Critical Periods of Development

In every pregnancy, a woman starts out with a 3-5% chance of having a baby with a birth defect. This is called her background risk. This fact sheet talks about the critical periods of development and types of birth defects that can result from exposures at different stages of pregnancy. This information should not take the place of medical care and advice from your health care provider.

What are critical periods of development?

In pregnancy, each part of the baby’s body forms at a specific time. During these times, the body can be very sensitive to damage caused by medications, alcohol or other harmful exposures. We call this specific time the “critical period of development” for that body part.

Does the chance types of birth defects change throughout pregnancy?

Yes, the risk depends on what body part is developing at the time of exposure. Once a body part has formed, it is no longer at risk to develop major birth defects, but some exposures could still affect its growth and function.

The chart on the next page shows the critical periods of development for different parts of the body. The chart starts from the time of conception when the egg and sperm join. The weeks listed on the chart are the “embryonic age” or “fetal age” of a pregnancy. Note that this is different from a common way of dating a pregnancy called “gestational age.” Gestational age begins with the first day of a woman’s last menstrual period. This day is usually two weeks before a baby is conceived. This means that you can change gestational age to embryonic/fetal age by subtracting two weeks. For example, 12 gestational weeks (since the day of your last period) is the same as 10 fetal weeks (since the first day of conception).

The dark bars on the chart show when each part is most sensitive to harmful exposures and at risk for major birth defects. Birth defects are typically classified as “major” if they cause significant medical problems and need surgery or other treatment to repair. Heart defects, spina bifida, and clubfeet are examples of major birth defects.

The lightly shaded bars show periods when the body parts are still at risk to develop minor birth defects and functional defects. “Minor” birth defects by themselves do not cause significant medical problems and usually do not require treatment or surgery. Minor birth defects can also be variations of normal development. Wide-set eyes and large ears are examples of minor birth defects.

Both major and minor birth defects are physical or structural changes. However, “functional” defects change how a part of the body works without changing its physical structure. Intellectual disability and hearing loss are both examples of functional defects.

The chart also shows the location of the most common birth defects that can occur during each week. In general, major defects of the body and internal organs are more likely to occur between 3 to 12 embryo / fetal weeks. This is the same as 5 to 14 gestational weeks (weeks since the first day of your last period). This is also referred to as the first trimester. Minor defects and functional defects including those affecting the brain are also able to occur later in pregnancy.
What is the greatest risk from a harmful exposure during very early pregnancy?

Harmful exposures during very early pregnancy have the greatest risk of causing miscarriage. A fertilized egg divides and attaches to the inside of the uterus during the first two weeks of embryo development. Very harmful exposures during this period (first four weeks after the first day of your last period) may interfere with the attachment of the embryo to the uterus. Harmful exposures during this time can also damage all or most of the cells of the growing embryo. Problems with uterine attachment and severe cell damage can both result in a miscarriage. Sometimes this miscarriage is before a woman even realizes that she is pregnant.

Less severe exposures during this time may only damage a few of the embryo’s cells. The cells of the embryo have a greater ability to recover at this early stage than they do later on in pregnancy. If a woman does not have a miscarriage, we believe that the exposures during this time are not likely to cause a birth defect.
We call the first four weeks of gestation the “all or none period.” “All” refers to high exposures damaging all of the embryo’s cells. This damage causes early miscarriage. “None” refers to exposures that are not high enough to have a significant effect on the pregnancy. We can use the rule of the “all or none period” to determine the risk of many different types of exposures. However, there are some important exceptions to this rule. Please contact MotherToBaby to discuss your specific exposure with our experts.

**What are the greatest risks from harmful exposures during the first trimester of pregnancy?**

The first trimester of pregnancy is defined as up to the 14\textsuperscript{th} week of pregnancy (13 weeks and 6 days) counting since the first day of your last menstrual period. Harmful exposures during the first trimester have the greatest risk of causing major birth defects. This is because many important developmental changes take place during this time. The major structures of the body form in the first trimester. These include the spine, head, arms and legs. The baby’s organs also begin to develop. Some examples of these organs are the heart, stomach and lungs. While the heart and stomach completely forms during the first trimester, the lungs continue to develop past the first trimester.

**What are the greatest risks from harmful exposures during the second and third trimesters of pregnancy?**

Harmful exposures during the second and third trimesters can cause growth problems and minor birth defects. Growth is an important part of the second and third trimester. The structures and organs that developed during the first trimester grow larger. Babies with growth problems may be much smaller or much larger than average. This size difference can put babies at risk for certain health problems.

Harmful exposures during the second and third trimesters can also cause functional defects like learning problems. The brain is part of the central nervous system and it develops during the entire pregnancy. Major, structural brain development lasts until about 16 fetal weeks (18 gestational weeks). However, the brain continues to develop for the rest of the pregnancy, after birth and through young adulthood.

While usually less well studied, some exposures in the second or third trimester might cause other pregnancy complications, such as premature delivery or low levels of amniotic fluid (the fluid that surrounds the developing baby in the uterus).

Finally, the use of certain medications and drugs at the end of pregnancy can cause withdrawal in some newborns. You should always tell your health care provider about all of the medications, supplements and/or drugs that you take.

**Does this mean that an exposure might be harmful at certain times during pregnancy but not at other times?**

Yes. Imagine your doctor gives you a new medication to take during your third trimester. We will call this “Medication A.” You read that Medication A increases the chance for heart defects. This means that babies may have a higher chance for major heart defects if their mothers’ take this medication during the heart’s critical period of development. We know that the heart’s critical period of development is from 3 to 6 embryonic weeks (5 to 8 gestational weeks). This means that using this medication in the third trimester cannot cause a major heart defect. Always talk to your health care provider before starting or stopping any medication.

**References:**

- Bleyl SB and Schoenwolf GC, 2010. What is the timeline of important events during pregnancy that may be disrupted by a teratogenic exposure? *Teratology Primer*, edited by Barbara Hales et al. The Teratology Society.