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In-vitro fertilization in France: 200,000 "test-tube" babies in the last 30 years

*Elise de La Rochebrochard**

Thanks to the contraceptive revolution, fewer and fewer unwanted babies are born. Today, couples want to choose the number of children they have, and the timing of their births. Expectations among potential parents are very high. Yet as age at childbearing increases, a growing number of couples now have problems conceiving, and are increasingly reliant on medical assistance to achieve a successful pregnancy outcome. At a time of renewed public debate on bioethics, Elise de la Rochebrochard explains how many children are born after *in-vitro* fertilization in France, how the country compares with its European neighbours, and how the situation is liable to evolve.

In 2003, one French birth in twenty was achieved after a medical treatment or procedure [1]. In other words, one or two children per class in today's French nursery schools were conceived with medical assistance. What form does this assistance take, and what is its demographic impact?

◆ An array of medical techniques

After one year of unprotected intercourse, 15 to 20% of couples wishing to conceive have still not achieved a successful pregnancy. Medical tests can be performed at this stage to determine the origin of the problem. For 38% of couples, combined infertility due to a problem affecting both partners is diagnosed [2]. In 34% of cases, the problems concerns the woman alone, in 20% the man alone, and in 8% the cause is unexplained. A range of medical treatments and procedures can be used to remedy medically diagnosed infertility, depending on the cause. Treatment often begins with ovarian stimu-

lation alone, before moving on, if necessary, to artificial insemination and *in-vitro* fertilization.

Ovarian stimulation is a procedure whereby the woman receives hormone injections for 8-10 days to stimulate the release of a mature egg. The child is then conceived naturally through normal sexual relations. There is no manipulation of sperm, egg or embryo, so this procedure is outside the scope of assisted reproductive technology (ART). An estimated 2.4% of women who gave birth in metropolitan France in 2003 became pregnant after ovarian stimulation [1]. This represents half of all medically assisted births in the country.

Artificial insemination (AI) involves placing sperm in the uterus during the ovulation period with the aim of achieving natural fertilization of the egg. With this procedure, only the sperm is manipulated, but not the egg or the embryo. The term AIH is used when the sperm is that of the husband or partner, and AID when the sperm comes from a donor. As artificial insemination requires only limited equipment and few technical skills, it may well have been practiced secretly since the 18th century.

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In-vitro fertilization (IVF) involves retrieving eggs from the woman's ovaries and collecting sperm from the man to fertilize them *in vitro* i.e. in a laboratory test-tube (hence the common expression "test-tube baby"). One to three embryos are then placed into the woman's uterus in the hope that at least one will implant and develop into a live baby. Louise Brown, the world's first baby conceived by IVF, was born in England in 1978. The first French test-tube baby was Amandine, born in 1982. Over the last 30 years, a range of IVF techniques have developed, notably ICSI in 1992 (see list of acronyms on page 3). IVF with ICSI involves selecting a single sperm cell and injecting it directly into the egg to "assist" the fertilization process (in standard IVF, the sperm enters the egg naturally).

◆ Assisted Reproductive Technology in figures

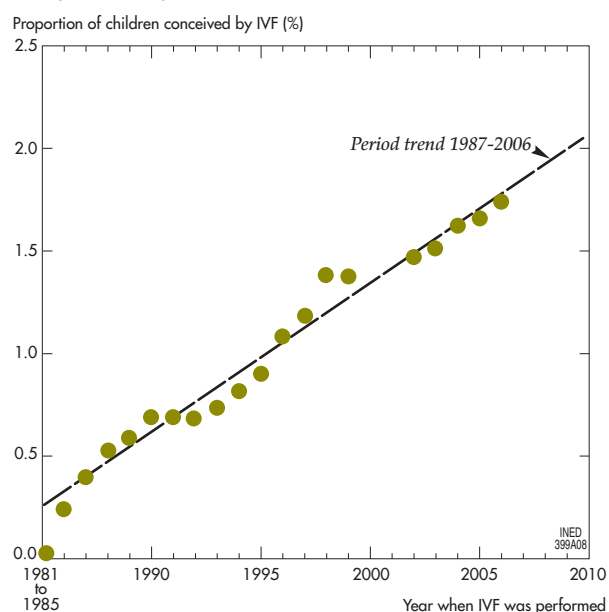
According to the latest report of the French biomedical agency (Agence de la biomédecine) published in 2007, 20,042 children were born after either artificial insemination (30%) or *in-vitro* fertilization (70%) practiced in a French centre in 2006 (Table 1). Taking account of the 9-month delay between conception and birth, this represents 2.5% (of which 1.7% IVF and 0.8% AI) of all births in France the following year, or one birth in forty.

The number of births obtained by IVF alone has increased steadily over the last twenty years, rising from 0.52% of births in 1988 to 1.74% in 2006 (i.e. an increase of +0.72% per decade) (Figure). If the trend continues, more than 2% of children could be conceived by IVF in France by 2010.

Since the technique was first introduced, a total of almost 200,000 children will have been conceived by IVF in France by the end of 2008 (Table 2). This steady

rise reflects both more frequent recourse to IVF and a better success rate (currently, 20-25% of attempts lead to the birth of at least one live child). The success rate drops sharply, however, for women aged 35-45, creating a situation of "urgency" for the treatment of older women [3]. IVF treatment also more frequently results in multiple births (one in five) as two embryos on average are transferred at each attempt. These twin births increase the rate of prematurity and of health problems among IVF babies compared with the general population of newborns. Even for single births, however, these risks are slightly higher among IVF babies [4]. The IVF procedure may be partly to blame, but also (and above

Figure – Increase in the proportion of children conceived by *in-vitro* fertilization (IVF) in France since 1981



(Elise de La Rochebrochard, *Population & Societies*, 451, INED, December 2008)

Table 1 – Number of children born after artificial insemination or *in-vitro* fertilization carried out in France in 2006

	<i>In-vitro</i> fertilization	Artificial insemination	Overall
The two social parents are also the genetic parents	13,635 (68%)	5,169 (26%)	18,804 (94%)
Donor sperm, egg or embryo	420 (2%)	818 (4%)	1,238 (6%)
Overall	14,055 (70%)	5,987 (30%)	20,042 (100%)

Source: Agence de la biomédecine (www.agence-biomedecine.fr/en/index.aspx). Annual report, 2007.

(Elise de La Rochebrochard, *Population & Societies*, 451, INED, December 2008)

Table 2 – Number of children conceived by IVF in the French population, 1981-2008

Year of <i>in-vitro</i> fertilization	Age in 2009 ^(a)	Overall ^(b)
1981-1988	20-27	9,943
1989-1993	15-19	25,090
1994-1998	10-14	39,668
1999-2003	5-9	54,693
2004-2008	0-4	69,049
Total	0 à 27	198,443

^(a): Age in 2009 is calculated by assuming that all children conceived in a given year are born the following year.

^(b): The numbers for 2000-2001 and for 2007-2008 are estimates based on an assumed linear increase in children conceived by IVF.

(Elise de La Rochebrochard, *Population & Societies*, 451, INED, December 2008)

all?) the genetic characteristics of the sterile parents. For example, there are concerns among scientists about the future fecundity of boys conceived by ICSI whose father suffers from severe male infertility.

These French data can be compared with world data available for 2000, though they are incomplete and of variable quality (1). An estimated 200,000 children were conceived by IVF in the world in 2000 alone, as many as the total number in France over the entire period 1981-2008. Around 5% of these births in 2000 occurred in France, versus more than 15% in the United States (though the proportion of IVF births with respect to total births is a modest 0.8%). According to the latest European figures (2) (for the year 2004), Germany and the United Kingdom have a proportion of IVF births similar to France. It is higher in Belgium (2.4%) and in the Nordic countries (2.8-2.9% and even 4.2% in Denmark). There are no figures for Italy and Spain where only half the ART centres communicate their data (3).

◆ IVF: from technically possible to socially desirable

The development of IVF has raised many ethical questions. To grasp the issues at stake, it is important to understand the technical aspects of this procedure. IVF provides a potential means to share reproduction between up to five "parents":

- the genetic "mother" who provides the egg,
- the genetic "father" who provides the sperm,
- the gestational "mother" who receives the embryo and carries it in her uterus,
- the partners (or individual) who desire the child and who are the sole parents in legal and social terms (referred to as the "social mother" and "social father").

These various reproductive options lead to different variants of IVF: with donor sperm, with donor egg, with embryo transfer to a gestational carrier, or with embryo transfer to another parental couple (embryo donation). In practice, however, 97% of children conceived by IVF in France have only two parents: the social mother is both the genetic mother and the gestational mother, while the social father is also the genetic father. In 2006, only 304 children were born as

(1) These data were published in 2006 in the journal *Fertility and Sterility*. Note that in France, the Public Health Code includes both artificial insemination (AI) and *in-vitro* fertilization (IVF) under the term ART. By contrast, many countries, in line with the WHO, have a more restrictive definition of ART excluding AI (both AIH and AID). Consequently, national ART statistics, where they exist, often primarily concern IVF.

(2) This report was published in *Human Reproduction* in 2006.

(3) The limited data available for Spain show that donor egg IVF cycles are much more common there than in the rest of Europe.

Glossary of acronyms

ART: Assisted reproductive technology

CECOS: Centres d'études et de conservation des œufs et du sperme (Centres for research and conservation of eggs and sperm)

PGD: preimplantation genetic diagnosis

IVF: *in-vitro* fertilization

AI: Artificial insemination

AIH: Artificial insemination with husband's sperm

AID: Artificial insemination with donor sperm

ICSI: Intracytoplasmic sperm injection

a result of IVF with donor sperm, 106 with donor egg, and 10 with donor embryo (Table 1).

In the case of artificial insemination (AI), the social mother must also be the genetic mother and the gestational carrier. The social father, on the other hand, is not necessarily the genetic father (in the case of AID). In 2006, the egg was fertilized naturally by the partner's sperm in 86% of births obtained by AI. Overall, children conceived with donor egg or sperm represent 6% of births obtained via AI or IVF methods (Table 2). Of these children, 90.6% were conceived with donor sperm, 8.6% with a donor egg and 0.8% with a donor embryo.

Genetic embryo manipulation is not technically possible as yet. However, in families where severe, incurable genetic diseases have already been identified, embryos can be "selected" to ensure that the children born are free of the genetic defect responsible for the disease. This technique is known as "preimplantation genetic diagnosis" (PGD). In France, PGD is authorized by the Public Health Code in exceptional cases, and only in three approved centres (Necker-Clamart in the Paris region, Strasbourg and Montpellier). In 2006, 46 children were born using this technique.

In France, these procedures are covered by the Bioethics Act of 1994, which was revised in 2004 and will be reviewed again in 2010. The Act is based on the following key principles:

- ART is available exclusively to heterosexual couples who are married or have been cohabiting for at least two years, of which both members are living and of reproductive age. Single people and homosexual couples are ineligible.

- Use of ART is authorized under only three circumstances: 1) medically diagnosed infertility; 2) risk of transmitting a serious disease to the child; 3) risk of transmitting a serious disease to one of the parents.

- Sperm, egg and embryo donation is free, voluntary

and anonymous. This means that a couple cannot choose the donor nor request that a donation be made by a family member.

- Fertilization with dual donation, i.e. both sperm and egg, is prohibited. At least one of the two social parents must be a genetic parent. The only exception is for embryo donation, which can be likened to pre-birth adoption of a child.

- Surrogacy (bearing a child on behalf of another woman) is prohibited. The social mother must be the gestational carrier. At present, both types of surrogacy are prohibited in France:

- *gestational surrogacy*, where the gestational carrier is not the genetic mother of the child (the egg may have been donated by the social mother or another egg donor);

- *traditional surrogacy*, where the carrier is also the genetic mother who provides the egg.

◆ Major differences in legislation across Europe

French legislation in the field of ART may change as social attitudes evolve and technologies advance. Large differences exist between countries, and even between close neighbours, a reality that encourages some people to travel abroad for treatments that are illegal in their own country (a practice known as “procreative tourism”).

In Belgium and Finland, and in the United Kingdom and the Netherlands, ART techniques are available to homosexual couples. The UK is planning legislation to permit IVF with intra-partner egg donation for lesbian couples [5]. This enables both women, social mothers of the child, to take part in the reproductive process, one by supplying the egg that will be fertilized by donor sperm (so she is the genetic mother) and the other by carrying the child (she is the gestational carrier).

Across Europe, the principle of gamete donor anonymity has been broadly debated in recent years and the legislation has been changed in several countries [6]. In 1984, Sweden abolished the principle of sperm donor anonymity, provoking a temporary drop in donor numbers (4). In a popular referendum in 1992, the Swiss voted to grant rights of access to genetic origins and to abolish sperm donor anonymity, with access to extensive information on the genetic “father” (name, first name, date and place of birth, place of residence, nationality, occupation and level of education, physical

(4) The profile of sperm donors also changed as a consequence. They are now older and more often already fathers of several children.

appearance). Likewise, in the United Kingdom, children conceived with donor egg or sperm and born after 1 April 2005 are entitled to know the identity of their genetic “parent”.

In France, citizens will be invited for the first time to express their views on these ethical issues in 2009 when the French Bioethics Act comes under review. The scope of debate will not be limited solely to experts, but will be opened to the whole of society via bioethics conferences, meetings, seminars and discussion forums. This will open the way for defining the future of assisted reproductive technologies in France.

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ABSTRACT

In 2003, one French birth in twenty (5%) was achieved after a medical treatment or procedure. In half of these cases (2.4%) conception was obtained through ovarian stimulation, and the other half by either artificial insemination (0.8%) or *in-vitro* fertilization (IVF) (1.7%). The proportion of births obtained after IVF alone has increased steadily over the last twenty years, rising from 0.52% of births in 1988 to 1.74% in 2006. This steady rise reflects both more frequent recourse to IVF and a better success rate (currently, 20-25% of attempts lead to the birth of at least one live child). In France, for 97% of children conceived by IVF, the social parents are also the genetic parents, i.e. no sperm or egg donations are involved. In 2006, only 304 children were born as a result of IVF with donor sperm, 106 with donor egg, and 10 with donor embryo.