RECURRENT FAILURE IN IVF

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ART FERTILITY CLINICS

Science Assisting Nature

STEPS TO ACHIEVE A PREGNANCY WITH IVF

ART CYCLE

ACCURATE DIAGNOSIS
To provide a tailored treatment

+

OVARIAN STIMULATION
To provide multiple gametes

+

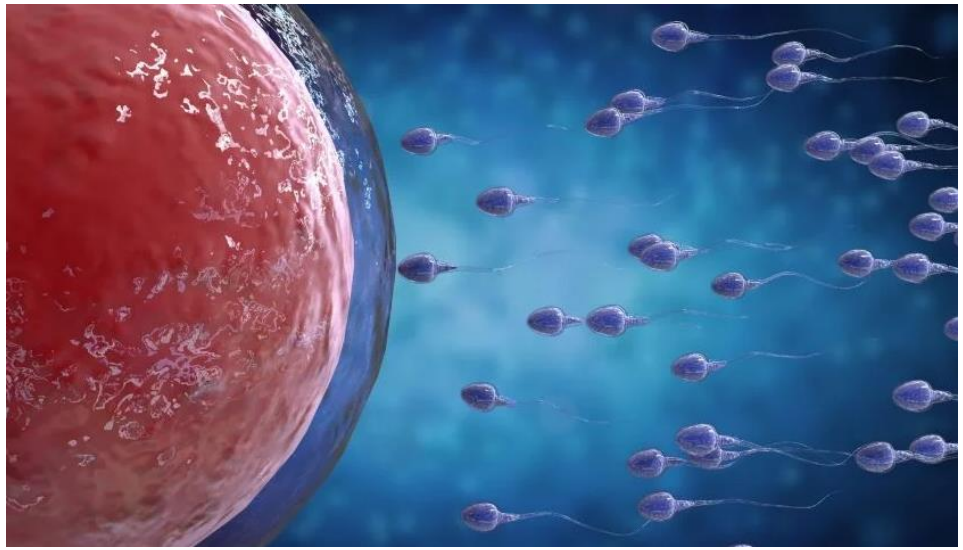
LABORATORY PROCEDURES
for fertilization and embryo development

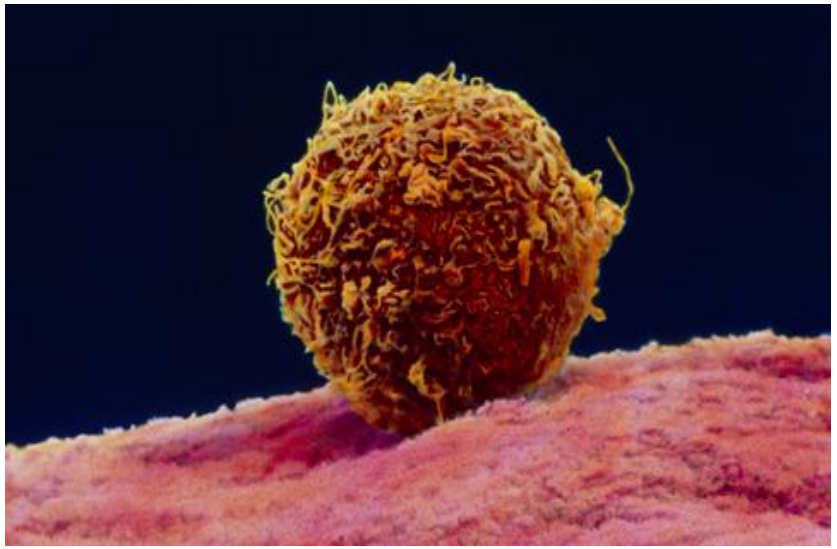
+

EMBRYO TRANSFER

+

LUTEAL PHASE SUPPORT





Suboptimal performance at any step decreases the chances of implantation and live birth.

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Ata et al, F&S 2021.

RECURRENT IMPLANTATION FAILURE (RIF): Difficult to Define and Less Common than assumed.

Despite numerous publications regarding RIF there is as yet no universally accepted definition.

Simon et al, JARG 2012, Das et al, F&S 2012.

As embryo quality, screening, and selection have improved, it is rightfully expected that success would be attained more quickly and that insights into an especially recalcitrant group might be identified after a lower threshold of transfers.

DEFINITION OF RIF

Failure to achieve a clinical pregnancy after transfer of at least **four good-quality embryos** (based on **morphological assessment**) in a minimum of three fresh or frozen cycles in a woman <40 years of age.

Coughlan C et al, RBMO 2014.

Perseveration is essential for success in the battle with infertility.

Somigliana et al, 2022.

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MAIN REASON FOR IVF FAILURE

EMBRYO ANEUPLOIDY (missing or extra chromosomes) is the most common cause of treatment failure.
Leading cause of embryo **developmental arrest**, **implantation failure**, and **miscarriage**.

Pirtea et al, F&S 2021.

TABLE 2

Blastocyst euploidy rates with comprehensive chromosome analysis according to female partner's age.

Study	< 35 y	35–37 y	38–40 y	41–42 y	> 42 y
Ata et al. 2012 (4)[a]	60%–63%	51%–55%	36%–39%	21%–25%	13%–17%
Demko et al. 2016 (6)[b,c]	60%	55%	45%	35%	20%
Barash et al. 2017 (3)[c]	62%	57%	44%	30%	
Hong et al. 2019 (7)[d]	74%	65%	47%	29%	15%
Irani et al. (5) 2020	55%	45%	32%	18%	8%

Note: [a]Published and unpublished data.
[b] Figures for only day five embryos.
[c] Based on approximations from the published figures and graphs in the original publications.
[d] Only women who underwent ovarian stimulation are included in the table.

Ata. Recurrent implantation failure. Fertil Steril 2021.

The aneuploidy rate in humans is very high.
Almost half of blastocysts are aneuploid, even in women under 35 years of age.
And the percentage increases with female's age.

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Barash et al, HR 2017. Ata et al, RBMO 2012. Irani et al HR 2020. Denko et al, F&S 2016. Hong et al, F&S 2019.

IMPLANTATION AND LIVE BIRTH RATE WITH EUPLOID EMBRYOS

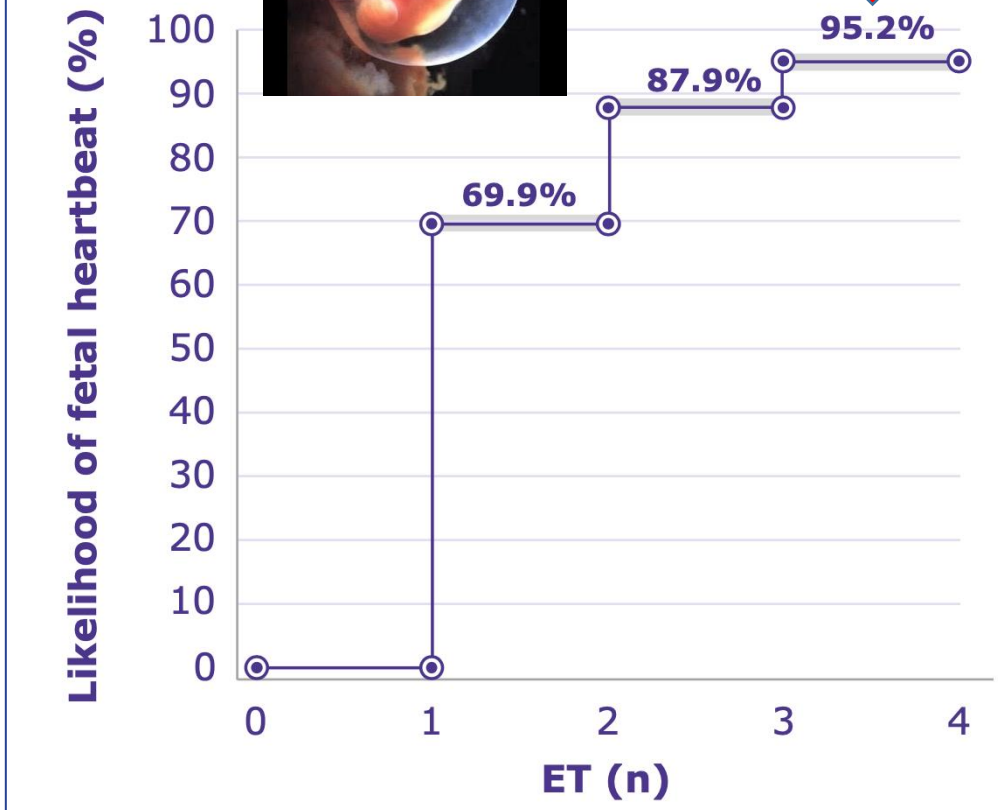
Rate of true recurrent implantation failure is low: results of three successive frozen euploid single embryo transfers

Paul Pirtea, M.D.,[a,b] Dominique De Ziegler, M.D.,[b] Xin Tao, Ph.D.,[c] Li Sun, Ph.D.,[c] Yiping Zhan, Ph.D.,[c] Jean Marc Ayoubi, M.D.,[b] Emre Seli, M.D.,[a,d] Jason M. Franasiak, M.D., H.C.L.D.,[a] and Richard T. Scott Jr., M.D., H.C.L.D.[a]

[a] IVIRMA New Jersey, Basking Ridge, New Jersey; [b] Hospital Foch, Paris, France; [c] Foundation for Embryonic Competence, Basking Ridge, New Jersey; and [d] Yale School of Medicine, New Haven, Connecticut

THE CHANCES OF LIVE BIRTH AFTER SINGLE EMBRYO TRANSFER OF EUPLOID EMBRYOS (correct number and healthy chromosomes) IS VERY HIGH!







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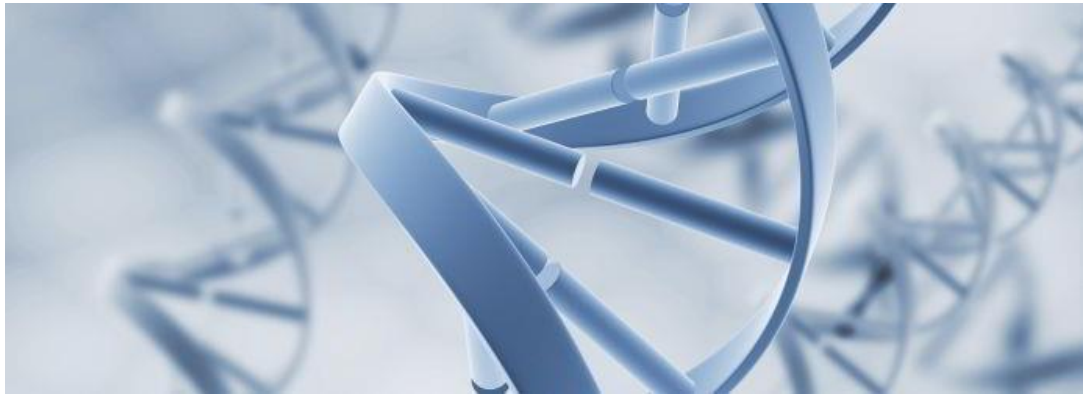
Pirtea et al. True Rate of RIF. F&S 2020.

RIF IS <5% AFTER 3 EUPLOID EMBRYO TRANSFERS

Most RIF are of **embryonic origin** which can be minimized by transferring **euploid** embryos



Low percentage of endometrial origin.
Receptivity and various therapies offered to women are expensive and not supported by scientific evidence.

Pirtea et al, F&S 2020.

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THE SOLUTION: PGT-A

- **Higher Pregnancy Rates** per transfer
- **Reduced Miscarriage Rates**
- **Reduced risk of abnormal offspring**
- Fewer wasted transfers (Implantation Faillure)
- Decreased time to pregnancy
- Optional **Single Embryo Transfer** (SET), reducing the likelihood of a multiple-gestation pregnancy.



Greater chance of having a healthy child in shorter time.

Tiegs et al, F&S 2020.

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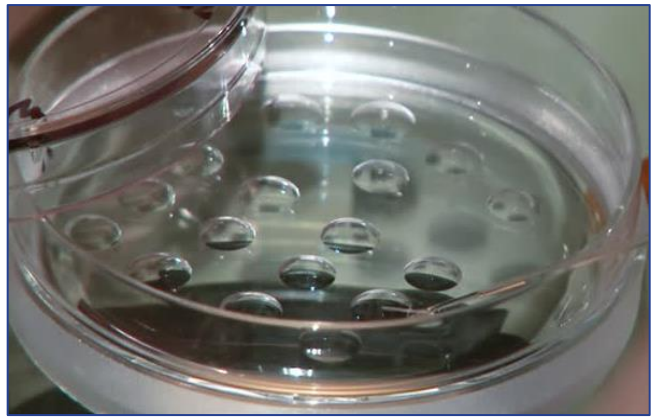
ART: PROVIDING THE BEST RESULTS

The latest IVF lab technology for optimal embryo quality and PGT-A outcomes. Highly specific biopsy techniques to control the variables impacting PGT-A outcomes, for maximum celular integrity and better outcomes.



Embryo culture media



Time-lapse incubators



Vitrification

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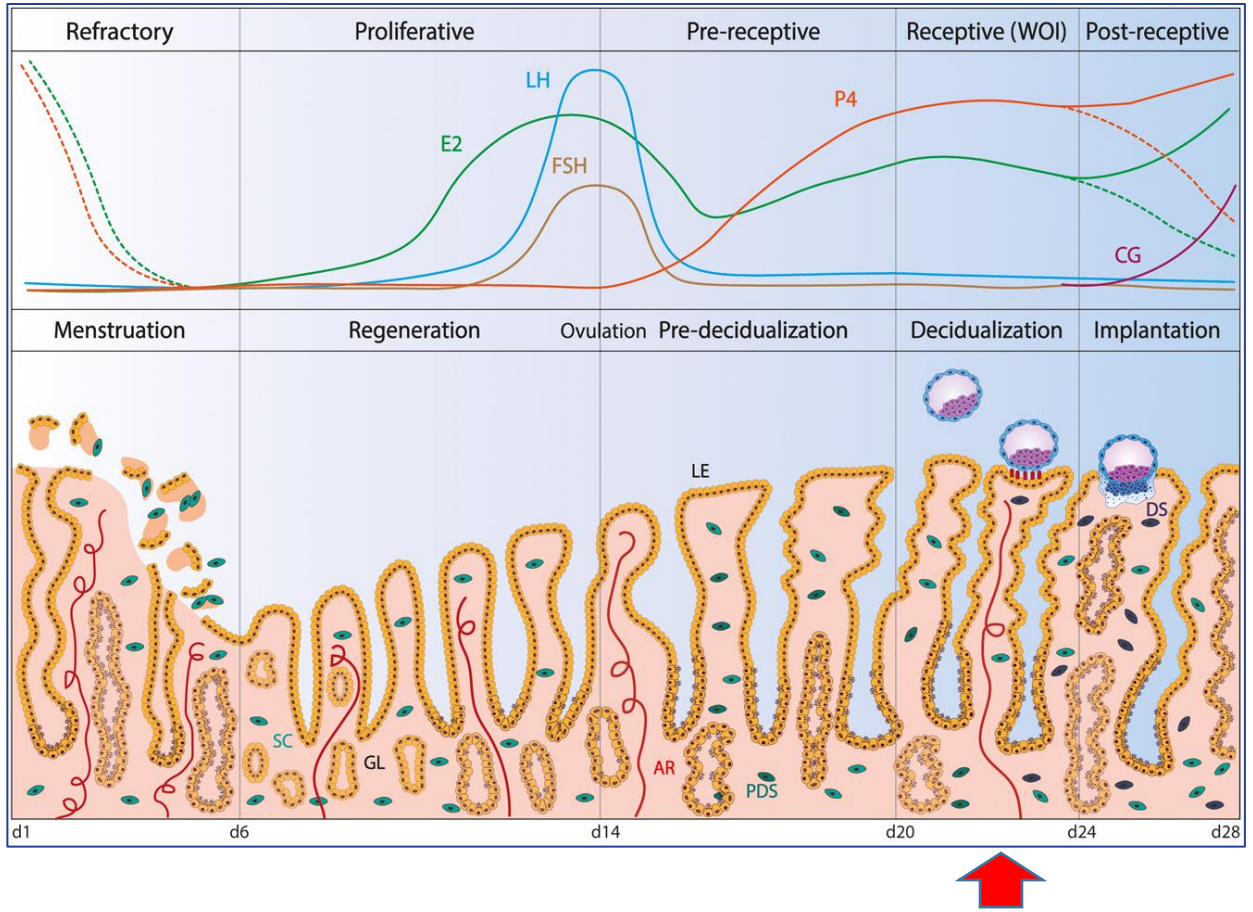
Capalbo et al, HR 2015. Fragouli et al, 2017. Swain et al, 2019. Rubio et al, F&S, 2019. Xiong et al, JARG 2021. Herrero et al, ESHRE 2019. Guzman Masias et al, ESHRE 2019.

The Timing of EMBRYO TRANSFER is Very Critical to a Successful Pregnancy



TO IDENTIFY THE WINDOW OF IMPLANTATION (WOI)

An embryo can implant only when the endometrium is receptive during the restricted WOI, which has unique histology, morphology and bulk tissue gene and protein signatures

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Wang et al, Nat Med 2020.

Our Proprietary EMBRYO TRANSFER protocol offers the highest successs rates

Highest implantation rates with FROZEN EMBRYO TRANSFER and NATURAL CYCLE PROTOCOL

GYNECOLOGICAL ENDOCRINOLOGY
https://doi.org/10.1080/09513590.2020.1740918

Taylor & Francis
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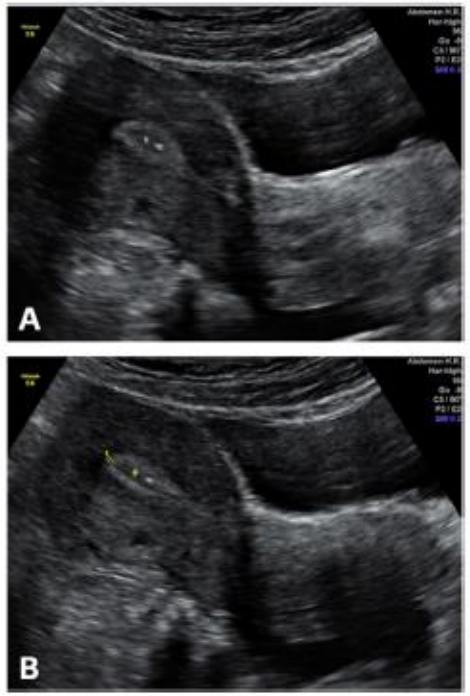
REVIEW ARTICLE

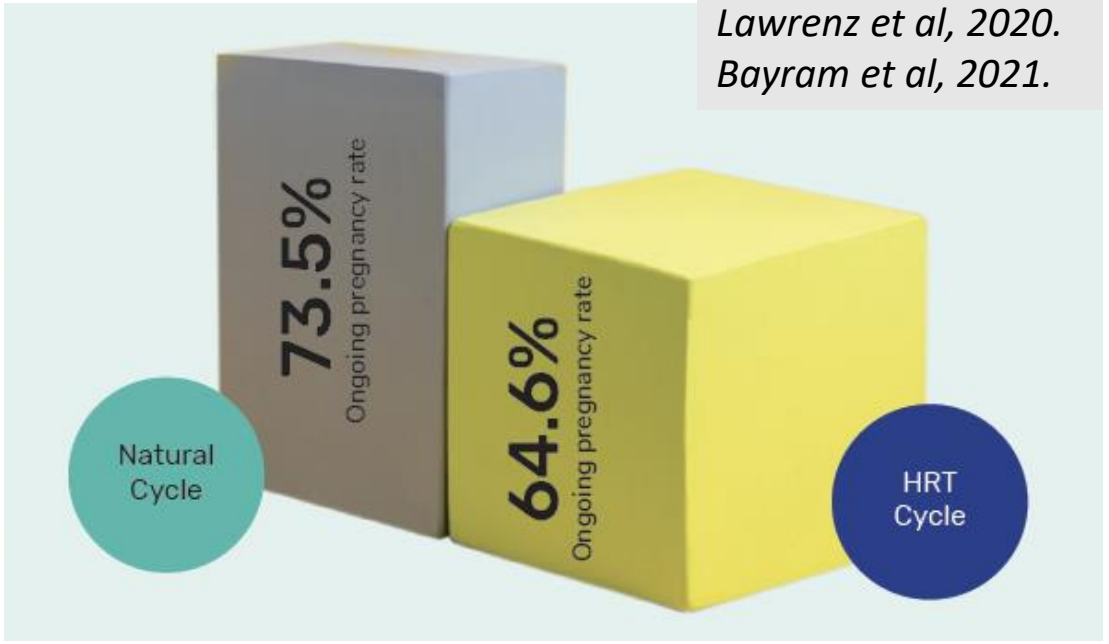
Check for updates

The ART of frozen embryo transfer: back to nature!

Barbara Lawrenz[a,b], Carol Coughlan[a], Laura Melado[a] and Human M. Fatemi[a]

[a]IVF Department, IVIRMA Middle-East Fertility Clinic, Abu Dhabi, United Arab Emirates; [b]Obstetrical Department, Women's university hospital Tuebingen, Tuebingen, Germany





Lawrenz et al, 2020.
Bayram et al, 2021.

1 RBMO VOLUME 00 ISSUE 0 2021

RBMO

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ARTICLE

The position of the euploid blastocyst in the uterine cavity influences implantation



BIOGRAPHY

Aşina Bayram received her Master of Science in Molecular Medicine from Yeditepe University in 2015 and Bachelor Degree in Molecular Biology and Genetics from Bogazici University in 2003. Since 2015, she has been working in ART Fertility Clinic, Abu Dhabi as a senior embryologist. Her primary research interests include embryology and reproductive biology.

Aşina Bayram[1,*], Neelke De Munck[1], Ibrahim Elkhatib[1], Ana Arnanz[1], Ahmed El-Damen[1], Andrea Abdala[1], Carol Coughlan[2], Nicolas Garrido[3], Laura Melado Vidales[1], Barbara Lawrenz[1,4], Human M. Fatemi[1]

KEY MESSAGE

The depth of embryo replacement inside the uterine cavity influences the pregnancy and clinical pregnancy rates as well as the implantation potential, and should be considered as an important factor to improve the success of IVF cycles.

The embryo transfer is a critically important procedure.

The best professionals (doctors and embryologist) for a smooth and precise procedure will deliver the best outcomes.

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ART: GETTING THE BEST OUTCOMES

ART CYCLE

ACCURATE DIAGNOSIS
To provide a tailored treatment

+

OVARIAN STIMULATION
To provide multiple gametes

+

LABORATORY PROCEDURES
for fertilization and embryo development

+

EMBRYO TRANSFER

+

LUTEAL PHASE SUPPORT

TAILORED PROTOCOLS → **LATEST TECHNOLOGY AND PGT-A with NGS** → **PERSONALIZED EMBRYO TRANSFERS**


frontiers in Endocrinology

Step-Down of FSH- Dosage During Ovarian Stimulation – Basic Lessons to Be Learnt From a Randomized Controlled Trial


Gynecological Endocrinology

Luteal phase serum progesterone levels after GnRH-agonist trigger - how low is still high enough for an ongoing pregnancy?

B. Lawrenz, S. Samir, L. Melado, F. Ruiz & H.M. Fatemi


GYNECOLOGICAL ENDOCRINOLOGY
https://doi.org/10.1080/09513590.2020.1740918

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REVIEW ARTICLE

The ART of frozen embryo transfer: back to nature!

Barbara Lawrenz[a,b], Carol Coughlan[a], Laura Melado[a] and Human M. Fatemi[a]

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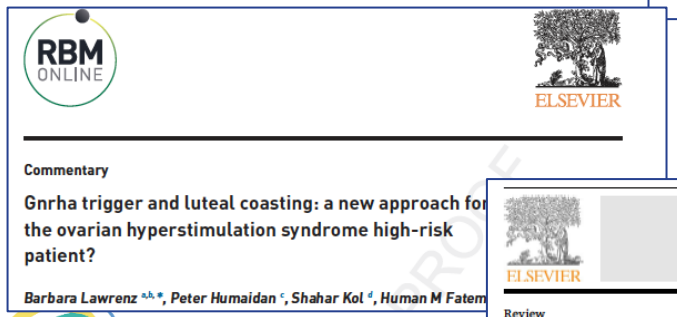
RBM ONLINE

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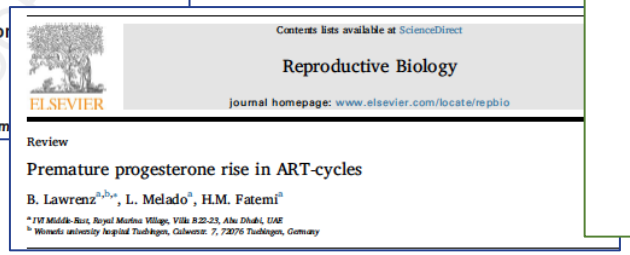
Commentary

Gnrha trigger and luteal coasting: a new approach for the ovarian hyperstimulation syndrome high-risk patient?

Barbara Lawrenz [a,b,*], Peter Humaidan [c], Shahar Kol [d], Human M Fatem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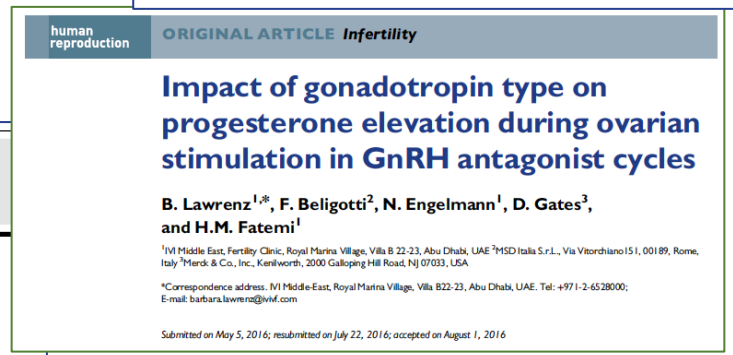
Review

Premature progesterone rise in ART-cycles

B. Lawrenz[a,b,*], L. Melado[a], H.M. Fatemi[a]


human reproduction ORIGINAL ARTICLE *Infertility*

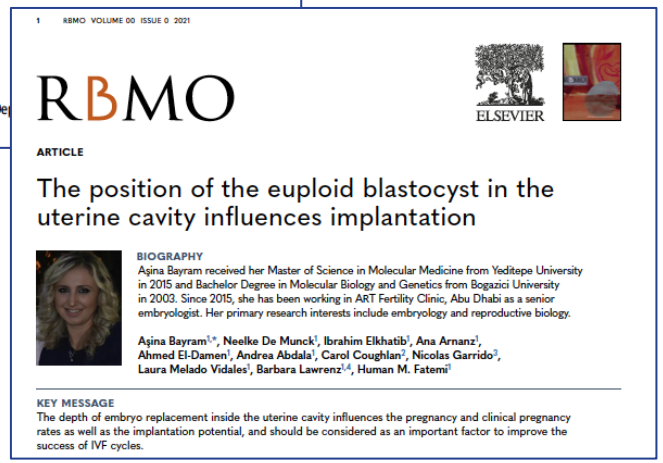
Impact of gonadotropin type on progesterone elevation during ovarian stimulation in GnRH antagonist cycles

B. Lawrenz[1,*], F. Beligotti[2], N. Engelmann[1], D. Gates[3], and H.M. Fatemi[1]

[1]IVI Middle East, Fertility Clinic, Royal Marina Village, Villa B 22-23, Abu Dhabi, UAE [2]MSD Italia S.r.L., Via Vitorchiano 151, 00189, Rome, Italy [3]Merck & Co., Inc., Kenilworth, 2000 Galloping Hill Road, NJ 07033, USA

*Correspondence address. IVI Middle-East, Royal Marina Village, Villa B22-23, Abu Dhabi, UAE. Tel: +971-2-6528000; E-mail: barbara.lawrenz@ivif.com

Submitted on May 5, 2016; resubmitted on July 22, 2016; accepted on August 1, 2016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Thank You



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