

Reproductive Effects Peak with Pesticide Exposure

Seasonal water contamination studied

By Paul Winchester, M.D.

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My name is Paul Winchester. I am a professor of neonatology at University of Indiana School of Medicine. When I was looking at the babies in our nursery one day in 2001, I became concerned about the frequency of birth defects and began looking for the reason. This research led me here to all these intelligent people [motioning to his fellow panelists: Warren Porter, PhD, Beyond Pesticides board member and professor of zoology and environmental toxicology at the University of Wisconsin-Madison, and Michael Skinner, PhD, professor of molecular biosciences at Washington State University] and to all of you. This is the summary of some of the findings we have made since we began our journey.

Basic truths

Basically, this is what we have learned, just so we do not have to argue whether pesticides are in your body or in your water. That is the "we hold these truths to be self-evident" part of this discussion.

- We know from extensive research that pesticides and



contaminants are in all of us all the time;

- We also know that it is not just one pesticide that we are contaminated with, it is a mixture of chemicals. (As Dr. Porter has said, pesticides are one part of a burden that we all carry.);

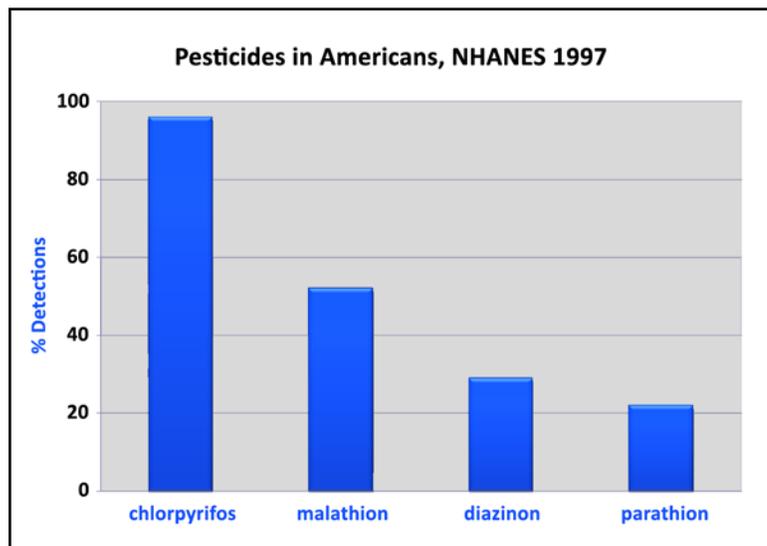
- We also know that the contaminants that we are loaded with –and this includes the 247 molecules of contaminants found in every single newborn baby born in America– each one of them is known to cause biological effects at very low doses;

- And the final truth is that our regulatory agencies have told us that we are safe.

Contaminated without consent

The National Health and Nutrition Examination Survey (NHANES) findings show that multiple pesticides are found in virtually every single American. [Slide #1] When the Environmental Working Group conducted the study to see how many pesticides an average person has in their body, they found that all of the volunteers are contaminated with everything from Teflon to plasticizers to flame retardants to DDT. DDT, remember, was banned almost 30 years ago and is still now found in 87% of every American measured. This is just another piece of the puzzle for us, because we may not like these molecules, but once we release them into the environment, whether we were right or wrong about them, we get to find out over the next 50 years.

If you look at placentas, an area a little closer to my



Slide 1. The National Health and Nutrition Examination Survey (NHANES) nearly all U.S. residents are contaminated with pesticides and other chemicals.

heart, we find mixtures of pesticides. If you look at animals around the planet, you find contamination. The remarkable thing is that many of these molecules, perfluorooctane sulfonate (PFOs), for example, are man's greatest accomplishment. We have now created molecules that are immortal! Immortal means that they will rise up into the atmosphere, be carried by the jet stream, and now they can appear in virtually every living organism on the planet, whether you are a seal, a dolphin or a robin's egg.

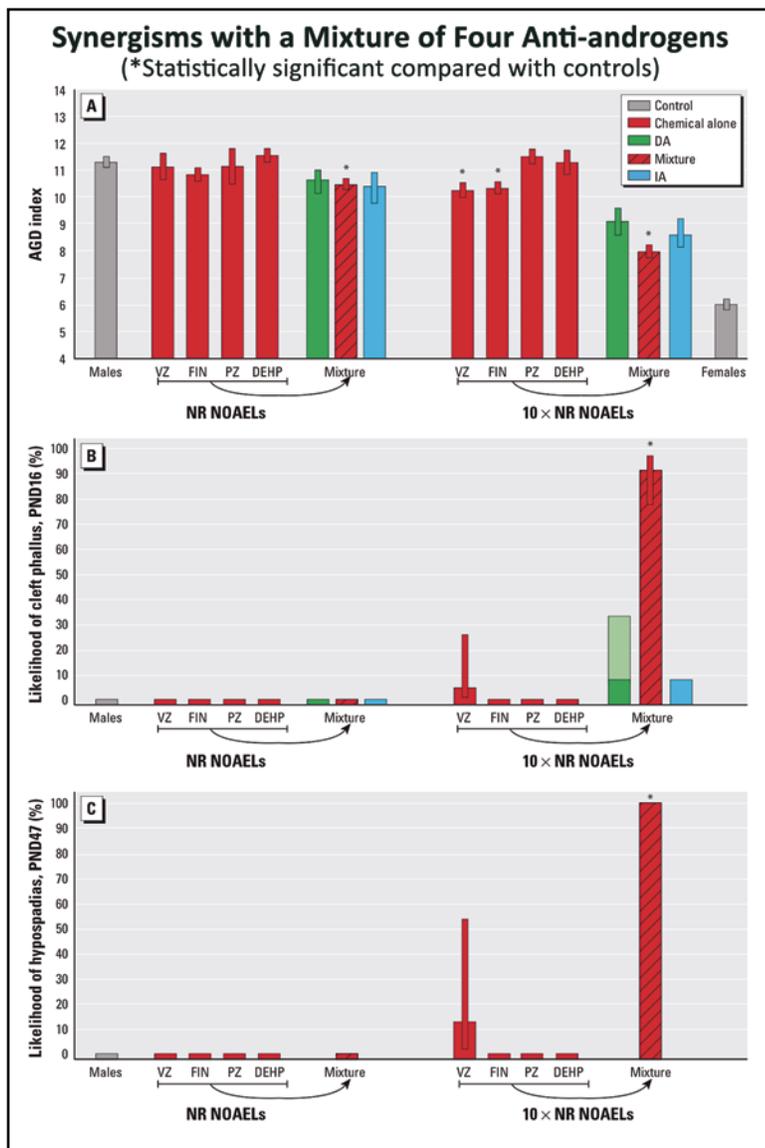
We have lots of evidence that shows mixtures are an important concept. The endocrine disrupting effects of vinclozolin mixed with three other molecules serves as a good example. Individually these molecules have very little effect, but mixed together they have elevated effect. [Slide #2] By the way, there are no Americans that have individual molecules, but when EPA requires testing of a product for safety, tests are performed on a single molecule, never the mixture combinations in your body.

The U.S. Geologic Survey (USGS) is showing us that the same is true for all rivers and streams in the U.S. They are all found to be contaminated. It is not a matter of whether they are contaminated, it is how many contaminants can be found. Slide #3 shows the 50th percentile; the average is 5 or 6 of these chemicals that are found in every single river or stream in the U.S.

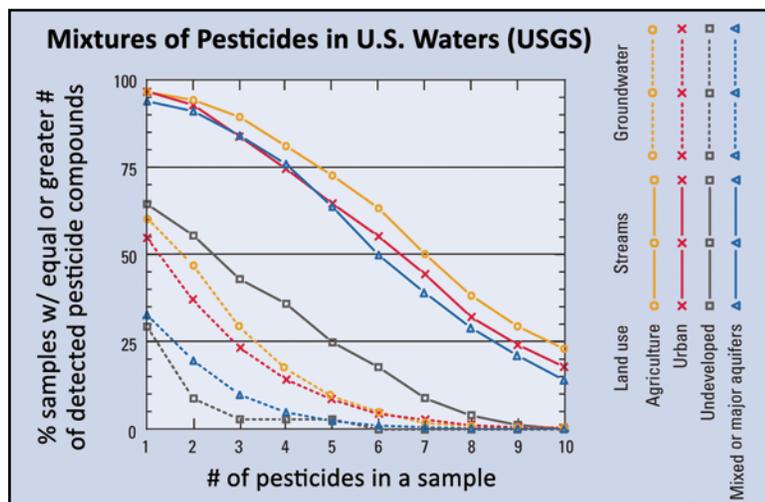
Paying the price later in life

Back to the question, "Are we safe?" One way to answer that is to ask, "Are we healthy?" When we talk about exposures to chemicals, we frequently forget that our mind has already been preset to imagine the type of harm that could befall us. I like to compare the concern about toxic harm to our understanding of fire: we know that it is harmful, but we also know you have to put your hand in it for a while before you actually get burned. So when we spray a fog of DDT on a group of playing children—and they run through the fog and come out the other side—we kind of think that is safe. It did not dawn on us that safety is a matter of measuring over years. It may be a matter of counting over generations before we can really have the sense of safety. Our cancer specialists have told us that carcinogenesis is important. And, we kind of learn that through the smoking story—if I smoke now, I will not get cancer until I am 50. So, yes, smoking causes lung cancer, but it is not going to kill me today.

The epigenetic story (inherited changes in gene expression without changes in DNA) is even more daunting. We have learned that the idea of toxicity that EPA uses is *entirely inappropriate* when it comes to our reproductive outcomes. When we are forming babies



Slide 2. Rodents exposed to phthalates (DEHP), finasteride (FIN), prochloraz (PRO) and vinclozolin (VZ) are less likely to cause birth defects when exposed to individually than in a mixture (Kortenkamp et al., 2009).

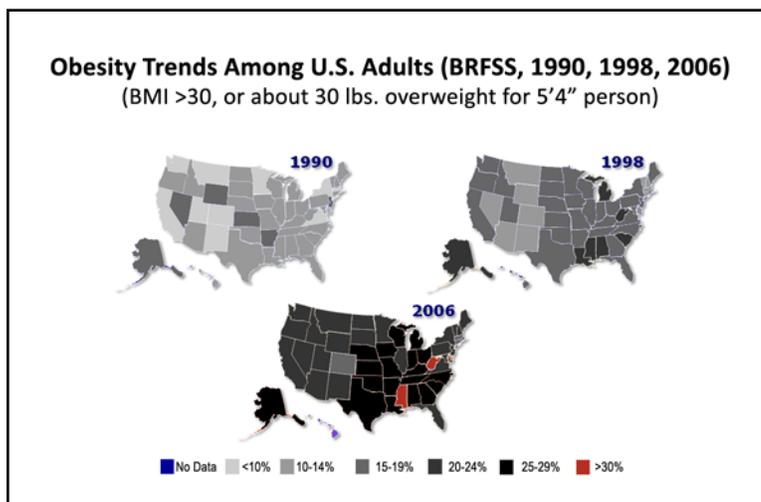


Slide 3. Data from the U.S. Geologic survey (USGS) shows that streams in the U.S. are contaminated with combinations of pesticides.

Children's Health Report Card 2007
(Environmental Working Group)

Autism	10X	increase early 80's - 1996
Male Birth Defects	2X	increase hypospadias, 1970-1993
Childhood Asthma	2X	increase 1982-1993
Acute Lymphocytic Leukemia	62%	increase in children, 1973-1999
Childhood Brain Cancer	40%	increase 1973-1994
Preterm Birth	23%	increase mid-80s-2002
Infertility	5-10%	of couples
Birth Defects	3-5%	of all babies
Sperm Counts	1%	decrease yearly 1934-1996

Slide 4. Data compiled by the Environmental Working Group in their 2007 Children's Health Report Card shows environmentally linked health effects are on the rise.



Slide 5. According to the Centers for Disease Control and Prevention's (CDC) Behavioral Risk Factor Surveillance System (BRFSS), the world's largest on-going telephone health survey system, obesity rates among U.S. adults has steadily increased from 1990 through 2006.

in the womb, we are actually forming an imprint of DNA that will set the stage for the rest of that person's life. When this imprint is altered by exposure to these products, then not only does your disease risk change for the rest of your life, but it may alter the lives of all of your descendants.

These environmental factors –weed killer, fungicide, insecticide, air pollution, nitrates, protein, calorie and/ or vitamin deficiency, plasticizer, PCBs, BPA, flame retardant, lead, mercury– are the list of things we have to worry about during pregnancy or conception. All of these have now been shown to be capable of imprinting DNA, which means they are potentially capable of altering our adult life, the spectrum of disease, and our descendants' lives. I was thinking of 'inherit the wind' here, but it really should be 'inherit the weed killer.'

More cures, more disease

Are we healthier today? Well indeed, you know, cure rates are up, but diseases are up. [Slide #4] We are doing better at taking care of premature babies than ever –I love to brag about it. But premature rates are up, autism rates are up, male birth defects are up, asthma is up, cancer is up, and infertility is up. The only thing that is down are sperm counts.

Yes, we are getting better at saving people with cancer. I notice this University, like every other community in the U.S., is building a Taj Mahal to cancer. In a neighborhood near you, you will find a heart center with valet parking, a maternal-fetal medicine center for high risk pregnancies, and a reproductive endocrinology center to help women get pregnant who are no longer capable.

We can compare disease rates between people who live near crop lands with the general public. Rates of cancer, asthma, obesity, attention deficit hyperactivity disorder (ADHD), major depression and premature menarche may all be linked. Slide #5 identifies the obesity story in the U.S., where light shading is good and dark is bad.

Autism: This disease has not only increasing instances of diagnosis but the younger ages are making the diagnosis.

Major depression: Many pregnant women now come to me already on an antidepressant. When did that start? Psychotropic drug use is up. My wife works in a school system as a nurse, and you have to be a pharmacist now to take care of kids in an ordinary school.

Child neglect and abuse: One of the most frightening aspects of fetal exposure to hormonally active drugs is that it makes females less good mothers when they grow up. This has been shown now in animal models and

it would predict, if it were true in humans, that we are having more abuse and neglect.

The age of menarche (first menstrual cycle): The long-term trend for age of menarche is shown in Slide #6. Tracking back to 1860, the present-day American experience shows where girls less than 11 years old are menstruating. So actually, you can say hormones are raging at an incredibly early age.

Prostate cancer rates are epidemic. **Breast cancer** rates are epidemic worldwide. Even in countries with low rates of breast cancer, breast cancer rates are up.

Global increase in diabetes: It is the same story. The lowest rate of diabetes is in Africa, but it has the highest rate of increase. The diabetes rate is not just increasing, but the age of onset is decreasing. When I was practicing in New Hampshire, I was seeing two-year-olds starting on insulin. Diabetes has been linked to pesticide levels. Research shows an increased risk of having diabetes with exposure to DDT and many other current use pesticides.

Diabetes affects the adult, but it also affects pregnancy and the baby. I just admitted a baby that looks just like babies we call "Buddha babies." The mother had diabetes. With too much sugar on board, the baby becomes very obese, but the baby's risk of birth defects of any kind is increased two- to four-fold. There is an increased risk of immaturity, jaundice, poor feeding, temperature instability and low blood sugar.

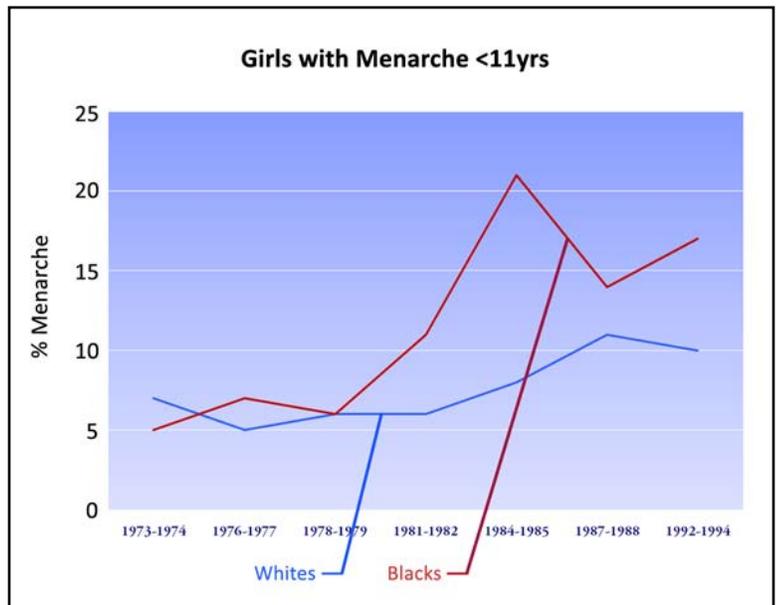
Many OBGYN diseases that are on the increase have now been linked to environmental contaminants, including, as Dr. Warren Porter mentioned, polycystic ovarian disease. There is not a woman here who does not have a friend who does not have that disease. When did that start?

Pregnancy-induced hypertension poses health risks. This is a disease that is now increasing in incidence. It causes premature babies and is linked to how closely exposed to pesticides you are.

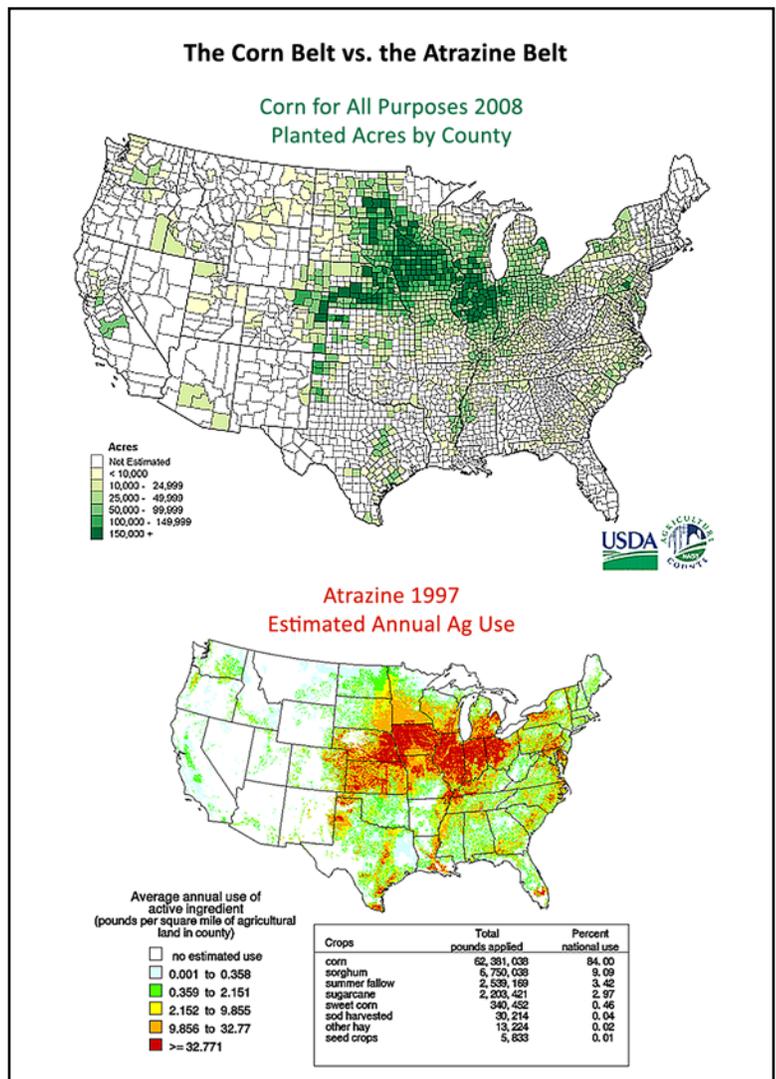
Can't find what you're not looking for

So my trouble in paradise really began when I looked at babies in the nursery at my hospital and asked about birth defects. What I found were two things.

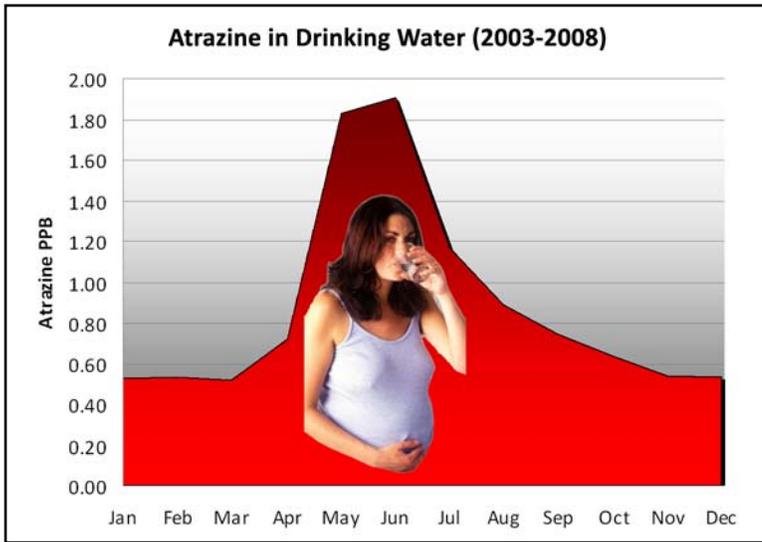
Indiana and 12 other states were not counting birth defects in 2001. I know birth defects and, according to the Centers for Disease Control (CDC), they are the leading cause of infant death in the U.S. The leading industrial country in the world was not counting the leading cause of infant death in a quarter of its states in 2001.



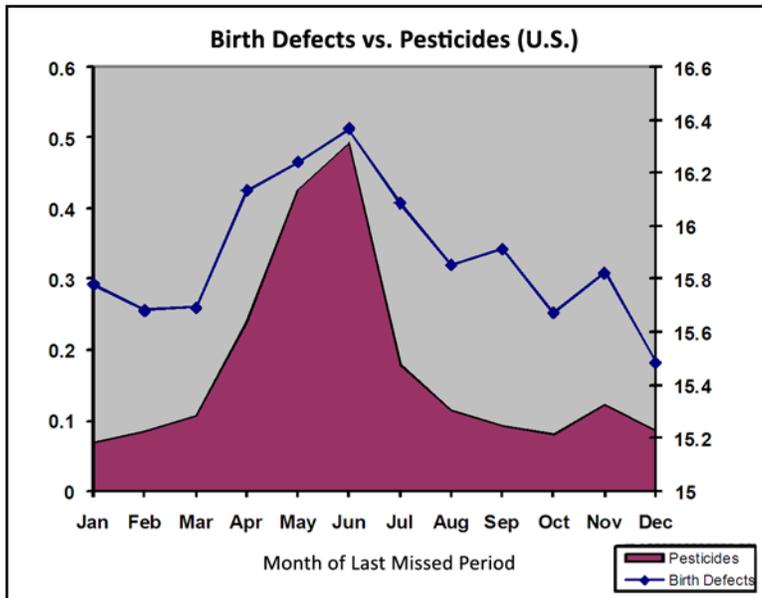
Slide 6. The percentage of U.S. girls whose age of menarche was under 11 has increased over the past two decades, especially in African American girls.



Slide 7. "The Atrazine Belt"



Slide 8. Like other contaminants, levels of the endocrine disrupting herbicide atrazine peak in June in Indiana water.



Slide 9. The national peak of pesticide water contamination in June mirrors the seasonal increase in rate of birth defects.

Birth Defects Linked to Season of Conception

Birth Defect Type	BIRTH DEFECTS (per 100,000)*		p-value
	April-July	Other Months	
Spina Bifida/Meningocele	21.93 (0.50)	20.31 (0.34)	<0.01
Other Circulatory/Respiratory	134.99 (1.25)	131.09 (0.85)	<0.01
Cleft Lip/Palette	83.09 (0.98)	79.07 (0.66)	<0.01
Polydactyl/Syndactily/Adactily	85.65 (1.00)	81.88 (0.68)	<0.01
Other Musculoskeletal/Integumental	223.49 (1.61)	217.36 (1.11)	<0.01
Down's Syndrome	46.23 (0.74)	43.22 (0.49)	<0.01
Other Congenital Anamolies	455.89 (2.33)	443.89 (1.59)	<0.01
Tracheo - esophageal fistula/Esoophageal atresia	13.33 (0.39)	12.32 (0.26)	<0.05
Other Gastrointestinal	32.22 (0.61)	30.82 (0.42)	<0.05
Other Urogenital	105.37 (1.11)	102.54 (0.76)	<0.05
Club Foot	58.17 (0.82)	56.23 (0.56)	<0.05

Slide 10. Birth defects with a statistically significant link to time of conception.

The other issue deals with what we learned about the water contamination rate in our state, and eventually the entire U.S. Nearly every contaminant we studied seems to peak in June. When I asked EPA to send me the information on Indiana, I calculated the rate of sampling by the water companies. It almost made me sick, because I realized that EPA allows water companies to not measure in the most contaminated month. So we realized they are not counting birth defects and they are not measuring the water in June! So we went looking.

It is relevant that my research team had met Tyrone Hayes, PhD [professor of biology at the University of California, Berkeley] at this point, and we live in the Corn Belt. We could rename it the "Atrazine Belt," because this is the atrazine story. [Slide #7] Dr. Hayes' research has shown that you are more likely to have eggs in your sperm-containing organs if you are a frog being exposed to atrazine. This means that an estrogen effect could be affecting children. At least if we live in the Corn Belt or the Atrazine Belt, we should be counting our babies to see if they are abnormal. Sure enough, if we look at the water in Indiana, we find that atrazine peaks as regularly as the Matterhorn. [Slide #8] I call this the June effect.

The timing of birth defects

We collected all the birth certificates from Indiana that contain birth defect information, which our state health department was not using. What we found, to make this story a little shorter, is that birth defects like spina bifida peak in June [conceptions]. Abdominal wall birth defects peaked in June. We also found premature birth peaked in June, sudden infant death peaked in June, and malformed genitals peaked in June. And while we were not counting spina bifida, we exceeded the national average for the time period. So a state that was not having problems with birth defects, just was not counting them!

In our national study, we found that the national water looks the same. The birth defects for the whole U.S. increase in women who conceive in the month of highest pesticide concentrations. The astonishing part of Slide #9 is not the findings, it is that I was the first one who did it. We have an entire CDC that could have easily asked this question. In fact, I think you could have asked somebody in kindergarten this question. That was the part that upset me the most.

Out of the 22 different birth defects, these 11 are significantly increased in months of increased pesticide contamination. [Slide #10] The other 11 were not significantly different. Now some investigators prefer that we report these as negatives, which suggests there

is no risk of these other disorders. However, if you notice, every single one of these numbers except one is greater in months of elevated pesticide contamination. The reason our study was successful is that we had 50 million babies to study. If we had 100 million babies, these probably would all become significant too. Birth defects increase during the time of conception when pesticide contamination is the highest.

By the way, this study was refused by the *Environmental Health Perspectives* journal, but thanks to the Scandinavians who were willing to publish it. So these are photos of kids with birth defects who I take care of every day. [Slide #11] Certain birth defects can be addressed through surgery –although we cannot do much about others, such as trisomy 18. We do have very expensive clinics that they can attend. We can repair their tracheoesophageal fistula and their heart defects. Wouldn't it be better if it did not happen?

Geography of birth defects and preterm birth

What about location? Well, to estimate pesticide exposure, we used the U.S. Department of Agriculture (USDA) pesticide usage data and found that the counties with the highest pesticide rates have the highest birth defect rates. Since then, one of my colleagues at Purdue University found that if you just do a satellite view of where you conceived your child, the closer you are to a cornfield, the more likely you are to have a birth defect.

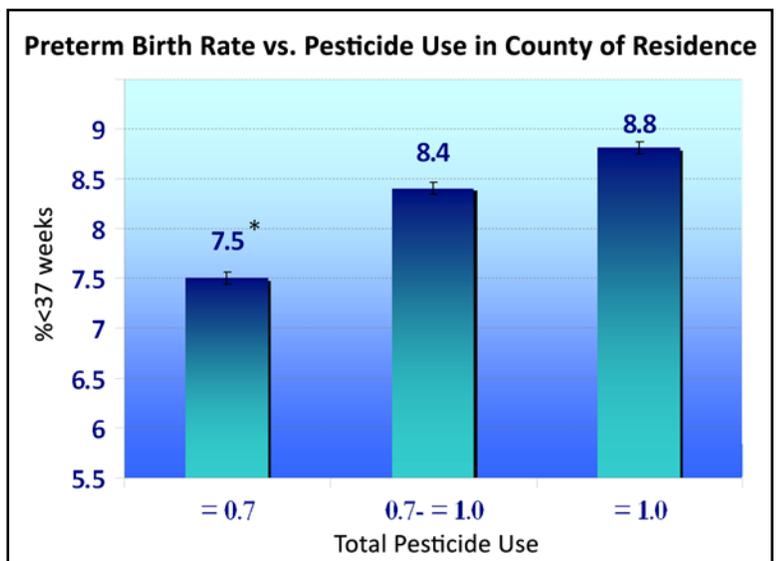
Preterm birth is next. If you take all the diseases linked to preterm birth, it is even more dangerous than birth defects. Because it is more common, it is increasing in an epidemic manner in the U.S.

Why don't we all know this? This is by far the most important fact of human health that I can think of. It determines the outcome of our human race; and it is epidemic. So, we took the California pesticide usage database, which is the best estimate of how much pesticide exposure you might have had (the California pesticide usage is gargantuan). We found that prematurity rates, if you control for other variables, goes up directly with the amount of pounds per person, or per acre, of pesticides that are used in a particular county. [Slide #12]

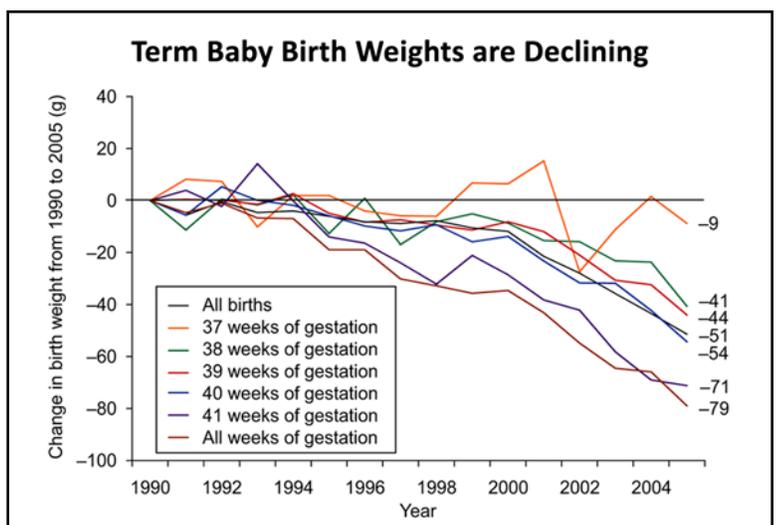
When we presented this last year, one of the participants in our audience asked, "Is this true?" And I said, well the U.S. government is actually funding a study in California that shows that when you measure pesticides in pregnant women, the ones with the highest levels have the shortest gestations. Fortunately, they also went further



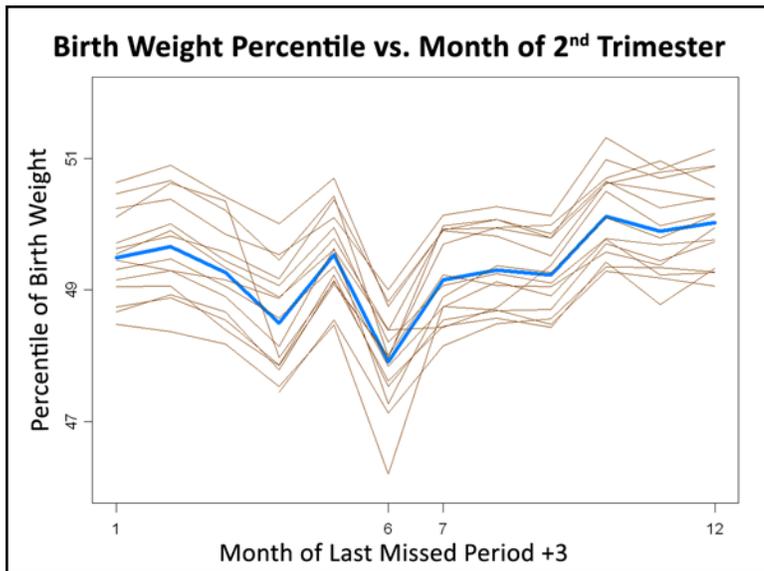
Slide 11. Children with various birth defects, linked to environmental factors.



Slide 12. Rate of preterm birth highest in counties with high pesticide usage.



Slide 13. Since 1990, birth weights in the U.S. have been decreasing. Birth weight is a predictor of lifetime health and IQ.



Slide 14. Birth weight is lowest when second trimester occurs in June-July.

to explain why some people that are exposed have problems and others do not. It turns out that what we really have is not just genes for prematurity, we have genes for detoxifying our womb, and some of us are better at it than others. The paraoxonase (PON) gene polymorphisms can determine which of those you are; as a pregnant mother, are you a good detoxifier, or are you a bad detoxifier? Those with the bad detoxifier versions of the genes are much more likely to have the premature babies.

Birth weight and more

Birth weight is our final item. We preface this by saying the newest development and recorded findings are that there is an epidemic not just of preterm birth, but of relatively smaller babies. It turns out over the last 15 years American babies are getting smaller. [Slide #13] Those of you who are dieting right now might think that

is a good thing, but those of us in the area of neonatal medicine know that the size of the baby is the best predictor of brain size and ultimately your lifetime risk of being on welfare, having a job, and having major disease of the heart, and so on. So it is not a good thing.

It is happening not just in term babies, but also in preterm babies. Babies are getting smaller. And so in California, once again as with the rest of the country, we find that pesticides are peaking in the middle of summer and the babies' birth weights, which reach the second trimester, have the lowest rates in those months. [Slide #14] This was found whether we measured their actual birth weight, relative birth weight or z-score [indicates how many standard deviations an observation is above or below the mean], and so we can say that if your baby was reaching the second trimester in May, June or July, you are much more likely to have a smaller baby.

Interestingly, in the same time period in California, that increases your risk of having an autistic child. In summary, we can say that growth restriction is another risk factor for having small babies.

And then finally, we did find that the Indiana University School of Medicine z-scores were lowest in the pesticide peak months in Indiana, and the same for having learning disabilities. Those babies are more likely to be conceived in those same months. So, perhaps we should be worried.

Dr. Winchester published the study, "Agrichemicals in surface water and birth defects in the United States," in the April 2009 issue of Acta Pædiatrica (Vol. 98, No. 4).

