The Heartland Study
Supporting Children's Health
In the Heartland and Beyond

White Paper: The Science that Gave Birth to The Heartland Study

Part I—Birth defects are the leading cause of infant death in the U.S.

Dr. Paul Winchester is the Co-Principal Investigator of HHRA's flagship project The Heartland Study and the Director of the NICU at Franciscan Health Hospital in Indianapolis, IN.

When Dr. Paul Winchester observed a spike in troubled pregnancies and birth defects in the Neonatal Intensive Care unit at Franciscan Health, Indianapolis, he had to find out why.

His journey to finding the data he needed exposed shocking gaps in our national health care monitoring system.

Dr. Paul started his search at the government's keeper of birth defect records – the Center for Disease Control (CDC). But when he requested the data, he was told that Indiana was one of 15 states in the U.S. without a birth defects registry. He was stunned to discover that Indiana didn't register birth defects, but even more stunned to learn that 15 states (30%) in the world's leading industrialized country weren't tracking the leading causes of infant death.

He was determined to get the data somehow.

Babies at risk – Doctors find a path

All 50 states track birth defects, like spina-bifida, that are evident at childbirth and do so via birth certificates. But since only about two-thirds of birth defects can be diagnosed when a baby is born, birth defects are undercounted in the 15 states without a registry.

But Dr. Paul was at least able to look at spina bifida rates as recorded on birth certificates to see how Indiana compared with other states. Two important trends caught his eye:

1. The incidence of spina bifida birth defects from 1991-2002 were higher in Indiana than the U.S, average, and
2. Spina bifida rates peaked and ebbed in certain months.

When these peak months were compared with peak use of agrichemicals, they matched. In fact, when all birth defects by month were tracked across all states over a decade and compared with peak use of agrichemicals, they matched.

How was Dr. Paul able to identify the use of agrichemicals in these areas? It's not like you can contact every farm in the Heartland and get their pesticide use data. Enter the U.S. Geological Survey (USGS) and its National Water Quality Assessment Project, which tracks and forecasts water quality across the U.S.

How does water quality figure into it? The nation's water quality is an excellent indicator because chemicals used on farms and lawns wash into streams, rivers, and lakes and some leach down into groundwater. NAWQA scientists test all these key parts of the nation's freshwater resources for pesticides, and find them with disturbing regularity.

Using the data collected by NAWQA, Dr. Paul compared amounts of agrichemicals in our water across each year to the occurrence of birth defects.

The deadly season

The upshot? The data showed that the incidence of birth defects was significantly higher in women who conceived a child during the peak season for agrichemical use in the Midwest (April-July), compared to women who conceived three or more months before, or four to six months after the peak herbicide spray season.

When these correlations were submitted for publication, most journals would not publish the findings. They claimed, correctly, that correlation does not prove causation. But correlations are often a first clue that guide scientists looking for answers to complex problems. Dr. Paul knew it was important to investigate more deeply whether the rising use of herbicides in Indiana, including several known to trigger birth defects, might be the cause, or one of the causes, of the rising frequency of certain birth defects and other reproductive problems he was witnessing in his NICU.

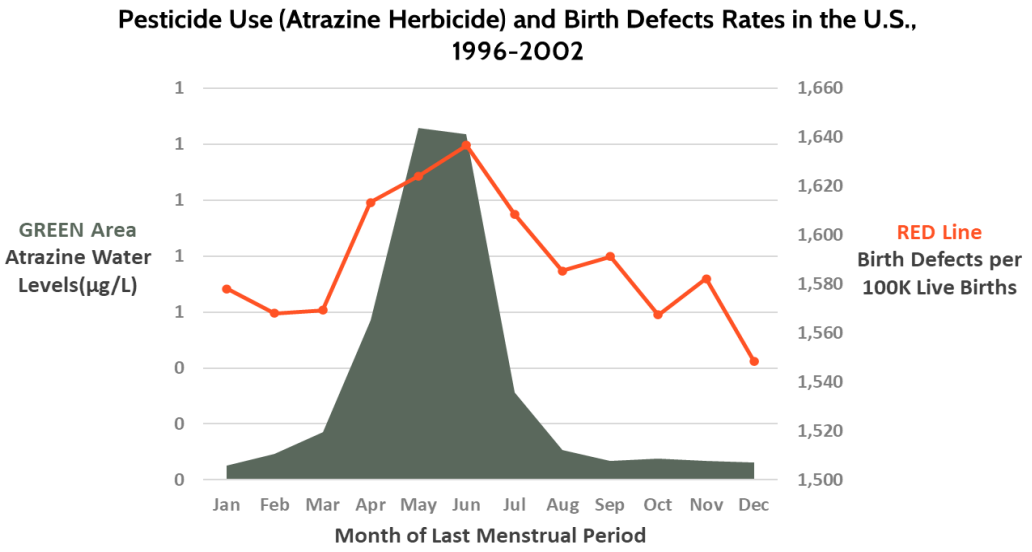
Part II—The Spark Catches

Finding the truth about healthy babies, human fertility and pesticides

If birth defects are the leading cause of infant death in the U.S., what is the second leading cause of infant death?

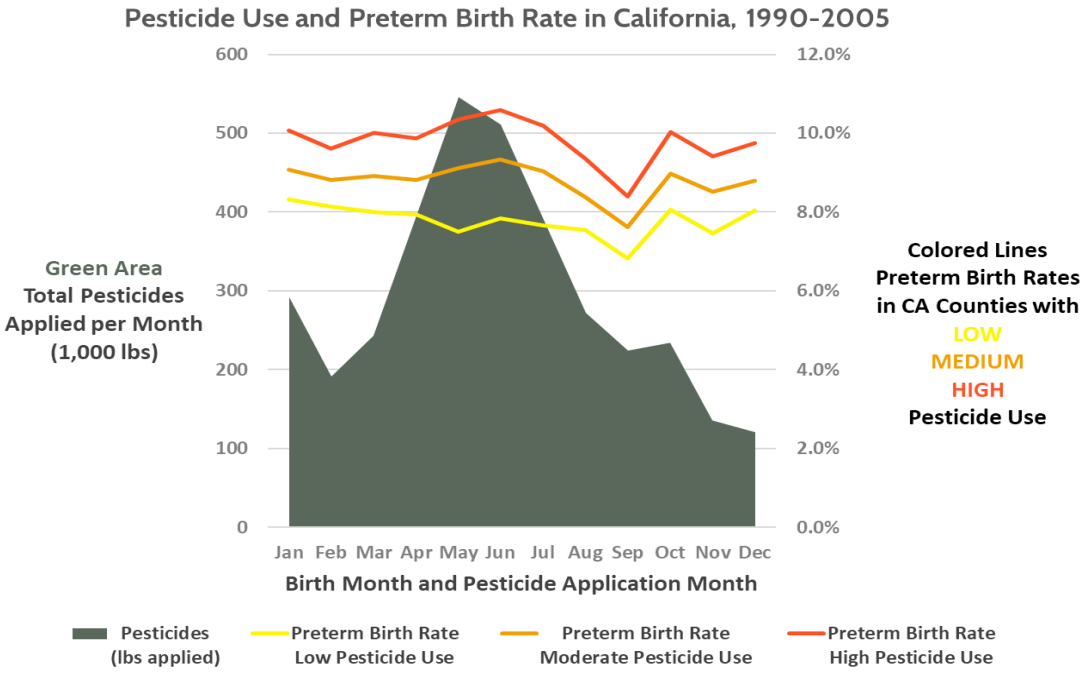
Preterm birth.

So Dr. Paul looked next at data on preterm births. He found that the preterm birth risk curve by month matched the birth defects curve: peaks in early summer and much lower levels over the winter.



In the case of preterm births, exposure to agrichemicals around the time of conception seemed to have the most impact. In fact, Dr. Paul and his team found that the highest risk of delivering a baby preterm occurred when women conceived in the month of peak pesticide use.

But how did he figure that out? Once again, Dr. Paul began the hunt for data. Fortunately, the state of California records pesticide use data for each county. That data enabled the team to show that women giving birth in high pesticide use counties had higher preterm birth rates (and shorter pregnancies). The shortest pregnancies occurred for women who conceived in the peak pesticide months (Winchester et al., 2016).



Looking Deeper

Once he saw "correlations" between adverse pregnancy outcomes and peak pesticide use months, Dr. Paul decided to look at other outcomes. He found that:

- Indiana Statewide Testing for Educational Progress (ISTEP) scores were lowest in children who were conceived in higher pesticide months.
- IEPs (special education needs) were highest in peak pesticide months of conception.
- Sudden infant deaths also spiked in peak pesticide use months.

For the month of June alone, which is the highest month for pesticide use in many states:

- IVF pregnancies were least successful in June.
- Birth month with shortest life span was for babies conceived in June.
- Abdominal wall defects and malformed genitalia peaked in June conceptions.

Can a mother's exposure to agrichemicals hurt her baby AND future generations?

That brings us to the next problem: Despite strong correlations between agrichemical use and adverse outcomes of pregnancy, Dr. Paul needed better evidence to determine whether low levels of pesticides in a woman's body during pregnancy could harm her unborn baby. Very few studies had measured chemical levels in moms-to-be.

Dr. Michael Skinner from Washington State University has explored the same issues in a series of provocative animal studies. He decided to test whether low-level exposures to agrichemicals could alter fetal development over multiple generations. Of course, you could not do that kind of test on humans, so he used rodents.

He began by exposing pregnant rats to a fraction of the dose known to cause acute effects to see what adverse health effects might occurr in the newborn rat pups. There were no observable health problems in the first generation. No birth defects, normal growth patterns and no pregnancy problems when the female pups matured and were bred. They all seemed perfectly normal.

Had his study followed EPA guidelines for reproductive studies, his team would have stopped at the second generation of rats. The chemical would have passed with flying colors. But Dr. Skinner and his team took the long view. They would continue to observe the rats through a couple of generations.

Sure enough, after a year and a half (that's three generations in rat years), everything changed in the group whose predecessors had been exposed to the chemicals. Kidney disease, immune problems, kidney cysts, premature onset of puberty, low sperm counts, tumors, obesity, premature ovarian failure and anxiety were just some of the diseases seen in the third generation.

Remarkably, neither these offspring nor even their parents had ever been exposed directly to the chemicals. This led Dr. Skinner to suspect that rather than changing the genes themselves, like in a mutation, exposure to toxins can actually change the way genes are expressed, usually by turning certain genes on or off at the wrong time, or never fully on or never fully off. And these "epigenetic" changes can be passed from one generation to the next.

This process is called epigenetic transgenerational inheritance. Many scientists now expect that a great grandmother's exposure to pesticides may increase the frequency of adult-onset diseases in her great grandchildren.

Dr. Skinner's group has now tested this effect using several pesticides and other toxics. His lab has published a handful of papers reporting that many chemicals can, in fact, alter the health of newborns two or three generations after an exposure to a chemical.

Doctors worry: Is the human race at risk?

But how does Skinner's findings in rats translate to humans? We are in the midst of an epidemic of obesity both in children and adults, premature puberty, childhood cancer, polycystic ovarian disease, fatty liver disease, lower sperm counts and infertility.

What if epigenetic transgenerational inheritance of disease is happening in humans, just as it did in Dr. Skinner's rats? This is one of the key research questions The Heartland Study is designed to answer.

Part III—The Spark becomes a Flame

Dr. Paul works exclusively with babies who require intensive care. He and his colleagues recognize that women have become more obese, have more chronic illness and are overall more likely to experience problems in the weeks just before they give birth, and then again, just after birth. And, their babies are more likely to end up in his NICU.

With all these maternal diseases, preterm births and infant birth defects on the rise, is it possible these conditions are somehow linked to a common cause, such as rising exposures to the herbicides Indiana farmers rely on in combating weeds?

That's what The Heartland Study aims to find out. Because Dr. Paul's initial findings were so compelling, a team of concerned scientists and researchers have joined the journey to truth.

Just as Dr. Paul met Dr. Skinner in the convergence of their respective scientific efforts, so did Dr. Charles Benbrook enter the story. Dr. Benbrook had been tracking the rise of agrichemical use for decades. He realized that all of the work done by Dr. Winchester, Dr. Skinner and many other scientists provided a solid foundation for a new study using state-of-the-art tools to trace the problems in Dr. Paul's NICU to their roots. Dr. Benbrook would help The Heartland Study grow as it's first Project Coordinator and then as the founding Executive Director of the Heartland Health Research Alliance, the non-profit that was launched to oversee this important research.

Elegant Design: The Heartland Study sets goal to test 2,000 pairs of moms and infants

The Heartland Study will be the largest multidimensional study of its kind ever undertaken anywhere in the world.

Creating a rock-solid scientific study is complicated. It must gather essential specimens and lots of information, and do so without imposing significant added burdens on busy doctors and pregnant women. The goal is to leave no stone unturned and rigorously pursue an answer to the question that inspired the study:

Do pregnant women exposed to agrichemicals suffer increased reproductive problems and adverse birth outcomes, and does this exposure trigger heritable changes to DNA expression that can cause disease in their children's children?

How will the Heartland Study team strive to answer this question?

By enrolling 2,000 mother-infant pair and tracking mom's health and the health of newborns. By studying the babies' development through at least age 3. By analyzing whether the women who are more heavily exposed to herbicides during pregnancy give birth to preterm or low-birth weight babies more frequently, or babies that experience other birth defects or developmental problems.

Closely follow babies until they are three

If babies can be tracked at least through the third year of life, scientists can usually pick up the early indications of problems like ADHD, autism, autoimmune disease and learning disabilities. Then scientists can use the tools of epidemiology to check for linkages between high exposures to herbicides and adverse birth outcomes. This is a tricky challenge because many factors influence the health of a woman during pregnancy and the health and development of a newborn. So, the epidemiologists on the HS team will be doing everything they can to rule out what are called "confounding factors" like smoking or diabetes or some other chronic disease.

Doctors at work to find answers

Dr. Paul's quest for solid evidence led him to join The Heartland Study team. This study was designed and is being carried out by a diverse team of scientists and clinicians. It is funded by the new non-profit called the Heartland Health Research Alliance. You can find out more about the team here.

The Heartland Study team is dedicated to coming up with the hard science needed to determine whether or not rapidly rising herbicide use across the Midwest negatively affects the health and development of children, possibly for generations to come.

Long-term clinical research studies like the HS are essential in order to rigorously establish whether herbicides are contributing most significantly to adverse birth outcomes. And if so, which ones?

Over several years now the federal government has cut funding for long-term kids' health studies, especially research on chemical exposures and environmental health risks.

This is why The Heartland Study and HHRA are relying on a long list of concerned individuals and foundations to carry out this important work. You too can help us enroll a mom and infant pair! If you'd like to contribute to a healthy future for babies, please let us know. There is much to do and all help is deeply appreciated!