

## Will My Baby Be Normal?

IVF is big. The one millionth IVF baby was born in 2003. By 2005, there were more than two million IVF babies. In the United States alone, at least one hundred thousand IVF cycles are performed and more than forty thousand IVF babies are born every year, accounting for more than one percent of U.S. newborns. In Europe, almost 4 percent of babies are the result of IVF. Although one hundred thousand IVF cycles per year in the United States may sound like a lot, all evidence shows that if the government or insurance companies were to pay for IVF treatment as they do for other medical treatments, there would be a tenfold increase in the number of IVF cycles performed in the United States. Although the average IVF program in the United States might perform several hundred cycles a year, if there were insurance coverage for IVF, these same programs would be doing up to two thousand cycles a year. That means that if it were not for financial limitations, there would be approximately one million cycles of IVF (resulting in four hundred thousand babies) performed every year in the United States alone.

Infertility is an epidemic not only in the United States. Already there are many millions of IVF cycles performed yearly throughout the world. The Australian government pays for IVF cycles and considers ART an important part of health care. In Melbourne alone, there are more than six thousand IVF cycles performed every year. In just one IVF center in Tel Aviv, Israel, more than four thousand IVF cycles are performed per year, and in Amman, Jordan (where perhaps the second-largest IVF program in the world is located), there are well over six thousand cycles performed every year in just one institution. In Tokyo, one program run by a single doctor does thirteen thousand IVF cycles per year. In any very large city with a population of more than ten million, one would have to estimate that the number of IVF cycles done each year would

exceed twenty thousand. Thus in the coming decade there will be many millions of IVF babies. Will those babies be normal?

The infertility epidemic is rampant in every modern society where women put off childbearing into their late twenties or midthirties. Approximately 25 percent of couples in any modern population in the world are infertile. Not only are infertility and IVF on the rise but about 30 percent of IVF children are twins, and 2 percent to 5 percent are triplets. Thus, for every million pregnancies, there are likely to be almost a million and a half babies. So if you think a million IVF babies born to date is a lot, there are plenty more on the way.

Huge numbers of our IVF patients clearly attest that their children are beautiful, normal, and intelligent. There are literally a million such happy anecdotes. Even women forty-six to fifty-two years old who had completely run out of eggs, after many years of facing their childlessness, finally chose donor eggs with IVF as their only alternative. These couples will attest to how normal their babies are, and what a joy and inspiration their children brought into what they referred to before as an “incomplete life.”

Nonetheless, there have been worrisome reports spread throughout newspapers, magazines, and TV about possible risks and an increase in abnormality or genetic problems with children born from this reproductive technology. You need to understand these scary stories in context. All pregnancies carry a risk (usually small) of an abnormal child. Every mother who has ever conceived naturally, without having to resort to any treatment, will tell you that her biggest fear for nine months was whether the baby would be normal. No expectant mother can breathe easily until she has counted her baby's toes. Even then, throughout the child's life, the next biggest fear for mom and dad is whether their child is developing normally. This is a risk that every couple has to undertake if they wish to be parents, whether they are fertile or not, or whether they need infertility treatment or not. But are the risks of having an abnormal child via infertility treatment any greater than in a normal, fertile population, and if so, how much greater?

Numerous population studies involving hundreds of thousands of children from a variety of countries, born from normally fertile couples without treatment, have consistently revealed that 3 percent of all children are born with some kind of congenital abnormality. Many more are born without abnormality but develop some sort of childhood dis-

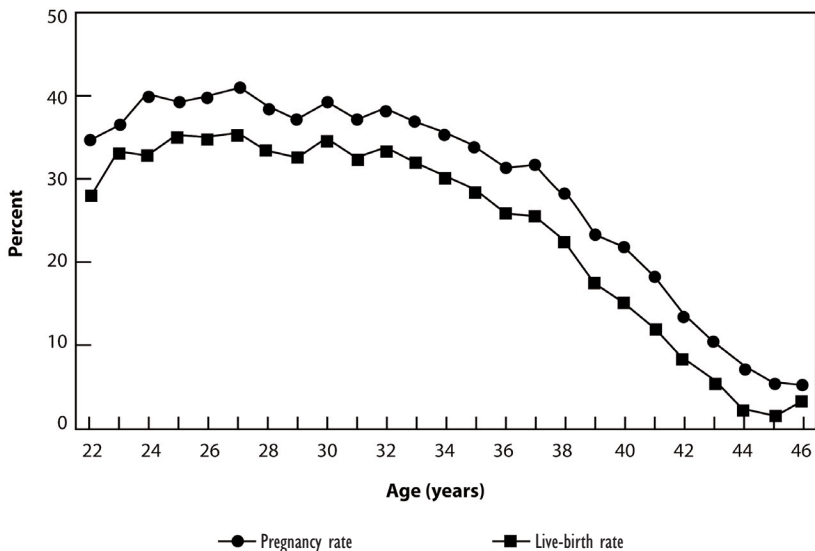
ease. Many of these problems can be corrected with pediatric surgery. Other defects don't even require correction, such as being born with an extra toe or an extra little finger. Defects that are readily correctable with surgery include cleft lip (which is cosmetically of concern, but can be repaired well), club foot, undescended testes, or hypospadias (when a male child has a normal penis, but with the opening positioned at the base rather than the tip). These "defects" can all be repaired quite routinely with modern pediatric surgery.

However, there are more frightening abnormalities, such as heart defects, which require major surgery; brain or spinal cord defects; and a whole host of other serious malformations. These malformations often have no specific genetic diagnosis and just represent relatively common errors in fetal development. They are simply the risk you take in deciding to have children, irrespective of whether or not you undergo any infertility treatment. All would-be parents are concerned about these risks, and they need to understand them. The question that scientists have been studying meticulously and methodically ever since the beginning of IVF is whether or not the reproductive technologies will result in an *increased* risk of any of these problems, and if so, which ones. In this chapter, I will discuss in detail how you can figure out your chances for getting pregnant with IVF treatment, as well as the odds (with or without IVF) of having a healthy child.

## **IVF Statistics and Your Biological Clock**

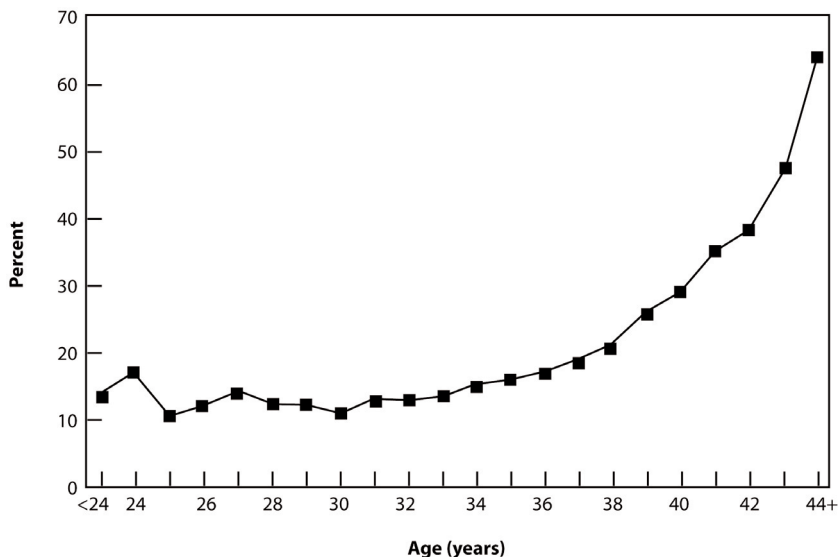
Universally, pregnancy rates begin to drop modestly in women over the age of thirty-two, and by age thirty-seven, they begin to drop quite precipitously. Figure 12.1 of this chapter demonstrates that the pregnancy rate per cycle for IVF, remarkably, can be superimposed exactly on the graph from chapter 3, comparing the decline in total number of eggs in the ovary with age (fig. 3.6). Similarly, the graph showing decline in IVF pregnancy rate with age can be superimposed on the graph in chapter 3 showing the decline with age in the number of antral follicles (fig. 3.9).

Figure 12.2 is a graph that is exactly the reverse of the pregnancy rate curve, showing the increased incidence of miscarriage with IVF pregnancies according to age. For women less than thirty-five years of age, there is a 15 percent chance of miscarriage. This is found in every population of fertile women. However, as a woman begins to progress beyond



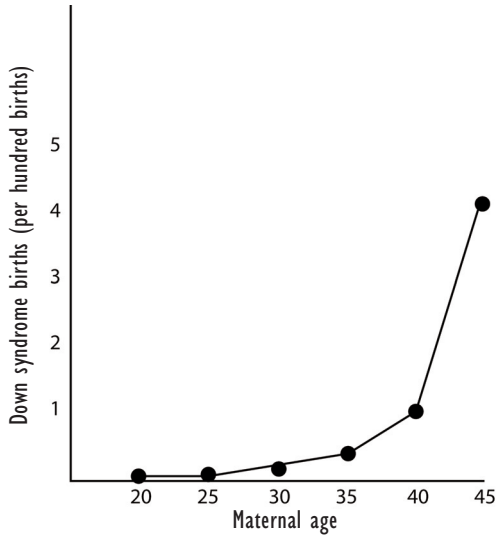
**FIGURE 12.1**

Pregnancy and live-birth rates for ART cycles by age of woman, 2000. Combined overall CDC Atlanta data of all IVF programs in the United States.



**FIGURE 12.2**

Miscarriage rates among women who had ART cycles by age of woman, 2000. Combined overall CDC Atlanta data of all IVF programs in the United States.



**FIGURE 12.3.** Maternal age and frequency of Down syndrome.

age thirty-five, her risk of miscarriage begins to rise, at first gradually and then quite drastically. By age forty-four, if she is lucky enough to get pregnant naturally or with IVF (it doesn't matter which), she has a 68 percent chance of miscarrying.

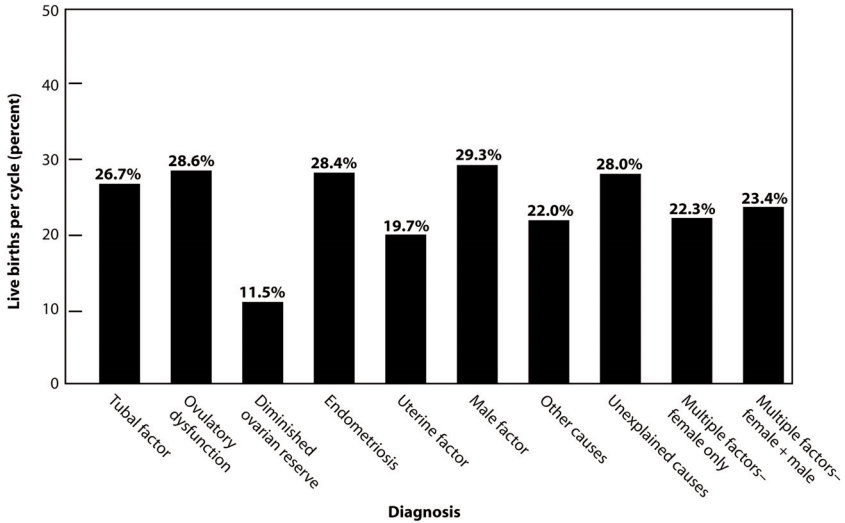
There is a big discrepancy between pregnancy and delivery in women over thirty years of age who have fewer than ten eggs. The older such a woman gets, with smaller numbers of available eggs, the greater the chance that she will miscarry even if she does get pregnant. This means that when only a few eggs are remaining in your ovary, those that are left are often of poorer quality. A look at figure 12.3 compares the risk of having a child with Down syndrome to a woman's age. Down syndrome (formerly called mongolism) represents a specific chromosomal error where the embryo has three copies of chromosome 21 instead of the normal two copies. This extra genetic material on chromosome 21 is what causes all the features of Down syndrome, which include reduced height, a simian crease in the eyes, reduced life span, and markedly retarded intelligence. This most feared of all congenital abnormalities occurs in over 1 percent of women aged forty, and in over 4 percent of women who have a child at age forty-five (as you can see from the graph).

These three phenomena — a reduced pregnancy rate with IVF in

women over age thirty-five, the increased miscarriage rate with or without IVF in women over age thirty-five, and the increased risk of chromosomal abnormalities such as Down syndrome after the age of thirty-five — are all related to the same genetic problem in your ovary. As your ovarian reserve diminishes with age, the quality and quantity of those eggs diminish each and every year, and that phenomenon is what is responsible for the ticking of your biological clock. That is the reason why only 2 percent of women in their early twenties are infertile, while 25 percent of women in their midthirties are infertile. The inexorable decline in ovarian reserve is the common, unifying theme for learning how to manage your biological clock and having a healthy, normal child. As you put off childbearing until you are ready emotionally, socially, and financially, you need to be able to plan with awareness what is happening hour by hour and year by year in your ovary. With the proper information, you can successfully keep track of this, plan your life, and avoid the terrible surprise you may receive by finally deciding to start your family after your clock has already run out.

Figure 12.4 demonstrates an attempt on the part of the CDC to try to figure out whether or not the live-birth pregnancy rate across a wide variety of IVF programs, good and bad, throughout the United States can be related to any specific diagnosis of the cause of the infertility. What those bars show (allowing for the usual variation and noise in any study) is that in trying to prognosticate success of treatment, the so-called diagnosis, the only thing that matters is diminished ovarian reserve. In other words, all that matters in determining pregnancy rate with treatment is whether or not you have a lot of eggs left. Whether your doctor tells you that he or she thinks your tubes are a problem, or that you don't ovulate properly, or that you have endometriosis, or that your husband has a sperm problem, or if nobody can figure out what your problem is, or if you have multiple factors (whether multiple female factors, or multiple male and female factors), none of this useless diagnostic categorization predicts your chance for having a healthy, live baby. It is only your age and your ovarian reserve that matter.

As your number of eggs diminishes with time, the ability of those remaining eggs to perform the complex process of meiosis (where the forty-six chromosomes become twenty-three) is hampered. Your egg must have exactly half the number of chromosomes that it began with (twenty-three) so that its chromosomes can combine with the sperm, which also has to have half the number it began with (twenty-three), in



**FIGURE 12.4**

Live-birth rates among women who had ART cycles by diagnosis, 2000. No difference for any diagnosis except “diminished ovarian reserve.” Combined overall CDC Atlanta data of all IVF programs in the United States.

order to result in an embryo with the normal number of forty-six chromosomes. Indeed, all the cells in your body must have forty-six chromosomes, twenty-three from the egg and twenty-three from the sperm. In the aging ovary, as the number of remaining eggs diminishes the likelihood of chromosomal errors increases. On average, this problem increases precipitously at age thirty-seven. However, it occurs at different ages in different women. You need to know how much reserve *your* ovary has, and at what age *you*, in particular, need to worry. If you are nearing that age, you either need to try to get pregnant soon or else have your eggs or ovarian tissue frozen for future pregnancy.

### Fears About IVF Offspring Not Related to Age

A frightening story came out in the *L.A. Times* on January 24, 2003. You need to know how to deal with and analyze reports like this about the alleged negative consequences of IVF. This newspaper reported an alleged link between several rare medical abnormalities, including retinoblastoma and Beckwith-Wiedemann syndrome, and IVF. Just to cover themselves, the authors of the article did say toward the end: “The

link between in vitro fertilization and birth abnormalities may still turn out to be spurious,” and “several fertility experts pointed out that other studies have found no heightened risks.” In fact, the retinoblastoma risk was later quietly debunked by a highly respected study from the Netherlands. However, the press had nonetheless accomplished their goal of selling good copy and creating unwarranted fears.

Beckwith-Wiedemann syndrome is extraordinarily rare, occurring in only about one in fifteen thousand natural births. Therefore, in any population of one million births (the number of in vitro fertilization babies born by 2003) there would have to have been at least sixty-two cases of Beckwith-Wiedemann syndrome. In the United States in just one year alone, more than thirty-five thousand babies have been born via IVF, so at least four would have to have had this condition. That is just the normal incidence. However, as soon as one mother experiences the tragedy of a child born with a rare congenital anomaly, such as Beckwith-Wiedemann’s, she will naturally go to the Internet and look for others who have had the same problem. The Brussels group has reported detailed, meticulous IVF follow-up on almost six thousand cases, and in that report, there was not one instance of Beckwith-Wiedemann syndrome. Of course, by the time fifteen thousand babies have been studied, there is most likely going to have to be a case of Beckwith-Wiedemann. But to evaluate whether you should be fearful of trying to have a baby with IVF technology, you need to compare your risks to that of a normal, fertile population.

An equally alarming article in the March 2003 issue of *Popular Science* attempted to terrify the public about the dangers of IVF, claiming that IVF is an unregulated procedure. In reality, IVF is the most carefully monitored and regulated field of medicine. Press hysteria was aggravated by the publicity-seeking claim of an off-the-wall, cultist religious group, the Raelians, that they were going to start to clone human beings. Cloning is not even remotely akin to what is performed in an IVF lab.

Because such hysteria can be generated by unknowledgeable sources, you will have to engage in some serious study on this issue in order to have peace of mind and be comfortable with whatever steps you decide to take, whether going through IVF, conventional fertility treatment, or simply remaining childless. In this chapter, I will give you the tools, the information, and the resources to decide for yourself.



## First Published Studies on Risk to Offspring from IVF or ICSI

First, let's discuss scientific reports which caused concern that ICSI or IVF might have dangerous consequences for the offspring. In a 1998 study from Sydney, Australia, children at one year of age conceived via ICSI were compared to a group conceived by routine in vitro fertilization, and to a similar-sized group conceived naturally. There were eighty-nine children in the first group, eighty-four children in the second group, and eighty children in the naturally conceived group. The Sydney paper found no significant difference in the incidence of major congenital malformations, abnormalities, or health problems among ICSI children, IVF children, and children conceived naturally. However, this report stated that 17 percent of children conceived by ICSI had either mildly or significantly delayed development at the one-year mark compared to only 2 percent of a control group of children conceived by IVF, and only 1 percent of children conceived naturally. This report stirred up considerable alarm and seemed to contradict the general, worldwide experience of infertility doctors and their patients. In fact, if anything, our observation of ICSI and IVF offspring is that, on average, they are much more intelligent and advanced in development than what we would see in the general population (I'll explain the reason for that later).

Five years later, in 2002, at a meeting of the European Society for Human Reproduction, the same group reevaluated and reexamined these children and found absolutely no developmental difference. There was no difference in intelligence or the incidence of health problems among any of the groups of children arising from ICSI, from conventional IVF, or from spontaneous conception. At the same time that the Sydney paper came out in 1998, the Brussels group had carried out a similar study for developmental milestones for children aged two years. Their results indicated that neither the ICSI nor the IVF children had any lower score than the general population, and there was no indication of ICSI children having slower mental development than their counterparts from fertile parents. In 2001, the medical journal *The Lancet* published a study of children recruited from twenty-two different fertility centers throughout the United Kingdom. The study looked at neuromuscular development, intelligence, postnatal health, and congenital

abnormalities in children conceived by ICSI, conventional IVF, and natural conception. They found no increased incidence of major congenital abnormalities in the ICSI group or the IVF group compared to the spontaneously conceived group of children. More important, there was no difference whatsoever between the ICSI or IVF offspring and the controls in neurodevelopmental scores or intelligence. So, at this point, there was no basis for fearing that there would be any difference between the children derived from ICSI versus those derived from spontaneous conception.

Then, in 2002, a series of alarming studies was published in the *New England Journal of Medicine*. One report came out of Western Australia. It involved 301 infants conceived with ICSI, as well as 837 infants conceived with conventional IVF. Those two groups were compared to 4,000 naturally conceived infants. It was simply a chart study, and no one had actually examined the children. This study claimed that 8.6 percent of the 301 children conceived by ICSI and 9 percent of the 837 infants conceived with conventional IVF had major birth defects diagnosed at one year of age. They compared this to the 4.2 percent diagnosed with congenital abnormalities from the naturally conceived group. I will discuss later in this chapter how that paper was completely in error.

In the same issue of the *New England Journal of Medicine*, an article was published by the CDC from Atlanta, stating that “among singleton infants conceived with IVF or ICSI, there was twice the incidence of low birth weight as in naturally conceived singleton infants.” Oddly, among twins, who would be expected to have a lower birth weight anyway, IVF and ICSI children had no greater incidence of low birth weight than the general population. That seemed to make no sense. It was strange that among singletons there would be a greater risk of low birth weight with IVF and ICSI patients than with the general population even though among twins there was no greater risk of low birth weight. (Of course, lower birth weight in itself is not a terrible consequence, unless it is associated with an increased risk of developmental and other health problems.)

Reading between the fine print of this otherwise concerning paper, one can see that this lower birth weight in singleton ICSI-IVF offspring was found only when there was a greater number of fetal heartbeats in the early ultrasound monitoring. In other words, these were twins that reduced to singleton, and so they would be expected to have lower birth

weight. Thus, even singleton children with lower birth weight are only a result of the multiple-birth problem, and there was no developmental problem associated with this slightly lower birth weight. Let me explain.

In order to increase the chance of pregnancy in IVF and ICSI, usually several embryos are placed into the uterus just to increase the chance of a pregnancy occurring, since the majority of human embryos are not going to develop. This means that there is, of course, a higher risk of multiple pregnancies, as with any infertility treatment (even the simplest fertility pills). This means it is possible for more than one embryo to implant. It is well known and established that high-order multiple pregnancies (greater than two) create a greater risk of premature birth and low infant birth weight. Thus, the lower birth weight of these ART offspring *cannot, in any respect, be attributed to any problem with ICSI or IVF itself, nor to the propensity of these parents to have low-birth-weight children.* Low birth weight is simply a risk associated with carrying more than one baby. In IVF programs that do not carelessly transfer large numbers of embryos, there will be no difference in birth weight among either singletons or twins compared to a naturally conceived population of singletons or twins.

### **Risks Associated with Multiple Pregnancy**

Clearly, the biggest issue for infertile couples to confront is the risk associated with a multiple pregnancy. However, this risk of multiple pregnancy can be completely controlled in IVF and ICSI, whereas with the general administration of fertility-promoting drugs, there is very little control. This means that IVF and ICSI are *safer* than the routine administration of fertility drugs. The popularly discussed septuplets from Iowa, whom I discussed in chapter 8, were, in truth, a medical tragedy, but not a tragedy related to IVF. The mother of the septuplets never underwent IVF. Indeed, if she had gone through IVF, the doctors could have carefully chosen the one or two best embryos to replace and could have frozen the extras so that she would have had a normal singleton, or at most twin, delivery. The big danger associated with IVF as compared to natural conception in a fertile population is the issue of transferring too many embryos, with the danger of more than two or three such embryos implanting. This results in low-birth-weight infants and premature delivery. But it is important to remember that this has

nothing to do with any intrinsic problem in the mother or father, or with IVF or ART.

Nonetheless, modern obstetrics is quite a remarkable science. Normal infant birth weight is somewhere between 5 1/2 and 9 1/2 pounds. In the past, premature infants with birth weights under 4 1/2 pounds were at severe risk, but now even infants of only three pounds have an excellent prognosis for survival without any obvious abnormality and free of any serious handicaps. Neonatal intensive care units that began to spring up in the 1960s, and that represent the standard of care throughout the United States, have even allowed the survival of infants weighing less than one pound, delivered as early as twenty-six weeks of pregnancy. It is truly one of the miracles of modern medicine that these extremely low-birth-weight infants can survive, and many appear to develop normally without serious handicaps. However, their condition is tenuous, the health risks are enormous, and infants born at less than thirty-two weeks or under three pounds are often at a clear disadvantage. That is why it is advisable to do whatever is possible to avoid carrying anything more than twins.

The best follow-up study of extremely low-birth-weight (premature) infants appeared in the *New England Journal of Medicine* in 2002 from Children's Hospital of Cleveland. It reported the outcomes of extremely low-birth-weight infants born twenty years earlier. They compared 242 survivors among *extremely* low-birth-weight infants, averaging only 2.3 pounds at birth, with 233 controls from the same population base in Cleveland who had normal birth weights. It was quite remarkable that these very-low-birth-weight infants on average had IQ scores only five points lower than their normal-birth-weight controls. An editorial (in that same issue of the *New England Journal of Medicine*) coming out of the Harvard School of Public Health entitled "Premature Infants Grow Up" remarked about the relative success of these children. In fact, the extremely premature children were "almost as successful as the members of the normal birth weight comparison group in completing school." The editorial noted that "despite academic and other developmental challenges, most of these adolescents who had very low birth weight have academic achievement at least equal to that of their normal birth weight peers." *Moderately* low-birth-weight children (those between three pounds and five pounds at birth) have *not been shown to have any more problems* than normal-birth-weight controls.

I was sitting at a baseball game with the son of a friend of mine one summer, and he introduced me to his roommate from college, a Phi Beta Kappa and a star on the tennis team. He is an extremely big fellow, and I teased him a bit about his size. It was then that I found out that twenty years earlier, he had been born prematurely, at a weight of only two pounds, and his parents and pediatricians had never expected him to survive. Yet here he was, intelligent enough to be Phi Beta Kappa in his third year of college, and a star tennis player. So large population studies do not necessarily reflect individual cases.

Although I would warn very strongly against any practice that would encourage the proliferation of low-birth-weight infants, such as a triplet or greater pregnancy, I must confess that of the ten triplet pregnancies that we have had in the previous decade (which worried me greatly), all have gone past thirty-two weeks of pregnancy and resulted in healthy children without any measurable handicaps. But such a good result requires enormous expense and continuous care during pregnancy from a skilled team of super-high-risk specialists.

### **Incidence of Birth Defects in ICSI and IVF Offspring Compared to Spontaneously Conceived Children: The Brussels Study**

Our greatest resource in studying this issue comes from the Dutch-speaking Free University in Brussels, an institution I have personally worked with for well over a decade. From the very inception of their IVF program in the early 1980s, the Brussels group has had a transparent methodological approach to following up every single pregnancy and every single child born from their IVF procedures. Every pregnant mother was offered amniocentesis with chromosome testing of the fetus. Every single newborn baby was examined in detail by pediatric specialists, neurologists, and geneticists. This examination and follow-up was carried out on a precise yearly basis, and any treatments necessary were carefully documented and recorded in a massive computer database. The details of their follow-up on each pregnancy and each child (almost ten thousand babies) over the course of these decades gives us the information we need in order to be comfortable with IVF. Such a prospective study (rather than anecdotal news stories) is the only way to discern what increased risk, if any, you take by embarking on IVF.

First, I will discuss the incidence of congenital abnormalities (obvious defects visible at birth), and in later sections I will discuss the issue of chromosomal abnormalities (defects in the chromosomes that would only be detected with genetic study by CVS, amniocentesis, or the study of the infant's cord blood at the time of delivery).

There seems to be a running battle between the Western Australia Epidemiology group and the Dutch-speaking Free University in Brussels, Belgium. The Western Australia group stated that children born as a result of ICSI were twice as likely to have a major birth defect than naturally conceived children in the general population. The Brussels group responded that the cases classified by the Western Australians as major congenital abnormalities were so minor as to have never been diagnosed in a routine population register of babies that were not specially being studied. For example, there were several cases of minor cardiac abnormalities, which are very commonly present at birth but often go undiagnosed in the general population because they are so minor and usually correct themselves by three to six months of age. When the Belgians eliminated those cases from the Western Australian evaluation, once again the incidence of congenital abnormalities (about 3 to 4 percent) was no different from what is routinely reported in a standard population of newborns conceived from a fertile population.

The Belgians have studied IVF and ICSI offspring in such detail and in such a transparent manner that they have the greatest credibility. In 2002 they reported impeccably detailed evaluations of 2,899 infants resulting from ICSI and 2,999 infants resulting from conventional IVF between the years of 1983 and 1999. This is the most detailed and reliable follow-up study ever performed on the health and genetics of infants conceived through IVF technology.

First, we will look at birth weight in ICSI as compared to birth weight in IVF offspring in almost six thousand births (see table 12.1). Of singleton births, only 1.5 percent of ICSI infants were very low birth weight (less than three pounds), and only 1.8 percent of IVF children were very low birth weight (less than three pounds). This was similar to the 2002 U.S. study from the CDC referred to on page 280. In a normal population, 1.4 percent of infants would be expected to have very low birth weight. It was readily apparent that neither IVF nor ICSI increased the risk of premature delivery or of low-birth-weight or very-low-birth-weight infants, other than what could be observed as simply a

consequence of multiple pregnancy. Note that the Brussels group had a very low incidence of multiple pregnancy, far lower than the United States, because of a more conservative approach to the number of embryos they transfer during an IVF cycle.

TABLE 12.1

**Comparison of 2,889 ICSI Offspring to 2,995 IVF Offspring  
(Prematurity and Birth Weight) — 2002**

	ICSI CHILDREN	IVF CHILDREN	EXPECTED IN NORMAL POPULATION
Average birth weight	2806	2920	16,730
Singletons	3224	3176	
Twins	2394	2382	
Triplets	1762	1769	
Quadruplets	—	1373	
Prematurity (<37 weeks)	902 (31.8%)	867 (29.3%)	
Singletons	126 (8.4%)	140 (9.0%)	
Twins	669 (54.6%)	600 (47.6%)	
Low birth weight (<2,500 g)	760 (26.7%)	784 (26.5%)	
Singletons	106 (7.1%)	121 (7.8%)	1,197 (7.5%)
Twins	593 (48.1%)	568 (45.1%)	
Very low birth weight (<1,500 g)	125 (4.4%)	167 (5.6%)	
Singletons	22 (1.5%)	28 (1.8%)	239 (1.4%)
Twins	64 (5.2%)	96 (7.6%)	

BONDUELLE ET AL., 2002

Only 3.4 percent of ICSI offspring and 3.8 percent of IVF offspring had any major congenital abnormality. There is also no difference in the incidence of these abnormalities related to the origin of the sperm, whether ejaculated or surgically retrieved from the testis or epididymis. In both ICSI and IVF offspring, as well as in the general population, there are slightly more boys than girls.

Looking at the minor malformations, which don't require surgery and result in no functional loss, again there was no difference from a normal population. Minor malformations include hairy ears, bilobe earlobes, large ears, moles, various septal defects in the heart that close and correct spontaneously over the first few months of life, phimosis of

the foreskin, a fifth finger, irregularity of toe length, etc. An enumeration of everything that could possibly be slightly off of perfect could scare any couple into not wanting to try to have children at all, but this is part of life. In any event, there clearly was no difference noted in this huge series of almost six thousand infants between the health of offspring of fertile couples and the offspring of ICSI and IVF procedures. For couples who wish more detail, I recommend they look up the scientific paper, which is located in the journal *Human Reproduction*, 2002, volume 17, issue no. 3, pages 671 to 694. However, I can summarize by saying that there is no greater risk of congenital abnormalities or other illnesses in children born via IVF or ICSI compared to those born via natural conception other than those related to high-order multiple pregnancy.