# INTRODUCTION

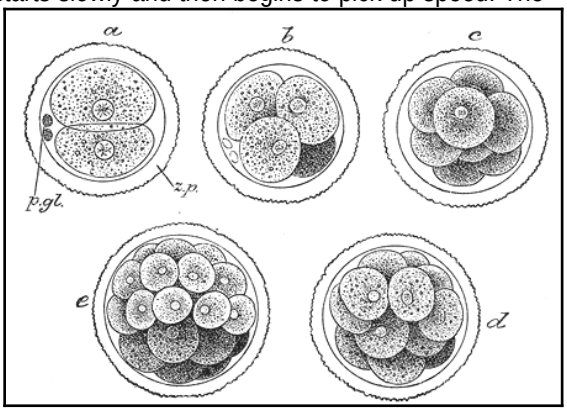
Although we are most familiar with the division of the prenatal period into trimesters, we do this only as a convenient way of dividing up the approximately 9 months (actually 266 days) of pregnancy into 3 equal segments. But biologically speaking, the term "trimester" has no real meaning. The three "stages" that do have biological meaning are not at all equal in length. The first, which is the subject of this chapter, is the germinal stage. It lasts only 2 weeks, from fertilization until the end of implantation. The second is the 6-week long embryonic stage, and it lasts from the end of implantation to the end of the second month. The last phase is the fetal stage, and it takes up the last 7 months of pregnancy and ends at birth.

In order to standardize the structural development of the germinal and embryological stages, a system of 23 stages was developed. Called the Carnegie Stages (after the Carnegie Institute), each is based on developmental structural changes and roughly corresponds to time since fertilization.

# GERMINAL DEVELOPMENT

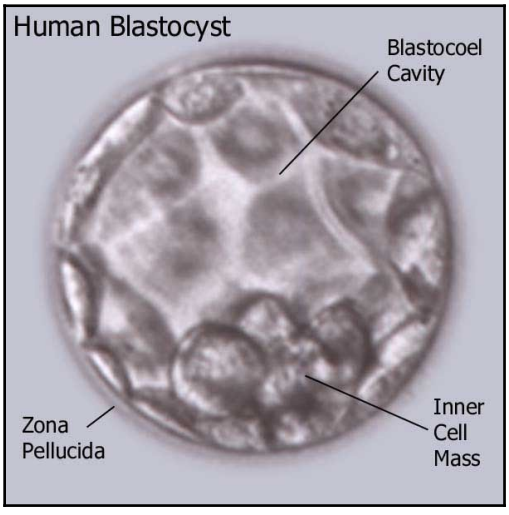
## The Zygotic Phase

Within 24 to 48 hours after fertilization, the single fertilized cell resulting from the fused union of the sperm and the ovum begins to divide. A series of mitotic divisions results, with a doubling of cells with each division. The nucleus splits in half, and the cell divides. This process, called cleavage, starts slowly and then begins to pick up speed. The first division results in 2 cells (called blastomeres), then these 2 cells produce 4 and so on. Every cell produced has the exact genetic information that the original cell has. The zygote, however, doesn't get any larger, because with each cleavage, the blastomeres are half the size of the previous cells (Gilbert, 1989).




## The Morula Phase

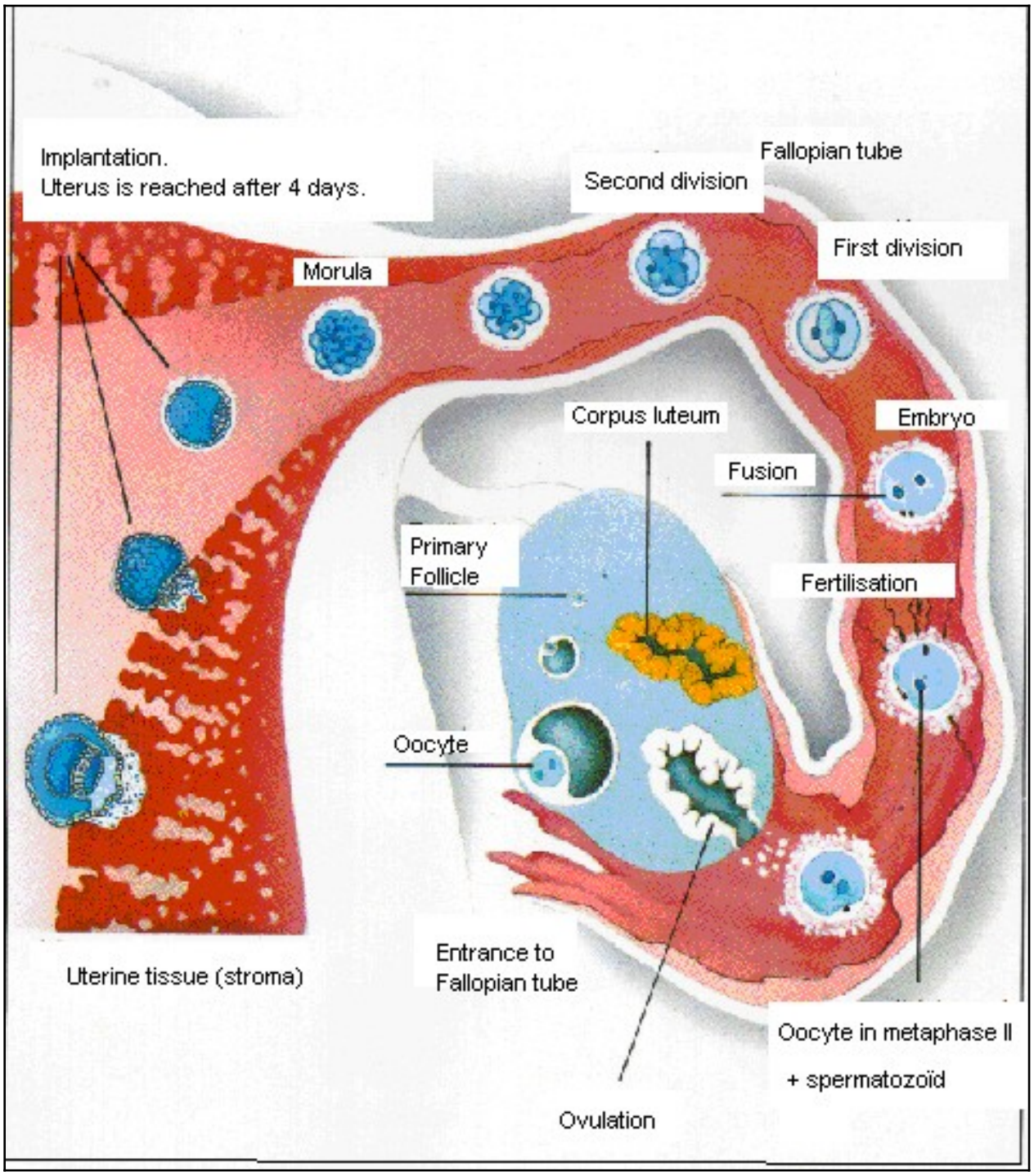
As this process continues, the zygote becomes a morula, a spherical mass with between 16 and 32 blastomeres. Even at this early stage, these cells begin to organize into the group of cells that will become the baby and another group that will become the placenta and umbilical cord (Nathanielz, 1992).




## The Blastocyst Phase

By day 4 or 5, a small fluid-filled bubble emerges in the morula, and it will continue to grow, eventually becoming the amniotic sac. At this point the morula becomes a blastocyst, and by the 6th day after fertilization has over 100 cells.

All of this takes place in one of the fallopian tubes, which connect the ovary to the uterus, the destination point of the blastocyst. As we noted earlier, the movement of the zygote/blastocyst is assisted by the fallopian cilia and the rhythmic contractions of the muscular walls of the tube. At this point it is encased in a non-adhesive protective shell known as the zona pellucida to prevent it from attaching to the wall of the fallopian tube (Norwitz, Schust & Fisher, 2001).




As it moves toward the uterus, the cells in the blastocyst continue differentiating. The outer ring of cells, called the trophoblast, will become the placenta, umbilical cord and amniotic sac. The inner mass of cells, called the embryoblast, will become the embryo itself. This inner cell mass, consists of stem cells, and at this point in development, they have the amazing ability to become any one of over 200 types of cells (Macdonald, 2005).

After approximately 6-7 days, the blastocyst enters the uterus and within 72 hours “hatches” from the zona pellucida, thereby exposing the trophoblast cells and allowing for adhesion to the wall of the uterus. This typically (but not always) takes place in the upper posterior (fundal) section of the uterus. The blastocyst will eventually “land” and begin the process of implantation, officially beginning the long months of pregnancy.

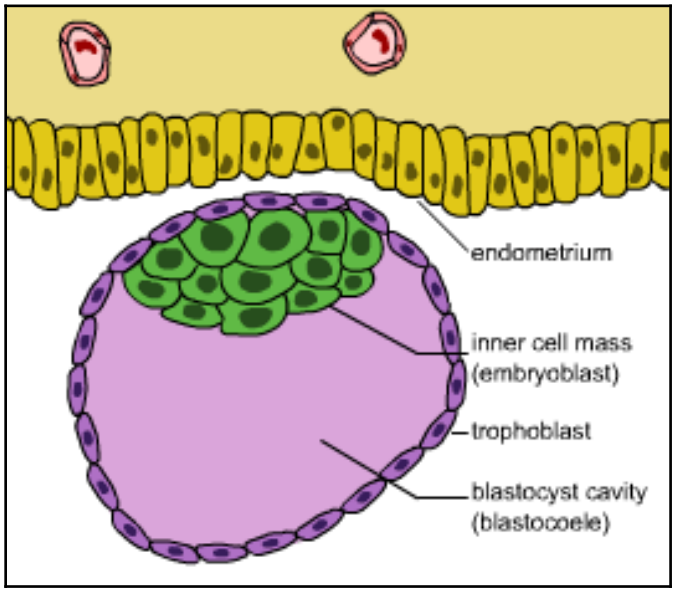
# IMPLANTATION

## The Three Stages of Implantation

The process of implantation includes three different stages (Staun-Ram & Shalev, 2005), the first 2 relatively short in duration and the third taking longer to happen.

### *Apposition*

The first stage, called apposition, includes the initial, somewhat unstable, adhesion of the blastocyst to the wall of the uterus. Small protrusions from the blastocyst (called microvilli) latch onto small protrusions (called pinopodes) in the wall of epithelium.




### *Stable Adhesion*

The second stage is a continuation of the first and is called stable adhesion, because the "latching-on" process involves more contact between the blastocyst and the uterine wall is thus more "secure".

### *Invasion*

The final stage is the invasion process, in which the blastocyst literally buries itself in not only the outer wall of the uterus (the endometrium), but also penetrates in second layer of the uterus, called the myometrium. This process results in the infiltration of the maternal blood supply, establishing the beginning of utero-placental circulation (Norwitz, Schust, & Fisher, 2001). By day 10 after fertilization, the blastocyst is completely buried in the wall of the uterus and the uterine epithelium has grown a layer of cells over the implantation site (Pijnenborg, Robertson, Brosens & Dixon, 1981).

Once this invasion occurs, the cells of the trophoblast begin interacting with cells in the uterus, giving and taking "orders" and influencing and being influenced by the mother's cells (Klimek, 2001; Vigano, Mangioni, Pompei, & Chiodo, 2003). This back-and-forth communication network establishes a chemical dialogue referred to as "cross talk" (Hill, 2001). It is the foundation on which successful pregnancy relies. Where there are problems and a failure to synchronize occurs, implantation will fail and a miscarriage will take place (Barnea, 2001; Jaffe, 2001).

## Testing for Pregnancy

The chemical dialogue of the "cross talk" means that pregnancy can be detected using "pregnancy tests". The cells of the trophoblast secrete a hormone called human chorionic gonadotropin (hCG), which prompts a woman's ovaries to continuing releasing progesterone. The result of this progesterone is the continued swelling and capillary growth of the endometrial wall near the blastocyst. This greatly increases the chances of the embryo's survival. The release of hCG also "tells" a woman's ovaries to temporarily (during pregnancy) stop ovulation and consequently menstruation (Nilsson & Hamberger, 2003 in Craig & Dunn page 78).

The presence of hCG can be detected in both urine and blood tests from implantation onward (about 12-15 days after fertilization). Urine tests are generally less accurate than blood tests, and can indicate a false result from a number of causes other than pregnancy.

# PROBLEMS IN IMPLANTATION

## Genetic Causes

It has been estimated that between 50 and 70% of all zygotes do not survive the first two weeks of the germinal period. Some of these are lost because of genetic issues. Missing (for example, Turner's syndrome) or extra genetic material (for example, Down Syndrome), damaged chromosomes (see photographs at right), or recessive inheritance (for example, Huntington's disease) can all be causes of lack of viability and miscarriage.

## Timing Issues

The timing of implantation has also been identified as potentially problematic. Research has found that the ideal time for implantation is 8-9 days after ovulation. The risk of pregnancy loss increases with each day following. Wilcox, Baird and Weinberg (1999) found that at day 9 implantation, 13% of pregnancies ended in loss, with each subsequent day resulting in a greater percentage of miscarriages; day 10 (26%), day 11 (52%), day 12 and following (82%).

## Maternal Causes

The uterine and fallopian environment can also be the source of implantation problems. It is estimated that 75% of pregnancy losses are due to failures of implantation (Wilcox et al, 1988). The causes of many of these miscarriages are never known, but evidence does indicate that the presence of certain maternal conditions and/or factors potentially increases the likelihood of failure to implant.

Regardless of the cause, failure to implant may result in a heavy menstrual period that arrives a little late and contains the unimplanted blastocyst. Women may never even know that they were temporarily pregnant (Craig & Dunn, 2007, 78).

### *Endometriosis*

A common source of implantation difficulties is endometriosis, a condition where the endometrial tissue from the uterus "migrates" to other parts of the body. It has been referred to as "reverse menstruation", because instead of flowing out of the body, the tissue flows into and attaches to the fallopian tubes, the ovaries, the pelvic cavity, the bladder, the rectum and in extreme cases even the lungs, arms, legs and brain. This tissue, wherever it migrates, continues to respond to hormonal changes in a woman's body over the menstrual cycle, building up and then sloughing off in 28-day cycles. Since there is often nowhere for this "flow" to leave the body, it builds up, causing inflammation, scarring, blood-filled cysts, and adhesion (the connection of 2 normally separated organs or bodily structures).

Endometriosis does tend to run in families affecting somewhere between 2-7% of all women and being a factor in 25-50% of women reporting infertility. But the presence of endometriosis does not always result in infertility, since only 30-40% of women with the condition are infertile.

Endometriosis can causes fertility problems in a variety of ways. The build-up of the endometrial tissues can simply get in the way and block access of the ova and sperm to each other, preventing fertilization. Even if fertilization occurs, the tissue can block access of the zygote to the uterus. The scarring in the uterus can cause the endometrium to be inhospitable and impenetrable to a blastocyst should it "land", thus preventing implantation. Adhesion of the various organs can prevent them from functioning and can be so extensive that are literally immobilized (Endometriosis, 2005).

### *Uterine Fibroids*

Another cause of implantation failure is the presence of non-cancerous tumors in the uterus. Called fibroids, they can be as small as a peanut or as large as a grapefruit and are relatively common, affecting up to 25% of all women. They tend to develop between the ages of 30 and 50 and are more commonly found in overweight and African-

American women, and in women who have not had children (Uterine Fibroids, 2006). Women who have taken birth control pills causing increased production of estrogen are also more likely to have fibroids, due to the stimulative effect that estrogen has on fibroid growth (Slupik & Allison, 1996).

Most women with uterine fibroids will not experience any symptoms. Symptoms, when they are present, include heavier-than-normal menstrual flow, pain in sexual intercourse, and bowel or urinary symptoms due to pressure from the fibroids. The presence of these symptoms depends on where the fibroids are growing and how large and numerous they are.

While fibroids do not necessarily cause infertility or miscarriage, they can at times impede movement and access of sperm, ova, and zygotes. For instance, they may block the cervix or a fallopian tube or may prevent a blastocyst from implanting in the uterine lining.

If a woman with fibroids does get pregnant, they may grow in size during the 9 months of pregnancy due to increased estrogen levels and blood flow. While most women are able to give birth, the baby may be born premature because there is simply not enough room in the uterus for both the baby and the enlarged fibroids.

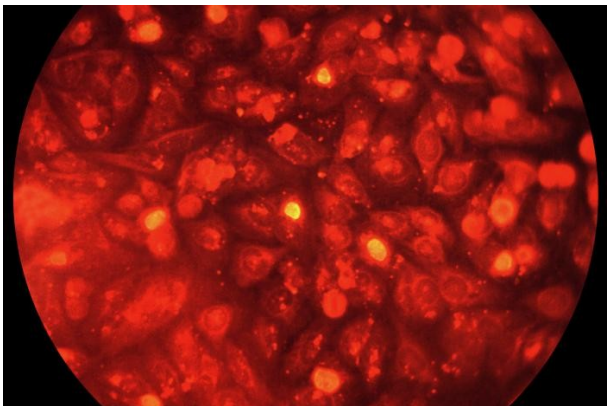
## *Previous Abortions*

According to Lurie and Shoham (1995), legal first or second trimester abortions do not significantly raise the risk factors for implantation problems later on. But late-term abortions do raise risks for a variety of reasons. The abortion procedure known as dilation and curettage (D&C) is associated with increased risk of cervical or uterine scarring. Implantation problems may be the result, due to the inability of the blastocyst to adequately adhere and survive the implantation process..

Further, any abortion (or other procedure) that requires the dilation of the cervix (to allow for the insertion of a suction tube) can weaken the cervical structures, causing what is known as an incompetent cervix. The result may be a premature dilation during pregnancy. While rare, any abortion that utilizes a suction tube (the majority of abortions), can result in perforation of the uterus or large blood vessel or the intestine. If this occurs, surgery is needed, which may cause complications of fertility. Finally, any foreign object entering the uterus introduces the possibility of uterine infection, which may also influence future fertility.

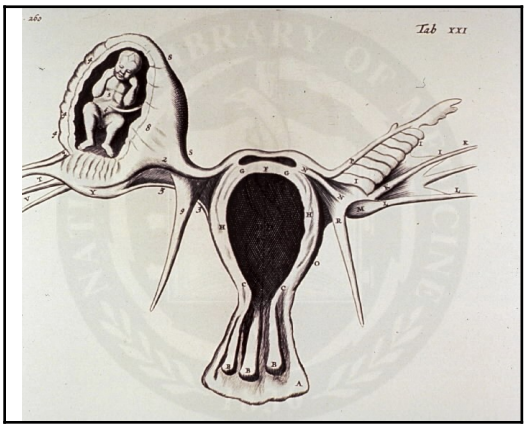
## *Previous Sexually Transmitted Infections*

Women who have experienced previous sexually transmitted infections, especially the bacterial infections Chlamydia and gonorrhea, are also at greater risk for fertility and implantation complications (Westrom, 1994). Both infections are associated with the incidence of ectopic pregnancy (discussed below) and pelvic inflammatory disease (PID) (Low et al, 2006). PID is caused by a migration of the bacterial infection from the vagina to the uterus, fallopian tubes and ovaries, resulting in inflammation and eventual scarring. Sexually transmitted infections are not the only cause of PID. Other potential causes may include a staph or strep infection, or any procedure which introduces the potential for infection (for example, a gynecological exam, IUD insertion, childbirth, miscarriage, abortion, or an endometrial biopsy).



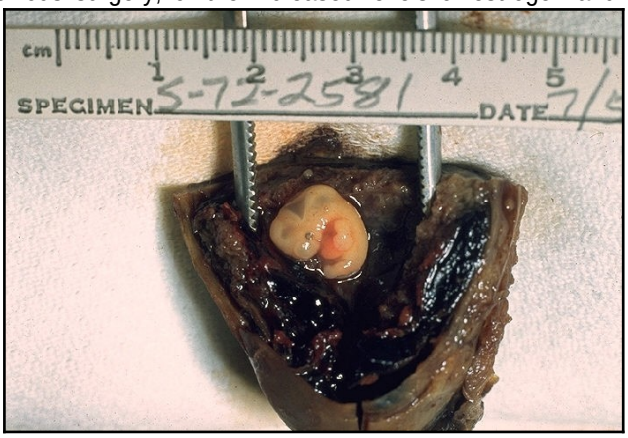
The symptoms of PID may range from nonexistent to severe. Particularly when caused by chlamydial infection, symptoms are typically absent and thus the infection is often ignored and PID may go untreated. When symptoms are present, they may include abdominal pain, irregular menstrual discharge, and painful sexual intercourse. Without treatment, PID causes normal tissue to scar, blocking access of sperm, ovum and zygotes to each other and the uterus. The scarring in the uterus can cause the endometrium to be inhospitable and impenetrable to a blastocyst, thus preventing implantation. If the zygote is blocked in the fallopian tube and cannot reach the uterus, the risk of ectopic pregnancy greatly increases.

PID results in infertility in approximately 1 out of 8 women who have the infection. Multiple episodes of PID increase rates of infertility. Approximately 1 million American women experience an episode of PID each year. Risk factors are increased for younger women, particularly teenagers, because their cervixes are not fully developed, increasing susceptibility. The more sex partners, and the more sex partners a woman's partner(s) has/have had, increase risk due to greater exposure to bacterial infections (CDC, 2006).




## Ectopic Pregnancy

As we have read above, a consequence of several maternal risk factors is the occurrence of implantation in a place other than the uterus, most often in one of the fallopian tubes (and thus sometimes called a "tubal pregnancy"). But implantation can also occur on the ovary, cervix, or even in the pelvic cavity. Ectopic pregnancies are most often caused by some blockage (for instance, a fibroid or endometriosis) or condition (for instance, scar tissue caused by a bacterial infection) which delays or prevents the zygote from reaching the uterus. Other potential causes may includes fallopian tube defects, previous surgery, or the increased levels of estrogen and progesterone caused by birth control pills (which slow zygotic movement through the fallopian tubes). The "morning after pill" (emergency contraception) has also been linked with greater increases in risk for ectopic pregnancy. But for many ectopic pregnancies, there is no known cause. These types of pregnancies are relatively common, occurring from 1-2½% of all pregnancies.




No matter what the cause, the implanted embryo cannot survive and if allowed to grow, can eventually produce in a rupture of the fallopian tube, resulting in severe abdominal pain and heavy internal bleeding. Untreated, an ectopic pregnancy can cause death. A procedure called a laparoscopy is performed to remove the implanted embryo.

# PROBLEMS IN FERTILITY

Numerous factors influence fertility, including genetics (Rutter, 2003), nutrition, ethnicity, culture, sexual behavior, timing, and many other variables. Among the most profound changes affecting fertility over the past several decades has been the introduction and common use of various birth control mechanisms as well as the selective use of abortion. When coupled with the delay of both first marriage and child-bearing typical of modern western societies (Hobcraft, 2003), it is clear that the patterns of procreation have changed significantly (Rutter, 2003). One example of these changing patterns is the rise in the industrial west of the proportion of multiple births relative to single births. Due to the relative increase in the number of factors affecting infertility, particularly maternal and paternal age, and coupled with significant technological advances in ameliorating infertility, it is not surprising that the result is an increase in the number of multiple births due to assisted conception (Derom & Bryan, 2000).

## Fertility Drugs

Two common types of fertility drugs are available for women having difficulty conceiving. Taking these drugs would normally be advised only after looking at other lifestyle factors that may influence fertility. These may include diet, smoking, alcohol and drug use, stress, and environmental exposure to toxins (Younglai, Holloway & Foster, 2004).

Other factors may affect male fertility problems, resulting in low sperm motility and sperm count. In addition, tight clothing may be a contributing factor in increasing scrotal temperature and thereby influencing sperm production adversely. Hormonal factors may also influence male infertility, particularly testosterone, LH (luteinizing hormone) and FSH (follicle-stimulating hormone). Thus, the fertility drugs discussed below may be prescribed for men as well. All of these facts should be considered by women seeking to get pregnant prior to the ingestion or injection of fertility medications.

### *Clomiphene*

Clomiphene (sold under the brand names Clomid and Serophene) is taken orally and works by stimulating hormone production and release of FSH and LH, triggering ovulation and the subsequent release one or more ova. Since FSH and LH have multiple effects on a woman's body, side effects can include ovarian swelling, breast tenderness, insomnia, nausea, depression, weight gain, fatigue, and general irritability. There is also a 1 in 10 chance of having a multiple conception (twins, triplets or more).

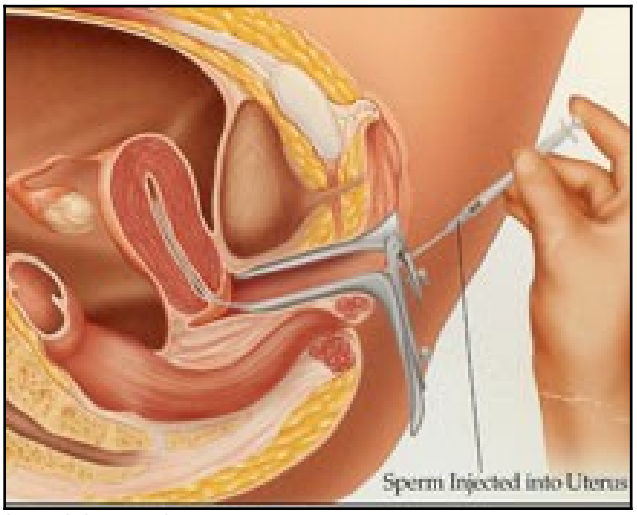
Clomiphene causes ovulation within 3 months in 80 percent of women. Forty percent of these women will eventually get pregnant. If clomiphene is not successful in producing pregnancy, then a second type of fertility drug called gonadotropins is often prescribed.

### *Gonadotropins*

Human menopausal gonadotropins (hMG) come in various forms and are sold under a variety of brand names (Pergonal, Repronex, Menogon, Fertinex, Follistim, Puregon, Pregnyl, Novarel, Profasi, Ovidrel). All variations of this class of fertility drugs include FSH or a mixture of LH and FSH and are administered by injection. The result is similar to clomiphene, except multiple ova are almost always produced and released at ovulation. This means that both the chances of getting pregnant are higher (up to 60% success rate) and the chances of conceiving multiples higher (up to 40%). Side effects include bloating, weight gain and fluid retention.

## Artificial Insemination (AI)

When endometriosis or some other factor is present that makes sexual intercourse difficult or when male factor infertility has been identified as the contributing factor in an inability to conceive, a technique called artificial insemination is used to increase the chances of conception. The woman tracks her menstrual cycles for several months, determining when her fertility may be at its peak. A sample of sperm is collected from the donating male and processed or "washed". This effectively reduces any debris or abnormal sperm, producing a highly concentrated dose of healthy, motile sperm. The sperm are then injected directly into the woman's uterus through a catheter. The process may be combined with fertility drugs to maximize success.




Advantages of the procedure include its relative quickness and the fact that it is generally less invasive than some of the processes discussed below. It only takes an hour or so and fertilization takes place normally in the fallopian tubes. The main disadvantage of artificial insemination is the "hassle factor". Couples must track the woman's menstrual cycle, and be available at the time of her maximal fertility to provide a sperm sample and then wait until it is washed and then have it inserted.

Success rates range from 40 to 50% and can be significantly increased with the concomitant utilization of fertility drugs (Comhaire & Thiery, 1986). Success rates decrease in older couples and when endometriosis and/or PID are present.

## Assisted Reproductive Technologies (ART)

When fertility drugs or artificial insemination are unsuccessful in producing pregnancy, more technologically complicated and invasive techniques are available. All are relatively expensive, have complications (Grudzinskas, 2000), and have no guarantee that they will work. All types of ART can also use donor (15% of the time) or non-donor (85% of the time) sperm and ova (CDC, 2004). Success rates vary considerably by type of contributing problem, age, and numerous other issues. According to the CDC (2004), success rates of all ART procedures resulted in no pregnancy 65% of the time, single-fetus pregnancy about 20% of the time, multiple-fetus pregnancy over 12% of the time, and ectopic pregnancy almost 1% of the time (CDC, 2004). But these pregnancies were not all successful, with over 15% resulting in miscarriages, about 54% in singleton births, and 29% in multiple births (CDC, 2004). Of live births, 64.6% were singletons, 31.6% were twins, and 3.8% were triplets or greater (CDC, 2004).

### *In Vitro Fertilization (IVF)*

In vitro fertilization is by far the most common ART process, accounting for over 99% (with and without ICSI which is discussed below) of ART procedures (CDC, 2004). It is a process in which ova are taken from the women's (or donor's) ovaries, often after she has taken several doses of fertility drugs to stimulate ova production. These ova are fertilized by the man's (or donor's) sperm outside the body (in a Petri dish or test-tube). Two or 3 days later, one or more zygotes are inserted into the uterus, usually by means of a catheter, with implantation naturally occurring. The process is often combined with drug treatments to insure the maximal receptivity of the endometrial wall of the uterus.

Due to the invasiveness of the procedure, potential side effects are numerous and include general discomfort, ectopic pregnancy, miscarriage, prematurity (Corabian & Hailey, 1999), and Ovarian Hyperstimulation Syndrome, resulting is thrombosis, enlarged ovaries, liver, kidney, and cardiorespiratory problems (Myrianthefs et al, 2000). There is also a relatively higher risk of multiple conceptions.

Success rates vary considerably depending on various factors, including hCG levels (Hauzman et al, 2001) and the age, with younger women having better outcomes than older women. The CDC reports success rates (live births) of between 31 and 34% of all women for the year 2002 (the last year the data are available).

### *Gamete Intrafallopian Transfer (GIFT)*

Accounting for only .2% of all ART procedures (CDC, 2004) and very similar to IVF, gamete intrafallopian transfer involves the harvesting of ova and the combination with sperm into a mixture that is injected directly into the fallopian tubes through a small incision in a woman's abdomen. Fertilization and implantation thus take place naturally. Success rates (live births) for GIFT are around 25% (CDC, 2004).

### *Zygote Intrafallopian Transfer (ZIFT)*

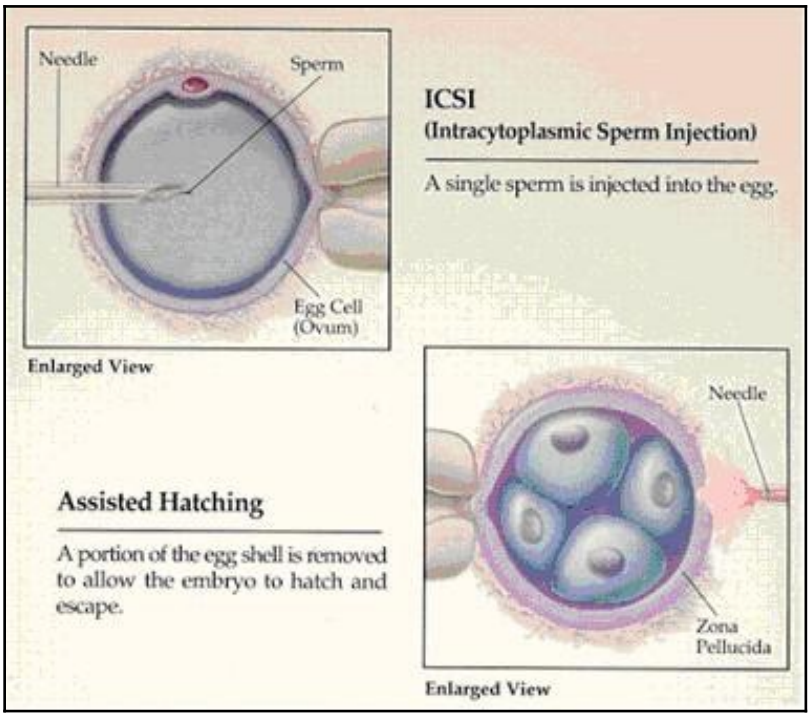
Accounting for only .5% of all ART procedures (CDC, 2004) and also very similar to IVF, zygote intrafallopian transfer involves the harvesting of ova and the fertilization by sperm outside the woman's body. The zygotes are then inserted into the fallopian tube (instead of the uterus as with IVF) with the expectation of natural implantation taking place. Success rates (live births) for ZIFT are around 26% (CDC, 2004).

### *Intracytoplasmic Sperm Injection (ICSI)*

Intracytoplasmic Sperm Injection (ICSI) is a procedure that is used when male factor fertility is an issue and is used in tandem with IVF (about half of IVF procedures also use ICSI). Ova and sperm are collected and the fertilization process is achieved artificially by injecting a sperm directly into an ovum. After 2 days, the resulting zygote(s) are then placed into the uterus, with the expectation of normal implantation. ICSI has several potential disadvantages, the most prominent being it short-circuits the natural process of conception which insures that only

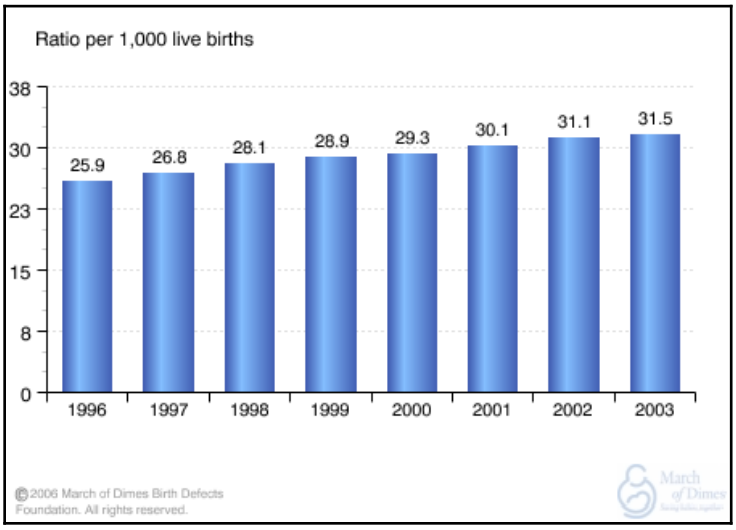
the strongest and hardiest sperm are able to fertilize an ovum. It also shares all of the IVF risk factors since it is a part of the IVF process.

### *Assisted Hatching*




With the IVF, ZIFT, and ICSI, procedures, fertilization takes place outside the women's body, so the natural processes may be subtly affected. One such process involves the protective shell of the ovum known as the zona pellucida. It encases the zygote and allows for smooth transition down the fallopian tube. But for implantation to occur, this shell must dissolve allowing for "hatching" of the blastocyst. This exposes the "sticky" cells of the trophoblast and increases the chances of adhesion to the endometrial wall. When fertilization takes place outside of the body, the zona pellucida does not naturally decompose and allow for "hatching" to take place. Thus, a procedure called "assisted hatching" is sometimes used to "help" the implantation process.

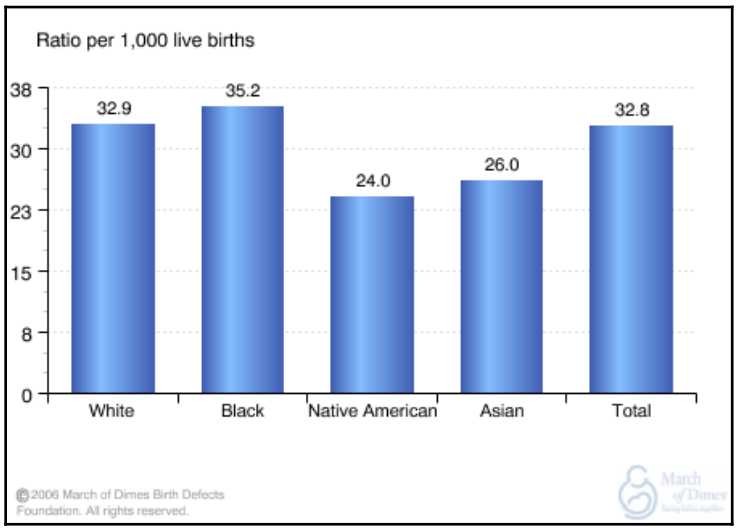
## MULTIPLE BIRTHS




While it is clear that the various assisted reproductive technologies do contribute to the greater likelihood of multiple births, such births also occur normally and naturally and have been a source of great interest and attention throughout history. The data show that the incidence of multiple births is increasing in industrialized countries. For instance, the proportion of twins in the United States has steadily increased since 1996.

The reasons for this steady increase include the above-cited influence of ARTs, but other factors may also play a role. For instance, folic acid supplements are thought to be a contributing factor. Women have been advised to take such supplements prior to conception to prevent neural tube defects such as anencephaly and spina bifida. A side effect of pre-conceptual folic acid intake is the increase in multiple conceptions. The increased use of oral contraceptives is also associated with increased risk of multiples. Women who have taken oral contraceptives for longer than 6 months and then conceive shortly after discontinuing their use double their chances of conceiving multiples.

The delay of childbirth generally and the resulting older age of first-time mothers contributes to the increased likelihood of multiples. Women over 40 are more than 4 times more likely to give birth to multiples than women under age 20. Further, the more babies a woman has had, the greater the chances with each subsequent pregnancy of being a multiple.




Finally, ethnicity also seems to affect multiple conceptions. As can be seen from the table at the right, women of African heritage have a significantly higher rate of multiple deliveries than white, Asian and Native American women. This is particularly true for those of Yoruba heritage, a large ethno-linguistic group in West Africa, primarily in Nigeria. The Yoruba have among the highest rates of twin births in the world, a ratio between 45 and 55 per 1000 live births. The all time winner for multiples is a small village in Brazil where the rate is over 100 per 1000 live births (Matte et al, 1996).

## Multiple Types

### *Non-identical Multiples*

Also known as fraternal, or dizygotic (or trizygtoic), these types of multiples develop from separate ova and separate sperm. As such, they are no more genetically similar than sibling brothers or sisters. After implantation, each multiple develops separate placentas and each has his or her own amniotic sac.

With parents of differing ethnic backgrounds, fraternal twins can be very distinct in the shade of their skin. Although rare, there have been documented cases where a woman has given birth to fraternal twins with 2 different fathers. If sexual intercourse with 2 different men happens relatively close together in time and during the window of fertility following ovulation, 2 separate ova may be fertilized by sperm from different fathers. It is thus possible to be a half-sibling and twin simultaneously.

Apart from some of the factors we noted earlier, non-identical twinning and other multiple conceptions do tend to run in families, but only on the mother's side, not the father's. But as we noted earlier, they are more likely to occur when ART procedures are utilized.

As you would expect statistically, for non-identical twins, about 25% are boy/boy combinations, about 25% are girl/girl and about 50% are boy/girl. Fraternal twins constitute about 2/3 of all twins, the identical type consisting of the other 1/3. As far as triplets go, non-identical triplets account for almost 95% of triplets, the rest being of the relatively rare identical type. It is also possible to have triplets where 2 are identical and the other is non-identical. So presumably, someone could be a twin and a triplet at the same time. About 500 sets of quadruplets are born in the United States each year and they are almost always of the non-identical type.

### *Identical Multiples*

Multiples that develop from a single ovum and a single sperm are called monozygotic. As such, each twin or triplet shares the exact same

gene pairs with his or her fellow multiples, and therefore must be the same gender. But quite amazingly, they do not share the same finger-prints.

Identical multiples do not tend to run in families and thus they seem to develop as a "quirk" of nature rather than caused by any predisposing factors. As such, rates of identical multiples are very similar are the world. Identical triplets are only about 5% of triplets overall and identical quadruplets are exceedingly rare. The latest case where this occurred was in April of 2006, when a 26 year-old woman from Madras, India gave birth to four identical girls. The chances of this occurring have been estimated as about 1 in 11 million. Indeed, since 1930, there have been fewer than 50 documented cases of identical quadruplets, with the majority of them being female.

Although we do not know why it happens, identical multiples result from a single zygote that splits into 2 (or 3) separate zygotes at some point early in its development, almost always before the 8th day and before implantation. This usually occurs with the first several zygotic divisions. There is no explanation for why this happens, it just does!

Some identical twins are "mirrored" and share traits exactly, but on opposite sides of their bodies. For example, one twin might be right-handed and the other left-handed. One twin may have a birth mark on the right thigh and the other at the same exact place on the left thigh. One twin's hair may part on the left and the other at the same place on the right. Mirroring can also produce a condition known as situs inversus, where the organs are on the opposite side of where they normally are (for instance, the heart is on the right instead of the left, called dextrocardia). Mirroring is associated with a relatively late "split" (over 9 days).

Identical twins and triplets come in three different types, depending on exactly when the "split" occurred which separated them into two or three persons. Each type differs in terms of amniotic sacs (amniotic) and placentas (chorionic).

### Diamniotic and Dichorionic (Triamniotic and Trichorionic)

These multiples, although identical**,** develop separate amniotic sacs and separate placentas. This type of identical is most likely to have "split" before day 3 after fertilization.

### Diamniotic and Monochorionic (Triamniotic and Monochorionic)

The most common type of identical twin (about 75%) involves separate amniotic sacs, but a shared placenta. Splitting most likely occurred between the 3rd and 8th day after fertilization. With triplets or even quadruplets, there can be a shared placenta with separate amniotic sacs, or any combination possible. For instance, 2 may share a placenta of even an amniotic sac, with the third (or fourth) having separate ones.

### Monoamniotic and Monochorionic


The rarest of all identical twin types results from a "split" between the 8th and 14th day after fertilization. These twins share the same amniotic sac and placenta. This type of twin is also most likely to have complications and most likely to miscarry.

One of these complications is called twin/twin transfusion syndrome (TTTS). Because these twins are sharing a placenta, there may be an imbalance in how much blood flow is reaching each. The result may be that one twin does not get enough blood and thus the oxygen and nutrients that it delivers and consequently develops slowly. The other twin may get too much blood, causing high blood pressure and stress

on his or her heart. But this twin grows faster and may be much larger than her sibling (see photo above). Approximately 3 out of 4 fetuses suffering from TTTS will die without surgical intervention.

### *Conjoined Twins*

Previously referred to as "Siamese twins", conjoined twins are monozygotic, monochorionic and mono-amniotic. Because they share the same amniotic sac and thus significant physical contact, the fusing together of skin at some point of the body during development can occur. Once delivered via a C-section, these conjoined twins are relatively easy to separate. With sharing organs, however, or when the fusing is substantial as in the photograph to the right, complications and difficulties are much more significant.

## CONCLUSION

The germinal period ends at the conclusion of implantation. Less than 2 weeks have passed since fertilization, but the accomplishments of any new embryo are considerable. She or he has survived considerable odds just to make it this far. The next chapter takes up the growth and tasks of the 6 week-long embryonic stage, when even more amazing events occur.

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