HHRA
Heartland Health Research Alliance

Reproductive Problems Linked To Pesticide Exposure

Here we review the types of reproductive problems that have been linked to pesticide exposure.

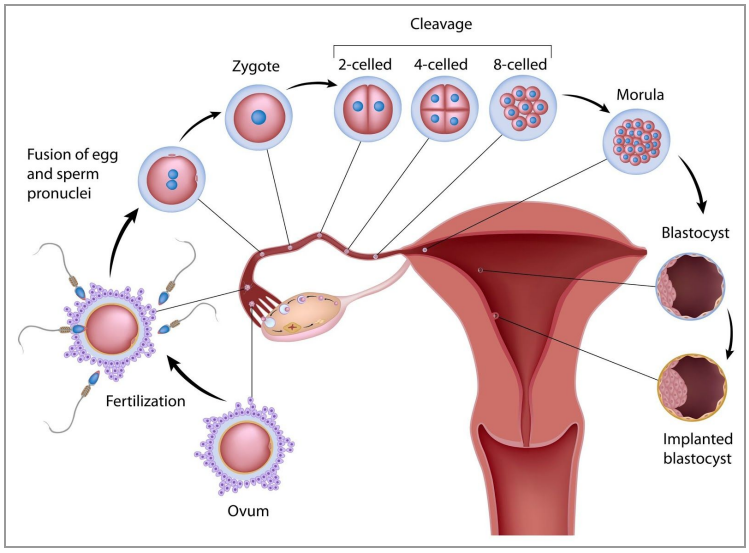
Failure to Conceive

Anecdotal evidence suggests that more and more couples are facing difficulties in conceiving and carrying a healthy pregnancy to term, and most Americans have family or friends that have struggled to have a baby.

While exact data are not available, scientists estimate that only around 30% of conceptions result in a live birth, and an even lower percent result in the birth of a child with no genetic or developmental "deficits."

In this context, the word "deficit" means: (a) a genetic polymorphism, mutation, or epigenetic change that causes, or heightens the risk of health or neurological problems later in life, (b) an observable birth defect, or (c) preterm delivery, low birthweight, or another factor known to be associated with health or developmental problems.

According to the Center for Disease Control's (CDC's) Infertility FAQs, "infertility is defined as not being able to get pregnant (conceive) after one year (or longer) of unprotected sex."



Fertility in women naturally declines with age, and is impacted by a myriad of factors such as genetics, current health status, uterine damage, chemical exposures, prescriptive and recreational drug use, and the quality of the sperm in question.

CDC goes on to explain that a successful pregnancy requires several things to happen in the correct order:

- An egg must be released;
- Sperm must fertilize the egg or eggs;

- Fertilized egg(s) must travel through the Fallopian tube into the womb/uterus; and
- Attach (implant) to the inside of the uterus.

A failure to conceive can arise from a problem with any of the above steps. While a critical step in the reproductive process, successful conception is just the beginning of an incredibly complex, nine-month process that entails a miraculous sequence of gene expression and cell division events, as a fertilized egg begins to divide and specialized cells, and then organ systems are created that become a living, breathing child.

Key Science: Pesticides and Failure to Conceive

- In 2015, the International Federation of Gynecology and Obstetrics released an opinion paper (di Renzo et al., 2015) warning of the "ubiquitous…threat to healthy human reproduction" posed by toxic environmental chemicals, including pesticides. The Federation calls out the need for "policies to prevent exposure to toxic environmental chemicals, work to ensure a healthy food system for all, make environmental health part of health care, and champion environmental justice."

Miscarriage

Spontaneous pregnancy loss prior to 20 weeks gestation occurs in over 15% of conceptions. The early loss of a once viable fetus is also referred to as spontaneous miscarriage or spontaneous abortion.

In many spontaneous miscarriages, women are not even aware they were pregnant, hence the uncertainty and undercounting in the frequency of spontaneous abortions.

"Recurrent pregnancy loss" is now defined as two or more spontaneous miscarriages ending a pregnancy prior to 20 weeks from the last menstrual period. While only a few percent of women experience recurrent pregnancy loss, its exact frequency and causes remain hard to pin down.

Drawing on the 2009 paper "Recurrent Pregnancy Loss: Etiology, Diagnosis, and Therapy," the most common causes of spontaneous miscarriage and pregnancy loss, in rough order of frequency, include:

- Endocrine and metabolic disorders including diabetes, thyroid disease, and luteal phase (the last phase of the menstrual cycle) defects;
- Anatomic abnormalities that interrupt blood flow in the uterus, such as intrauterine adhesions, and uterine fibroids and polyps;
- Unexplained environmental etiologies including exposures to chemicals, organic solvents, radiation, and other toxicants; and
- Genetic factors such thrombotic mutations.

Though The Heartland Study, HHRA will shed new light on the contribution of prenatal herbicide exposures to spontaneous miscarriage rates, and pioneer methods to link chemical exposures to epigenetic changes.

Key Science: Pesticides and Miscarriage

Research has linked herbicide exposure to increased risk of spontaneous miscarriage, including for glyphosate, the # 1 herbicide in the U.S. and the world that is widely applied throughout the Midwest. We summarize some key studies below, or access all relevant records in our bibliography here.

- From 1999-2002, a trio of epidemiological studies were released that looked at the rate of spontaneous miscarriages among farm families. Two (Arbuckle et al., 1999 and Arbuckle et al. 2001) analyzed data from the Canadian Ontario Farm Family Health Study, and found increased miscarriage rates following preconception exposure to some herbicides (phenoxy acetic acid herbicides, glyphosate, and thiocarbamates.) A third study of farmers from Minnesota's Red River Valley (Dr. Vincent Garry's key paper from 2002) found a "modest but significant increase in risk for miscarriages" for women whose spouses applied fungicides and herbicides, and for women who were directly engaged in pesticide application.
- Two more recent papers by Medardo Avila-Vasquez point out that agricultural communities in Argentina with high glyphosate application rates have dramatically increased rates of miscarrage and other health problems. See Avila-Vasquez et al., 2015 and Avila-Vasquez et al., 2018 for the details.

Low Birthweight and Preterm delivery

The CDC's National Center for Health Statistics provides an overview of Birthweight and Gestation for the U.S. In 2017, CDC reports that:

  - 318,873 babies, or 8.3% of all live births, were born with low birthweights (less than 2500 grams, or 5.5 pounds);
  - 4% were born with very low birth weights;
  - 382,726 babies were born preterm, or just under 10% of all live births.

Low birthweight babies are at greater risk for many health problems, including newborn respiratory distress and infections, developmental delays in childhood, and are even more likely to develop chronic illnesses like diabetes and heart disease. So yes, an extra pound or two at birth can make a big difference!

The CDC offers these definitions of gestational length, birth rates and outcomes:

- Full term delivery- Birth of a baby after 39 weeks of pregnancy.

- Preterm birth rate- The number of births delivered at less than 37 completed weeks of gestation per 100 total births, based on the obstetric estimate of gestation.
- Early preterm birth rate- The number of births delivered at less than 34 completed weeks of gestation per 100 total births, based on the obstetric estimate of gestation.
- Late preterm birth rate- The number of births delivered at 34–36 completed weeks of gestation per 100 total births, based on the obstetric estimate of gestation.
- Birth rate at 34, 35, and 36 weeks- The number of births delivered at the specified completed weeks of gestation per 100 total births, based on the obstetric estimate of gestation.
- Singleton births- Births in single-gestation pregnancies.
- Multiple births- Births in multiple-gestation pregnancies (i.e., twin and triplet and higher-order births).

In a web resource called "Why Is 40 Weeks So Important," the New York Department of Health highlights that a full term delivery:

- Reduces the risk of several health problems stemming from difficulty breathing, keeping warm, and nursing normally;
- Lowers the incidence of newborn jaundice; and
- Provides time for the baby's brain and neurological system to fully develop (this part of the brain is responsible for more complex thinking and it doubles in size during the last few weeks of pregnancy), lessening the risk of ADHD, autism, and metabolic or reproductive disorders as adults.

Key science is highlighted below, or see all relevant bibliography items on gestational length here and birthweight here.

Key Science: Pesticides and Birthweight/Preterm Delivery

- In 2018, a Heartland Study research team published a paper found a "significant negative correlation" between urinary glyphosate levels and shorter gestational lengths. In other words, women with higher amounts of the herbicide in their urine were more likely to have shorter pregnancies, if not necessarily preterm delivery (Parvez et al., 2018).

Several other studies have reported an association between low-birth weight and/or pre-term delivery and pesticide exposures, including:

- Earlier in his career, Heartland Study Co-PI Dr. Paul Winchester researched the incidence of preterm birth and shortened gestation in areas with high pesticide use in California. In a paper published in 2016, he and his team identified an association between higher pesticide exposure and shorter gestation and lower birth weights (Winchester et al., 2016).

- Research on transgenerational, epigenetic impacts of herbicide exposure reported in 2018 that pregnant rats exposed to glyphosate were more likely to have offspring that in turn had shorter pregnancies, and gave birth to lower birthweight pups (Milesi et al., 2018).

Birth Defects

Sadly, about one in 33 infants born in the U.S. annually has one or more birth defects.

According to the CDC, "when discussing exposures and risk factors in regards to birth defects, we are talking about anything the fetus is exposed to as well as anything that may alter conditions within the womb. This includes everything the mother may come into contact with during pregnancy."

The CDC goes on to highlight that most structural birth defects are associated with development of the fetus that occur early in pregnancy, during the "periconceptional" period (the month before and first 3 months after conception).

Thus, a significant share of birth defects research focuses on possible causes in the first trimester of pregnancy (the first 12 weeks).

Types of Birth Defects

The most common categories of birth defects are:

- Congenital heart disease – An abnormality in the heart that develops before birth.
- Down syndrome – A genetic chromosome 21 disorder causing developmental and intellectual delays.
- Cleft lip and cleft palate – Openings or splits in the roof of the mouth and lip.
- Spina bifida – A birth defect in which a developing baby's spinal cord fails to develop properly.
- Club foot – A birth defect in which the foot is twisted out of shape or position.
- Phenylketonuria – A birth defect that causes an amino acid called phenylalanine to build up in the body.
- Edwards' syndrome – A condition that causes severe developmental delays due to an extra chromosome 18.

The Eunice Kennedy Shriver National Institute of Child Health and Development provides further details on common birth defects in two major categories: Structural Birth Defects, and Functional or Developmental Birth Defects.

Our Research on Birth Defects

Research cannot always definitely prove exposure causes birth defects, but instead measures impacts on risk of a certain outcome.

Instead, results are reported as changes in birth defects risk for exposed pregnancies compared to unexposed.

The Heartland Study is designed to explore possible linkages between prenatal herbicide exposure levels and birth outcomes, including the frequency of birth defects.

Known birth defects are relatively rare, collectively impacting just 3% of newborns. The frequency of specific birth defects is much lower. This is why epidemiological studies exploring the impacts of chemicals or other environmental causes on birth defects need to track birth outcomes in a large number of pregnancies. This is one reason for the Heartland Study's ambitious goal of bringing at least 2,000 mother-infant pairs through our research protocol.

The Heartland Study will calculate risk ratios that reflect the odds of a given birth defect or adverse birth outcome occurring in the group of pregnant women most heavily exposed to herbicides, compared to the group that is exposed to the lowest average levels.

The CDC provides these benchmarks for evaluating the outcomes of epidemiological studies like the Heartland Study:

- Higher risks – a doubling or more – suggests an association between the exposure and the condition in question. This may mean the studied exposure/risk factor contributes to the birth defect.
- Decreased risks – one half or less – indicates a protective effect. The exposure appears to prevent the birth defect from occurring.
- No change in risk – implies that the exposure and the defect are not closely related.

Several studies have reported associations between herbicide use and exposures and birth defects. We highlight a few below, or you can see all relevant bibliography records here.

Key Science: Pesticides and Birth Defects

- Exposure to the herbicide atrazine has been linked to increased incidence of hypospadias, a rare birth defect in male babies where the opening to the urethra is on the underside of the penis instead of the tip (Winston et al., 2016), and chanal atresia or stenosis, a condition where the back of the nasal passage is blocked (Agopian et al., 2013A, Agopian et al., 2013B).
- Heartland Study Co-PI Paul Winchester documented that pesticide use was correlated with increased birth defects in the U.S. in 2009 (Winchester et al., 2009).
- Research on the Ontario Farm Family Study in Canada that was published in 2008 found that parental exposure to dicamba herbicide was significantly correlated to increased risk of birth defects in male babies (Weselak et al., 2009).
- A key paper from 2002 found that farm families in Minnesota's Red River Valley that conceived babies during the spring planting (and spraying) season were significantly more likely to be born with birth defects (Garry et al., 2002).

Developmental Impacts

The pathway from fertilized egg to the day of birth, and life passages through infancy, childhood and adulthood, can be disrupted, delayed, or driven off course in a variety of ways, with widely varying consequences.

Birth defects are one, often unmistakable example of adverse developmental effects, but many others cannot be diagnosed at birth, and may or may not manifest as an infant grows older.

Most recent pesticide-related developmental research has focused primarily on effects that alter or impair the integrity of the neurological, immune, or reproductive systems. Such impacts encompass a broad array of adverse outcomes:

- Reduced IQ, behavioral problems, ADHD and autism;
- Autoimmune diseases and heightened vulnerability to pathogens, cancer, and other factors that can trigger illness; and
- Abnormal sexual development and reproductive performance and inclinations.

In particular, the now proven, adverse impact of certain insecticides on neurological development has received intense focus by scientists worldwide. Such impacts can lead to reduced IQ and a number of behavioral and learning disabilities. The rich literature on this topic is accessible via our bibliography under the tags developmental impacts and neurodevelopmental toxicity.

Recent research has also linked herbicides, and in particular glyphosate, to various neurodevelopmental disruptions leading to adverse birth outcomes like autism.

The largest and most sophisticated population-based study of pesticides and autism was published in the British Journal of Medicine in 2019. The von Ehrenstein et al study was conducted by a University of Southern California led team, and reported a 33% elevation in the risk of autism spectrum disorder coupled with learning disabilities among children with autism, compared to matched controls.

Surprisingly, living near areas where glyphosate-based herbicides were applied was a more significant factor in autism than living near where the OP insecticides chlorpyrifos, diazinon, and malathion were applied.

For this reason, the Heartland Study protocol includes annual developmental assessments at ages 1, 2, and 3, and hopefully through age 16 (pending funding), to enable calculation of odds rations linking herbicide exposure levels and autism, as well as other developmental and behavioral outcomes.

Key Science: Pesticides and Developmental Effects

- For a recent review of known research on the pesticide exposure and autism and ADHD, see this meta-analysis (Roberts et al., 2019).
- This case study by Dr. William Shaw looks at one farm family whose triplets with autism spectrum disorder all showed elevated urinary glyphosate levels (Shaw, 2017).
- A team of French scientists found that low-dose pre- and postnatal exposure to glufosinate ammonium herbicide induced autism-like symptoms in mice (Laugeray et al., 2014).
- For more on why this all matters, see HHRA Science Advisory Board member Dr. Bruce Lanphear's article "The Impact of Toxins on the Developing Brain" (Lanphear, 2015) and this perspective on the economic impacts of neurodevelopmental deficits caused by endocrine-disrupting chemicals like many herbicides (Attina et al., 2016).