INFORMED CONSENT FOR PGS-PGD

Definitions

PGS: Pre-implantation genetic screening
PGD: Pre-implantation genetic diagnosis
Aneuploidy: Alteration in the number of chromosomes (higher or lower than 46 chromosomes)
Translocation: Alteration in the structure of chromosomes involving two of them without altering final number of chromosomes (46 balanced).
Inversion: Alteration implying a rearrangement of the genetic information within the same chromosome.
PCR: Polymerase chain reaction. Technique used to generate a higher amount of DNA copies.
NGS: New generation sequencing. Technique used to analyze the number and structure of chromosomes.
Mosaic: a normal embryo has 46 chromosomes in all of its cells. An embryo with mosaicism has a certain percentage of its cells with 46 chromosomes and another percentage with more or less chromosomes. Since the clinical consequences of this alteration are unknown, this Institution considers that they cannot be transferred to the uterus.

Purpose

The purpose of PGS is providing the possibility of transferring chromosomally normal embryos to the uterus.
The purpose of PGD is providing the possibility of transferring to the uterus chromosomally normal embryos or embryos having all of the genetic material (balanced translocations/inversions).

Procedure steps

Obtaining embryo/s: by means of ICSI.
Embryo transportation: They must be transported by the fertility center of origin by the following means:

1. For pronuclei: fresh within six (6) hours after fertilization, transported in incubator.
2. Embryo/blastocyst biopsy: If they are transported within the first 4 hours after biopsy, the biopsy can be refrigerated and for times between 4 and 24 hours after biopsy, it can be transported frozen with dry ice.
3. Embryo (72 hours) or blastocyst (days 5 to 7): Cryopreserved in liquid nitrogen.

Embryo thawing: For cryopreserved embryos. The fresh pronuclei go directly to the next step.
Embryo culture: All embryos are allowed to evolve until they become blastocysts (day 5 onwards).
Embryo biopsy: it is the extraction of cells from the embryo (trophectoderm) since day five (5).
Embryo cryopreservation or re-vitrification: All biopsied embryos will be cryopreserved o re-vitrified, after signing the corresponding consent.
Analysis: The DNA of each embryo's cells is amplified through PCR. Then the matrix obtained from the NGS is analyzed. This step of the procedure analyzes the amount of DNA in each chromosome revealing if there is a correct number of chromosomes or not, plus the presence of translocations and mosaicisms. During this process, cells are destroyed to obtain DNA. This analysis takes several days.
Embryo transportation: Biopsied embryos are returned after cryopreservation to the fertility center of origin, where they will be stored.
Embryo donation for research or discard: Only performed with embryos presenting aneuploidies or presenting unbalanced translocations.
Viable embryos' thaw and transfer: performed in a future cycle under the indications of the fertility center of origin.

Risks

Related to culture: not obtaining embryos in the blastocyst stage due to an arrest in embryo development.
Related to un-biopsied embryo thawing: there is a risk that embryos do not survive the thawing process, this risk being below 20%. In case no embryo survives, the analysis will be cancelled.
Related to the biopsy: not being able to obtain the cells in order to have a diagnosis. The embryo could be damaged during the biopsy procedure due to its own features and quality, and this might affect future embryo development.
Related to the transportation: if the biopsy is not transported according to what we described above.
Related to the analysis: It could happen that the material is not enough to carry out the genetic study (non-amplified embryo). It could happen that reaching to conclusive results is not possible due to the embryo quality.
Related to the transfer: transfer cancellation due to non-viable embryos or if the embryos do not survive the thawing process.

Results / Success rates

PGS: There is a low percentage of false positive (<0.1%) or negative (<2%), in addition to limitations to identify specific diseases (associated to a single gen - monogenic) since PGS is a technique is mainly used to analyze the variations in the number of complete chromosomes and it does not evaluate their integrity in relation to small breaks, segment

inversions, etc. This method can detect if there is mosaicism in embryos, where one of the cell lines presents a numeric alteration (monosomy o trisomy), it can be detected as long as the proportion between both lines is over 20%. If an embryo has a mosaicism in a single chromosome, where the amount of monosomic and trisomic cells is similar, the result can be considered "normal".
PGD: The limitation of this technique is that it can only detect unbalanced chromosome changes (higher to 5 Mb). It also detects between 70% and 80% of triploidies and it does not detect polyploidies.
Pre-implantation genetic tests (chromosomal) can determine if the embryo is affected with a chromosome anomaly. Therefore, the probabilities of conceiving a baby with a chromosomal anomaly will be reduced by more than 90% after PGS-PGD. However, we recommend patients they undergo some sort of pre-natal genetic diagnosis during the first trimester of pregnancy, in case of ultrasound-biochemical findings that may lead to suspect there is some kind of anomaly.

Information provided to the patient/s
I/we have read and understand the information above in relation to the procedure I/we will undergo.

I/we have had the chance to ask questions to the physician in charge and clear all doubts about the procedure, its risks, benefits and eventual complications related to the procedure I/we will undergo. The explanations I/we have received have been provided in a clear and simple language.

I/we have been informed that all medical data related to this procedure are confidential, including my/our medical record, diagnostic tests and/or images according to article 2 sub-section d) of Law No. 26,529 on Patient's rights in relation to health professionals and health institutions, modified by Law No. 26,742, Regulatory Decree No. 1089/2012 and articles 8 and 10 of Law No. 25,326 on Personal Data Protection. Disclosure of such information (whether totally or partially) will only take place in exceptional circumstances under legal requirement, relieving Cegyr from the physician-patient privilege or in extraordinary circumstances based on Cegyr's founded criteria.

I/We have been informed about and provide consent to the use of non-identifying data about the outcome of this treatment to be reported to several national and international databases for statistical and/or scientific purposes, according to the laws regulating the matter.

I/We have been informed that I/we can obtain, at any time, a copy of my/our medical record, according to the provisions of Law No. 26,529 of Patient's rights in relation to health professionals and health institutions (art. 12 and following) modified by Law No. 26,742, Regulatory Decree No. 1089/2012 and Law No. 25,326 on Personal Data Protection.

I/We have been informed and understand that I/we can withdraw this consent jointly or individually at any time before the blastocyst biopsy. Consent withdrawal must be notified irrefutably and in writing to the health center providing the services, expressly stating the will to withdraw this consent and discontinuing the procedure. I/We understand that in case we had embryos at the time the consent is withdrawn, I/we will be legally responsible for them and their maintenance costs.

I/We have been informed and understand that performing PGD or PGS **does not eliminate** the need for standard pre-natal tests, through invasive or non-invasive methods during the first trimester of pregnancy.

I/We have been informed and understand that in the case of heterosexual patients, sexual abstinence is essential during the entire treatment period. Abstinence is necessary to avoid the possibility of a spontaneous pregnancy, which would invalidate the results of the PGS or PGD tests.

I/We have been informed and understand that the results of the PGS cannot be used to select the sex of the embryo to be transferred in view of social concerns.

I/We have been informed and understand that it is recommended that patients receive the appropriate genetic advice before deciding to authorize this test.

I/We have been informed and understand that performing an opening in the zona pellucida or embryo outer layer does not prevent the development of the embryo or its implantation. I/We have been informed that no part of the future fetus will be absent when the trophectoderm is biopsied. The procedure can delay the development for a few hours, but the embryo will continue its normal development.

I/We have been informed and understand that embryos with unbalanced translocations, arrested embryos and non-viable embryos (presenting aneuploidies that are incompatibles with life), can be donated to Cegyr for research or discarded according to our decision.

I/We have been informed and understand that embryos presenting viable aneuploidies (compatible with life) or mosaicism, can be donated to Cegyr for research, can be discarded or cryopreserved according to our decision. I/We have been informed and understand that if I/we do not wish to transfer these embryos in the future, it must be clearly stated in a specific written consent.

CONSENT

By signing this document I ……..……[1] together with……..……..[2] **express my will,** fully conscious and freely, to perform the technique ……..……[3], to my/our embryos and I/we **AUTHORIZE** the medical professionals of the health center to apply the treatment and or techniques to me/us that they consider necessary for that purpose.
In addition, in case of resulting non-viable embryos, I ……..……[1] together with ……..……..[2] consent to the embryos' ……..……..……..[4]. In case of resulting viable embryos but with chromosomic alterations (for example: trisomy 21, 18, 13, monosomy of chromosome X, mosaicism, etc.) I ……..……[1] together with ……..……..[2] consent to the embryos' ……..……..[5].

In case of legal conflicts in the interpretation of this document, we agree to submit ourselves to the jurisdiction of the Civil Courts of the City of Buenos Aires.

It is the responsibility of the patients to inform the health center during the entire cryopreservation period of any changes to the indicated address. Otherwise, the following address will be the valid one for the purposes of this consent.

[1] Please state name and last name
[2] Please state name and last name or cross out the line
[3] Please state PGD or PGS accordingly
[4] Please state discard or donate for research
[5] Please state discard, donate for research or keep under cryopreservation

PATIENT 1

Last name and names:……..… Identity card number/Passport:…….Age:……

Address:……..……..……PC/ZC:……....

City:…….State.:……..Country:…….

Phone number:……..Mobile phone number:……..E-Mail:……

……
Signature, printed name and date

PATIENT 2

Last name and names:……..… Identity card number/Passport:…….Age:……

Address:……..……..……PC/ZC:……....

City:…….State.:……..Country:…….

Phone number:……..Mobile phone number:……..E-Mail:……

……
Signature, printed name and date

TREATING PHYSICIAN ……
Signature, seal and date

Two (2) copies of this consent are signed in this act. One of the copies of this consent will be delivered to the patient/s and the remaining one will be filed at the Health Center.