

Together. All the way™

# More babies born with EmbryoGlue

Proven to increase clinical pregnancy rate and live birth rate when used for embryo transfer<sup>1</sup>



# EmbryoGlue for successful transfer

Embryo transfer is one of the most sensitive and critical procedures in IVF treatment. EmbryoGlue®, a hyaluronan-rich transfer medium, is designed to promote embryo implantation. Few interventions in embryo transfer have improved the success rate as significantly as EmbryoGlue according to the clinical evidence<sup>2</sup>. EmbryoGlue has been shown to promote successful implantation and increase the pregnancy and live birth rate without increasing the risk of adverse events<sup>1</sup>.



## What is it?

EmbryoGlue is a medium developed exclusively for embryo transfer and is the only existing transfer medium with a proven implantation-enhancing effect<sup>1</sup>. EmbryoGlue has the basic composition of a rich blastocyst culture medium and contains recombinant albumin and a high concentration of hyaluronan. It can be used for transfer of all embryo developmental stages, including cleavage embryos, blastocysts after assisted hatching, biopsied embryos and cryopreservation. The use of EmbryoGlue for embryo transfer can increase the clinical pregnancy rate and live birth rate<sup>1</sup>.



## How to optimise transfer

A meta-analysis from 2022 on transfer interventions showed that three methods stand out with positive outcomes in terms of clinical pregnancy rate and with significant clinical evidence for their effectiveness<sup>2</sup>.

- 1 Hyaluronic acid-enriched media (EmbryoGlue)
- 2 Ultrasound guidance
- 3 Soft transfer catheter

# The proven effectiveness of EmbryoGlue

Since the market introduction of EmbryoGlue in 2003, multiple studies have been published regarding its effectiveness. Three reviews on the effect of hyaluronan in transfer media have been published by the Cochrane Library in 2010, 2014, and 2020.

The Cochrane Review in 2020 on "Hyaluronic acid in embryo transfer media for assisted reproductive technologies" by Heymann et al. concludes:

“Moderate-quality evidence shows improved clinical pregnancy and live birth rates with the addition of hyaluronic acid as an adherence compound in embryo transfer media in ART”

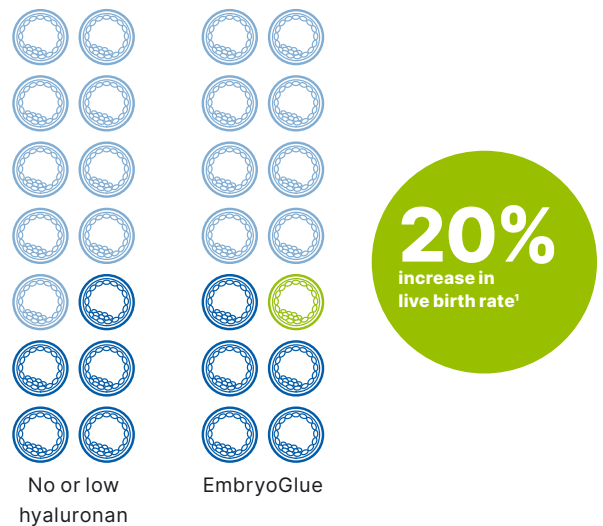
The miscarriage rate was reduced in some studies but did not reach statistical significance in the total data set. The review includes a total of 26 randomized, prospective, controlled trials including a total of 6704 patients undergoing IVF/ICSI treatment. The embryo transfers were performed in either a transfer medium containing no or a low concentration of hyaluronan or EmbryoGlue with a high concentration of hyaluronan.

## What is the clinical outcome of using EmbryoGlue?

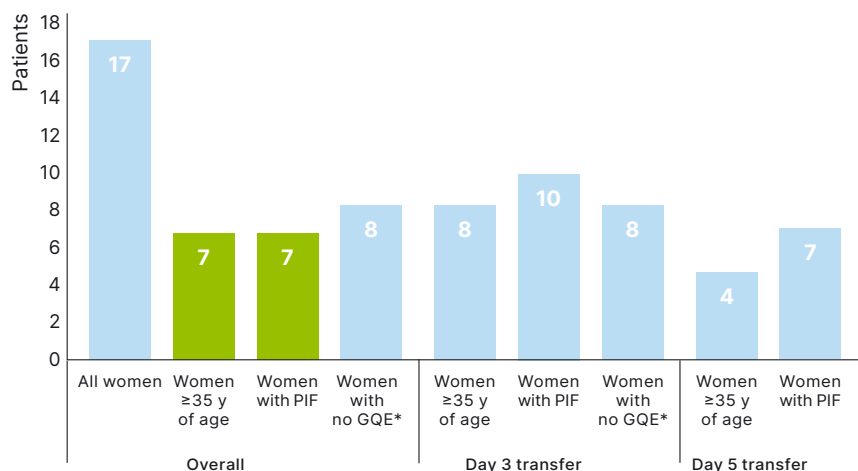
The live birth rate increased from 33.3% to 40.2% with the use of EmbryoGlue. According to a number needed to treat (NNT) calculation, based on the Cochrane Review, one additional live birth was achieved for every 14 transfers. For a clinic with 700 cycles annually, this is one additional baby born per week, or a 20% increase in live births<sup>1</sup>.

The number needed to treat varies between patient groups, and the strongest benefit is seen in women ≥35 years of age and women with Previous Implantation Failures (PIF)<sup>3</sup>.

### Number Needed to Treat = 14

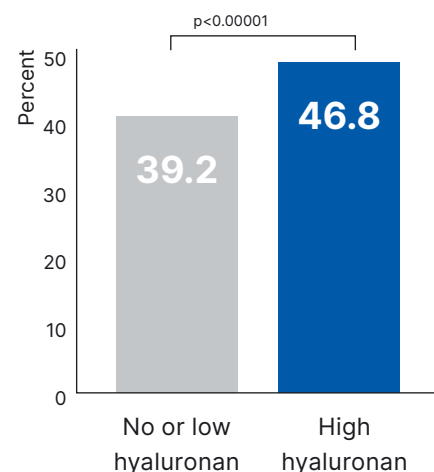


## Numbers Needed to Treat in different patient groups<sup>3</sup>



\*Good Quality Embryos

## Clinical pregnancy rate<sup>1</sup>



# How does it work?

EmbryoGlue is a transfer medium containing a high concentration of an implantation-promoting macromolecule, hyaluronan.

Hyaluronan is the main glycosaminoglycan present in follicular, oviductal, and uterine fluids and can significantly contribute to the high-viscosity environment of the female reproductive tract<sup>4,5,6,7</sup>.

The synthesis of hyaluronan increases dramatically on the day upon which implantation is initiated, and it decreases to near basal levels by the next day, indicating its importance for the implantation event. Other types of glycosaminoglycans do not show elevated synthesis at the time of implantation<sup>8,9</sup>.



## Possible mechanisms for the implantation-promoting effect of hyaluronan

### Improved adhesion

Hyaluronan is known to increase cell adhesion, and thus it can support the initial attachment of the blastocyst to the endometrium<sup>10</sup>.

### Rapid mixing with uterine secretions

Hyaluronan facilitates the rapid diffusion of the contents of the transfer medium into the viscous secretion of the uterus. An aqueous medium containing an appropriate concentration of hyaluronan produces a medium with a far higher viscosity in comparison to a solution only containing proteins. EmbryoGlue has the highest viscosity compared to other common transfer media<sup>11,12</sup>.

### Receptor cross-linking

The hyaluronan surface-adhesion receptor CD44 is present throughout development from the oocyte to the blastocyst stage<sup>12</sup>. The CD44 receptor is also expressed on human endometrial cells at the time of implantation<sup>13,14</sup>. Another type of hyaluronan receptor, RHAMM/IHABP, is also expressed on the embryo surface at the implantation stage, suggesting a possible receptor-mediated process where hyaluronan cross-links the receptors on the embryo and endometrial cells<sup>15</sup>.

// The inclusion of hyaluronan is not only associated with increased embryo development and viability, and there is also a distinct benefit of having hyaluronan in the transfer medium. From every perspective, the inclusion of hyaluronan in both culture and transfer media makes physiological sense, and the data clearly support multiple benefits to the embryo. //

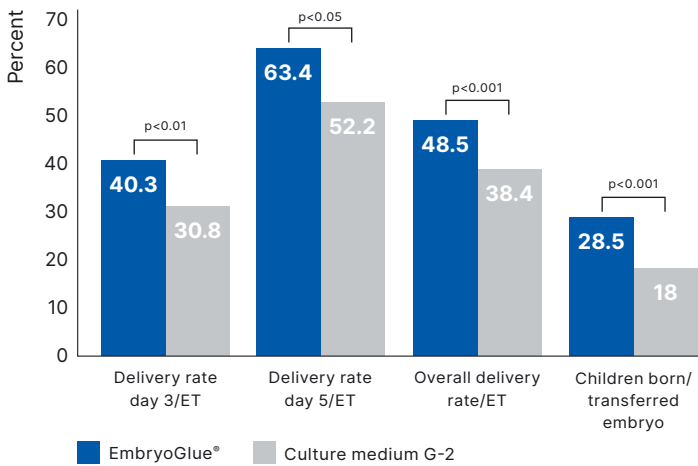
*Professor David Gardner, Distinguished Professor, School of BioSciences, University of Melbourne and Scientific Director, Melbourne IVF and the inventor of EmbryoGlue*



# EmbryoGlue is as safe as standard of care

When using an implantation-promoting medium, one may be concerned that embryos without the potential to become a healthy baby may implant; however, no increase in adverse events, such as early or late miscarriage, has been shown<sup>1,17,18</sup>. Due to the increase in implantation with EmbryoGlue, it is recommended to be used with a single embryo transfer policy<sup>1,17</sup>.

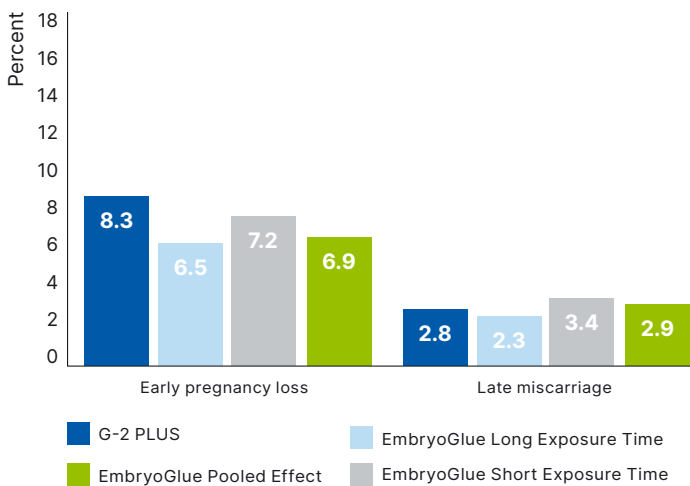
## Increased live birth rate in all development stages



In 2011 Balaban et al. performed a follow up study on pregnancies obtained by Urman et al. (2008), with the use of EmbryoGlue. The study included almost 1300 embryo transfers.

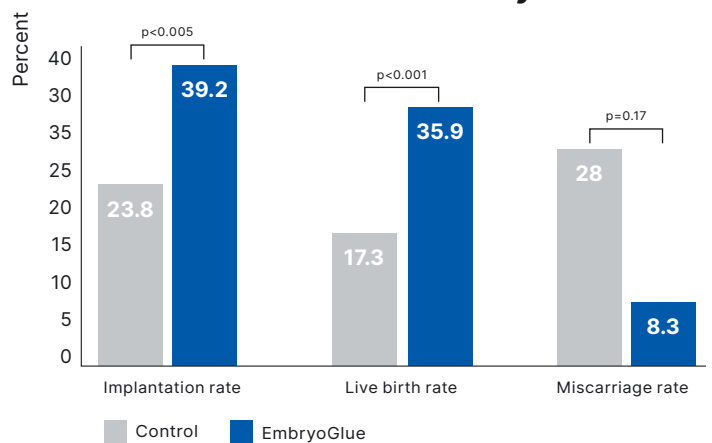
The results showed a significantly increased delivery rate with the use of EmbryoGlue independent of day of transfer<sup>3,19</sup>.

## No increase in pregnancy loss



Adeniyi et al. (2021) investigated a total of 3391 fresh embryo transfers in a study between 2011 and 2015 using three different protocols – low hyaluronic acid (G-2 PLUS), short (10-30 min) EmbryoGlue exposure, and long (2-4h) EmbryoGlue exposure. The purpose of the study was to assess the safety and efficacy of implementing EmbryoGlue as a transfer medium. The results showed no increase in pregnancy loss or miscarriage and an overall improvement in live birth events<sup>17</sup>.

## Outcomes of PCOS patients after fresh SET in EmbryoGlue



According to Kandari et al. (2019), the use of EmbryoGlue for time-lapse SET in women with PCOS significantly increases the implantation rate and live birth rate with lower miscarriage rates compared with conventional embryo transfer medium<sup>18</sup>.

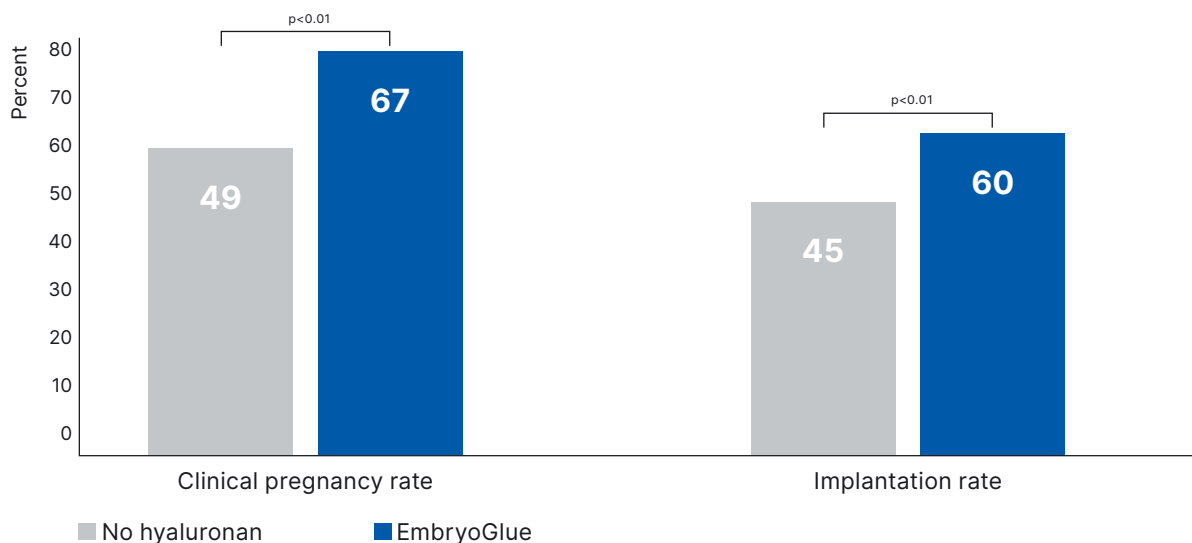
# PGT patients and EmbryoGlue - a perfect match

PGT (Preimplantation genetic testing) treatment requires a lot of time, effort, and resources in your clinic. The increased complexity is estimated to add six hours of working time for every cycle that includes genetic testing, which is the reason why you want to give your embryos the best chance of implantation.

Data indicates that PGT embryos benefits from being transferred in EmbryoGlue. A retrospective study showed the clinical outcomes from 830 transferred embryos (557 in the control group with no hyaluronan added and 273 transferred with EmbryoGlue). The data showed an increase in both implantation rate and clinical pregnancy rate<sup>20</sup>.

Patient groups offered PGT <sup>21,22</sup>	Patients groups benefiting most from EmbryoGlue <sup>3,23,24</sup>
<ul style="list-style-type: none"> <li>• Older patients &gt;35</li> <li>• Patients with previous implantation failure</li> <li>• Blastocyst transfer</li> <li>• Patients with recurrent miscarriage</li> </ul>	<ul style="list-style-type: none"> <li>• Older patients &gt;35</li> <li>• Patients with previous implantation failure</li> <li>• Blastocyst transfer</li> <li>• Transfer of cryo-preserved embryos/blastocysts</li> </ul>

## Frozen embryo transfers with PGT embryos



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The reintroduction of EmbryoGlue as the embryo transfer medium unexpectedly coincided with statistically significant improvements in clinical outcome metrics – chemical, clinical, and ongoing pregnancy - specifically for frozen embryo transfers in PGT cycles. Using EmbryoGlue as the transfer medium instead of buffered media proved to be simple, cost-effective, and clinically efficacious. //

*Dr Mike Reed, Laboratory Director at the Fertility Center of New Mexico, USA*

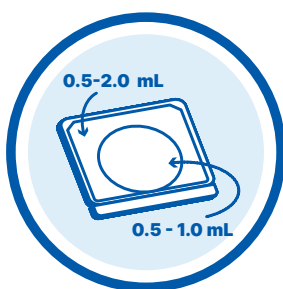


# EmbryoGlue is easy to use

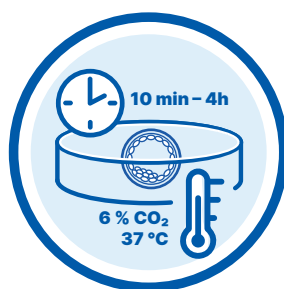
It is important to pay attention to the lab and transfer workflow in the clinic when using EmbryoGlue. Being a well-studied transfer medium, EmbryoGlue has more data on transfer optimisation than other products<sup>17,25</sup>. For transfer protocols, the preparation of dishes, embryo equilibration time, and catheter loading are important factors that can affect the results.

## 3 things to remember

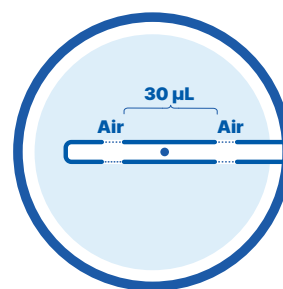
Follow the instructions for use to ensure stable osmolality, pH and temperature. Below are three important lab procedural steps to follow. Please contact your Vitrolife representative for clinical support.



Dish volumes



Embryo equilibration



Catheter loading

## Choose the size that best fits your clinic's needs

EmbryoGlue is available in two different sizes, 10 mL and a patient pack of 5 vials. The 5 × 1.5 mL kit is tailored for 5 transfers using 1 vial each. This single-use transfer solution offers added convenience and safety to an already superior product.

Product	REF	Description	Size
<b>Media for Embryo transfer</b>			
EmbryoGlue®	10085	Transfer medium	10 mL
EmbryoGlue® 5X1.5 mL	10168	Transfer medium	5 × 1.5 mL

Based on the regulatory status, not all products are available in all countries. Please contact your local sales representative for information on availability in your country.



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