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One in thirty children in France conceived through assisted reproductive technology

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The world's first 'test tube baby', Louise Brown, will turn forty on 25 July 2018. Elise de La Rochebrochard provides an overview of assisted reproductive technology (ART) in France since its inception. She specifies how many children conceived through ART are born in France each year, explains the methods used and the proportion of children born from gamete donation, and estimates the total number of births by ART from its beginnings.

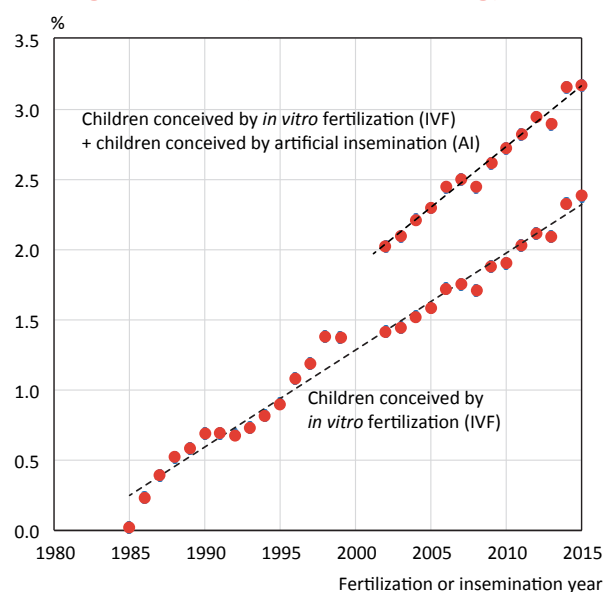
The world's first 'test-tube baby', Louise Brown, will turn forty on 25 July 2018. The birth of this English woman marked a genuine revolution in assisted reproductive technology (ART). This technique makes it possible to fertilize an egg with a sperm cell outside the woman's body in the biologist's 'test tube', or, according to the technical term, *in vitro* (Box 1). Before this first *in vitro* fertilization (IVF), assisted reproductive technology was limited to 'artificial' insemination (AI), in which sperm from either the woman's partner or husband (AIH) or a donor (AID) is deposited on her cervix or inside the uterus to fertilize an egg inside her body.⁽¹⁾

One child in thirty now conceived using assisted reproductive technology

In France in 2018, one child in thirty (3.4%) is expected to be conceived using ART techniques, either IVF or AI (Figure 1 and Box 2). IVF is now the dominant technique, representing 70% of all ART-conceived babies in France. The first French 'test-tube baby', named Amandine, was

conceived in 1981 and born on 24 February 1982. Since then, the number of *in vitro* fertilizations in France has been rising continuously and at a remarkably linear rate (Figure 1). The share of babies conceived *in vitro* has been rising 0.5% every seven to eight years. In 2011, 2.0% of children in France were conceived through IVF, and if this trend continues, the figure should reach 2.5% in 2018; that is, one baby in forty, or over 20,000 children.

Figure 1. Children conceived annually in France through assisted reproduction technology (ART)



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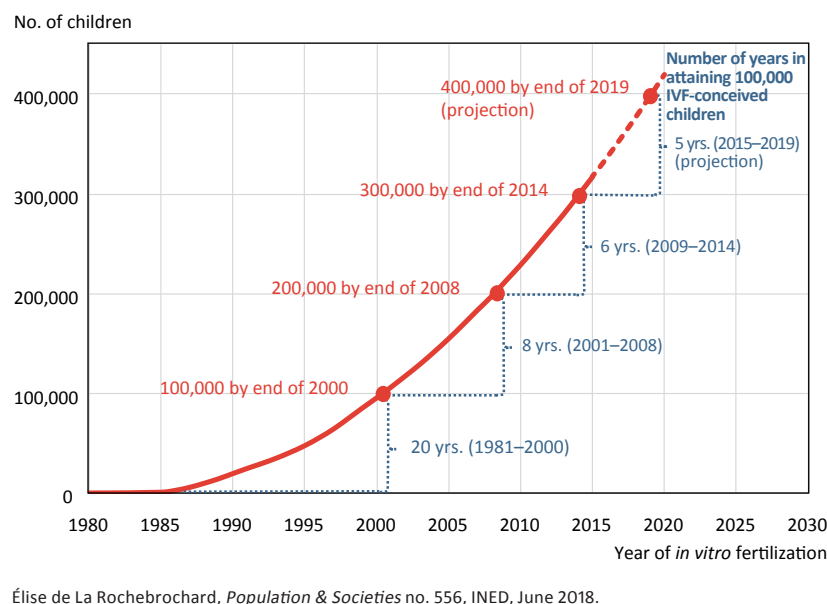
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(1) Medical infertility treatment often begins with simple hormonal stimulation, i.e. involving neither artificial insemination nor *in vitro* fertilization. That treatment is not included in ART because there is no manipulation of sperm, oocytes, or embryos. We have no statistics on how often simple hormonal stimulation treatments are used or on the number of children thereby conceived.

Box 1. Acronyms

- AI:** artificial insemination
- AID:** artificial insemination by donor
- AIH:** artificial insemination by husband (or partner)
- ART:** assisted reproductive technology
- CBRC:** cross-border reproductive care
- CECOS:** *Centre d'étude et de conservation des œufs et du sperme humains*, France's centres for the study and preservation of human eggs and sperm
- ICSI:** intracytoplasmic sperm injection
- IVF:** *in vitro* fertilization

Figure 2. Running total of children conceived by *in vitro* fertilization (IVF) in France since 1981



The increasing use of IVF has been bolstered by technical advances that now make it possible to treat male factor infertility just as well as female factor infertility. Initially, IVF was only designed to counter female factor infertility due to damaged or blocked Fallopian tubes. But since 1992, a new IVF technique has also helped to treat male factor infertility: intracytoplasmic sperm injection (ICSI). It involves selecting a sperm cell and inserting it directly into the oocyte. The use of ICSI has increased considerably: in 2012–2015, two out of three *in vitro* fertilizations in France were brought about through this method.

France will soon have 400,000 children conceived through IVF

The IVFs performed during the first two decades of its practice in France (1980–2000) made it possible for 100,000 children to be born (Figure 2). The development then gathered momentum, as the number reached 200,000 children by the end of 2008 and 300,000 by the end of 2014. If the trend continues at the rate observed over the last thirty years, France should have a total of 400,000 children conceived *in vitro* by the end of 2019. The same dynamic is found for the world at large. In 2013, the International Committee Monitoring Assisted Reproductive Technologies (ICMART) estimated that five million babies had been conceived by IVF across the world, half of them over the previous six years [3]. Among children conceived by IVF, there is a significant proportion of multiple births. In France in the 1990s, no fewer than 130 babies were born per 100 deliveries subsequent to IVF. Initially, to increase the chances of

obtaining a pregnancy, physicians would transfer many embryos, often four or more at a time (39% of cases in France in 1988). However, multiple births considerably increase health risks to the children involved. Physicians gradually became aware of this and began transferring fewer embryos to reduce the risk of multiple births: three embryos (around 40% of cases in 1997), then two embryos (approximately 60% of cases in 2009). Currently, the number of births per 100 deliveries following IVF stands at 110 – a frequency that is still much higher than in the case of ‘natural’ pregnancy (101 children per 100 deliveries). Today, the objective is to further reduce twin birth frequency by transferring one embryo only, freezing others as the case may be and transferring them in later attempts. In France, over 40% of IVFs performed in 2015 involved the transfer of a single embryo, and that proportion is expected to increase in the coming years. Finland and Sweden lead the way with strong, proactive policies that have made it possible to achieve 80% of IVFs using single-embryo transfers.

Only 5% of ART-conceived babies involve third-party donors

ART is often associated with having recourse to a third party to conceive a child, through sperm or egg donation, embryo donation (in the case of one couple receiving embryos from another couple), or surrogacy. In reality, nearly all ART-conceived babies in France (95% in 2015) develop out of gametes from their two parents. Most third-party donations in France are of sperm (accounting for 4% of ART births in France, or

approximately 1,000 children per year); very few involve egg donation (1% of ART births, or approximately 250 children per year). Embryo donation is statistically negligible (0.01% of ART births, or twenty-five to thirty children a year), and surrogacy is illegal in France.

Gamete donation in France is free and anonymous. It is managed by CECOS centres,⁽²⁾ commonly known as sperm and egg banks. There are not enough donors in France to meet demand from infertile heterosexual couples of reproductive age, particularly their demand for oocytes. Current French law restricts access to ART to these couples, though part of French society would like to see it extended to others. As the law stands now, those excluded from ART include women age 43 or over who request an oocyte, as a woman's oocytes age more quickly after age 37; single women and female same-sex couples requesting sperm; male same-sex couples needing an egg donation and a surrogate; and women requesting to use surrogacy because they cannot carry a pregnancy to term.

French people who do not have access to ART involving third-party donors may decide to seek what is known as cross-border reproductive care (CBRC) in order to use ART outside France, often in other European Union (EU) countries [4]. Heterosexual couples of reproductive age can request reimbursement for such cross-border care from the CNSE (France's foreign health-care reimbursement office), which in 2015 received 1,499 requests of this type. However, CBRC is often perceived as illegal, and it is unlikely that all eligible parties apply for reimbursement. Furthermore, those excluded from ART cannot be reimbursed for this care by the CNSE.

ART with a third-party donor within the European Union: an unbalanced landscape

Approximately 10% of the IVFs performed in the European Union take place in France, according to the 2013 European report on ART activity (Box 2). This proportion is less than France's share of EU births (15%). By contrast, Germany accounts for 13% of IVFs in the EU, identical to its share of births (13%). Italy accounts for 12% of EU IVFs and only 10% of EU births. Despite these intercountry variations, IVF activity across the sizeable EU states broadly corresponds to their demographic weight: the five major countries taken together (the United Kingdom, France, Germany, Italy, and Spain) account for 63% of births and virtually the same proportion of IVFs (62%).

The situation is quite different for ART involving third-party donors. France accounts for no more than 2% of EU oocyte donations. Germany and Italy account for no donations because each prohibits them. These three demographic heavyweights, together representing no less than 39% of the EU's female population aged 20 to 44, are therefore far behind in terms of oocyte donation. Their nationals have to cross borders to achieve their parenthood intentions [5], creating a phenomenon of cross-border care seeking whose magnitude has yet to be determined. Destination countries include Spain, Greece, and the Czech Republic, the last two representing only 2% of EU births each. Those three countries alone account for 77% of EU oocyte donation: Spain dominates at 59%; the Czech Republic and Greece donate respectively 9% and 8% of oocytes within the EU.

The same imbalance is found for sperm donation, which, once again, particularly affects Germany, Italy, and France. As mentioned, only heterosexual couples have access to donated sperm in France, a situation that induces those excluded from ART – specifically, single women and female same-sex couples – to cross borders for reproductive assistance. The situation is the same in Germany, though little is known about sperm donation in that country since statistics for it do not figure in the European Union report (Box 2). In Italy, sperm donation is illegal. In the EU, sperm donation is essentially performed in three countries: Denmark and Belgium represent, respectively, only 1% and 2% of EU births but 26% and 20% of EU sperm donation, while Spain accounts for 8% of EU births and 19% of EU sperm donation.

Within the European Union, ART involving a third-party donor is concentrated in a few countries receiving Europeans unable to access donated gametes in their home countries. This strong concentration of donations within just a few (often small) countries raises ethical questions about donation organization. To meet demand from the EU population, those countries have to recruit a considerable number of donors, which cannot be based on just the altruism of the local population. Some female donors are likely to be young, economically vulnerable women motivated by the financial compensation of €400 to €2,000 paid out by the centres [6].

In January 2018, a series of public debates on bioethics was launched in France, calling upon French society to consider, among other things, possible changes to ART legislation. Among the issues being debated is whether access should be extended to all women, including single women and same-sex couples, which could lead to revisions to France's bioethics law within the year. The choices France makes will have consequences beyond its borders, either accentuating or curbing the current concentration of ART services involving gamete donation within just a few countries.

(2) CECOS stands for *Centre d'étude et de la conservation des œufs et du sperme humains*, France's centres for the study and preservation of human eggs and sperm.

Box 2. Information sources

FRANCE

1981–1999: periodic IVF activity reports by the GEF research group on IVF; these reports later published by the Ministry of Health. Data supplemented by FIVNAT registry data. See Table 2 of Reference [1] for an overview of the data.

Note: Data for the years 2000 and 2001 are not available from these sources; the number of children conceived through IVF for each of these years was estimated on the assumption of a linear trend.

2002–2015: annual ART activity reports on IVF and AI published by the Agence de la Biomédecine. Data on open access at <https://www.agence-biomedecine.fr/AMP>

2016–2019: projections on the assumption of a linear trend

For all years, see INSEE's total births statistics, based on civil registries. Data on open access at <https://www.insee.fr>

EUROPE

IVF activity statistics regularly published in Europe by the European Society for Human Reproduction and Embryology [2]. These reports extend beyond the European Union to include such countries as Russia. The analysis presented here was limited to the 28 EU member-states, specifically the 26 that participated in the 2017 report on ART activity for the year 2013 (Luxembourg and Slovakia are missing). Across the 26 countries, there are a total of 1,083 IVF centres; the report covers the activity of 957 of them (88%). France, Italy, Germany, and the United Kingdom together have 513 centres, of which 512 have provided data. Only 130 of the 198 centres in Spain provided data. The estimates presented here were adjusted on the assumption that the IVF centres included in the report are representative of all activity in the country. Oocyte donation is included in IVF activity. Sperm donation is measured by AID activity, as information on sperm donation for IVF is not presented. Some EU countries – notably Germany and the Czech Republic – do not communicate information on AID.

Demographic statistics (on natality, women of reproductive age, etc.) are published by Eurostat.

Open access: <http://ec.europa.eu/eurostat>

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Abstract

In France, one child in thirty is now being conceived through one of two methods of assisted reproductive technology (ART), either *in vitro* fertilization (IVF) or artificial insemination (AI). One baby in forty in that country is born using IVF. This share has been growing at a linear rate for over three decades. Altogether, 300,000 children were conceived in France by way of IVF from 1981 to late 2014. If this trend continues, the total will stand at 400,000 children by the end of 2019. Only 5% of ART activity in France involves gametes donated by a third party, primarily sperm, while there is a considerable shortage of donated eggs (oocytes). French law currently restricts ART to heterosexual couples of reproductive age. In this legal and organizational context, some French people go abroad to obtain donated gametes, particularly to Spain, Greece, the Czech Republic, Belgium, or Denmark.

Keywords

Assisted reproductive technology (ART), *In vitro* fertilization (IVF), Cross-border reproductive care, Births, France, Europe.



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