

IVF Treatment Add-Ons

HFEA Traffic Light Rating

Green: <u>more than one good quality RCT</u> which shows that the procedure is effective and safe.

Amber: there is a <u>small or conflicting</u> body of evidence, which means further research is still required and the technique cannot be recommended for routine use.

Red: if there is <u>no evidence</u> to show that is safe and effective

More information: https://www.hfea.gov.uk/treatments/treatment-add-ons/

Hyaluronate enriched medium (Embryo Glue) is rated amber

What is Hyaluronate enriched medium (Embryo Glue)?

Hyaluronate enriched medium contains a substance called hyaluronan, which may improve the chance of the embryo implanting in the womb. It is added to the solution in the dish in which the embryos are kept before being transferred to the patient. Embryo glue is an example of a Hyaluronate enriched medium.

Are there any risks?

There are no known risks from using Hyaluronate enriched medium (Embryo Glue).

What is the evidence for Hyaluronate enriched medium?

At the October 2019 Scientific and Clinical Advances Advisory Committee (SCAAC) meeting the Committee evaluated the evidence base for Hyaluronate enriched medium. Minutes of this discussion and the evidence used to inform this discussion is available <u>here</u>.

There is one high quality study in this review which shows that the use of Hyaluronate enriched medium improves live birth rates, other studies in the review were of moderate quality. Further high-quality studies are needed



before doctors can be confident of the benefits of Hyaluronate enriched medium. <u>https://www.vitrolife.com/products/ivf-media--oil/embryoglue/</u>



Time-lapse imaging (embryoscope) is rated amber

What is time-lapse imaging (embryoscope)?

In IVF, time-lapse imaging (embryoscope) is used to help select the embryos most likely to develop into a baby.

In conventional IVF, the embryologist will check the developing embryos each day under a microscope, which involves removing them from the incubator for a brief period.

Time-lapse imaging (embryoscope) allows the embryologist to take thousands of images of the embryos as they grow without disturbing them. Not only does this mean the embryos do not have to be removed from the incubator, it also allows the embryologist to get a continuous view of each embryo as it develops, rather than just viewing them once a day.

The embryologist can then choose a specific embryo for implantation based on criteria such as rate of development and the number and appearance of cells.

Are there any risks?

No, there are no known risks to the woman or her embryos from time-lapse imaging (embryoscope).

What is the evidence for time-lapse imaging?



At the June 2018 Scientific and Clinical Advances Advisory Committee (SCAAC) meeting the Committee evaluated the evidence. <u>Minutes of the June 2018 discussion and the evidence used to inform this discussion are available here</u>.

There have been various studies to try and see if time-lapse imaging can improve birth rates. Initial research has shown some promise, but it's still very early days.

Indeed, being undisturbed while they grow may improve the quality of the embryos but there's certainly not enough evidence to show that time-lapse imaging improves your chance of having a baby, which is something you may want to consider if it's being offered to you at an extra cost. https://www.vitrolife.com/products/time-lapse-systems/embryoscope-time-laps e-system/

This Cochrane review has further information on the evidence for time-lapse imaging.





Improved ongoing pregnancy rate and live birth rate¹



Early pregnancy loss reduced¹





IMSI is rated red

What is IMSI?

Intracytoplasmic morphologically selected sperm injection (IMSI) is an advanced sperm selection method similar to that used in intracytoplasmic sperm injection (ICSI). The IMSI technique involves using a microscope to view sperm under very high magnification (over x6000). This allows clinics to view detailed images of sperm.

Are there any risks?

IMSI is a non-invasive test performed on a semen sample as an additional step in the ICSI process. The risks associated with the use of ICSI also apply to IMSI; there are no significant additional risks to the patient or embryo.

Find out more about ICSI

What is the evidence for IMSI?

At the October 2019 Scientific and Clinical Advances Advisory Committee (SCAAC) meeting the Committee evaluated the evidence base for IMSI. Minutes of this discussion and the evidence used to inform this discussion is available <u>here</u>.

There have been several Randomised Controlled Trials (RCT) within the last decade. Systematic reviews suggest that IMSI could be beneficial in specific situations such as previously failed ICSI attempts. The research that has been carried out does not support the use of IMSI over standard ICSI. One small study found that IMSI had improved pregnancy outcomes in older patients, however this study was carried out with a small number of participants and the link, if any, between IMSI and older eggs is not fully understood.





PICSI is rated red

What is PICSI?



Physiological intracytoplasmic sperm injection (PICSI) is a technique used to select sperm to use in Intracytoplasmic sperm injection (ICSI) treatment. It involves placing sperm with hyaluronic acid (HA), a natural compound found in the body. PICSI identifies sperm that can bind to HA and these sperm are selected for use in treatment.

Are there any risks?

PICSI is a non-invasive procedure performed on a semen sample as an additional step in the ICSI process. Risks associated with the use of ICSI also apply to PICSI; there are no significant additional risks to the patient or embryo.

Find out more about ICSI

What is the evidence for PICSI?

At the October 2019 Scientific and Clinical Advances Advisory Committee (SCAAC) meeting the Committee evaluated the evidence base for PICSI. Minutes of this discussion and the evidence used to inform this discussion is available <u>here</u>.

There have been several studies comparing PICSI with standard ICSI, but there is very little evidence to suggest any benefit of using it. A large RCT was recently carried out which showed that using PICSI did not increase the chances of having a baby.

The results of this large RCT did suggest that PICSI may be beneficial in relation to a potential reduction in miscarriage. It is important to keep in mind that this evidence was the secondary outcome, that is, it was not the aim of this research. This means that the study was not designed to investigate the effect of PICSI on miscarriage rate, making these secondary results less reliable. For this reason it is important to discuss your individual circumstances with your doctor.





Assisted hatching is rated red

What is assisted hatching?



The egg and early embryo are surrounded by a thick layer of special proteins called the zona pellucida. Before an embryo can implant in the womb it has to break out or 'hatch' from its zona pellucida. Some people think that assisted hatching - using acid, lasers or other tools to thin or make a hole in the zona pellucida - helps the embryo to 'hatch'.

Are there any risks?

There is always some risk of damaging embryos with these types of procedures.

What is the evidence for assisted hatching?

At the October 2019 Scientific and Clinical Advances Advisory Committee (SCAAC) meeting the Committee evaluated the evidence base for assisted hatching. Minutes of this discussion and the evidence used to inform this discussion is available <u>here</u>.

<u>The National Institute for Clinical Excellence (NICE)</u> is the national body advising doctors on treatments. It says:

"Assisted hatching is not recommended because it has not been shown to improve pregnancy rates."

NICE also says that further research is needed to find out whether assisted hatching influences birth rates and to examine the consequences for children born as a result of this procedure.



Some clinics believe assisted hatching can lead to higher birth rates in specific subgroups of patients. There is however no good quality evidence to support the use of assisted hatching for any patient.



Artificial egg activation calcium ionophore is rated amber



What is egg activation?

When a sperm meets an egg, it triggers a process called 'egg activation' which starts off the process of embryo development, while at the same time allowing only one sperm to fertilise the egg. If the egg doesn't activate, then it won't develop.

Egg (or oocyte) activation may be stimulated by chemicals called calcium ionophores. These chemicals can be added to the embryo in the lab.

Are there any risks?

In theory, egg activation using calcium ionophores could cause embryos to have abnormal numbers of chromosomes, which would cause the pregnancy to miscarry. Currently, there's not enough evidence to decide whether these risks are a serious concern.

Given the possible risks, clinics offering this treatment should only do so for selected patients who have had failed fertilisation and should be able to justify their reasons for doing so.



What is the evidence for egg activation?

At the October 2019 Scientific and Clinical Advances Advisory Committee (SCAAC) meeting the Committee evaluated the evidence base for egg activation. Minutes of this discussion and the evidence used to inform this discussion is available <u>here</u>.

In the few studies done to date, egg activation using calcium ionophores may improve fertilisation rates in ICSI cycles where the egg and sperm have failed to activate in previous treatment cycles. However, there are no RCTs to show that it is effective and there are no follow up studies on the safety of this technique.



The HFEA opinion on egg activation can be seen at:

https://www.hfea.gov.uk/treatments/treatment-add-ons/artificial-egg-activatio n-calcium-ionophore/