Genesis of Twins and Multiple Pregnancy

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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 may be:

- **Monozygotic (identical):** arising when a single ovum is fertilized and divides into 2 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 maternal age.
- **Dizygotic (non-identical):** develops when two ova are fertilized with each fetus having its own placenta, chorion, and amnion. They represent about 70% of twin pregnancies.

Monozygotic Multiples

Monozygotic multiples are **2 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 cleaved** in the course of its development. This can take place at 3 different times:

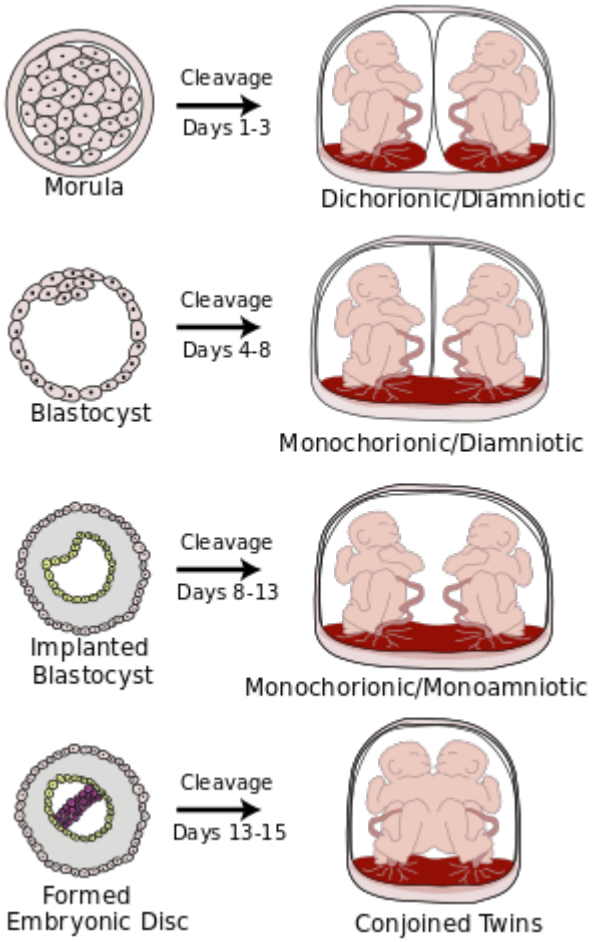

Image: Chorionicity and amnionicity in monozygotic twins. By: Kevin Dufendach. License: CC-BY 3.0

The first time the egg-cell may separate takes place on the first day or before the 3rd day; namely in the **2-cell stage**. The zygote has already completed the first division; this means that the zygote has divided very rapidly without the new formation of cell material. It has thus divided without changing its size. The 2 cells resulting from this division can develop further independently and form 2 blastocysts. This results in the formation of separate/fused placentas i.e. 2 chorions and 2 amnions. Thus, diamniotic dichorionic multiples are formed. They resemble dizygotic twins and represent one-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

becomes the **trophoblast**, while the inner cells remain together in a cluster of cells called the **embryoblast**.

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

The last time separation can occur 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 becomes the **syncytiotrophoblast.** The inner part of the trophoblast retains its structure and is now called the **cytotrophoblast**. The cells of the embryoblast are now differentiated into 2 cell layers: the highly cylindrical epiblast which forms the amniotic cavity and the **hypoblast** which forms the yolk sac.

The 2 cell layers lie on one another at a site called the **germinal disc**. From this disc, the actual embryonic body develops. This development begins with gastrulation, in which cells from the epiblast migrate between the 2 discs. The transformation and migration of these cells lead to the formation of the **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 the so-called **Siamese twins/conjoined twins**.

Division beyond day 15 of development results in incomplete twinning.

Development of monozygotic multiples

Due to their early division, dichorionic-diamniotic multiples undergo ‘normal’ development. Each child has its **own placenta**, its **own chorionic cavity**, and **its own amniotic 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 2 embryoblasts within a trophoblast. As the placenta is formed later, it is logical that these multiples **share a placenta and a chorionic cavity. However, they have their own amniotic 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, chorionic cavity, and amniotic cavity.**

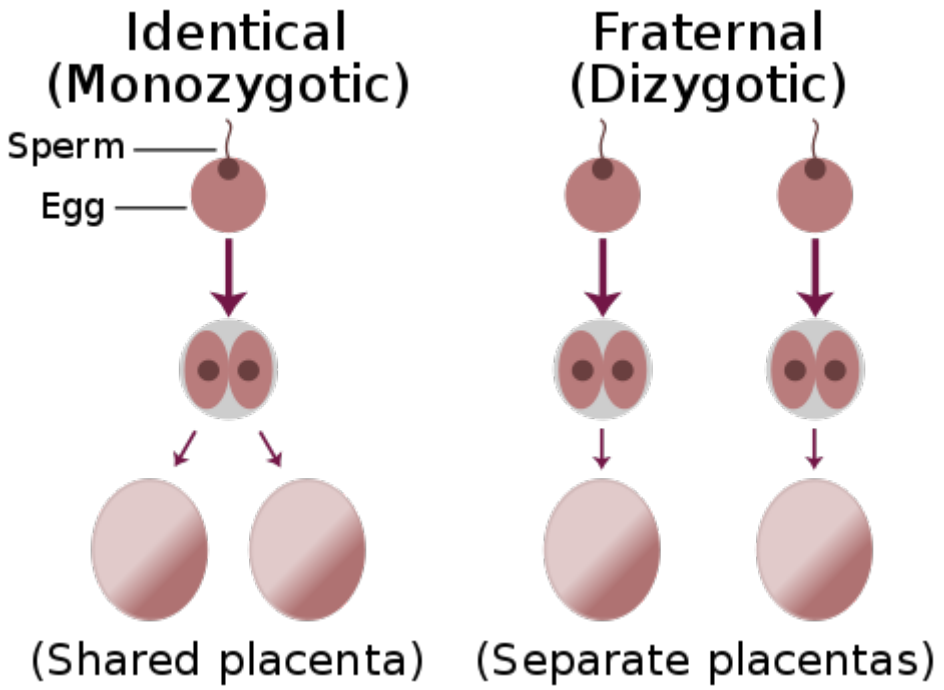

Image: Comparison of zygote development in monozygotic and dizygotic twins. In the uterus, a majority of monozygotic twins (60–70%) share the same placenta but have separate amniotic sacs. In 18–30% of monozygotic twins, each fetus has a separate placenta and a separate amniotic sac. A small number (1–2%) of monozygotic twins share the same placenta and amniotic sac. Fraternal twins each have their own placenta and own amniotic sac. By: Trlkly (Original by Wikipedia Editor User:ChristinaT3). License: CC BY-SA 3.0

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 quadruplet pregnancies have a probability of 1:13 million. They represent the highest documented number of identical multiples.

Dizygotic Multiples (fraternal twins)

Dizygotic multiples are described as 2 or more children who have developed **from several oocytes fertilized by different sperms** within a pregnancy. They have **different genomes** and are therefore similar to siblings born at different times. They can even be fertilized by sperms from different men since sperms can remain functional for up to 5 days in the uterus.

Formation of dizygotic multiples

If 2 **oocytes** ovulate simultaneously and are fertilized by 2 different sperms, twins are formed. If one of the zygotes divides, triplets (1 in 40,000) develop. If both zygotes divide, they form quadruplets (1 in 13,000,000 is accurate). In rare cases, it can also happen that one of the fertilized eggs divides 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 1 of the 2 twins has split off a monozygotic twin.

Due to today's **possibilities of artificial insemination**, the **probability** of multiple pregnancies has significantly **increased**. For example, with the use of fertility-enhancing drugs, 3 oocytes can ovulate at the same time and be fertilized by 3 different sperms. These are then trizygotic triplets. All 3 have different genotypes and can therefore also be of **different sexes**.

Development of dizygotic multiples

Dizygotic twins develop independently of each other in **2 different oocytes**. Therefore, both embryonal states form their own membranes: each child has its **own placenta**, as well as its **own amnion** and **chorionic cavity**. If the 2 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 chorionic 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 industrialized countries in the last decade. This can be mainly attributed to artificial fertilization, which often transfers 2 or even more fertilized eggs into the uterus to increase the chance of success. Other types of fertility treatment have contributed to the increase in dizygotic multiple pregnancies in affluent countries.

Special Features of Twins

Twin pregnancies lead to **premature babies** more frequently compared to single pregnancies. In addition, there is an increased risk that the twins will die in the **perinatal period** (22nd week of pregnancy to the 7th day after birth). The **perinatal mortality** of twins is **10–20%**. For single pregnancies, it is only 2%. The significantly higher perinatal mortality is usually due to maturation disorders or low birth weight.

Investigations show that only about 29% of all twin pregnancies result in 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 unbalanced nutrient supply and resorption of the malnourished twin.

Rarer than resorption is the mummification of the twin (**the fetus papyraceus**). In about 10% of cases of a common chorion, a twin is not supplied enough with blood. As a result, its growth is reduced and twins of different sizes are produced **(twin-twin transfusion syndrome)**.

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

Clinical Indicators of Multiple Pregnancies

- Discomforts associated with pregnancy are worsened i.e., severe backache, varicosities, and abdominal distension.
- Uterus is larger than expected for the date
- Unexplained excessive maternal weight gain
- Polyhydramnios
- Clinical ballottement of more than one fetus by a multiplicity of small fetal parts during an obstetric examination
- Recording of different heart rates all asynchronous with each other and mother's 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 labor and an abdominal ultrasound performed 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-twin transfusion syndrome
- Placenta previa
- Multiple pregnancies of triplets and above
- Non-vertex presentations of both twins
- Non-vertex presentation of a 2nd twin that is of greater weight than the 1st twin

Vaginal delivery in case of:

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

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Notes