main qualities to be considered in selecting a donor for TDI are an assurance of good health status and the absence of genetic abnormalities. The donor should be of legal age and, ideally, less than 40 years of age, because increased male age is associated with a progressive increase in the prevalence of aneuploid sperm and an increased risk of autism in offspring. Selection of donors with established fertility is desirable but not required. Psychological evaluation and counseling by a qualified mental health professional is recommended strongly for all sperm donors. Psychological consultation should be required for individuals in whom there appear to be factors that warrant further evaluation. In cases of directed donation, psychological evaluation and counseling are recommended strongly for the donor and his partner as well as for the recipient female and her partner, if applicable. No owner, operator, laboratory director, or employee of a facility performing inseminations may serve as a donor in that practice. Neither the patient's physician nor the individual performing the actual insemination can be the sperm donor.

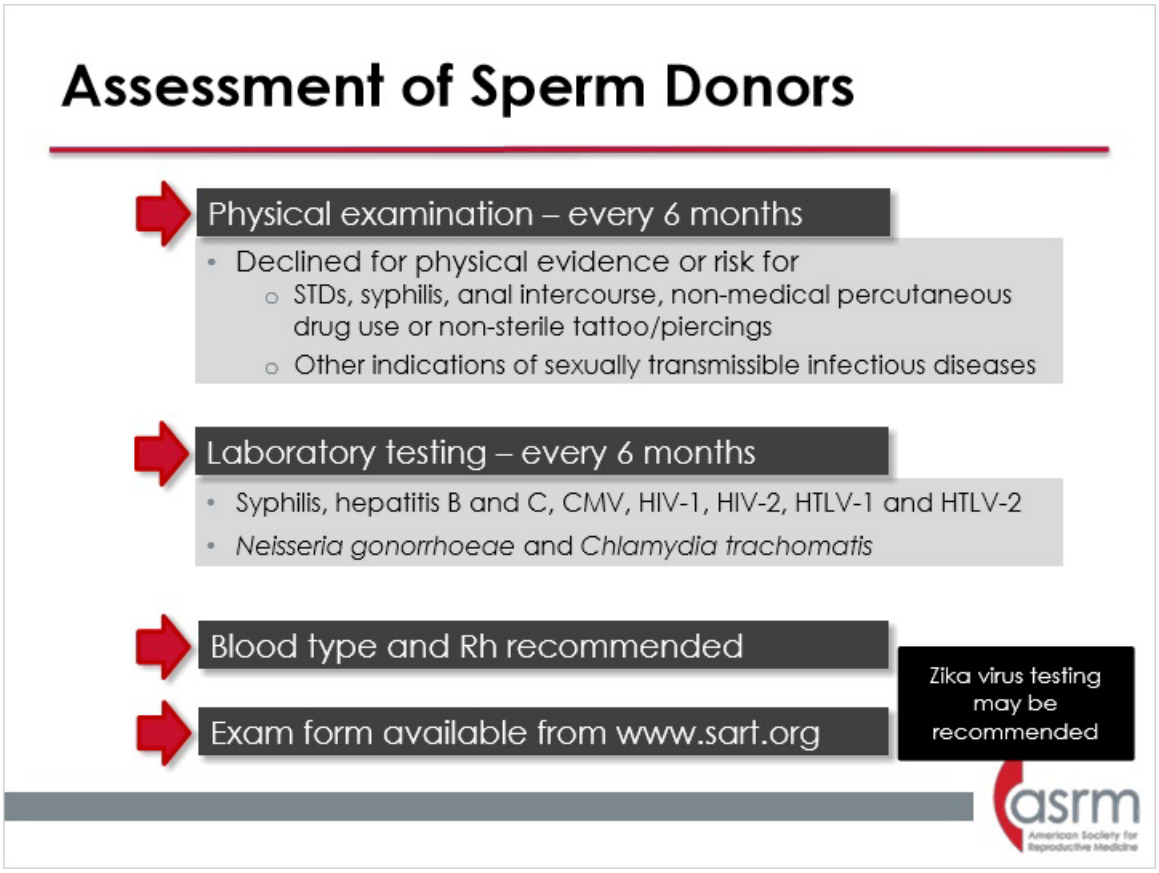
1.34 Assessment of Sperm Donors



Notes:

Genetic evaluation for heritable diseases should be performed in potential sperm donors. Testing for cystic fibrosis carrier status should be performed on all donors. Other genetic testing should be performed as indicated by the donor's ethnic background in accordance with current recommendations after obtaining a proper family history. Some institutions perform chromosomal analyses on all donors, but such evaluation is not required. In addition to being healthy and having no history to suggest hereditary disease, a complete personal and sexual history should be obtained. Specific criteria for exclusion of prospective sperm donors are detailed in the ASRM Practice Committee Report on gamete and embryo donation. Generally, prospective donors are excluded if they have a history or exposure to high risk behaviors or sexual partners that increase the possibility of transmission of HIV, STIs, etc. during gamete donation. A complete list of screening questions is available as "Donor medical history interview questionnaire" at www.sart.org.

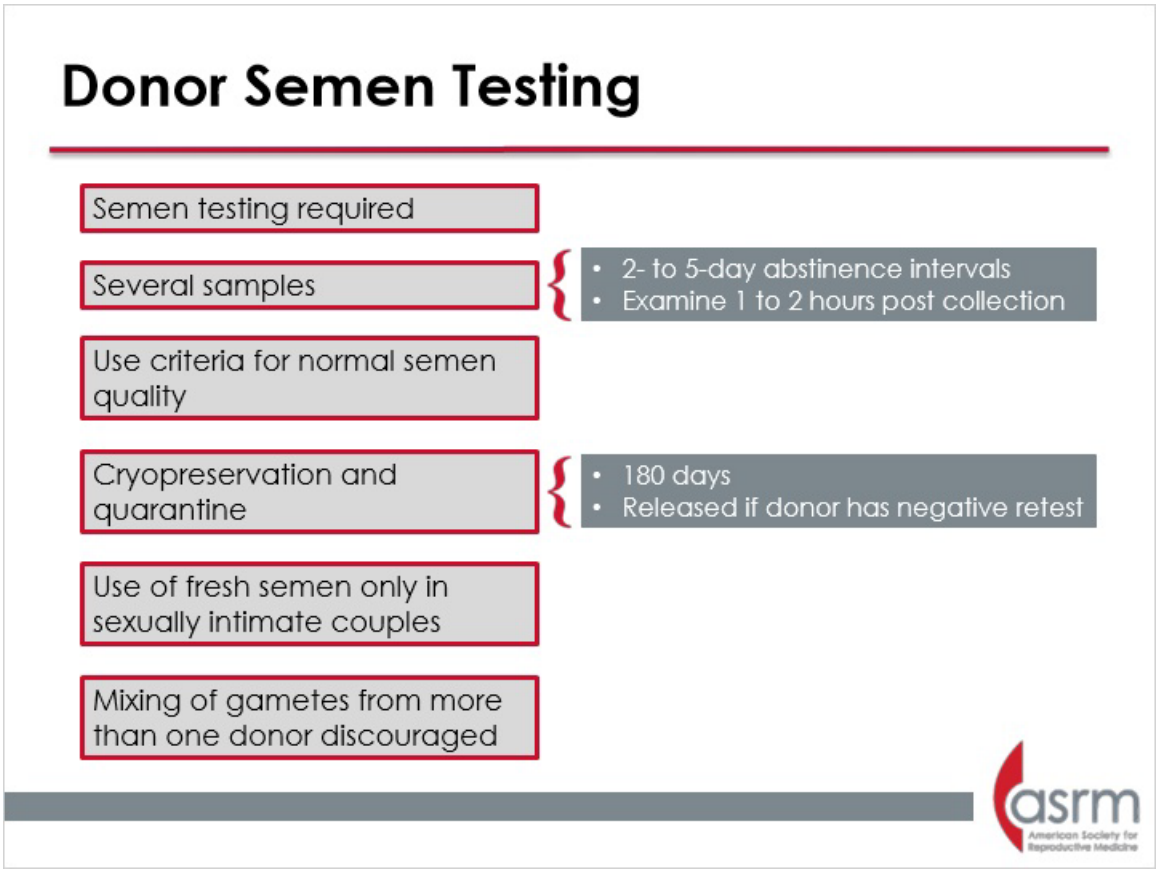
1.35 Assessment of Sperm Donors



Notes:

Before acceptance, and every 6 months while remaining an active sperm donor, donors should undergo a complete physical examination and should be declined for physical evidence for risk of sexually transmitted diseases, syphilis, anal intercourse, non-medical percutaneous drug use, recent tattooing or piercing in which sterile procedures were not used; as well as other medical indications of sexually transmissible infectious diseases. Laboratory testing, performed initially and every 6 months, should include syphilis, hepatitis B and C, CMV, HIV-1, HIV-2, HTLV-1 and HTLV-2, as well as *Neisseria gonorrhoeae* and *Chlamydia trachomatis*. Initial blood typing and Rh factor is recommended. A form for physical examination of male donors is available through www.sart.org. Health care providers should elicit pertinent information from male partners about possible exposure to Zika virus. If partner has been exposed further testing will be required.

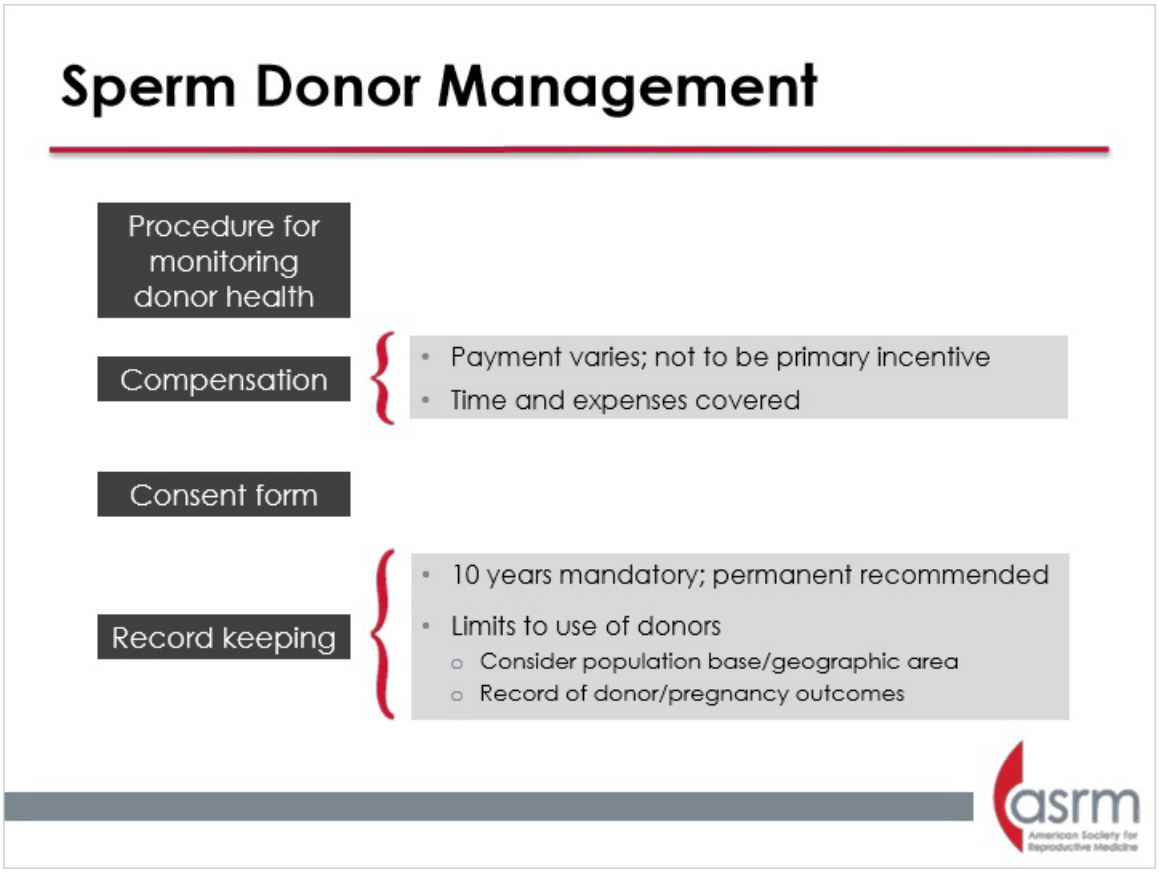
1.36 Donor Semen Testing



Notes:

Semen testing is required for all sperm donors. It is suggested that several samples be examined (each after a 2- to 5-day abstinence interval) before proceeding with a more extensive evaluation. Each sample should be examined within 1 to 2 hours after ejaculation into a sterile container. The criteria used to judge the normality of the sample can vary among laboratories. There are no uniformly accepted standards, but, in general, the minimum criteria for normal semen quality can be applied. Following anonymous semen donation, FDA regulations require that the semen sample be cryopreserved and quarantined for 180 days (6 months) and released only after repeat testing of the donor is negative. Fresh semen use can only be justified for sexually intimate couples due to the potential for HIV and STIs to be transferred prior to seroconversion. ASRM recommends cryopreservation and quarantine for all known donor specimens, just as for anonymous semen donations. The mixing of gametes from more than one donor or from a partner and donor is discouraged, as the genetic origin of the resulting embryo is unknown.

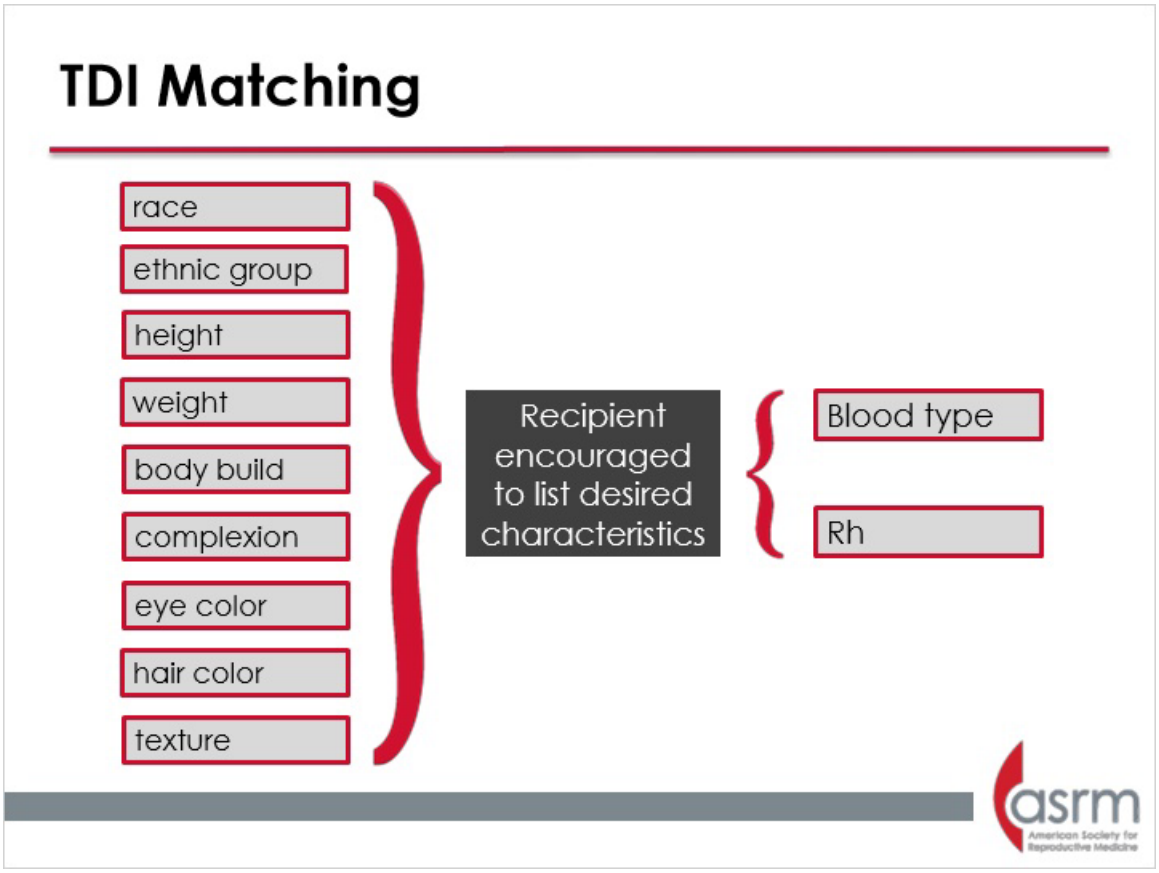
1.37 Sperm Donor Management



Notes:

Programs that solicit and use sperm donors must have donor management procedures in place. Careful screening and testing of donors and an ongoing procedure for monitoring donor health status reduces the risks for transmission of infections to recipients of donor insemination. Compensation and payments to donors varies from area to area but should not be so high that it becomes the primary incentive for the donor. It is appropriate to compensate the donor for his time and expenses. Donor consent is essential, and should include the donor's firm denial of having risk factors for STIs and genetic diseases and acknowledgement of his responsibility to notify the donor program of changes in his health or risk factor status. The FDA requires that donor screening and testing records be kept for at least 10 years; however a permanent record and ongoing follow-up is recommended. In addition, consideration of limits to use of donors should include the population base and geographic area. A record of clinical outcomes for the each insemination cycle should be maintained to assist in limiting donor use and in the event that a previously unidentified heritable disease is encountered that is attributable to the donor.

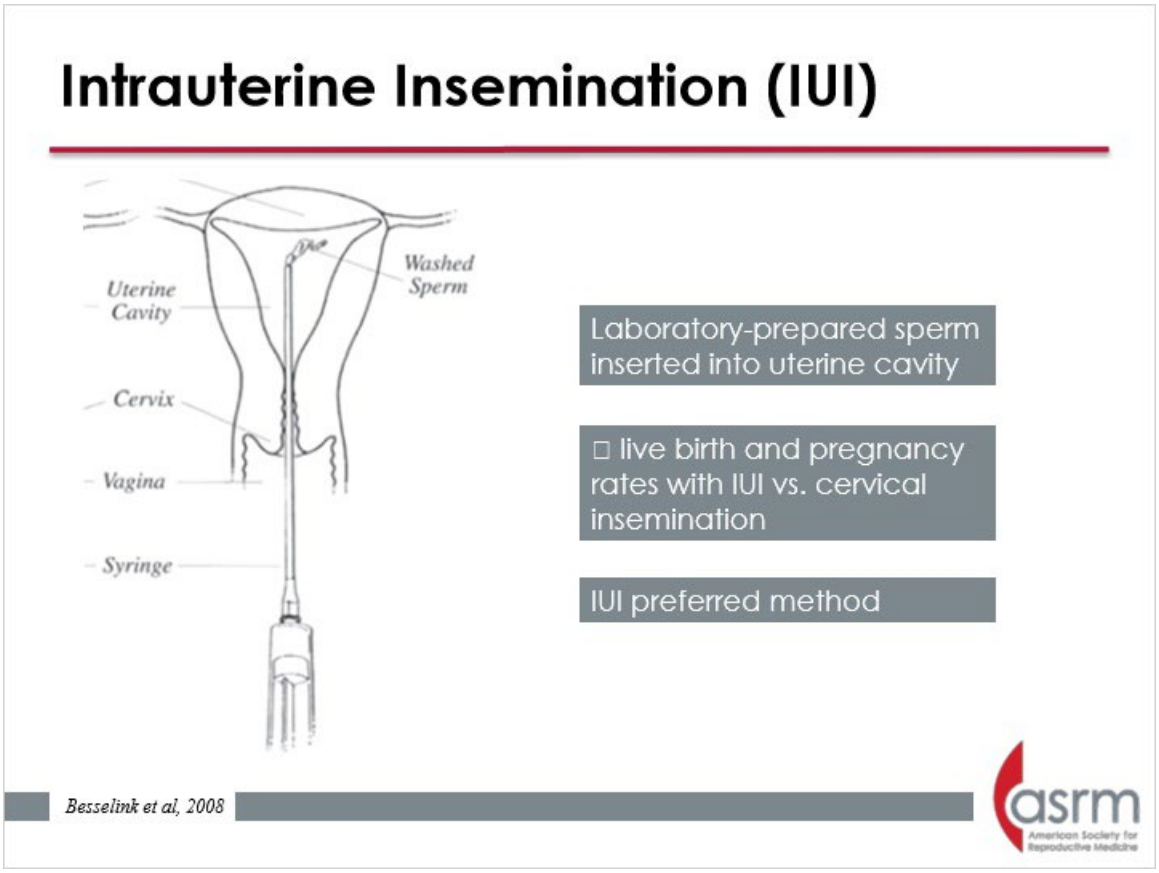
1.38 TDI Matching



Notes:

There are several methods for matching the recipient's male partner and the sperm donor. The recipient couple should be encouraged to list the characteristics that they desire in a prospective donor, including race and/or ethnic group, height, body build, complexion, eye color, and hair color and texture. Consideration should be given to blood type and Rh factor, particularly for Rh-negative recipients. If the use of donor sperm creates the potential for Rh incompatibility, recipients should be informed of the obstetric implications of the condition.

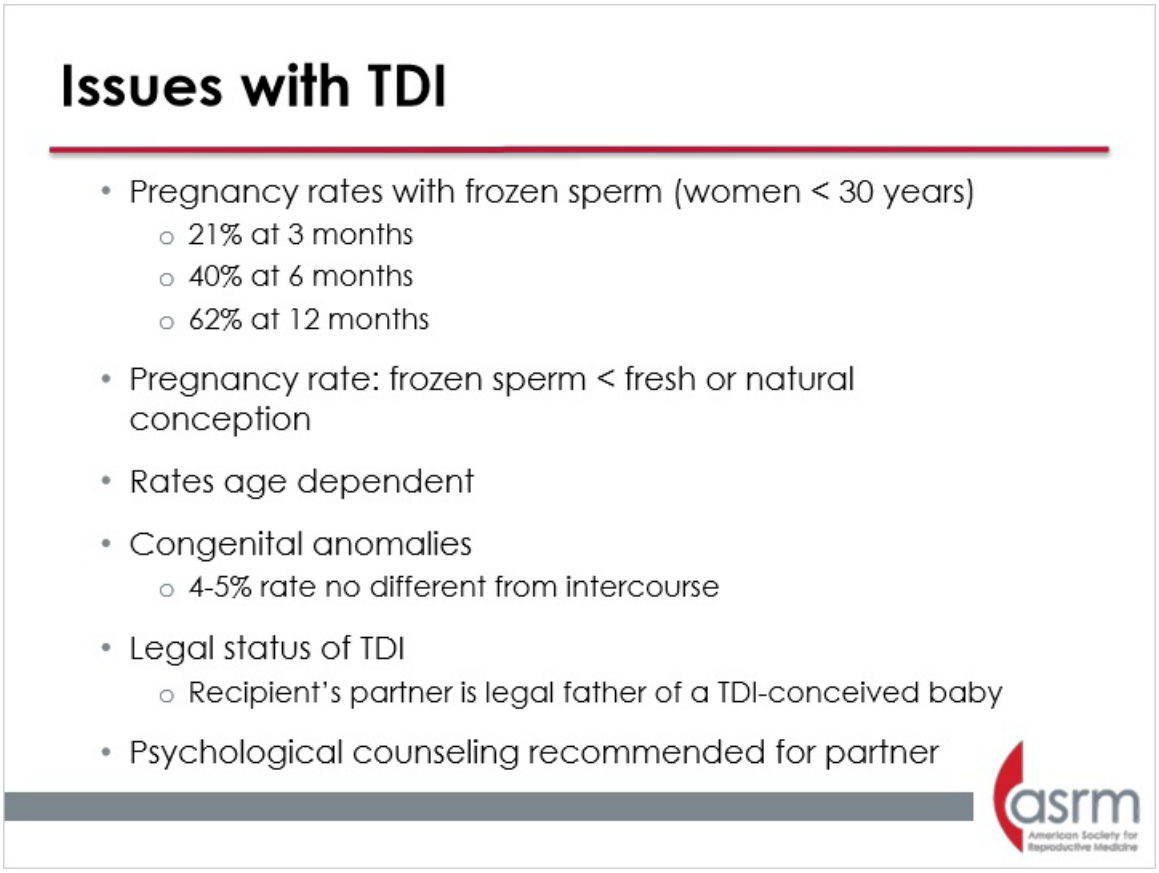
1.39 Intrauterine Insemination (IUI)



Notes:

Intrauterine insemination is a procedure in which laboratory-prepared sperm are inserted into the uterine cavity through a cervical catheter. Alternatively, cervical insemination can be used, in which sperm are deposited within the cervix. However, a Cochrane review of 232 studies showed that the rates of live birth and pregnancy improved with the use of IUI rather than cervical insemination in stimulated cycles using cryopreserved sperm for donor insemination. Thus intrauterine insemination is the preferred method.

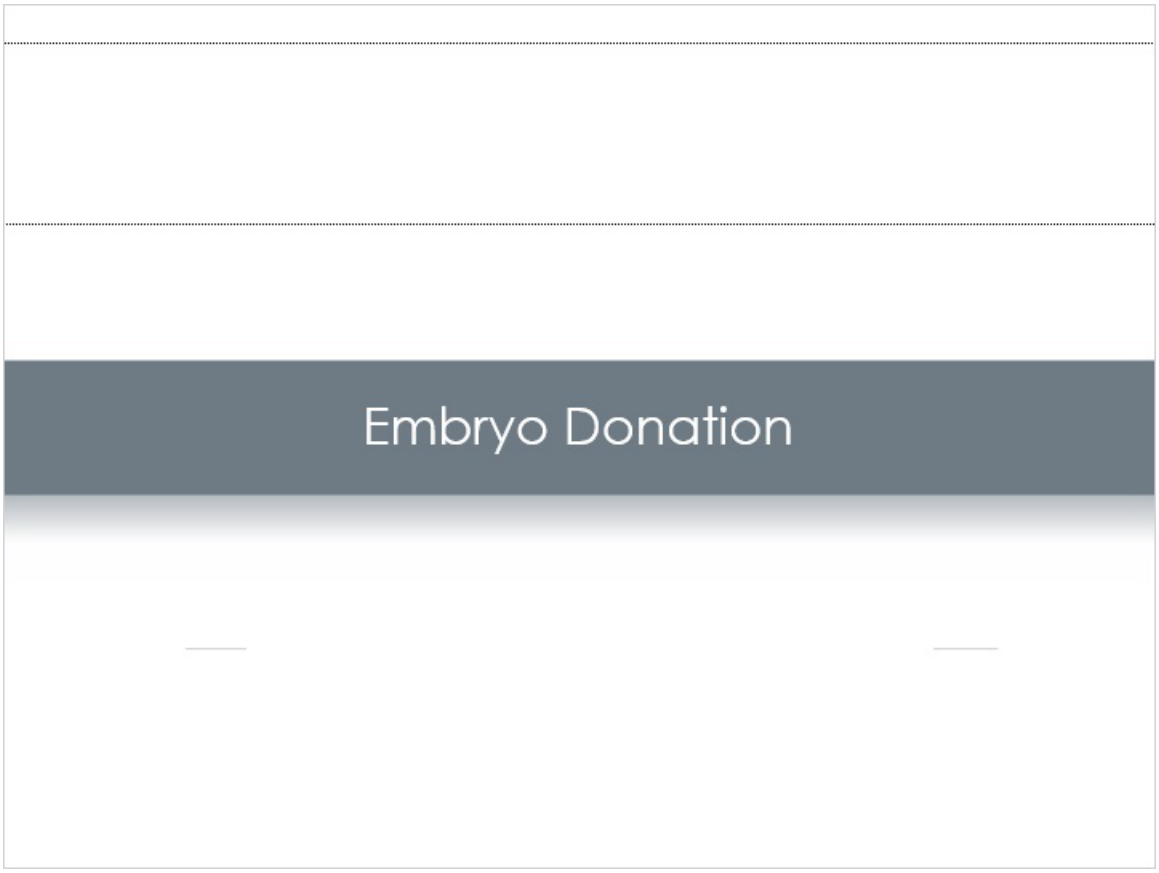
1.40 Issues with TDI



Notes:

There are certain issues associated with therapeutic donor insemination that patients and clinicians should consider. Because of safety issues, cryopreserved sperm are used for most inseminations. However, the pregnancy rate with frozen sperm is lower than with fresh sperm or natural conception. For women under age 30, pregnancy rates are 21% at 3 months, 40% at 6 months and 62% at 12 months. Pregnancy rates with use of frozen sperm are also age dependent, with decreased rates in older women. The rate of congenital anomalies with donor sperm is about 4 to 5%, which is not different from the rate with natural conceptions. Regarding the legal status of TDI: once the recipient's partner signs a consent form, he becomes the legal father of a TDI-conceived baby. Psychological counseling should be offered to recipient's partner, as about 80% of men experience guilt at not being able to produce a child without the aid of a donor.

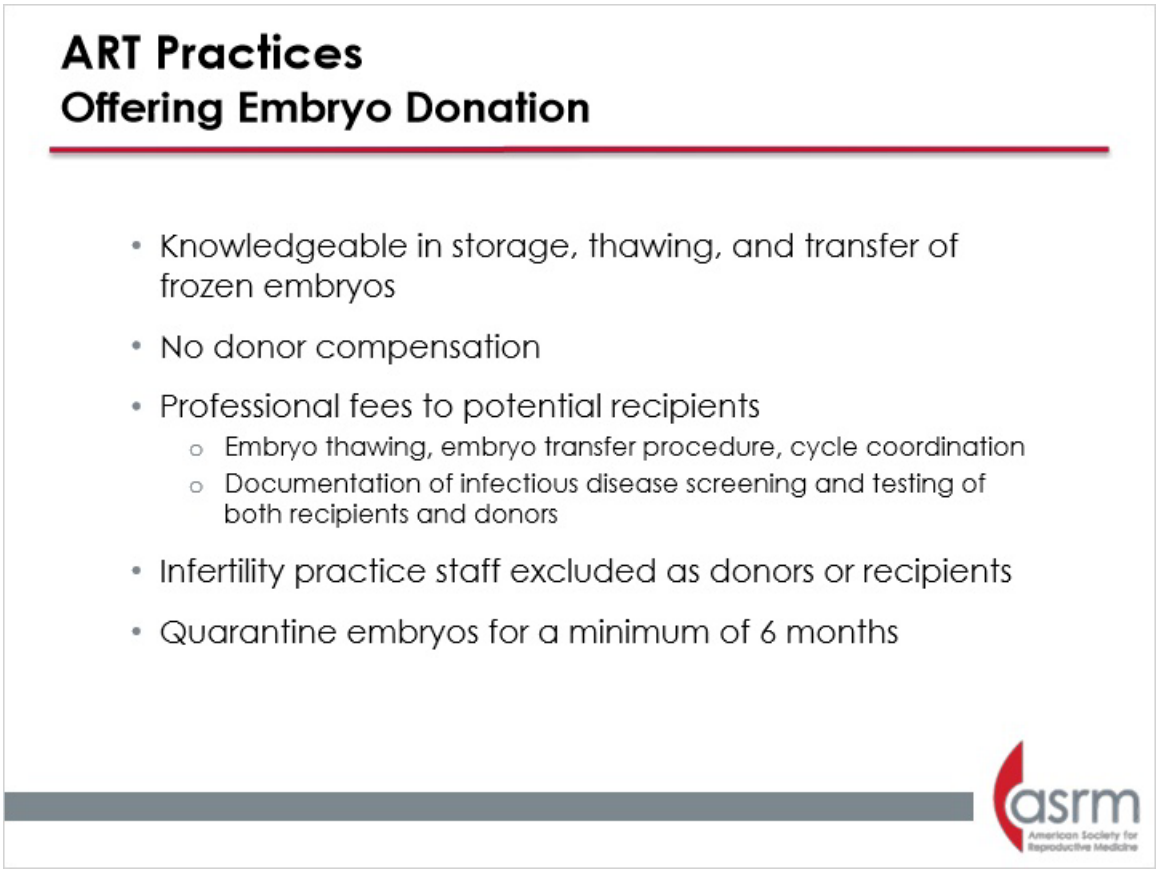
1.41 Embryo Donation



Notes:

Donation of embryos to support the family-building efforts of others is an important option for patients considering the disposition of cryopreserved embryos in excess of those needed to meet the patients' own fertility goals. It is important to use appropriate terminology when referring to this procedure. Application of the term ''adoption'' to embryos is inaccurate, misleading, and could place burdens upon infertile recipients that are not appropriate. As adoption refers to a specific legal procedure that establishes or transfers parentage of existing children, the term embryo donation should be used.

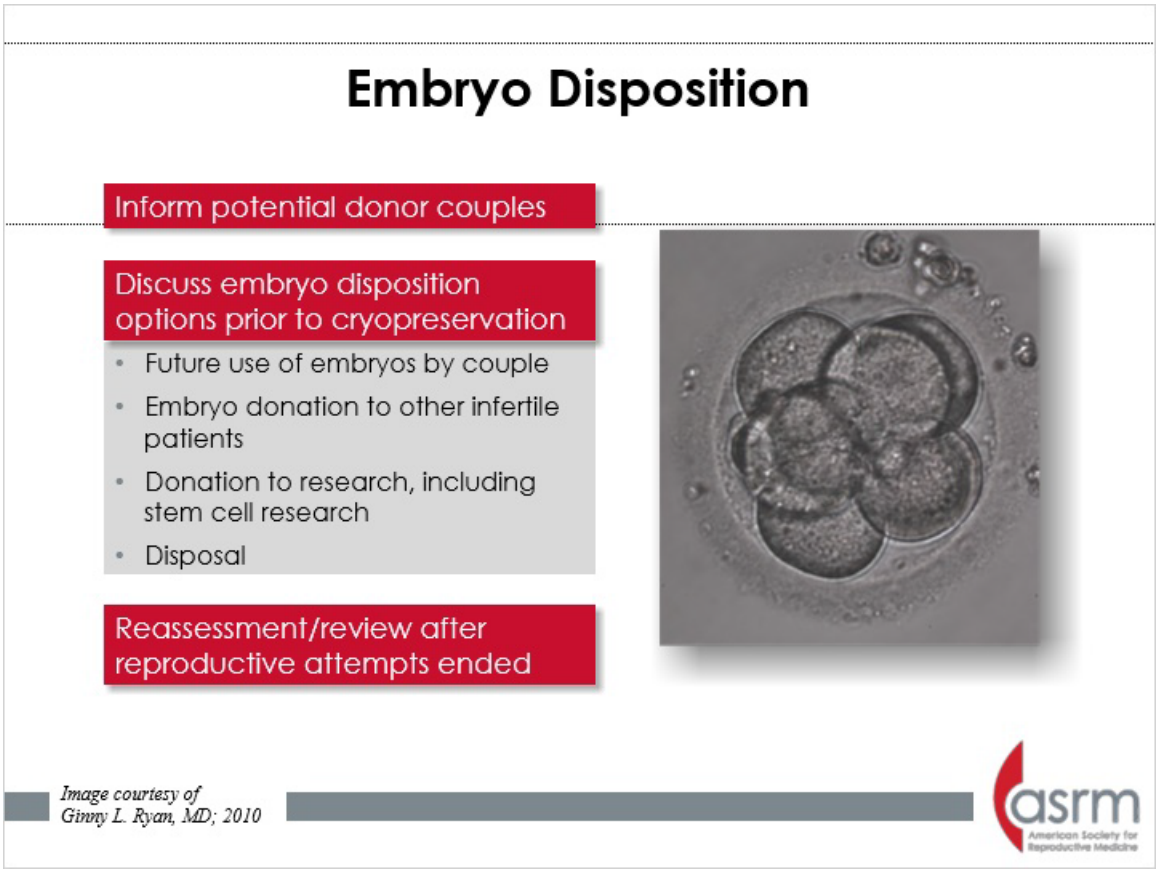
1.42 ART Practices



Notes:

ASRM has developed recommendations for ART practices offering embryo cryopreservation and embryo donation. The practice should be knowledgeable in the storage, thawing, and transfer of frozen embryos. The selling of embryos per se is ethically unacceptable and donors should not be compensated for their donated embryos. However, the practice may charge a professional fee to the potential recipients for embryo thawing, the embryo transfer procedure, cycle coordination and documentation, and infectious disease screening and testing of both recipients and donors. Physicians and employees of an infertility practice should be excluded from participation in embryo donation (as donors or recipients) within that practice. Embryos should be quarantined for a minimum of 6 months before the potential donors are screened and tested.

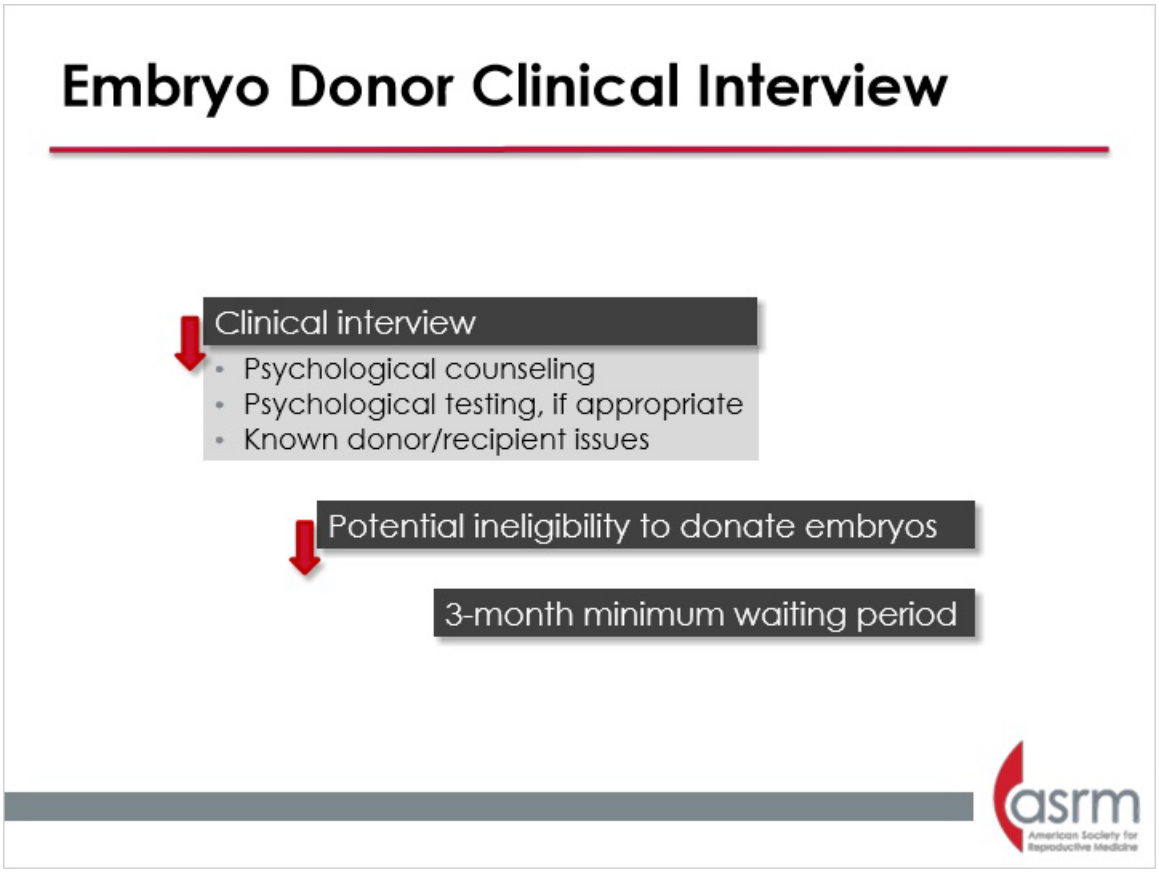
1.43 Embryo Disposition



Notes:

Potential embryo donor couples should be informed about all aspects of their medical treatments and the relevant psychological and ethical issues inherent in donating embryos. There should be a discussion of embryo disposition options before cryopreservation. Current options include the couple's own future use of the embryos via cryopreservation, donating the embryos to other infertile couples, donating the embryos for research, including stem cell research, and disposal. Policies on cryopreservation may vary from center to center and couples must sign appropriate forms indicating their informed consent. All potential donor couples should be advised at the time of the IVF procedure that additional screening and testing may be required if they elect to donate their embryos. After couples have concluded their own reproductive attempts, embryo disposition options should be reassessed.

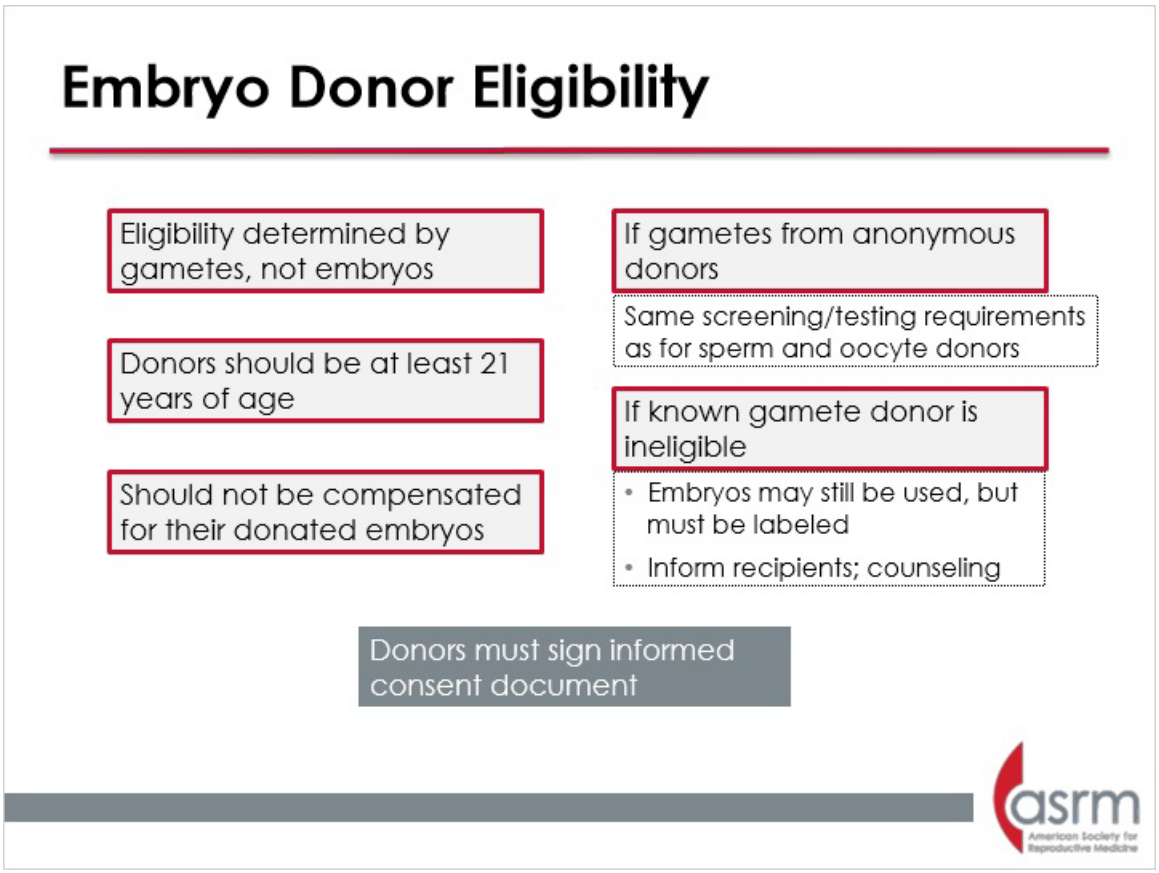
1.44 Embryo Donor Clinical Interview



Notes:

The decision to proceed with embryo donation is complex, and patients may benefit from psychological counseling to aid in the decision. Psychological consultation with a qualified mental health professional is strongly recommended for all patients considering embryo donation. The assessment should include a clinical interview and, where appropriate, psychological testing. The physician should require psychological consultation for patients in whom there appear to be factors that warrant further evaluation. In circumstances involving known donors, psychological evaluation and counseling is strongly recommended for the donors. The potential impact of the relationship between the donor and recipient should be explored. It is important to ascertain whether the donor is informed about any plans that may exist relating to future contact. The assessment should occur after couples have concluded their own reproductive attempts and have clearly indicated their desire to donate embryos. The couple should be counseled about their possible ineligibility to donate embryos. A minimum 3-month waiting period with appropriate follow-up assessment is recommended between the time a couple signs the consent form to donate embryos and the actual donation to a recipient couple.

1.45 Embryo Donor Eligibility

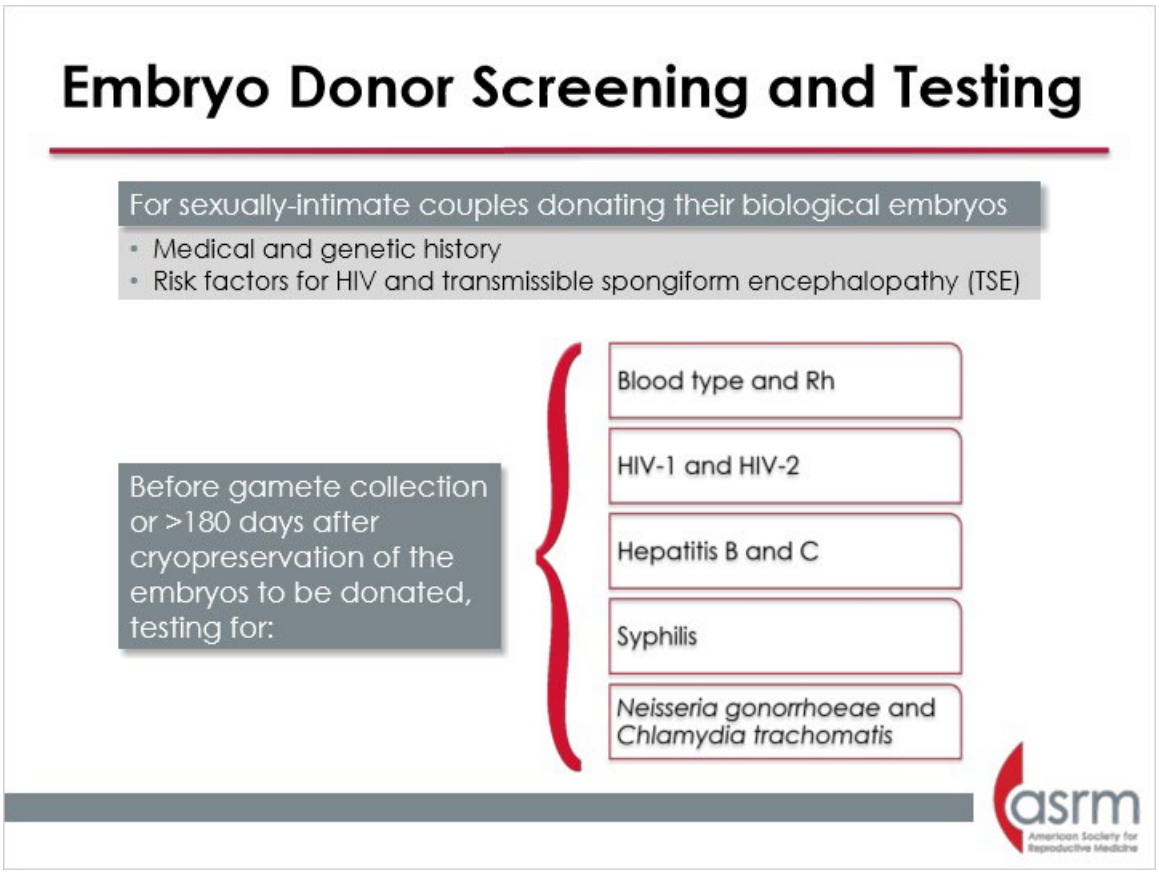


Notes:

Eligibility of donors is determined by the eligibility of the gametes, not the embryos being donated. Donors should be at least 21 years of age and should not receive compensation for their donated embryos. If the embryos are derived from anonymous gamete donors, those donors must be determined as eligible by the same screening and testing requirements for anonymous sperm and/or oocyte donation. If one or both of the donors is known to the recipient, gametes from the known donor that were determined to be ineligible can still be used and those embryos are not prohibited from use according to current FDA rules, provided that the tissue is labeled to indicate any associated increased risks and that physicians using samples are aware of the status of the results. Although the FDA does not require informing the recipients of the test results, ASRM recommends that the recipients be informed and counseled appropriately before transfer of the embryos.

All embryo donors must sign an informed consent document indicating their permission to use their embryos for embryo donation.

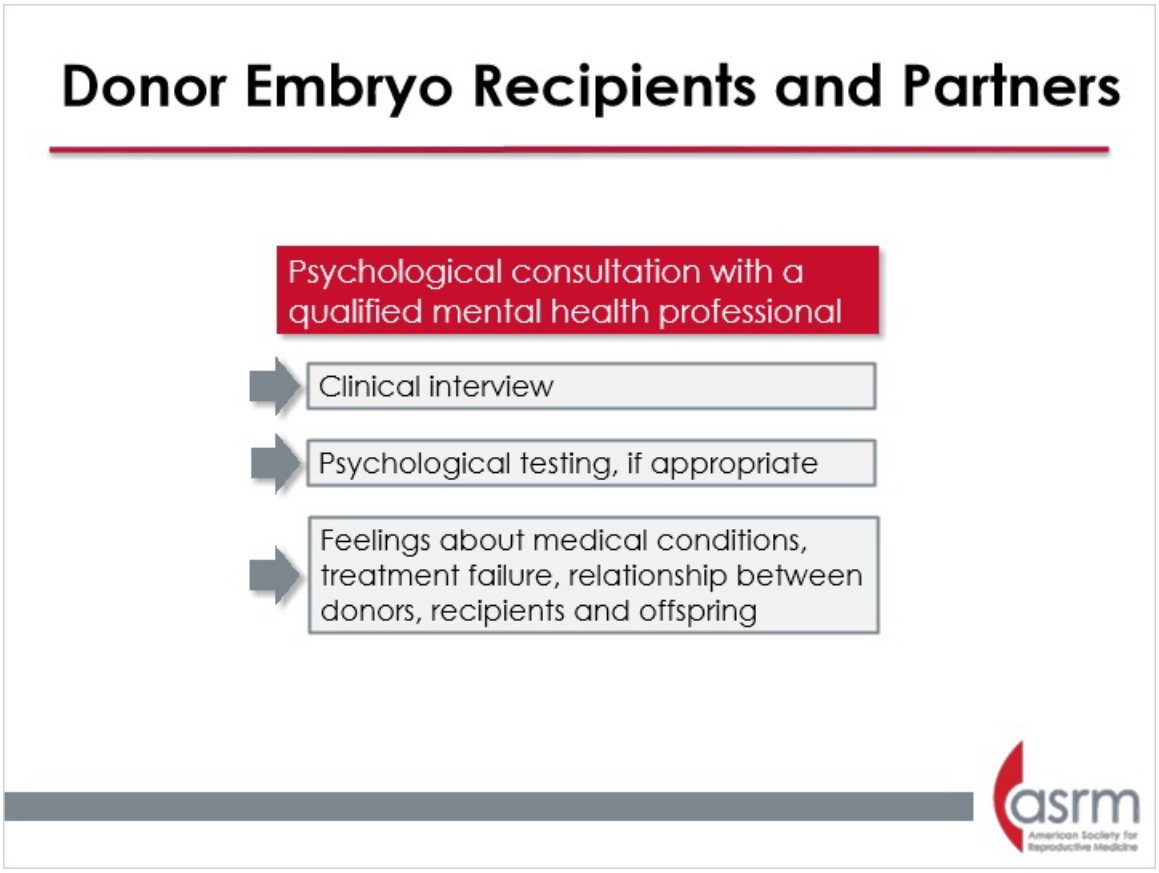
1.46 Embryo Donor Screening and Testing



Notes:

Embryos derived from the gametes of a sexually-intimate couple and created for use by that couple are exempt from the requirements for donor screening and testing before creation of the embryos. The following guidelines apply to sexually-intimate couples who decide to donate unused embryos that are the product of their own biological gametes. They must provide a medical and genetic history and be screened for relevant risk factors for human immunodeficiency virus (HIV) and transmissible spongiform encephalopathy (TSE) and must submit to blood tests for infectious diseases and blood typing before gamete collection or more than 180 days after cryopreservation of the embryos to be donated. Tests include those shown here.

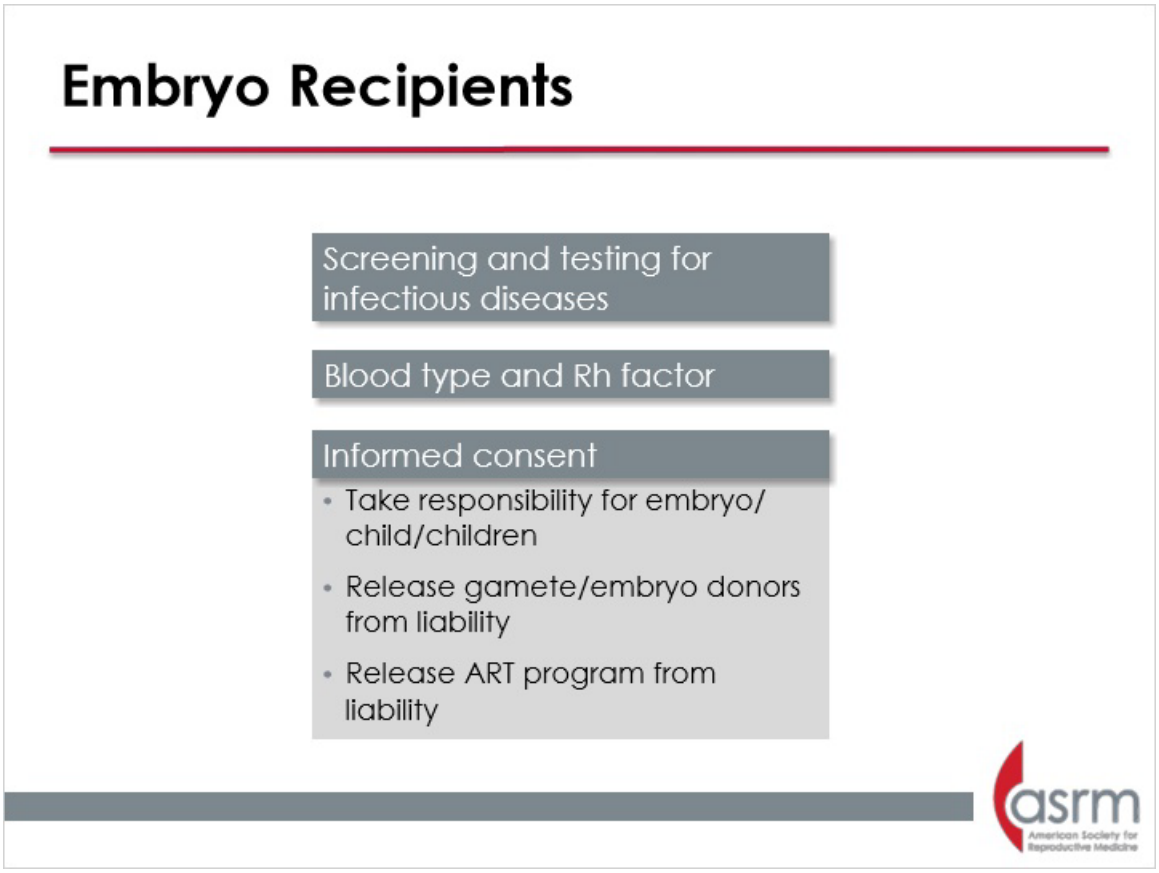
1.47 Donor Embryo Recipients and Partners



Notes:

For recipients of donor embryos and their partners, psychological counseling with a qualified mental health professional is strongly recommended. The assessment should include a clinical interview and, where appropriate, psychological testing. The physician should require psychological consultation for patients in whom there appear to be factors that warrant further evaluation. The recipient and her partner should be counseled about their subsequent feelings concerning the medical conditions that made necessary the use of donor embryos. The impact of treatment failure should also be addressed, including coping with treatment termination, the grieving process, and developing alternatives for the future. Relative issues, such as the impact of the relationship between known donors, recipients, and offspring, should be explored. This assessment should attempt to exclude significant psychiatric illness and current substance abuse and to evaluate their ability to cope with the stress of ART.

1.48 Embryo Recipients

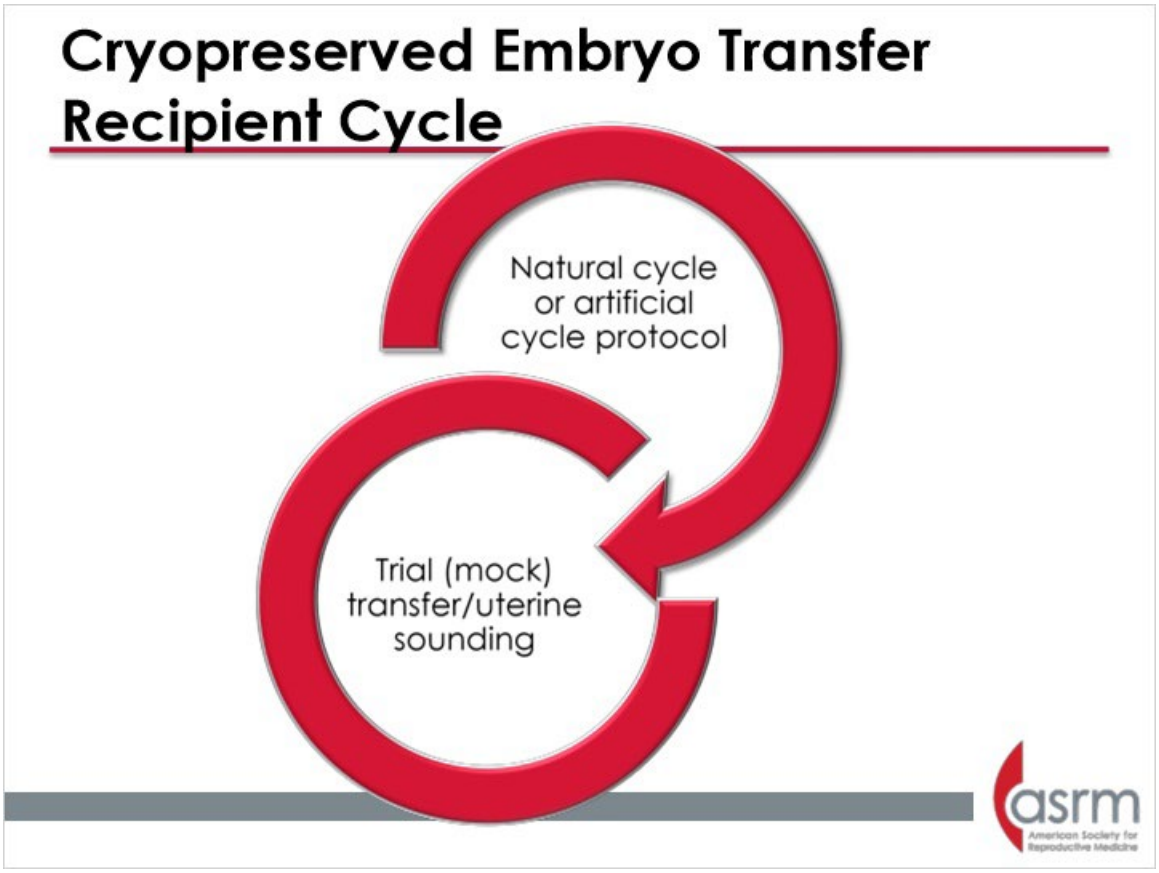


Notes:

Recipients of donor embryos should be advised of screening and testing requirements and be prepared either to not use or to assume the risks related to the use of donor embryos. Screening and testing for infectious diseases is similar to that of the donors. Although not required by the FDA, recommended tests also include blood type and Rh factor. If the use of donor embryos creates the potential for Rh incompatibility, couples should be informed about the obstetric significance of this condition.

Informed consent is also essential for embryo recipients, who must take full responsibility for the embryo and any child or children that may result from the transfer. Recipients must release the gamete donors from any and all liability from any potential complications of the pregnancies, congenital abnormalities, heritable diseases, or other complications of the embryo donation. The ART program should also be absolved of liability from potential complications of pregnancy, congenital abnormalities, and heritable diseases.

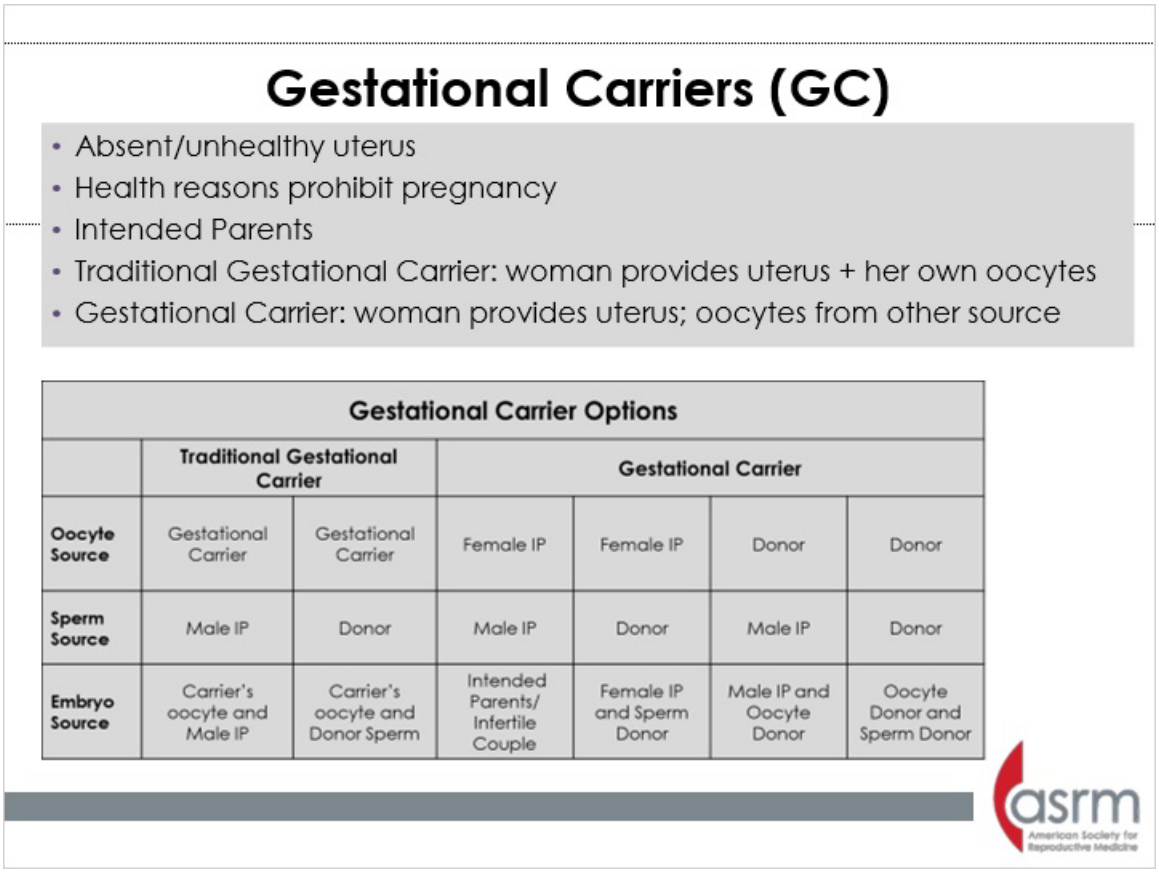
1.49 Cryopreserved Embryo Transfer



Notes:

Women receiving donated cryopreserved embryos will use either a natural cycle or artificial cycle protocol for optimal timing of transfer. The transfer is timed based on the developmental stage of the embryos when they were frozen. A trial (mock) embryo transfer or uterine “sounding” may be done to predict and avoid difficult embryo transfer.

1.50 Gestational Carriers (GC)

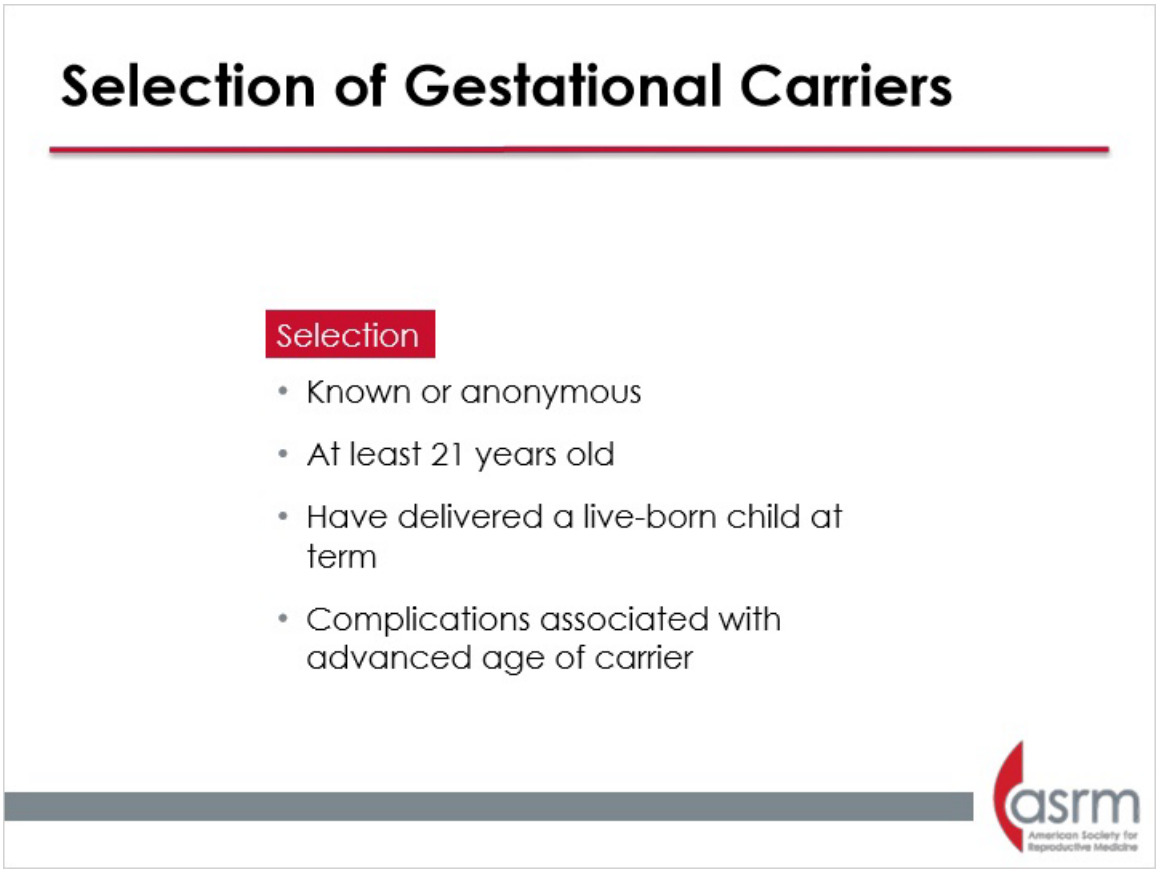


Notes:

Use of a gestational carrier may be an option for infertile couples when the female partner's uterus is absent or unhealthy, or when she cannot carry a pregnancy due to health reasons. A traditional gestational carrier, previously known as a surrogate, is a woman who donates her oocytes and is the gestational carrier for a pregnancy resulting from fertilization of her oocytes either through an ART procedure or insemination. The traditional gestational carrier has a genetic and biological link to the pregnancy she might carry, thus the biologic father and his partner usually must adopt the child after its birth.

In contrast, a gestational carrier is an individual in whom embryos created by the intended parents are transferred into the carrier's uterus, which has been prepared hormonally to carry a pregnancy. Since the gestational carrier does not provide the oocyte, she is therefore not genetically related to the child. Other sources of gametes and embryos may be used with gestational carriers, as shown in this table.

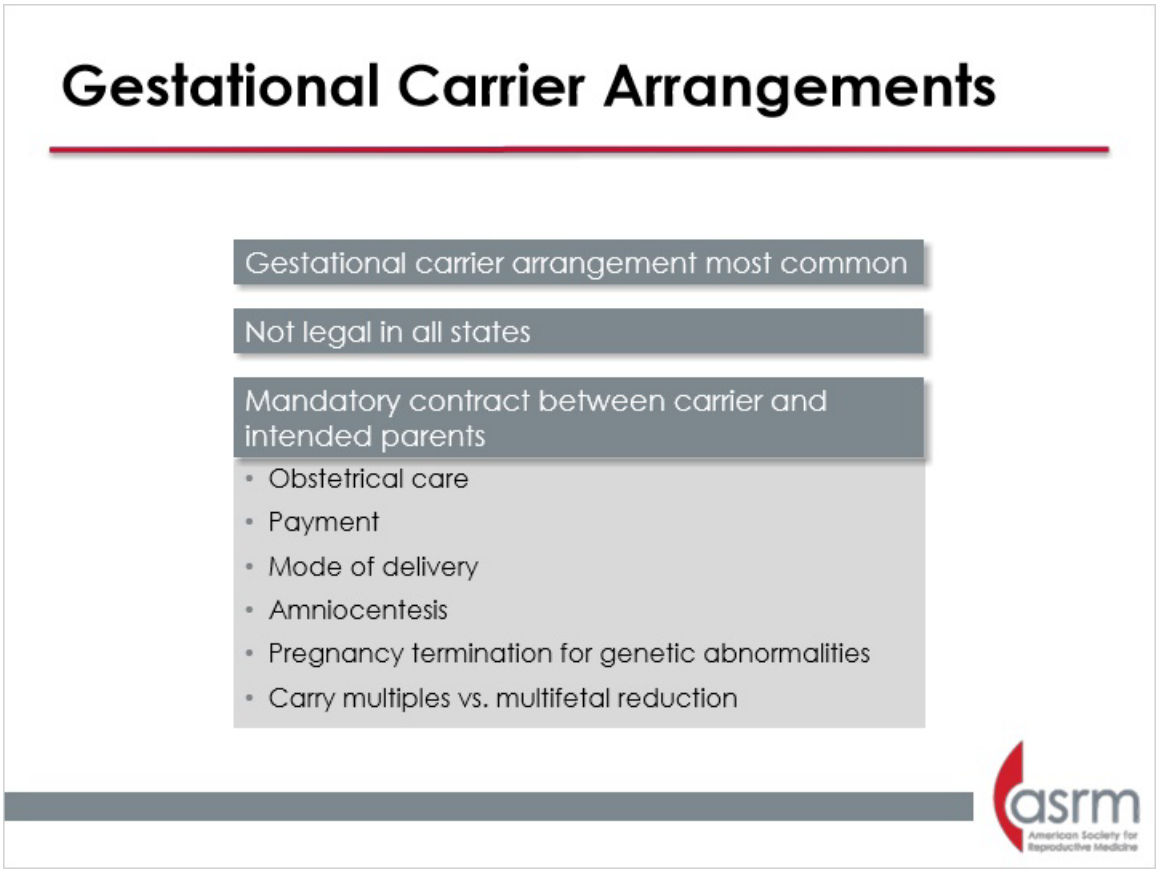
1.51 Selection of Gestational Carriers



Notes:

Known carriers are typically relatives or friends who volunteer to carry the pregnancy. Anonymous carriers are identified thorough agencies that specialize in recruiting women to become gestational carriers. The carrier should be a minimum of 21 years of age and have delivered a live-born child at term. The use of a gestational carrier of advanced age is particularly challenging. The obstetric complication rate, especially the incidence of gestational hypertension or gestational diabetes is much higher. Certainly evaluation of a woman's overall health and appropriate screening for underlying medical conditions that might complicate a pregnancy, as well as counseling regarding the obstetric risk should be performed if considering an older carrier.

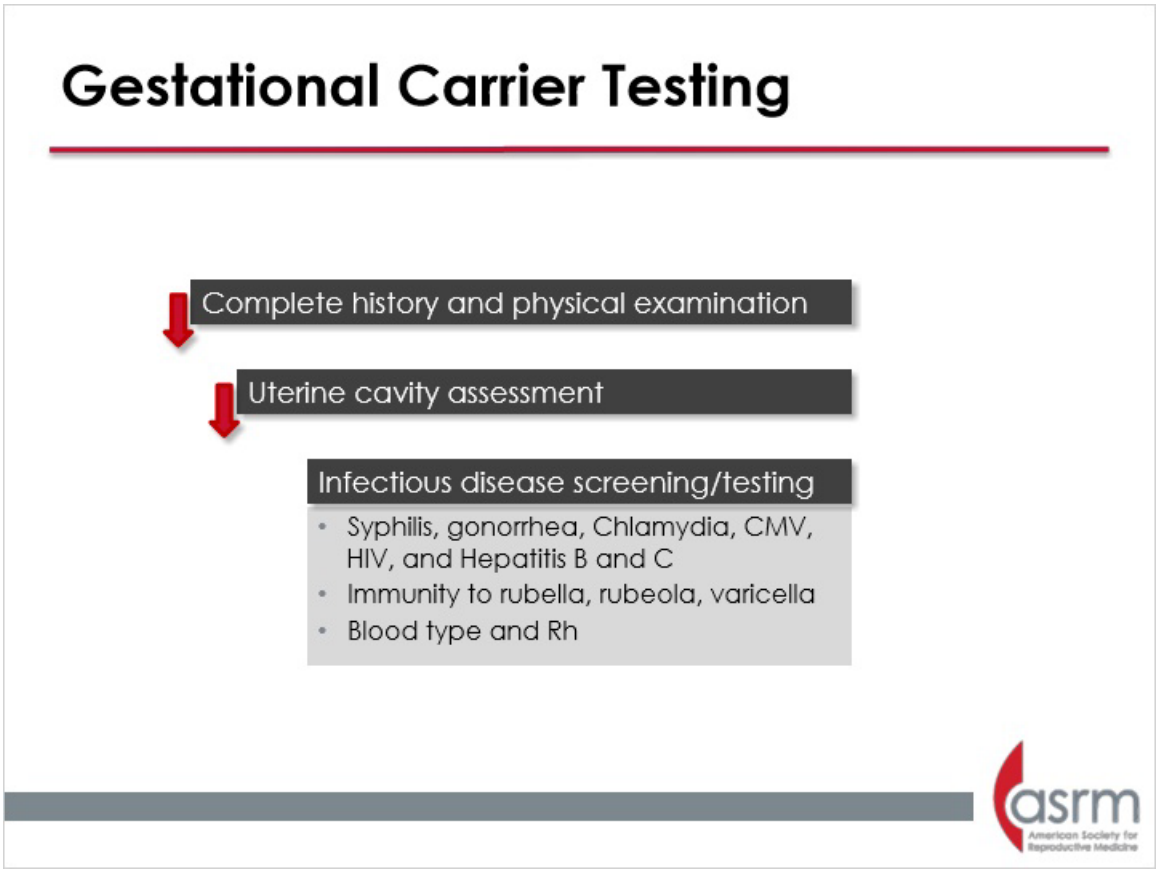
1.52 Gestational Carrier Arrangements



Notes:

Traditional gestational carrier arrangements often are controversial with the potential to be complicated legally, ethically, and psychologically. Despite the requirement for IVF to create embryos, the utilization of a gestational carrier, legally, is the more common approach conducted in the United States. Such arrangements are not legal in all states and a contractual agreement between the carrier and the intended parents is mandatory. Contracts should include language that outlines provisions for obstetrical care, compensation to the gestational carrier for services, the mode of delivery, testing such as amniocentesis, pregnancy termination for genetic abnormalities, and, in the case of multiple gestation, continuing the pregnancy or multifetal reduction.

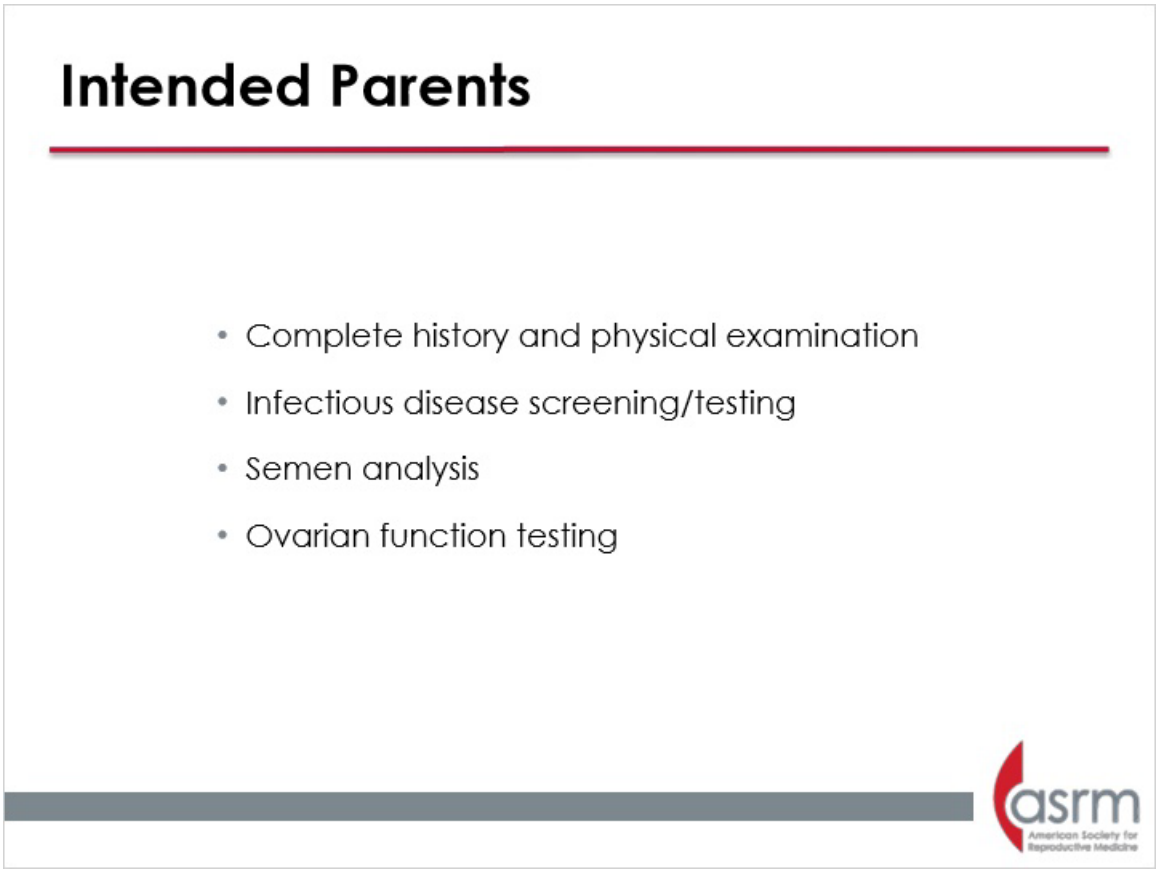
1.53 Gestational Carrier Testing



Notes:

The carrier should undergo a complete medical history including a detailed obstetric history, lifestyle history, and physical examination. The carrier should have an assessment of her uterine cavity with hysterosalpingogram, sonohysterogram, or hysteroscopy. The same infectious disease screening and testing for gamete donors should be performed, including syphilis, gonorrhea, Chlamydia, CMV, HIV, and Hepatitis B and C. The carrier should also be screened for immunity to rubella, rubeola and varicella. In addition, her blood type and Rh should be noted.

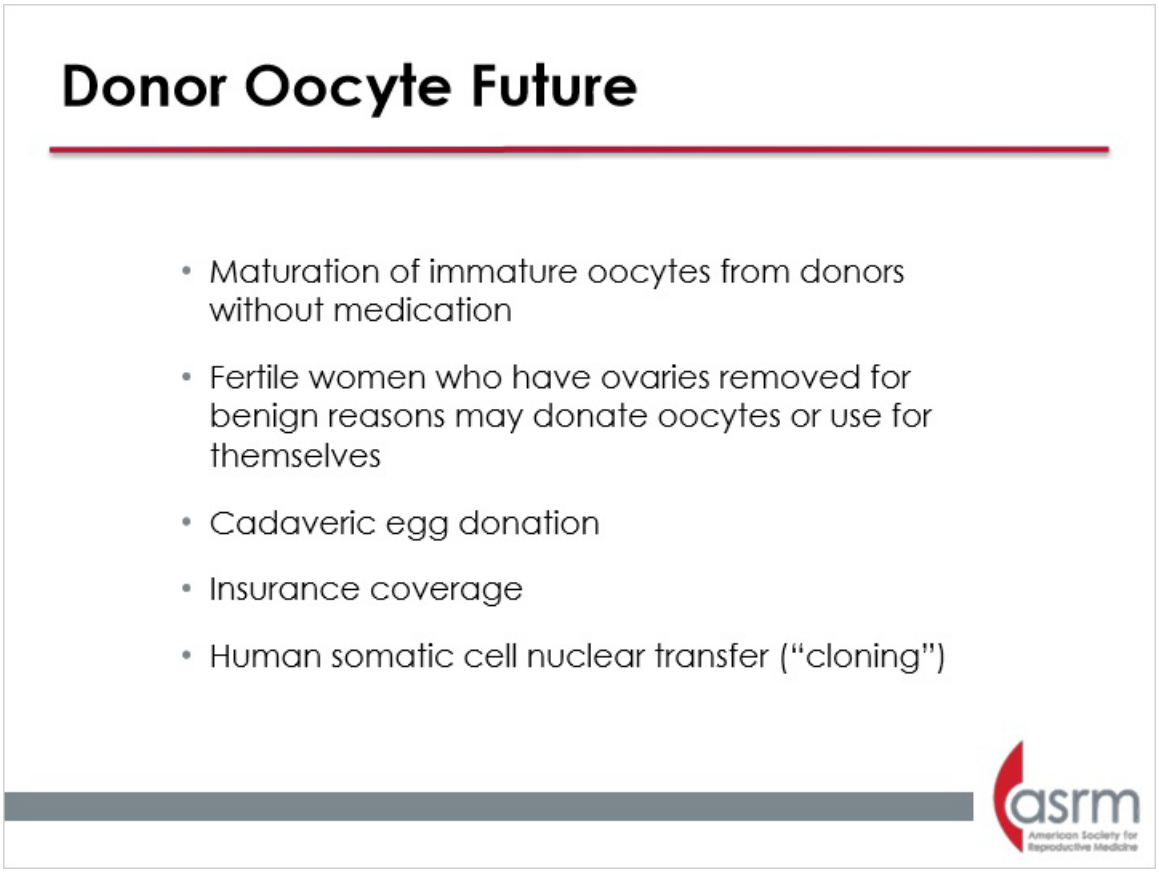
1.54 Intended Parents



Notes:

The intended parents should both undergo a complete medical history and physical examination. They should undergo the same infectious disease screening and testing as for all gamete donors. Semen analysis should be obtained for the male partner, and an evaluation of ovarian function should be performed for the female partner.

1.55 Donor Oocyte Future



Notes:

As technology improves, new options for oocyte donors will become available, and may include techniques for maturation of immature oocytes from donors without medication. It is also possible that fertile women who have their ovaries removed for benign reasons may donate oocytes or use for themselves. Cadaveric egg donation may be a consideration. Progress in health care insurance reform may have implications for coverage of oocyte donation. While human somatic cell nuclear transfer, also known as "cloning" technology may be progressing, the ASRM Ethics Committee does not recommend it at the present time.

1.56 Thank You

Notes:

We hope this module has provided you with a greater understanding of the clinical and medical issues and guidelines related to third-party reproduction and that you will be able to use this information in your care of patients.