



Short communication

Founding pioneers of IVF update: Innovative researchers generating livebirths by 1982

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ABSTRACT

This commentary adds accuracy and interesting information to the story of the founding pioneers of IVF which was published in this journal in 2018, at the 40th anniversary of the first IVF livebirth, namely Louise Joy Brown born 25 July 1978. Table 1 in that first publication is now updated to reflect extended information about Team 1 comprising the acknowledged “Fathers of IVF”, but whose work is better tabulated as Team 1a from the NHS days in Oldham; and Team 1b covering the new period of private practice at Bourn Hall in Cambridge. With the passing of pioneer Ian Craft, co-author of the first article, further information came to light at his memorial service. There has now been some adjustment to the last few months of 1982, with correct inclusion of Israel into the list along with an interesting exposé of the two major pioneer facilities of that country. The previously cited third Australian groups (Team 12) have now been appropriately relegated to 1983, a year which experienced a plethora of IVF facilities around the world and the beginning of the IVF population boom.

1. Introduction

At the 40th anniversary of the birth of Louise Joy Brown on 25th July 1978, the technology of in vitro fertilization is celebrated worldwide as the number of offspring now exceeds 8 million from reported registers, and likely exceeds 10 million taking into account countries with inadequate reporting systems. For those IVF pioneers whose efforts were concurrent with those of the acknowledged “Fathers of IVF”, namely Patrick Steptoe and Robert Edwards, the current numbers indicate that IVF technology is being applied widely around the world, but in a large proportion of individuals their outcomes indicate a poor-prognosis scenario. Each of the early pioneers faced this problem as their standard outcome and, by Louise Brown’s 4th birthday, or even the end of 1982, the only clinic able to report a 10% livebirth outcome for their initiated efforts, was that established by Steptoe and Edwards at Bourn Hall, Cambridge.

As a member of two of the founding pioneer teams, I was aware of the historical events in each of the relevant countries enabling a joint publication with my mentor Professor Ian Craft to tabulate those historical achievements [1]. Sadly, Craft passed in June and his Obituary, which was compiled by myself with eminent embryologist Joyce Harper, expressed Craft’s breadth of talent [2]. His passing also brought earlier colleagues from both the medical and science areas of IVF to his memorial and provided an opportunity to update the historical data on

which we had compiled our earlier report.

2. Updated data

Table 1 now makes 3 adjustments:

2.1. Team 1a

Team 1a comprising the acknowledged “Fathers of IVF” Patrick Steptoe and Robert (Bob) Edwards, along with nurse/embryologist Jean Purdy, completed their working arrangements at Kershaw’s Cottage Hospital in Oldham, Manchester in August 1978, soon after the birth of the first IVF infant Louise Joy Brown on 25th July 1978 at the Oldham and District General Hospital (ODGH). The second surviving infant Alastair MacDonald was born at Stobhill Hospital in his parent’s hometown of Glasgow, Scotland [3]. Louise Brown was conceived following embryo transfer at 11:50 pm on 12th November 1977 and the conception of Alastair MacDonald followed an embryo transfer at 11.15 pm on 20th May 1978. A further pregnancy was achieved following an embryo transfer at 10.50 pm on 19th July 1978. That final pregnancy delivered at 21 weeks gestation on 26 November and is recorded as an early neonatal death, the 600 g male infant having respirations for 2 h [3]. They subsequently re-established at Bourn Hall in Cambridge, UK in a private setting without the previous NHS advantages. The Kershaw

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Table 1

Lists the pioneer IVF centres which established livebirths from IVF, beginning with Louise Brown in July 1978 and documenting 9 successful centres to her 4th birthday (July 1982); thereafter another 3 centres to the end of 1982.

Team	Country	City	Main Members/ ^a First twins/ ^a extra info	First Livebirths
1a	Britain	Oldham, Manchester, UK	Steptoe, Edwards, Purdy ^a second surviving birth	Jul - 78 ^a Jan - 79
1b	Britain	Bourn Hall, Cambridge, UK	Steptoe, Edwards, Purdy, Further members: Webster, Fishel, Cohen ^a First twins	July - 81 ^a Sep - 82
2	India	Kolkata/Calcutta, India	Mukherjee, Muckherjee, Battacharya	Oct - 78
3a	Australia	Melbourne, Australia	Wood, Johnston, Lopata	Jun - 80
3b	Australia	Melbourne, Australia	Wood, Leeton, Trounson ^a First twins	May - 81 ^a Jun - 81
4	USA	Norfolk, Virginia, USA	Jones, Seeger-Jones, Garcia, Acosta, Veek ^a First twins	Dec - 81 ^a Mar - 83
5a	France	Clamart, Paris, France	Frydman, Testart, Lasalle, Papeirnik	Feb - 82
5b	France	Sèvres, Paris, France	Cohen, Plachot, Mandelbaum	Jun - 82
6	Britain	London, UK	Craft, Yovich, Green, Shelton, Bernard ^a First twins (also first IVF live birth) ^a sperm/egg to uterus	^a Apr - 82 ^a Aug - 82
7	Germany	Erlangen, Bavaria, Germany	Trotnow, Kniewald, Habermann	Apr - 82
8	USA	Los Angeles, California, USA	Marrs, March, Mishell	Jun - 82
9	Australia	Perth, Western Australia	Yovich, Pusey, De Atta, Reid, Grauaug ^a First twins; ^a monozygotic	Jul - 82 ^a May - 83
10	Sweden	Stockholm, Sweden	Hamberger, Nilsson, Wikland, Enk	Sep - 82
11	Israel	Sheba, Ramat Gan, Israel	Maschiach, Dor, Ben-Rafael	Sep - 82
12	Austria	Vienna, Austria	Feichtinger, Kemeter, Szalay ^a First twins	Oct - 82 ^a Nov - 82

Team 1b reported a 15% pregnancy rate, being 38 of 250 single embryo transfers to December 31, 1982 [8].

Team 2. Note several different spellings for Dr Subhash Mukherjee including Mukhopadhyay also Mucherjee and Subhas Mukerji, Subhas Mukherjee. In Western publications, Mukherjee is most common [5]. Wikipedia uses Mukhopadhyay, but describes 11 variations.

* The first IVF twin live births - in order 1. Melbourne, Australia (Team 3b; June 1981); 2. London, UK (Team 6; April 1982); 3. Cambridge, UK (Team 1b; September 1982, possibly earlier but not before May 1982); Vienna, Austria (Team 12; November 1982). Two others twin pregnancies from these pioneer centres ensued in 1983 (Team 4; March 1983 and Team 9; May 1983; the first monozygotic twins).

hospital facility was embraced by the OGDH hence the NHS covered the running costs for the ward beds and operating theatre along with the attendant nursing staff, many of whom worked extra time voluntarily. In this setting the patients did not pay for their hospital stay or treatment [4]. The Bourn Hall Clinic opened on 28 September 1980 and the first cohort of 23 patients was admitted for natural cycle IVF [5]. This **Team 1b** had continued their protocol of natural cycle tracking hence each of the women had a single embryo transferred. One of these “pioneer patients” conceived and, following a perfectly normal pregnancy, delivered a healthy child at term in July 1981; this was soon followed by another term IVF baby a few weeks later. These were natural cycle pregnancies, following the protocol from the Kershaw era of 1977–1978 and the team were able to report a pregnancy rate of 15% being 38 of 250 single embryo transfers to December 31, 1982 [8]. However, in the private setting with patients paying for treatment, the team soon re-explored ovarian stimulation, initially with Clomiphene, but subsequently adding gonadotrophins (HMG; human menopausal gonadotrophin) in those with poor responses. Other practices which had previously established at Kershaw also became modified. These included the idea of conducting embryo transfers (ETs) in the late-day /evening (meaning between 5pm–9pm). However, the conceptions of both Louise Brown and Alastair MacDonald followed ETs conducted near midnight as the “IVF Fathers” had other commitments in the earlier evening on those occasions [3,5,6]. Although persisting with Natural cycle and HiGonavis testing for the natural LH surge continued through the early eighties, HCG triggers were re-introduced enabling a more orderly and efficient utilisation of the operating theatre facility for OPU’s. A third practice, namely that of undertaking ETs in the knee-chest position for those women with anteversion of their anteverted uterus was gradually changed to ETs in the supine, lithotomy position when trans-abdominal ultrasound with partially filled bladder was introduced. All these processes had been introduced on sound reasoning by **Team 1a** [7] and may still have a place today for some women with recurrent implantation failure. Continuing with their analytical scientific approach to IVF, **Team 1b** published many articles examining each

variation of their protocols. Their first report detailed their earliest results to December 1982 [8] but their proudest publication covered the birth of 500 babies conceived by IVF at Bourn Hall by 1985, some of which were now derived as frozen embryo transfers (FETs) [9].

2.2. Team 11

Team 11 is now replaced by one of the Israeli pioneers, namely the team headed by Professor Shlomo Maschiach at Sheba, in Ramat Gan, a suburban district of Tel Aviv. Their healthy female infant was born in September 1982 and is celebrated as the first “home-grown IVF infant” of Israel. This curious comment relates to the unique historical background of IVF in Israel [10]. A religious Torah was proclaimed by the Israeli Knesset on 11 February 1981 and provided licence approval for two IVF units - one headed by Maschiach at Sheba; the other, based at Hadassah University Hospital in Jerusalem, was headed by Professor Joseph Schenker. As it worked out it was Schenker who drew media attention with the first IVF birth on 11 February 1982. A healthy female born by Caesarian section at Hadassah. However, what was not clarified at the time, was the fact that this girl was “conceived” at Bourn Hall where her mother had the embryo transfer procedure on 26 May 1981. She had actually been referred by Schenker to Steptoe prior to Schenker receiving his IVF licence. It is certainly a happy pioneer story and both of the IVF females, now in their late 30’s, are frequently celebrated in the Israeli media. Schenker delivered his team’s first “home-grown” infant in April 1983. Both teams remain highly respected in Israel and have assisted in the training of many skilled IVF clinicians and embryologists who are now world-renowned.

2.3. In the original Pioneers article, Team 12

Team 12 referred to two Australian facilities who had reported pregnancies in the latter part of 1982 but, having now re-checked their documentation, it has emerged that the livebirth outcomes actually occurred during 1983. In particular I would like to mention Professor

Doug Saunders from the Royal North Shore Hospital (RNSH) in Sydney, whose consultant Obstetrician/ Gynaecologist David Smith, actually took over the position with Ian Craft from myself when I departed at the end of 1980. He delivered the first two RNSH IVF infants on the same day in February 1983. Another Consultant from the facility of Professor Saunders, Rick Porter, followed David Smith in London and helped Ian Craft pioneer the first successful use of a GnRH agonist in IVF [11].

3. Conclusion

The revised Table is still true to the original premise with 9 Teams achieving livebirths by the fourth birthday of the first IVF live birth. The extra 3 teams completed the year 1982 and were added in as they were distinctly independent, with most contributing unique ideas into the field. If the Table 1 was extended into 1983, it would reflect the arrival of many IVF facilities around the world and the beginning of the IVF livebirth population explosion.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.repbio.2019.12.008>.

References

- [1] Yovich JL, Craft IL. Founding pioneers of IVF: independent innovative researchers generating livebirths within 4 years of the first birth. *Reprod Biol* 2018;18:317–23.
- [2] Yovich JL, Harper JC. Obituary: emeritus professor Ian Logan Craft FRCS FRCOG: a ‘universal genius’ with scientific and artistic qualities. *Reprod Biomed Online* 2019;39(4):545–6.
- [3] Edwards R, Steptoe P. *A Matter of Life. The story of IVF - a medical breakthrough.* Cambridge UK: Finestrade Ltd and Crownchime Ltd; 1980. 224 pages.
- [4] Johnston MH, Elder K. *The Oldham Notebooks: an analysis of the development of IVF 1969-1978. VI. Sources of support and patterns of expenditure.* *Reprod Biomed Soc Online* 2015;1:58–70.
- [5] Gosden R. *Let there be life. An intimate portrait of Robert Edwards and his IVF revolution.* Williamsburg, Virginia USA: Jamestowne Bookworks; 2019. 362 pages.
- [6] Elder K, Johnson MH. *The Oldham Notebooks: an analysis of the development of IVF 1969-1978. II. The treatment cycles and their outcomes.* *Reprod Biomed Soc Online* 2015;1:9–18.
- [7] Steptoe PC, Edwards RG, Leeton JF, Trounson AO, Johnston IWH, Lopata A, et al. Embryo replacement and fetal growth. In: Edwards RG, Purdy JM, editors. *Human conception in vitro.* London: Academic Press Inc; 1981. p. 413–20.
- [8] Edwards RG, Steptoe PC. Current status of in-vitro fertilization and implantation of human embryos. *Lancet* 1983;8362(2):1265–9.
- [9] Steptoe PC, Edwards RG, Walters E. Observations on 767 pregnancies and 500 births after human in-vitro fertilization. *Hum Reprod* 1986;1(2):89–94.
- [10] Birenbaum-Carmeli D. Pioneering procreation: israel’s first test -tube baby. *Sci Cult (Lond)* 1997;6(4):525–40.
- [11] Porter RN, Smith W, Craft IL, Abdulwahid NA, Jacobs HS. Induction of ovulation for in-vitro fertilisation using Buserelin and gonadotropins. *Lancet* 1984;324(8414):1284–5.