



## Monopaternal Superfecundation in an *In Vitro* Fertilization Cycle: A Case-Based Review

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### Abstract

**Background:** Superfecundation refers to oocyte fertilization from multiple sexual intercourses in the same menstrual cycle, bringing about multi-zygotic pregnancies from mono- or heteropaternal superfecundations.

**Case:** We reported a case of a couple who had unprotected intercourse occurred 2 to 4 days before oocyte retrieval. And monopaternal superfecundation of heterosexual twins occurred after the transfer of one embryo. Unprotected intercourse around the time of oocyte retrieval will put women receiving IVF at greater risk of superfecundation, which would disturb the treatment of PGT, and affect maternal-fetal health for high-order pregnancies.

**Conclusion:** Women receiving IVF should avoid unprotected intercourses around the time of oocyte retrieval.

**Keywords:** Superfecundation; *In vitro* fertilization; Case-based review

### Abbreviations

IVF: *In Vitro* Fertilization; AMH: Anti-Müllerian Hormone; Gn: Gonadotropin; LH: Luteinizing Hormone; hCG: human Chorionic Gonadotropin; E2: Estradiol; ET: Embryo Transfer; PGT: Preimplantation Genetic Testing

### Introduction

Superfecundation refers to oocyte fertilization from multiple sexual intercourses in the same menstrual cycle, bringing about multi-zygotic pregnancies from mono- or heteropaternal superfecundations [1]. Heteropaternal superfecundation is associated with sexual intercourses with different men, and monopaternal superfecundation associated with one man. According to three cases in 39,000 records from a paternity-test database, there existed a frequency of 2.4% heteropaternal superfecundation among natural dizygotic twins, with their parents involved in paternity issues [2]. Monopaternal superfecundation is probably much more common because under normal circumstances it is not recognized, and its prevalence has been estimated to be 8% of all dizygotic twins [3].

### Case Presentation

Here, a case of a couple who had monopaternal superfecundation of heterosexual twins after the transfer of one embryo was reported. Informed consent was required for this couple.

A 31 years-old female was hospitalized in our IVF unit for secondary infertility. She experienced an abortion after a natural pregnancy in 2012 and suffered from menstrual disorder for 3 years afterwards (with a cycle of 30-40 days). Sonography showed that the left fallopian tube was adhesive, and the right fallopian tube was unobstructed. In 2019, three cycles of ovulation induction were conducted but the pregnancy failed. Before the IVF cycle in 2021, her AMH level was 7.9 ng/ml and her BMI was 18.75 kg/m<sup>2</sup>. Her husband's semen was examined in March 2021, showing that the sperm concentration was 72.2 × 10<sup>6</sup>/ml, the movement rate was 61%, the proportion of normal sperm was 1.5%, and most of the sperms were amorphous. Diagnosis: Secondary infertility, Left fallopian tube adhesion, Male dyspepsia.

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Then an IVF was decided on. Controlled superovulation stimulation was conducted with 150IU of Gn, triggered on the 12<sup>th</sup> day of Gn, E2 3057.5 P0.66 LH1.0. Thirteen oocytes were aspirated. Five D3 embryos and three blastocysts were obtained. Finally, one eight-cell embryo was transferred. The hCG level was 2034 mIU/ml on the 14<sup>th</sup> day after ET. Transvaginal ultrasound examination performed 5 and 7 weeks after ET showed two intrauterine gestational sacs with a single embryo with cardiac activity in each. The NT indicated double chorionic double amniotic sac twins at 10 weeks after ET.

The woman had regular prenatal examinations, and no pregnancy complications occurred during pregnancy until 33 weeks' gestation on January 13<sup>th</sup>, 2022, when she prematurely delivered a 2024-g boy and a 1905-g girl. The couple questioned whether they had transferred the wrong embryo. After careful examination of laboratory records and transfer records, it was indeed an eight-cell embryo that was transferred. The couple recalled having unprotected intercourse two days and four days before oocyte retrieval. The doctors explained that another fetus resulted from natural conception in the same cycle. Then, a paternity test was performed and the monopaternal superfecundation was confirmed genetically.

## Discussion and Literature Review

Superfecundation was first recognized with heteropaternal superfecundation, which is the result of sexual intercourse with different men [2]. However, monopaternal superfecundation is probably much more common because under normal circumstances it is not recognized.

When the number of sacs detected was bigger than the number of embryos transferred during IVF, three possible mechanisms were observed, including: Division of transferred embryos, superfecundation, or a combination of both [1]. The division of embryos during the 3<sup>rd</sup> to 8<sup>th</sup> days is the most commonly-seen cause for twin- or multiple pregnancies [1,4]. However, for this couple, it was obviously a case of superfecundation, which was further confirmed as a monopaternal superfecundation by paternity testing.

In the presence of naturally conceived embryos, superfecundation after IVF may occur in addition to the transferred embryos. As monopaternal superfecundation after IVF was first reported by Amsalem [1], it showed the couple had intercourses during the period between retrieval and transfer. At the time of oocyte retrieval, some oocytes may spill into the peritoneal cavity, while others may ovulate a few hours later. In the event of unprotected intercourses around the time of retrieval (or even during a few days before), *in vivo* fertilization may occur with viable sperm, leading to superfecundation.

Superfecundation may increase the possibility and multiplicity of multiple pregnancies in IVF. Patients should be informed of the risks arising from superfecundation-induced high-order multiple pregnancies. Indeed, increased incidence of maternal and perinatal risks during multiple pregnancies could be observed, including miscarriage, pregnancy loss, fetal death, low birth weight, and preterm delivery [1]. Despite the fetal reduction operation, the risks of miscarriages, bleeding, premature membrane rupture, and chorioamnionitis, are still higher than that of the single pregnancy [5].

Superfecundation might be more common in couples undergoing Preimplantation Genetic Testing (PGT) because most of them are fertile couples with the added effect of controlled ovarian stimulation. In case of superfecundation in a cycle of PGT, there is a growing risk of conceiving a baby with an undesirable genetic trait for the couple (single gene disorder, aneuploidy, or particular sex). Therefore, couples receiving PGT should be informed of the possibility of superfecundation and clear written instructions to avoid unprotected sexual intercourses before transplantation. If the number of pregnancy sacs is found bigger than the number of embryos transferred or a patient is found having a fetus different from that detected in the embryo(s) transferred, PGT laboratory case records of the couple should be carefully reviewed. For PGT with X-linked diseases, in case of simultaneous pregnancies of "different" sexes, the fetus can be reduced where applicable.

Superfecundation could be prevented by avoiding unprotected intercourse around the time of oocyte retrieval. A suitable time frame is from 1 week in advance to 2 days after the oocyte retrieval: A so-called "safe period" principle. As the response to controlled ovarian stimulation differs from each other, it's difficult to predict the exact day of oocyte retrieval accurately. Unprotected intercourses from the start of ovarian stimulation should be avoided according to usual practice, especially for PGT couples.

In summary, unprotected intercourse around the time of oocyte retrieval will put women receiving IVF at greater risk of superfecundation, which would disturb the treatment of PGT, and affect maternal-fetal health for high-order pregnancies. Women receiving IVF should avoid unprotected intercourses around the time of oocyte retrieval.

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