#### PROJECT REPORT





# Archiving the work of Dr. Subhas Mukherjee: The architect of India's test tube baby

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Received: 15 January 2024 / Accepted: 9 February 2024 / Published online: 14 March 2024 © Indian National Science Academy 2024

#### Abstract

India's first test baby-Kanupriya, also known as Durga, was born on 3 October 1978, just 67 days after the birth of Louise Brown in England. She was the brainchild of Dr. Subhas Mukherjee, a reproductive biologist from Kolkata, India. This idea was way ahead of its time. Thus, it met with harsh criticism and rejection. Dr. Subhas faced severe humiliation, constant repudiation, and multiple transfers. This led to his tragic death on 19 June 1981. In 1997, Dr. T. C. Anand Kumar, former director of the Institute of Research in Reproduction (now ICMR-NIRRCH), Mumbai, who had headed the team that led to the birth of India's first 'scientifically documented' test-tube baby 'Harsha' in 1986, assessed Dr. Mukherjee's diaries, papers, and handwritten notes on his technique and after that credited Dr. Mukherjee by extensively writing about his pioneering feat. In 2002, after 21 years of his death, ICMR recognized his work for the first time. Dr. Mukherjee's method of combining in vitro fertilization and cryopreservation of human embryos is the currently preferred technique of medically assisted reproduction. Dr. Edwards was awarded the Nobel Prize for creating a test tube baby in 2010. Though Dr. Subhas Mukherjee was the first Asian to discover such a process and the first to discover live birth from frozen embryos, he never got recognition during his lifetime. Till now, he has not received any honor of such magnitude. Much of Dr. Subhas's work remains unpublished because of restrictions and prohibitions by the authorities. We believe, there is a need to preserve and document Dr. Mukherjee's work to make it a familiar name in India. For this purpose, meticulous, unbiased, and thorough analysis of all the available material was necessary. This project was undertaken with this intention.

**Keywords** Assisted reproduction · IVF · Test-tube baby · Superovulation · Cryopreservation

#### 1 Introduction

The twentieth century witnessed tremendous advancement in the world of science. One of the most influential was the success of in vitro fertilization. Louise Brown was the first baby born via IVF on 26 June 1978 by the efforts of Dr. R. G. Edwards and Dr. Patrick Steptoe in England. Just 67 days

The project was accomplished under the sponsorship of Indian National Commission for History of Science during the period July 2019 to June 2022.

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later, the world's second test tube baby 'Durga' was born in Kolkata, India. She was the brainchild of a brilliant scientist 'Dr. Subhas Mukherjee', a clinician with expertise in endocrinology, obstetrics, gynecology, and reproductive biology. Both Dr Mukherjee and British scientist Dr Edwards started work at the same time. Unlike his counterparts in England, Dr. Mukherjee used gonadotropins for ovarian stimulation, a transvaginal approach for ovum pick up and cryopreserved the embryos. Dr. Subhas Mukherjee was the first one to cryopreserve an eight-cell embryo, storing it for 53 days, thawing, and transferring it into the uterus, resulting in a successful and live birth as early as 1978, 5 years earlier than anyone else had done so. The techniques used by Dr Mukherjee were more advanced than his British counterparts and later became the standard approach for IVF. Moreover, he carried out this work at his apartment with a few simple equipments. In U.K., Dr. Edwards and Dr. Steptoe were highly appreciated for their commendable research, and Dr. Edwards was awarded the Nobel Prize in Physiology and



Medicine in 2010. Sadly, none of Dr. Subhas' brilliant work was acknowledged on the other side of the world. Instead, he was humiliated and ostracized. Dr. Subhas Mukherjee's work was quenched by multiple transfers and repudiation. Unfortunately, this led to his sorrowful demise on 19 June 1981.

After Dr. Subhas' unfortunate death, his collaborator in the IVF project and close friend, Prof. Sunit Mukherjee (professionally a food technologist), along with Mrs. Namita Mukherjee (w/o Dr. Subhas Mukherjee's), set up a Research Centre named "Dr. Subhas Mukherjee Memorial Reproductive Biology Research Centre" at Behala, Calcutta to keep his memory alive. Here, they preserved all the documents and equipment used by Dr. Subhas. They also organized memorial lectures on Dr. Subhas' birth anniversary every year.

In 1996, Dr. T. C. Anand Kumar, former director of IRR (now ICMR-NIRRCH) was invited by Prof. Sunit Mukherjee for 'Subhas Mukherjee Memorial Oration'. Prof. Sunit Mukherjee showed him all the notes of Dr. Subhas Mukherjee because Dr. Kumar and his team were credited for the birth of India's first 'scientifically documented' baby, Harsha, in 1986. After analyzing the said documents, Dr. T. C. Anand Kumar understood the merits of Dr. Subhas' work. Disheartened by the tragic end of Dr. Subhas' life, Dr. Kumar did everything he could to give him the credit he deserved. In April 1997, he published an article in Current Sciences titled 'Architect of India's first test tube baby: Dr. Subhas Mukerji' in the historical notes section, where he credited Dr. Subhas as the architect of India's first test tube baby (Kumar, 1997). In this article, he briefly explained the method used by Dr. Subhas, which was different and more practical than Dr. Edwards's and Dr. Steptoe's methods. Notably, Dr. Subhas' method is used as the standard procedure of IVF across the globe.

The major highlights of his innovative works are as follows. Sadly, he did not receive any credit for these works. (i) He was the first to use gonadotropin hormones to stimulate the ovaries before retrieving the oocytes. However, the credit goes to Dr. Jones from the USA, who did this work in 1981. (ii) Cryopreservation and successful transfer and implantation of the cryopreserved embryos in a simple setup in his apartment with the help of a few general instruments and one incubator. (iii) The cryopreservation was manually performed by adding alcohol to dry ice. (iv) He attained a live birth following the uterine transfer of a frozen-thawed embryo (Mukerji et al., 1978). (v) Trounson and Moore from Australia attained their first pregnancy in 1983 using cryopreserved embryos, which unfortunately did not result in a live birth. (vi) He mentioned in his notes that human oocytes need to be incubated prior to insemination with sperm to attain better fertilization rates. However, the first paper in published literature is from Trounson in 1983 (Trouson & Mohr, 1983). (vii) He aspirated the oocytes through the vagina. This technique was unheard of in human IVF till 1986, when vaginal ultrasound probes became available. (viii) He even used to carry out sperm activation in protein-supplemented Tyrode's solution, which is done in IVF clinics even today using more developed media.

Dr. Kumar also wrote about the hardships he faced and the irresponsible blundering actions of the authorities during that time. Dr. TC Anand Kumar then delivered Dr. Subhas Mukherjee Memorial's lecture, where he said there's no doubt that Dr. Subhas was the pioneer of India's first test tube baby and the world's first cryopreserved baby. He also convinced ICMR to mention Dr. Subhas briefly in their official document—National Guidelines for Accreditation, Supervision & Regulation of ART Clinics in India. Due to the honourable efforts of Dr. T. C. Anand Kumar and Prof. Sunit Mukherjee, Dr. Subhas Mukherjee is respected and remembered as someone who invented the most efficient process for the birth of test tube babies, even with a lack of resources. In 2010, Dr. Edwards was awarded the Nobel Prize for developing in-vitro fertilization. Though Dr. Subhas Mukherjee was the first Asian to discover such a process, he never got his recognition during his lifetime.

Prof. Sunit, very respectfully, had kept all the documents left behind by Dr. Subhas. This includes his handwritten papers, scientific notes, personal diaries, journals, documents of correspondence with the authorities, invitation letters from national and international conferences, personal letters, and newspaper and magazine articles related to Dr. Subhas. Even at the age of 88, he used to look after the Subhas Mukherjee Memorial Reproductive Biology Research Centre all by himself. Much of Dr. Subhas's work remained unpublished because of restrictions and prohibitions by the authorities.

# 2 Objective

In 2018, the co-PI of this project, Dr. Rajvi, visited Kolkata and made a courtesy call to meet Dr Sunit Mukherjee and see the archives of Dr. Subhas Mukherjee. It was a shock to see dusty cupboards and boxes of papers, documents, books, photographs, and news cuttings scattered in a nondescript industrial estate. Prof. Sunit Mukherjee was nearly in tears that the path-breaking work done by his friend would be lost with him. Randomly looking at some documents, she realized there was much more in these papers and diaries. We believe that there is a need to preserve and document Dr. Mukherjee's work to make it a familiar name in India. For this purpose, meticulous, unbiased, and thorough analysis





<sup>&</sup>lt;sup>1</sup> National Guidelines for Accreditation, Supervision & Regulation of ART Clinics in India, ICMR https://main.icmr.nic.in/sites/default/files/art/ART\_Pdf.pdf.

of all the available material was necessary. Our main aim was to create awareness and archive all the facts and figures regarding Dr. Subhas Mukherjee. Objectives of this project were to (i) collect all available scientific notes, research papers, newspaper and media cuttings, photos, personal correspondence, and thesis of Dr. Subhas Mukherjee. (ii) archive the necessary documents available. (iii) compile documents to make a book on the medical history of India's first test tube baby. (iv) display selected documents, notes, and photos in Science/Medical exhibition (v) submit a report to MCI to include Dr Mukherjees contribution to the medical curriculum.

The work was carried out by (i) scheduling a meeting with Prof. Sunit Mukherjee at Kolkata, (ii) collecting the documents related to research work done by Dr. Subhas Mukherjee, (iii) delivering presentations/talks (iv) interviews, and (v) publications.

# 3 Methodology used for the study

In the first phase of our project, we visited 'Dr Subhas Mukherjee Memorial Reproductive Biology Research Centre' at Behala, Kolkata. We met Prof. Sunit Mukherjee, a colleague and close friend of Dr. Subhas Mukherjee. He was kind enough to give us the documents he had preserved for 42 years. He also gave us a 5-hour-long interview with major insights into Dr. Subhas Mukherjee's life and briefly spoke about the process of successfully making the dry ice bath used for cryopreservation. He also gave us some insights into Dr. Mukherjee's thought process and about his humiliation and struggles. Prof. Sunit Mukherjee had dedicated all his life to sharing his dear friend's recognition. This interview was recorded with the help of a filmmaker and is now transcribed for reading. Unfortunately, a few months after the meeting, on 4 January 2020, Prof. Sunit passed away at the age of 89 years.

We scanned all the documents collected from Kolkata, sorted them into fifteen major categories and subcategories, and titled them suitably. The following categories of documents were sorted out:

- (1) Newspaper and magazine cuttings from 1978 onward during his lifetime and after his death
- (2) Dr. Mukherjee's scientific notes and research publications
- (3) All the reports from Dr. Anand Kumar giving "credit" to Dr. Subhas Mukherjee
- (4) Letters from patients
- (5) Letters of invitation from different parts of the world to Dr. Mukherjee for a talk on IVF
- (6) Some of his hand-written notes
- (7) Notes about patients and their files.

- (8) Dr. Mukherjee's earlier correspondence with the university.
- (9) The correspondence with the investigation committee formed to verify the "claim" made by Dr. Subhas Mukheriee
- (10) Mrs Namita Mukherjee's correspondence with the Chief Minister and Government officials after the demise of Dr. Subhas Mukherjee
- (11) Documents related to the Memorial centre and Prof. Sunit Mukherjee
- (12) Photographs
- (13) Personal documents
- (14) Recognition
- (15) Miscellaneous

# 4 Research work by Dr. Subhas Mukherjee

Going through the documents, we have realized that Dr Subhas had also worked in many other areas apart from IVF. These are:

# 4.1 Hormone human chorionic gonadotrophin

He demonstrated that HCG originating from endometrium helps in the maturation of the ovum, builds corpus luteum, and contributes to the binding of the embryo to the walls, creating a placenta that helps to supply blood to the embryo. These observations helped him lay the foundation for building an embryo outside the mother's body. In 1975, Dr. Subhas published his paper entitled 'Purification and Polyacrylamide gel electrophoretic characterization of human endometrial gonadotrophin from non-pregnant human endometrial tissue' in *India Journal of Physiology and Allied Sciences*, Vol. 29, no. 02.

# 4.2 Polycystic ovarian syndrome

Dr. Subhas hypothesized that emotional stress is one of the causes of Polycystic Ovarian Syndrome. He believed that there is a close association between stress and PCOS. He also performed few biochemical assays to confirm this and published two papers.

#### 4.3 Methods of measuring hormones

Dr. Subhas had performed many hormonal assays. His Ph.D. thesis was also on 'A New Bioassay Method for Luteinizing Hormone depending on the Depletion of Rat Ovarian Cholesterol.' This study explained a new technique to determine the activity of luteinizing hormones in the form of a bioassay (Mukherji et al., 1965).





# 4.4 Studies related to hermaphrodites/sexual abnormalities

We found many patients' data and case studies indicating that Dr. Subhas used to treat people with sexual abnormalities. It is noteworthy that these conditions were considered taboo during that time, and such people had to suffer through a lot of mental stress due to social stigma.

#### 4.5 Contribution to nutrition

During the Bangladesh war, many refugees migrating to India fell prey to malnutrition. The protein deficiency was treated by Dr. Mukherjee, who gave the refugees Fish Protein Concentrate (FPC) in 1971. The FPC was prepared from sea fish with 80% protein content in Norway.

# 5 Other findings

# 5.1 Obtaining hormones

While analyzing the documents provided by Prof. Sunit Mukherjee, we came across many significant documents. Firstly, Dr. Subhas was questioned about how gonadotropin, which he used to stimulate the ovaries, was obtained and used in various other studies. Documents revealed that his close relative, Mr. Bimal K Banerjee, visited Germany often and would provide Dr. Subhas with medicines, mainly hormones, for his work (Fig. 1).

# 5.2 First cryopreservation of human embryo

One more thing about which the authorities and the scientific community were skeptical regarding the IVF experiment was the procedure of cryopreservation of the embryo. Prof. Sunit Mukherjee was a cryobiologist who handled the cryopreservation part of the experiment. In the documents, we found a letter from the 'Indian Oxygen Plant' at Taratala under Prof. Sunit's name. The letter explains that they had ordered Liquid Nitrogen Storage Dewars as claimed by the team and mentioned by Prof. Sunit in the books 'Two Beautiful and Minds' and 'A Tale of Subhas-Namita-Sunit' (Fig. 2).

#### 5.3 Legal notice to the whole team

Another crucial document we found, was a legal notice from Mr. Prabhat Kumar Agarwal and Mrs. Bela Devi Agarwal—parents of Durga alias Kanupriya. As per our knowledge, all the literature speaking about Dr. Subhas' IVF experiment says that the parents of Kanupriya chose complete

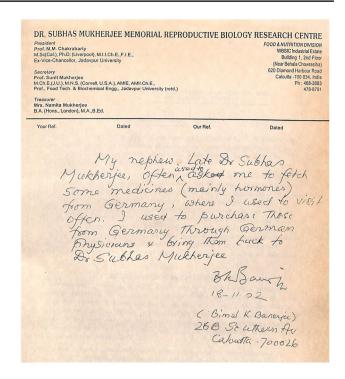


Fig. 1 Affidavit by Mr. Bimal K. Banerjee

anonymity in fear of social ostracization and hence never came forward. We found a legal notice in the form of a stern warning stating that the couple was unhappy with Dr. Subhas revealing the scientific details of the experiment leading to Kanupriya's birth. This was probably in reaction to Dr. Subhas giving lectures at multiple conferences. It was stated that strict legal action would be taken against the team if they revealed any more information. It is noteworthy that the notice also included Dr. Kailash Chaudhary. He was the family doctor of Agarwals who had referred them to Dr. Subhas. This proves the extent of social pressure they were all under (Fig. 3).

#### 5.4 Interview of Dr. Subhas by CBS news in 1979

Among the letters sent to Dr. Subhas, we found one written by CBS News just a few weeks after Durga's birth. They had requested an interview for a documentary on assisted reproduction titled 'The Baby Makers'. We went through the CBS archives on their website and found this documentary listed, but the video was unavailable. We contacted CBS news, but they replied that their archives consist primarily of music and films, and it is impossible to search for one interview. We then looked through the archives of old libraries in the US and found that the documentary was listed in many. We contacted one of them and found that they had it in VHS tape form. Fortunately, one of our associates was in the same city.





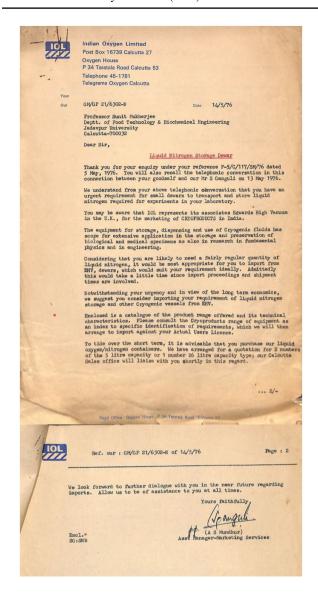


Fig. 2 Liquid nitrogen storage Dewars

He re-recorded the video and sent it to us. In the documentary, Dr. Subhas is seen along with Prof. Sunit Mukherjee. They shared the details of their cryopreservation technique and gave insight into the ethical dilemma around IVF.

#### 6 Interviews taken

We identified some of Dr. Subhass associates through the collected documents and Prof. Sunit's interview. We met many, like (i) Dr. Manju Mukherjee, the former Head of the Department of Biochemistry at Calcutta University, where Dr. Subhas Mukherjee used to work. (ii) Dr. Debajyoti Das, a lecturer at Presidency College Kolkata where Dr. Subhas had studied, (iii) Dr. B. N. Chakravarthy who worked with Dr. Mukherjee and used to share the same clinic, and Dr

Subhas had his last published paper on the association of PCOS and emotional stress. Sadly, he passed away on 15 April 2022. (iv) Ms. Kanupriya Agarwal (Durga), India's first IVF baby herself. (v) Mr. Prabhat Kumar Agarwal, Durga's father who briefly spoke about how they met Dr. Subhas and how he handled their case. (vi) We also interviewed Mrs. Bela Devi Agarwal (Druga's mother) through video conferencing. She gave us many details about the IVF procedure that Dr. Subhas had used. She also told us about how they managed to maintain secrecy around her pregnancy and their decision to choose anonymity to this day. This is the first interview given by Bela Agarwal. (vii) We have contacted and interviewed Dr Subhas Mukherjee's brotherin-law Mr. Amitav Banerjee. He also had a few documents with him, which he kindly showed us. (viii) Dr. Amit Roy was a colleague of Dr. Subhas. He shed light on his reputation as a scientist and how he suffered as the controversy unfolded. He also gave us insights about the scenario of medical science during that time in Kolkata. (ix) We also managed to meet Mrs. Karpagam, wife of Dr. T. C. Anand Kumar. She kindly gave us many relevant documents, which included the letters exchanged between Dr. R. G. Edwards and Dr. T. C. Anand Kumar regarding IVF and Dr. Subhas Mukherjee (Fig. 4). We also got the original affidavit signed by Mr. and Mrs. Agarwal confirming that Durga's birth was through IVF, done by Dr. Subhas Mukherjee (Fig. 5).

# 7 Publication outcomes

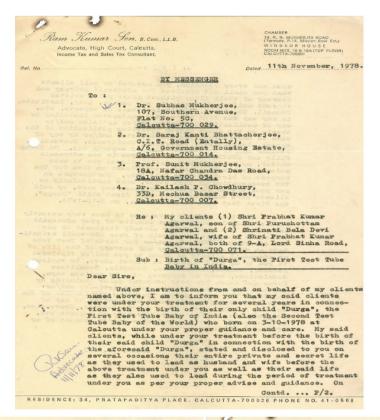
A booklet was prepared which gives a general idea of the life and works of Dr. Subhas Mukherjee with the title 'Dr. Subhas Mukherjee-A Visionary and Pioneer of IVF'. This booklet was launched at ICMR-NIRRCH's Golden Jubilee Celebration and International Conference on 20 February 2020 in the presence of the former Union Minister of Health and Family Welfare and Science and Technology- Dr. Harsh Vardhan. This is available on our institute's website.<sup>2</sup>

We had sent an abstract to the Editor of *Journal of Assisted Reproduction and Genetics* about an article about Rewriting history- Dr Subhash Mukherjee: first to lead to a live birth following the use of frozen human embryos. The editor has asked us to send the manuscript. We are in the process of finalizing the manuscript. We have written an essay on Dr. Mukherjee's work on stress and PCOS—a concept far ahead of his time. In February 2023, we published an article in 31st issue of ISSRF Newsletter titled, 'Remembering Dr. Subhas Mukherjee—The trailblazer of IVF in India' (Mukherjee et al., 2023).





<sup>&</sup>lt;sup>2</sup> https://nirrh.res.in.



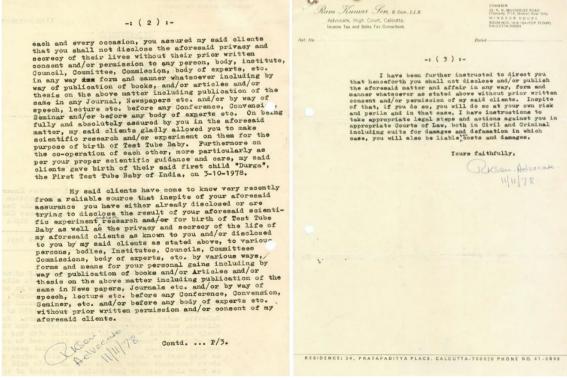


Fig. 3 Legal notice to the team





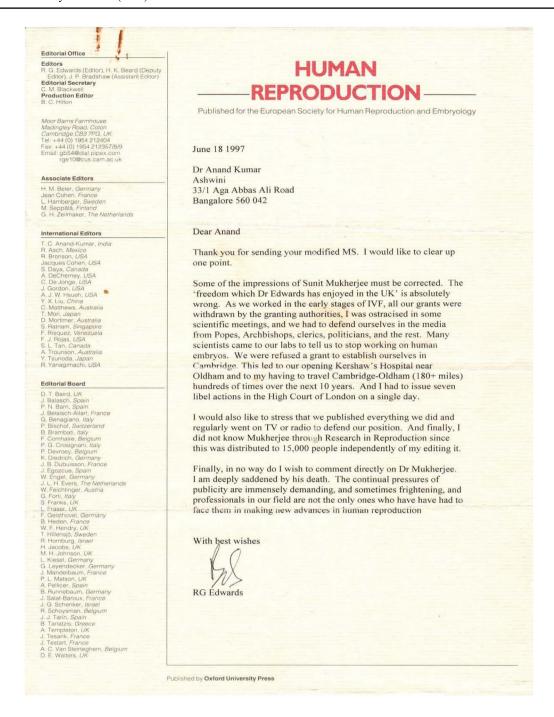


Fig. 4 Letter written by Dr. R. G. Edwards to Dr. T. C. Anand Kumar

#### 8 Presentations/talks organized

On 16 January 2021, we conducted an online symposium 'Memory of Dr. Subhas Mukherjee-A tribute on his 90th Birth Anniversary'. The symposium covered a broad spectrum of topics, starting from the need to keep his memory alive to his pioneering IVF work and other research contributions. It also included insights into his life stories, Kanupriya's (a guest speaker) thoughts on test-tube babies and

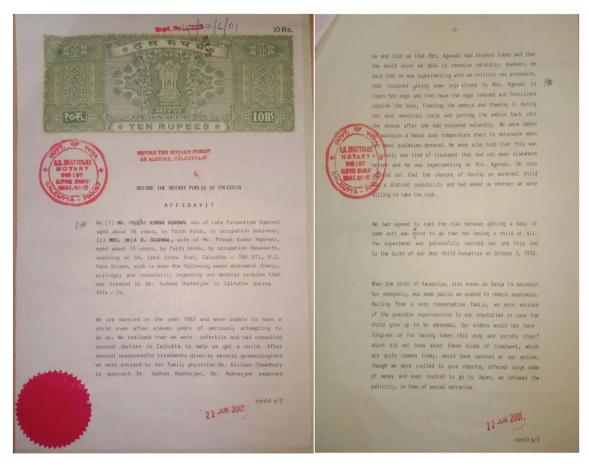
IVF, and the latest techniques and current IVF protocols. The webinar was live streamed and is available on YouTube.<sup>3</sup>

On 19 June 2021, on the 40th death anniversary of Dr. Subhas, a webinar titled—'Justice for the Forgotten Hero' was conducted. Prominent speakers like Dr. Gautam Khastagir and Dr. Sadhan De gave a talk along with Dr. Srabani





<sup>&</sup>lt;sup>3</sup> https://www.youtube.com/watch?v=3FsHmJaNYlQ.



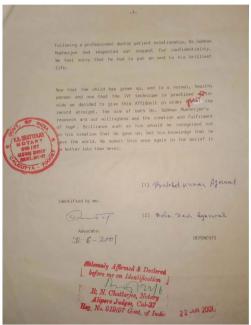


Fig. 5 Affidavit by Mr. and Mrs. Agarwal





Mukherjee and Dr. Rajvi Mehta. Kanupriya was also a guest in this webinar.

In October 2021, the 9th Annual Conference of Academy of Clinical Embryologists of India titled "Creation of Life in In vitro" was organized online. Two orations titled "Journey of IVF: a talk on Dr. Subhas Mukhopadhyay" were conducted at this conference. One was delivered by Dr. Sudarshan Ghosh, a close associate of Dr. Subhas Mukherjee, and our co-PI, Dr. Rajvi H. Mehta, delivered the other. This oration was attended by a considerable number of accomplished as well as young doctors and scientists. The entire oration is available online.<sup>4</sup>

One of the scientists of our institute, ICMR-NIRRCH, Dr. Deepak Modi, spoke about Dr. Subhas Mukherjee at Dr. APJ Abdul Kalam Govt. College, Silvassa Dadra Nagar Haveli on 23 February 2022. This was part of 75 Points from the Annals of History S&T in India. Nearly 200 students physically heard the talk, and an additional 400 students viewed it online. The talk is still available on YouTube.<sup>5</sup>

#### 9 Conclusion

There is no doubt that the work done by Dr. Subhas Mukherjee was highly commendable. His tragic end is a loss to the entire country. According to an estimate by WHO, approximately five million children have been born worldwide through ART interventions. However, the pioneering contributions of Dr. Subhas Mukherjee in advancing IVF techniques is still shrouded from the world. The method he

formulated remains the technique of preference even today, showing how advanced his thought process was and how significant his achievements are in the field of IVF. His astounding research was a hope for countless couples suffering from social and emotional distress. His tragic end is a loss to the entire country. He may have left this world early, but his legacy will and should continue through his outstanding contributions to reproductive biology.

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<sup>&</sup>lt;sup>5</sup> https://www.youtube.com/watch?v=iCTWgJNE07U.





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