



FROM CONCEPT AND TEST-TUBE TO ROBOTICS: FIFTY YEARS OF ASSISTED REPRODUCTION RE-EVALUATED

DR. JACQUES COHEN^{1,2,3,4}

1: Professor Emeritus Conceivable Life Sciences, New York

2: IVF 2.0, Liverpool, UK

3: Laboratoire d'Immunologie, CHU de Reims, Hôpital Robert Debré, Reims, France

4: Université de Reims Champagne Ardenne URCA, Reims, France

The evolution of assisted reproductive technology (ART) is built upon more than two centuries of foundational biological discovery and technological innovation. Key early breakthroughs include the recognition of spermatozoa by van Leeuwenhoek in 1677, the mammalian oocyte by von Baer in 1827, and the microscopic visualization of fertilization by Hertwig in the 1870s. These advances, together with early work in tissue and embryo culture, chromosomal heredity, mitosis and meiosis (Boveri, Sutton, 1900), and micromanipulation instrumentation pioneered by Chambers (1922), provided the scientific basis for experimental mammalian development outside the body. The first mammalian embryo transfer from one animal to another in Cambridge in 1890 demonstrated the feasibility of supporting gestation beyond the biological mother, and in 1923 J.B.S. Haldane articulated the concept of extracorporeal human incubation, remarkably anticipating the principles of IVF long before their realization.

Clinical IVF reached its first major milestone in 1978 with the birth of Louise Brown through the combined efforts of Robert Edwards, Patrick Steptoe, and Jean Purdy. In the same year, Subhash Mukhopadhyay achieved a parallel clinical success in India, establishing an important and pioneering contribution to the history of human IVF. Publications were forthcoming from the UK, Australia and the USA in 1980. Rapid progress followed in the 1980s, including the development of media reflecting uterine and oviductal physiology, precision incubator systems, cryopreservation and advances in high-resolution microscopy and micromanipulation.

Cryopreservation quickly became integral to clinical practice. Early work by Gerard Zeilmaker and his team in Rotterdam (1983), resulting in successful births from cryopreserved 8-cell embryos, represented a crucial step in human embryo freezing, contemporaneous with but preceding by a few months the widely cited report by Trounson. The next year this was followed by the Bourn Hall team's publication of the first successful freezing of the human blastocyst. These innovations expanded IVF into a cycle-based technology rather than a single-opportunity procedure.

Micromanipulation provided a second foundational leap starting in 1986 by Gordon and Talansky who successfully succeeded in an artificial male factor model in the mouse to artificially assist fertilization by opening the zona pellucida to allow spermatozoa entry. Techniques such as partial zona dissection (PZD) based on zona drilling, and subzonal insemination (SUZI) in the late 1980s established a cellular-surgical approach that led directly to intracytoplasmic sperm injection (ICSI) in 1992, enabling treatment of severe male-factor infertility. Similar technical principles allowed safe biopsy of the preimplantation embryo, first for monogenic disorders in 1990 (PGT-M) by Alan Handside and his team and later in 1994 for aneuploidy assessment (PGT-A), further broadening clinical possibilities.

Today, artificial intelligence and robotic automation are transforming IVF once more. AI supports objective embryo evaluation and decision-making, while robotics now manages key steps including time-lapse culture, semi-automated vitrification, cryostorage tracking, and remote or semi-autonomous ICSI. Fully integrated Day-0 automation, spanning oocyte handling, denudation, sperm preparation, and insemination, is entering clinical validation at Conceivable and will be published in 2026.

Viewed across its full scientific trajectory, IVF is transitioning from an artisanal laboratory practice to a standardized, scalable, and increasingly accessible global discipline, one with the potential to improve outcomes, reduce variability, and expand reproductive choices worldwide.

Take Home Messages

- ☞ **IVF stands on centuries of discovery:** from the identification of gametes and chromosomes to advances in cell culture, microscopy and micromanipulation that enabled human conception outside the body.
- ☞ **Parallel global innovations shaped early IVF success:** including the landmark achievements of Edwards–Stephens–Purdy in the UK and Mukhopadhyay in India in 1978, underscoring a truly international scientific milestone.
- ☞ **Cryopreservation and micromanipulation revolutionized clinical IVF starting in the 1980s:** enabling cycle-based treatment, assisted fertilization and ICSI for severe male-factor infertility, and embryo biopsy leading to PGT-M and PGT-A.
- ☞ **The role of the embryologist shifted from observation to precision microsurgery:** defining IVF as a highly skilled artisan field, but still vulnerable to operator-dependent variability.
- ☞ **AI and robotics are now transforming IVF into a scalable, standardized discipline:** with the first automation of Day-0 procedures poised to improve consistency, efficiency and global accessibility of reproductive care.