**INFERTILITY SERVICES: INTRACYTOPLASMIC SPERM INJECTION (ICSI) CLINICAL GUIDELINES**

**Purpose:** To provide an understanding of fertility preservation among individuals faced with the potential loss of fertility secondary to treatment for cancer and other medical conditions.

**Detailed Steps/Screen Shots**

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| **1. Background Information** | • A male factor is involved in 40% - 60% of all infertility cases  
• The frequency of the ICSI procedure performed in the United States in 2009 was 64%.  
• Fertilization may be compromised by one or more of the following sperm abnormalities:  
  – Low count (oligospermia) - <20 million/ml  
  – Low motility (asthenospermia) - <50% motile  
  – Abnormal morphology (teratospermia) - <30% normal  
• A history of poor or failed fertilization in a previous in vitro fertilization (IVF) cycle suggests that fertilization problems may recur in subsequent IVF cycles  
• Complete failure of fertilization occurs in <5% of IVF cycles  
• Poor fertilization (<25% fertilization rate) may occur in ≤20% of IVF cycles.  
• Head directed anti-sperm antibody has been associated with fertilization failure.  
• Sperm recovered directly from testicular or epididymal tissue may be severely limited in quantity and may lack natural fertilizing capacity  
  – The use of round spermatids (immature sperm) for injection is considered experimental  
• Oocytes, particularly in women ≥40 year of age may have a thickened and/or hardened zona pellucida, impairing the ability of sperm to penetrate the egg naturally.  
• A limited number of available oocytes may necessitate the use of ICSI to ensure an acceptable number of zygotes.  
• In IVF, standard fertilization enjoys a 70% fertilization success rate  
• In IVF, ICSI enjoys a 80% fertilization success rate  
• The fertilization failure rate for standard IVF is <5% but may be as high as 25% in cases of borderline semen.  
  – There is no established definition of borderline or sub-optimal semen.  
  – There are no reliable tests that exclude fertilization failure prospectively  
• ICSI is being used increasingly for patients without a male factor  
• Using ICSI in non–male factor patients does not appear to be associated with improved fertilization, pregnancy, or live birth rates. The benefits of ICSI for this population, if any, are unclear.  
• Children conceived as a result of ICSI have similar physical and intellectual development compared to children conceived spontaneously.  
• There may or may not be a small increased risk of congenital abnormalities in children conceived through ICSI  
  – This may be due to the bypassing of the sperm selection process that occurs with natural fertilization  
  – It may also be due to the presence, duration, and type of infertility, as well as the age of the mother and the father  
• This guideline applies to patients seeking advice on whether or not to utilize ICSI to fertilize their or an egg donor’s oocytes. |
## Clinical Management

### 2. Indications
- Oligospermia, asthenospermia, or any combination thereof
- Antisperm antibodies thought to be causing infertility
- Prior complete fertilization failure or poor fertilization rates with standard IVF protocols
- History of Polyspermy
- Frozen sperm limited in number and quality
- Sperm recovered directly from testicular or epididymal tissue
- Specific oocyte defects impairing sperm-egg interaction e.g. abnormalities of the zona pellucida
- Limited number of oocytes (<6)
  Embryologist's discretion

### 3. Best Practices
- The frequency of ICSI should not exceed 65% of all fresh IVF cycles.

### 4. Case Example

| Case Example | A 39 year old couple with tubal factor infertility presents for an IVF cycle. The initial evaluation reveals a sperm count of 15 million/ml (normal ≥ 20 million/ml) and a test of ovarian reserve demonstrated an FSH of 10.5. The ovarian stimulation yielded 10 oocytes of which 6 were mature. The couple questioned their physician as well as the embryologist regarding the best method to fertilize the oocytes. This couple has two indications for ICSI. First and foremost, there is a male factor present characterized by relatively mild oligospermia. Second, there are a relatively limited number of oocytes available for fertilization, and there is a high probability that at least 50% or higher may be chromosomally abnormal. Consequently, it is important to maximize fertilization potential. ICSI was recommended. Interestingly, on stripping the oocytes of their surrounding cumulus cells, the embryologist noted thickening of the zona pellucida, another relative indication for ICSI. On the same day, another patient, also with tubal factor infertility, underwent an oocyte retrieval. This was her first IVF cycle at age 32. Her partner's semen analysis was entirely within normal limits. Fifteen oocytes were retrieved, all of which were mature. She and her husband were wondering if they too should have the ICSI procedure, fearing the possibility of complete fertilization failure. This couple was counseled to have conventional IVF, without ICSI. There is no male factor involved and there are an abundant number of oocytes available. The anticipated fertilization rate of at least 70% is as good as that for ICSI and conception outcomes are the same as for ICSI. The risk of total fertilization failure is <5%. The couple agreed to conventional fertilization. Surprisingly, only 3 oocytes fertilized. The embryos were cultured to the blastocyst stage and an eSET was performed. The remaining blastocysts were cryopreserved. Pregnancy outcome is pending. If the patient does not conceive from this fresh or subsequent frozen cycle, ICSI would be performed on a subsequent fresh cycle due to the low fertilization yield. |
5. Bibliography

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