OOCYTE MATURATION DEFECT

Oocyte Maturation Failure, Oocyte Defect Syndrome, Bad Eggs Syndrome, Meiotic Arrest, Oocyte Arrest, Maturation Arrest Of Human Oocytes

Defect during oocyte maturation.

About Oocyte maturation defect

Oocyte maturation arrest is a complex problem not clearly understood; only few cases showing a complete oocyte maturation failure has been reported previously, still the exact incidence remains unknown. Failure to resume meiosis (a specialized type of cell division that reduces the chromosome number by half) in vivo may arise at one of the following three levels: absent or incomplete luteinizing hormone (LH) surge; derangements in the signaling mechanisms from the surrounding cumulus cells; and intrinsic oocyte factor.

In the natural cycle, the resumption of oocyte meiotic maturation and ovulation process is controlled by the mid cycle secretion gonadotrophins by the hypophysis; this pre-ovulatory gonadotrophin surge is thought to be the primary stimulus by which oocyte maturation is reinitiated. In vivo, this surge lasts about 48 hours.

Maturation arrest of human oocytes may occur at various stages of the cell cycle. A total failure of human oocytes to complete meiosis is rarely observed during assisted conception cycles. Oocyte maturation arrest may be the cause of infertility in some couples previously classified as having unexplained infertility. The recognition of oocyte maturation arrest as a specific medical condition may contribute to the characterization of the yet poorly defined entity currently known as ‘oocyte factor’ (oocyte secretes its own factors to regulate microenvironment in close neighbourhood of surrounding cells). The cellular and genetic mechanisms causing oocyte maturation arrest should be the subject of further investigation.
Maturation arrests in human oocytes (Pic. 1) can occur at:

1. Germinal vesicle (GV) stage (Pic.2) when oocytes are awaiting the gonadotrophin signal or the release from an inhibitory follicular environment. Germinal vesicle (GV) stage oocytes have no ability to participate in the early steps of fertilization. Maturation promoting factor controls the resumption of meiosis from the diplotene arrest. Any disruption in the signaling events with maturation promoting factor leads to the arrest of the oocyte before the germinal vesicle breakdown (GVBD). The process of GVBD is triggered through stimulation of the cumulus cells by luteinizing hormone (LH).

2. At metaphase one (MI) and were unable to complete meiosis up to metaphase two (MII).
   - **Meiosis I arrest (MI)**
     There are several processes between meiosis I and metaphase of meiosis II. They include chromosome condensation, formation of the metaphase spindle, separation (partition) and segregation (random spacing) of the homologous chromosomes. The final process of the first meiotic division is the formation of the first polar body. MI arrest is classified when the arrest is before the development of the first polar body. This situation occurs when there is some disruption in signal transduction pathway or abnormally meiotic spindle, which is responsible for abnormal separation and segregation of chromosomes.
   - **Meiosis II arrest (MII)**
     Meiosis II imply that oocyte is „mature“ and capable of fertilization. Unfortunately there are women, which are producing oocytes with MII morphology, but they are still not capable of formation an embryo even with fertilization. The cause of this condition is unknown.

3. Oocytes did not respond properly to fertilizing sperm.
   - **Mixed arrest**
     There are also patients, which produce oocytes arrested at more than one stages of meiosis.

As it is difficult to identify maturation arrest of oocytes unless and ART (assisted reproduction techniques) procedure is done, such women are subjected to extremes of financial, emotional and physical burden due to repeated failures of infertility treatment.

More information on the physiology and pathophysiology of oocyte maturation with knowledge of cellular and genetic mechanism causing oocyte maturation arrest is necessary before the exact nature of defects interfering with meiotic competence can be determined and effective therapy can be suggested. Based on a candidate gene approach, the genetic or microarray analysis of patients will help to identify genes and pathways involved in
complete failures. One can infer from these cases that “oocyte factor” probably may explain the reason for “unexplained infertility”. So patients with unexplained infertility should proceed with IVF (in vitro fertilization) instead of ovulation induction with timed intercourse or intrauterine insemination (IUI).

**Associated diseases**
- unexplained infertility
- rheumatoid arthritis

**Complications**
- infertility

**Risk factors**
A total failure of human oocytes to complete meiosis is rarely observed during assisted conception cycles.

### Impact on fertility

When the arrest occurs in early stages of development, oocyte is not capable of following maturation. In other cases when oocyte reaches the correct nuclear maturation stage (MII) several of them did not have sufficient time to complete cytoplasmic maturation; i.e., they did not have time to accumulate all the mRNAs (messenger ribonucleic acid) and proteins required for early development as RNA (Ribonucleic acid) synthesis ceased when meiosis resumed. Physiological inhibition of spontaneous nuclear maturation in vitro for a period of time sufficient to complete cytoplasmic maturation, will be required to improve developmental competence.

### Prevention

This condition cannot be prevented.

### Symptoms

- infertility
- repetitive production of mostly immature oocytes
- inability of in vitro maturation
- fertilization failure despite intracytoplasmic sperm injection

### Therapies
Self therapy

There is no self therapy for this condition.

Conventional medicine

Pharmacotherapy

No pharmacotherapy can be used to treat this condition.

Surgical therapy

Oocyte maturation defect cannot be treated surgically.

Assisted reproduction

Research aimed at understanding the mechanisms that control meiosis has relevance for practical applications as the oocyte, in addition to its important role in determining fertility, is a major player in reproductive biotechnologies such as in vitro maturation (IVM), in vitro fertilization (IVF), cloning and transgenesis (the process of introducing an originating externally gene—called a transgene—into a living organism so that the organism will exhibit a new property and transmit that property to its offspring). When mammalian oocytes that are competent to re-initiate meiosis are removed from their follicles and cultured, they undergo spontaneous resumption of meiosis with progression to MII in the absence of gonadotropins, demonstrating that a signal(s) from the follicle holds oocytes in prophase arrest. Spontaneous oocyte maturation allowed the development of in vitro maturation (IVM), a reproductive technology which involves artificial removal of cumulus-oocyte complexes (COC) from antral follicles and culturing them in standard cell culture conditions for 24-48 h until they reach metaphase II. Moreover, IVM has the potential to exploit the large supply of oocytes available within ovaries in the case of ovariectomy. A proportion of these oocytes are then competent to develop following in vitro fertilization.
Therapies

Egg donation
Process by which a woman donates eggs for purposes of assisted reproduction or biomedical research.
Learn more at: www.fertilitypedia.org/edu/therapies/egg-donation

ICSI
A micromanipulative fertilization technique in which a single sperm is injected directly into an egg.
Learn more at: www.fertilitypedia.org/edu/therapies/icsi

Sperm donation
The procedure in which a man (sperm donor) provides his sperm for fertility treatment.
Learn more at: www.fertilitypedia.org/edu/therapies/sperm-donation

Standard IVF
A process in which an egg is fertilised by sperm outside the body: in vitro. Own or donated gametes may be used.
Learn more at: www.fertilitypedia.org/edu/therapies/standard-ivf

Sources
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“Reduced developmental competence of immature, in-vitro matured and postovulatory aged mouse oocytes following IVF and ICSI (https://rbej.biomedcentral.com/articles/10.1186/1477-7827-6-58)” —by Lacham-Kaplan and Trounson licensed under CC BY 2.0


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