Genesis of Twins and Multiple Pregnancy

A large number of embryological processes must be carried out for the development of a new human being. There are numerous sources of error that can lead to malformations up to stillbirths. However, deviations can also occur within these processes, which lead to the development of two or more children, that is to say, twins or generally multiple births. This article explains how exactly this is done, what forms of multiples exist and how frequently they occur.

Introduction

Twins and multiple pregnancies arise from various scenarios such as:

- **Monozygotic twins/ multiples (identical)** arise when a single ovum is fertilized and divides into two or more independent units of development. They occur in 2.3—4 per 1000 live births in all races. The occurrence is not influenced by heredity or mothers age.
- **Dizygotic twins (non-identical)** develop when two ova are fertilized with each fetus having its own placenta, chorion, and amnion. They represent 70 % of twin pregnancies.
Monozygotic Multiples

Monozygotic multiples are **two or more children** who have developed from the **same fertilized egg**. Monozygotic multiples, therefore, have the **same genetic material** and therefore look identical.

Pathogenesis and formation of monozygotic multiples

For the formation of monozygotic multiples, the fertilized ovum (**zygote**) must be cut through in the course of its development. This can take place at three different times:

The first time at which the egg-cell may separate may take place on the first day or before the third day; namely in the **two-cell stage**. The zygote has already completed the first division; this means that the zygote has divided very rapidly and without new formation of cell material. It has thus divided without changing its size. The two cells resulting from this division can develop further independently and accordingly form two blastocysts. This results in formation of separate/fused placentas i.e. 2 chorions and 2 amnions. Thus, Diamniotic dichorionic multiples are formed. They resemble dizygotic twins and are represent a third of monozygotic twins.

The next time the zygote can separate is in the **early blastocyst stage**. During this stage, the first cell differentiation has already taken place. The external cells of
the **morula**, now formed by many divisions, form an epithelium-like complex, which later forms the so-called **trophoblast**, while the inner cells remain together in a cluster of cells called the **embryoblast**.

This stage is before amnion formation (day 4- day 8) and division results into a single placenta, common chorion and 2 amnions thus, **monochorionic-diamniotic multiples** can develop. This is the most common form of monozygotic multiples representing 2/3rds of monozygotic multiples.

The last time at which the child’s system can separate is as a **two-leaved germinal disc which occurs in day 8—13 of development**. The blastocyst has already entered the uterus. For this, the trophoblast is invasively growing into the mucous membrane of the uterus. The outer part dissolves its cell borders and the so-called **syncytiotrophoblast**. The inner part of the trophoblast retains its structure and is now called **cytotrophoblast**. The cells of the embryoblast are now differentiated into two cell layers: the highly cylindrical epiblast that forms the amniotic cavity and the **hypoblast** that forms the yolk sac.

The site on which the two cell layers lie on one another is called the **germinal disk**. From it develops the actual embryonic body. This development begins with the gastrulation, in which cells from the epiblast migrate between the two disks. The transformation and migration of these cells lead to the formation of the so-called **primitive strip**, which, for the first time, gives the embryo a caudal and cranial end by the subsequent formation of the **chorda dorsalis**.

If several primitive streaks develop, **monochorionic-monoamniotic multiples** develop. This is the only form of multiples which, due to their narrow localization in case of a faulty closure of the body wall, can lead to duplications or so-called **Siamese twins/conjoined twins**.

Division beyond day 15 of development results into incomplete twinning.

### Development of monozygotic multiples

Due to their early division, dichorionic-diamniotic multiples undergo a “normal” development. Each child has its **own placenta**, its **own chorion cavity**, and its **own amnion cavity**. If the blastocysts nest very close to one another during pregnancy, the **placentas may be fused**. **Anastomoses** may form between the different chorion vessels.

Monochorionic-diamniotic multiples develop from two embryoblast within a trophoblast. As the placenta is formed later, it is logical that these multiples **share a placenta and a cortical cavity. However, they have their own amnion cavity**.

Monochorionic-monoamniotic multiples are separated only after the formation of the amniotic cavity and the yolk sac, but within a trophoblast. These multiples, therefore, have a **common placenta, corium cavity and amniotic cavity**.
Probability of several multiples

The probability of giving birth to several multiples depends on the number of multiples. Monozygotic twins have an incidence of 1:250, while the probability of obtaining monozygotic triplets is significantly lower with 1:200 million. Monozygotic quadruplets are created with a probability of 1:13 million. They represent the highest documented number of identical multiples.

Dizygotic Multiples (fraternal twins)

Dizygotic multiples are described as two or more children whom have developed from several oocytes fertilized by different sperm within a pregnancy. They have different genomes and are therefore no longer similar to siblings born at different times. They can even be fertilized by sperm from different men since they can remain functional for up to five days in the uterus.

Formation of dizygotic multiples

If two oocytes ovulate simultaneously and are fertilized by two different sperms, twins are formed. If one of the zygotes divides, triplets develop. If both zygotes divide, they form the basis for quadruplets. In rare cases, it can also happen that one of the fertilized eggs is dividing several times. This can lead to an even higher number of multiples.

It should be noted, however, that multiples, which have been produced by the division of the zygote, are monozygotic multiples. The above-described forms of multiples are, therefore, more precisely mixed forms. Thus, the said triplets are dizygotic twins, and one of the two twins has split off a monozygotic twin.
Due to today's **possibilities of artificial insemination**, the **probability** of a multiple pregnancy has significantly **increased**. For example, with the use of fertility-enhancing drugs, three oocytes can ovulate at the same time and be fertilized by three different sperms. These are then, so to speak, trizygotic triplets. All three have different genotypes and can therefore also be of **different sex**.

### Development of dizygotic multiples

Dizygotic twins develop independently of each other in **two different oocytes**. Therefore, both embryonal states form their own membranes: each child has its **own placenta**, as well as its **own amnion** and **chorion cavity**. If the two embryos are very close to one another, the placentas may be fused together, as in the case of dichorionic-diamniotic multiples. Similarly, anastomoses can arise between the chorion vessels.

### Probability of dizygotic multiples

**Two-thirds of all twins are dizygotic twins.** Their frequency among the multiples is, therefore, the highest and even increases with the age of the mother. While the birth rate of monozygotic multiples has remained more or less constant over the years, the number of dizygotic multiples has risen significantly in the industrialized countries in the last decade. This can be mainly attributed to artificial fertilizations, which often transfer two or even more fertilized eggs into the uterus to increase the chance of success. Another factor contributing to the increase in dizygotic multiple pregnancies in affluent countries is fertility treatment.

### Special Features of Twins

Twin pregnancies lead to **premature babies** more frequently compared to single pregnancies. In addition, there is an increased risk that twins will die in the **perinatal period** (22nd week of pregnancy to the seventh day after birth). The **perinatal mortality** of twins is **10% to 20%**. For single pregnancies, it is comparatively only **2%**. The significantly higher perinatal mortality is usually due to maturation disorders or a low birth weight.

Investigations show that only about **29%** of all twin pregnancies are also leading to twin births. **This dysfunction of a twin during pregnancy** has various causes: the death of one of the twins can, for example, be caused by an unbalanced nutrient supply and disappear by resorption.

It is rarer that the resorption is replaced by a mummification of the twin, that is, by the **fetus papyraceus**. A common chorion leads in about **10%** of the cases that a twin is not supplied enough with blood. As a result, his growth is reduced and twins of different sizes are produced. One speaks of **transfusion syndrome**.

In a few cases, **fetal inclusion** or the **fetus in fetu** may occur. Here, one of the twins is incorporated into the others. After inclusion, the fetus in fetu ceases to grow normally. It usually remains undetected for a long time, unless the surviving twin causes premature troubles. However, the fetal inclusion is so rare that no possible cause is known.

### Clinical Indicators of Multiple Pregnancies

- All annoyances of pregnancy are worsened i.e., severe backache, varicosities, and abdominal distension
- Uterus is larger than expected for dates
- Unexplained excessive maternal weight gain
- Polyhydramnios
- Clinical ballottement of more than one fetus by multiplicity of small fetal parts during obstetric examination
- Recording of different heart rates all asynchronous to each other and mothers heart rate with variances of more than 8 beats per minute
- Palpation of another fetus after delivery of one infant

**Management of multiple pregnancies:**

Mothers with suspected or confirmed diagnosis of multiple pregnancies should be admitted after showing the first signs of labour and an abdominal ultrasound done to ascertain the position of each fetus as well as to estimate the weight of each fetus.

**Delivery is either via**

C-section in case of:

- Suspected twin to twin transfusion syndrome
- Placenta previa
- Multiple pregnancies of triplets and above
- Both twins are in a non-vertex presentation
- Non-vertex presentation of second twin that is of greater weight than twin A

Vaginal delivery in case of:

- Vertex presentation of both twins
- Non-vertex twin B which is of equal or less weight than twin A

**Review Questions**

The correct answers can be found below the sources.

**1. Which of the following statements regarding the formation of multiples is true?**

A. The first time at which monozygotic multiples can be formed is in the early blastocyst stage.
B. The last possible time for the formation of monozygotic multiples is in the early blastocyst stage.
C. Monozygotic multiples can develop even after the end of the gastrulation.
D. The earliest possibility of division of the zygote in monozygotic multiples is during the two-cell stage.
E. After the implantation, no division into monozygotic multiples is possible anymore.

**2. Which of the following statements on the development of multiples is true?**

A. Dichorionic-diamniotic multiples share a placenta, but each has a chorionic and amniotic cavity.
B. Monochorionic-diamniotic multiples share a placenta and chorionic cavity, but each has an amniotic cavity.
C. In monochorionic-monoamniotic multiples, a fusion of placentas can occur in the very near implantation.
D. Dichorionic-monoamniotic multiples are the most common form of monozygotic multiple births.
E. Dizygotic multiples develop in a common placenta.

3. Which of the following is true?

A. Twin pregnancies do not represent an increased risk for either mother or children compared to single pregnancies.
B. The transfusion syndrome is caused by an unbalanced blood supply in common chorion.
C. The number of monozygotic multiple births has increased rapidly lately by the new possibilities of artificial insemination.
D. Higher age of the mother raises the chances for a single pregnancy.
E. Dizygotic twins have the same DNA and therefore must be of the same sex.

References


**Correct answers:** 1D, 2B, 3B

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