

# ISM1™



Prof. Yves Ménézo  
Inventor, ISM media series

*“ISM1™ is based on decades of research and refinement of media development. It is a very rich cleavage-stage medium which fully supplies the embryo with the elements required for good metabolic and physiological function. ISM1™ is designed to imitate the micro environment and to reduce in vitro culture stress. It contains components such as glucose and derived metabolites, amino acids, nucleotides, vitamins, and cholesterol. ISM1™ is the first commercially available cleavage-stage culture medium to include the sulphur amino acid methionine required for methyl transfer in the vital genomic imprinting process.”*

Prof Ménézo has been associated with ART for more than 30 years. He was the first to gain a successful pregnancy following blastocyst culture & transfer and the first to formulate a commercially available blastocyst culture medium (Menezos' B2) in the early 90's. ISM1™ was launched in 2001 and has since proven its worth as a successful culture medium worldwide.

# Fertilization and Culture: Which medium to choose?

Introduced more than 20 years ago, Universal IVF Medium has become one of the most popular and tested IVF media on the market. Culture media have since advanced into richer, more composite products, optimized towards human embryo physiology and development.

A modern culture medium, such as ISM1™, is a complex fluid supplying amino acids, nucleotides, vitamins, and metabolites adjusted specifically to each stage in embryo development.

## Mimicking nature - what does the embryo need?

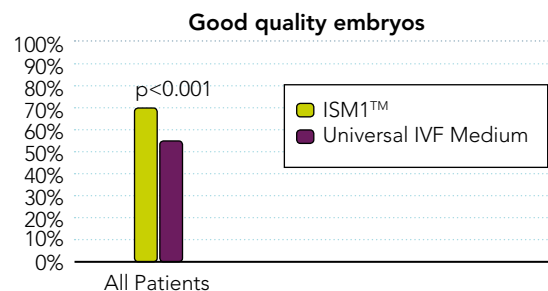
High glucose is optimal for fertilization, but not optimal for Day2- Day3 culture, since the embryo is unable to properly metabolise glucose at this time. ISM1™ is a complex, low-glucose medium, giving significantly better culture conditions for the embryo (e.g. Gardner et al 2004)

## ISM1™ best for culture, Universal IVF Medium best for fertilization

### Multicenter sibling study comparing fertilization and culture in Universal IVF Medium and ISM1™ (Erb et al 2004)

Result:  
Significantly better fertilization rates in Universal IVF Medium  
Significantly more 'good quality' embryos for both fresh transfer and cryo in ISM1™.

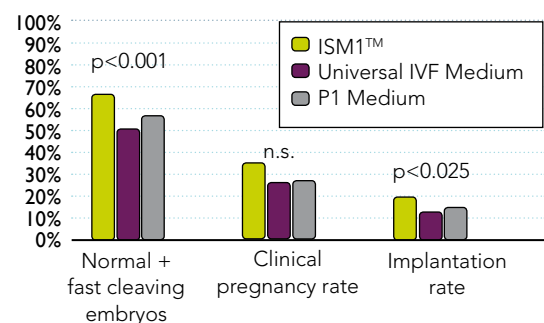
n=216 cycles



### Comparison of fertilization and culture in Universal IVF Medium, ISM1™, and P1 Medium (Michaeli et al 2007)

Result:  
Significantly higher fertilization in Universal IVF Medium.  
Significantly higher implantation rate and percentage of normal/fast cleaving embryos in ISM1™.

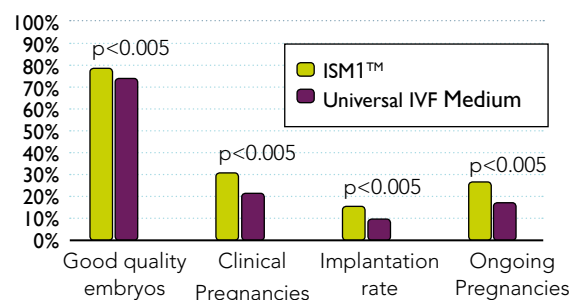
n=732 cycles



### Comparison of culture in Universal IVF vs. ISM1 (Xella et al 2009)

Result:  
Significantly more good-quality embryos, ongoing pregnancy rates, and implantation rates in ISM1™.

n=726 cycles



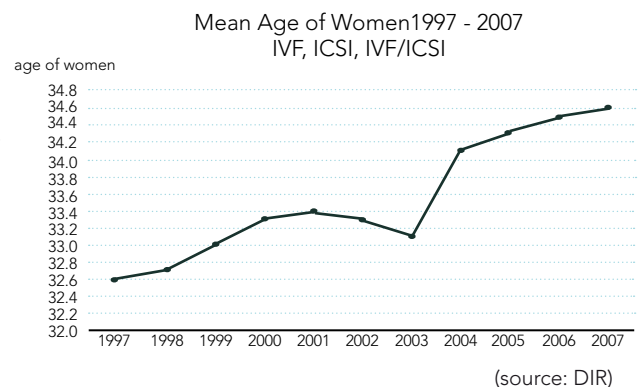
# Aging women: The battle of IVF

## Age at time of IVF treatment is rising in Germany

Women are born with a fixed pool of oocytes, and with age, esp >35yrs, there is a progressive decline in biochemical regulatory functions of the aging oocyte, including mitochondrial function and depletion of the endogenous pool of amino acids. This is the major factor in fertility decrease with age.

Essential amino acids are often omitted from cleavage-stage media, f.ex. Methionine, an essential sulphur amino acid involved in genomic methylation and imprinting.

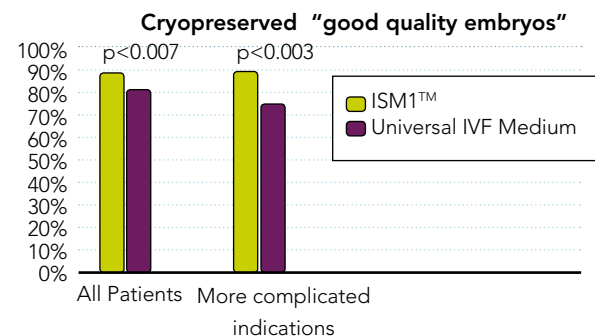
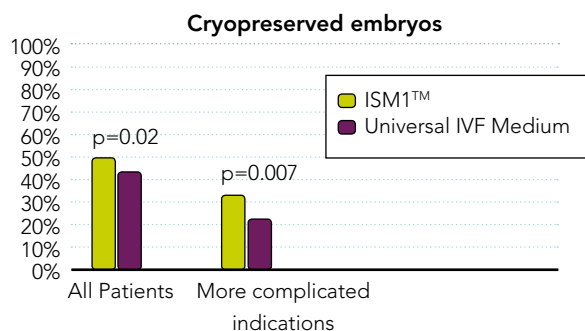
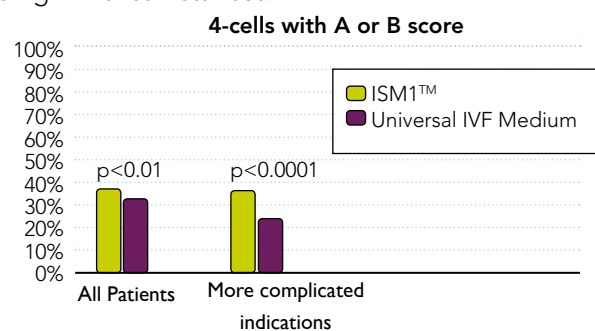
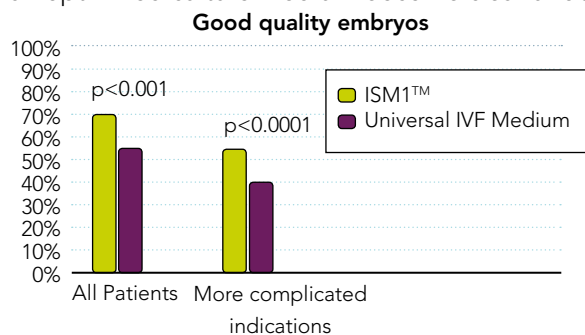
ISM1™ is a rich cleavage-stage medium containing high levels of pyruvate and both essential and non-essential amino acids - including methionine – thus supplying factors that are vital to aging oocytes.



## Multicenter sibling study comparing Universal IVF Medium and ISM1™ (Erb et al 2004)

Data analysed for "complicated indications" (= older women 38-42yr + anovulation, endometriosis, unexplained infertility.)

The significant improvement of ISM1™ is even greater in patients with complicated indications. The benefits of an optimized culture medium become clear under demanding IVF circumstances.



## Culture tips

- Monitor pH** pH may vary between media according to medium composition and buffer strength. Confirm regularly that your incubator CO<sub>2</sub> reading is correct, and that the pH level in each medium is within range. Outlying pH values may impede embryo development.
- Low O<sub>2</sub>** Recent studies are finally confirming that reduced oxygen tension (~5%) improves developmental competence of embryos (references available from ORIGIO.)
- Incubators** Every opening of incubator door involves a lengthy relapse time of temperature, CO<sub>2</sub>, and Relative Humidity equilibration. Use of mini incubators (single patient incubators) reduces these issues.

# Statements from clinics

Marc Van den Bergh, Certified Senior Clinical Embryologist, Leiter Fertilitätslabor - IVF Laboratory Director, Kantonsspital Baden A.G.

*"Under the supervision of my promoter Prof. Ménézo I composed for several years my own "In House" sequential media, which enabled me to measure the glycolytic activity of the human blastocyst between day 4 and 5. When stricter quality control regulations were needed to obtain the ISO certification of our laboratory, it was from the beginning clear that MediCult produced the media corresponding closely to my vision of "embryo culture with high performances".*

*Since we introduced in 2005, ISM1™ in combination with the Universal IVF Medium we were able to keep our clinical pregnancy rate continuously 3 to 5% above the Swiss national mean as published by the Swiss National IVF Register."*

Dr. med. Peter Fehr and Brigitte Greutmann, Zentrum für Reproduktionsmedizin, Schaffhausen

*"For years we use ISM1™ as culture medium for cryocycles. The embryo quality we observe as well as the pregnancy rates did convince us."*

Vera Baukloh, Partnerschaftsgesellschaft Drs. Fischer, Naether, Rudolf, Hamburg

*" The use of ISM1™ (from the end of 2006 on) increased our pregnancy rate per transfer slightly but significantly. This fact was especially obvious in cases with subsequent culture periods of more than three days where this increase reached almost 20%."*



Lars Johansson, Ph.D.E, MSc.CE  
Director of embryology, ORIGIO a/s

*" Since the introduction of ISM1™ in our center, in 2004 the percentage of top quality embryos ( $p < 0.001$ ), cryopreserved embryos ( $p < 0.0001$ ) and implantation rates were substantially increased ( $p < 0.001$ ) and the ongoing pregnancy rates was almost doubled from 31 to 51%. The patients we treated were severe male factor (100%) combined with obese women, within all age groups (40-60%), which even further strengthened my belief in the quality of ISM1™."*

## References & Further reading

- Erb, K et al 2004: A multicenter study comparing sibling oocytes cultured in ISM1™ versus Universal IVF Medium". Study available from ORIGIO.
- Fechtali et al 2004: Comparison of two embryos culture media in IVF and ICSI therapy, Abstracts of the 20th Annual Meeting of the ESHRE, Berlin, Germany, i147
- Gardner et al (Ed.) 2004: Textbook of Assisted Reproductive Techniques, Laboratory and Clinical Perspectives, Taylor & Francis
- Michaeli et al 2007: In vitro fertilization outcome using three types of culture media containing different concentrations of glucose for developing cleavage stage embryos. A comparative study. *Fertility and Sterility* 88(suppl 1): S324
- Steele et al 2006: Comparison of MediCult Sequential Medium ISM1 with Non-Sequential Universal IVF Medium in an IVF/ICSI Programme. *British Fertility Society Summer College, Oral communication (OC12)*.
- Xella et al 2009: Embryo quality and implantation rate in two different culture media: ISM1 versus Universal IVF Medium. *Fertility and Sterility (epub ahead of print)*

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