Research to Real Life: How Scientific Research Affects YOU

The Boston University Superfund Research Project (BUSRP) scientists and researchers are often asked questions by community partners, health professionals, health advocates, agency personnel and the public about what their research means in real life settings and the scientific methods they use to conduct the research.

Frequently Asked Questions

The following questions and answers were written by BU SRP scientists to help translate some of the more common scientific methods and explain what they mean in the real world and to human health. They are designed in a "Who, what, when, where and why" format and include the following topics:

- **How** does it work?
  Exposure Biomarkers – How do we analyze toxic chemicals in people's bodies and what does it mean. Does exposure =risk?
  by Patricia Fabian, ScD and Susan Korrick, MD, MPH

- **Why** do we do it?
  Fish studies – Why do we spend money and time studying a species like zebrafish? How is this research relevant to human health?
  by Mark E. Hahn, PhD

- **What** does it mean?
  What is **environmental epidemiology**? What are **odds ratios** and what do they mean in scientific studies?
  by Ann Aschengrau, ScD

- **What** is it, **How** and **why** do we do it?
  What is a **risk assessment**? How do we conduct **risk assessments** and what are they used for? Why is there criticism of **risk assessment**-based guidelines and standards?
  by Wendy Heiger-Bernays, PhD

How does it work?

Exposure Biomarkers

by Patricia Fabian, ScD and Susan Korrick, MD, MPH

Question: What are exposure biomarkers?
Answer:
Exposure biomarkers, also known as biological markers of exposure, are chemical measurements present in human tissue or fluid samples. Scientists estimate how much of a particular chemical has entered our bodies by measuring the levels of a certain chemical or its byproduct in various human tissues or fluids such as urine, stool, breast milk, nail or hair.

We are exposed to chemicals all of the time from the food we eat, the water we drink, the air we breathe, as well as the household and personal care products we use. Chemicals may also be found at workplaces including, for example, places where manufacturing occurs and standard office buildings. After being exposed to certain chemicals from eating, drinking, breathing or skin contact, they may enter the blood stream, get metabolized, and/or become stored in part of the body, or eventually get excreted in urine or via other pathways. That is why scientists are able to analyze exposure biomarkers. Most people are exposed to chemicals that can have adverse health effects just from daily activity, but with proper precautions, this doesn't mean they have to stop doing those activities.

Question: Why do exposure biomarkers use so many different tissues? For example, what is the difference between exposure biomarkers measured in blood compared with urine or toenails?
Answer:
The choice of tissue for an exposure biomarker depends on a number of factors including which tissues in the body may store the chemical and the chemical's half-life. A chemical's half-life is a measure of how quickly it is excreted or removed from the body, that is, the time it takes for the body to eliminate half of the chemical to which it was exposed. Chemicals with short half-lives may be removed from the body within hours of exposure. For example, after drinking water or eating food that has arsenic in it, the body can excrete the arsenic within hours of exposure via the urine. In this case, measuring arsenic in urine is a standard way to assess arsenic exposure. The chemical structure of arsenic also means that, after exposure, not only is it excreted in the urine, but some is also deposited in hair and nails. This means that hair and nails can also be useful tissues for measuring arsenic exposure.

Other chemicals have long half-lives and, after exposure, can stay in the body for years or even decades. For example, the chemical structure of organochlorine chemicals such as PCBs and certain pesticides such as DDT means that, after exposure, the chemicals are deposited in fatty tissue where they can remain for many years. Because of this, measuring PCBs or DDT in the blood or breast milk (both of which contain fat) are more useful tissues for measuring this type of exposure.

The choice of tissues for exposure biomarkers is also often influenced by whether it is possible for the chemical to get into the tissue from outside of the body, which is called external contamination. As an example, in some regions of the U.S. and elsewhere, there are high lead levels in soil. If individuals walk barefoot in this soil, their toenails may contain high lead levels without their internal organs having had lead exposure. In this case, lead levels in toenails would not be an accurate reflection of internal exposure which is the exposure of interest for health.

Lastly, choice of tissues for exposure biomarkers may depend on practical considerations including convenience (clipping toenails is easier than drawing blood) and whether there are established laboratory analysis methods for measuring that chemical in a particular tissue.

Question:
When chemicals are found in exposure biomarkers, does that mean the chemicals will cause health problems?
Answer:
Everyone is exposed to chemicals that can be hazardous to health but finding a chemical in someone's blood, nails or other tissues does not necessarily mean that it will make the individual sick. The amount of chemical in the body and the toxicity of the chemical both help determine whether the chemical will impact health. For example, manganese is a metal that is essential for health. At moderate levels of exposure, it is good for you, but at high levels of exposure, it can cause damage to the nervous system. Certain people may be more susceptible to chemical health effects than others. Nervous system damage from lead exposure can be worse in children than in adults, as an example.

Question:
How are exposure biomarkers used?
Answer:
Exposure biomarkers are very important tools for determining whether, and how much, a given person or group of people have been exposed to a chemical. At times, they are used as part of medical care, like when screening for childhood lead poisoning. They are also a critical part of many research studies that investigate whether exposures to certain chemicals may have adverse health effects in the population.

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What does it mean?

Environmental epidemiology, odds ratios.

by Ann Aschengrau, ScD

Question: What is environmental epidemiology?
Answer:
Environmental epidemiology is a field of study that examines the relationship between exposures to environmental hazards, (including chemicals, disease carrying-organisms, radiation, heat and cold, noise, stress), and health or disease outcomes. There are many challenges in this field because the focus is on populations who are experiencing exposures in their daily lives, rather than deliberate exposures such as clinical trials for pharmaceuticals. The exposures often rely on people's ability to recall events and activities that they engaged in months and years ago. The outcomes are also often subtle such as changes in brain function and are difficult to measure like academic performance during childhood.
The goal of most environmental epidemiological studies is to determine if there is an association between an exposure and a disease (say, outdoor air pollution and childhood asthma), and if so, to assess the strength of that association. Epidemiologists use various measures to assess the strength of an association, depending on the design of the study.

Question: What are odds ratios and what do they mean in scientific studies?
Answer:
An odds ratio is typically used in case-control studies. In this type of study, the investigator selects a group of cases with disease (say, children with asthma) and a group of controls (say, children without asthma) and compares their exposures (say, air pollution levels around their homes) using an odds ratio.

Mathematically, the odds ratio compares the odds of developing the disease among exposed people (those who develop asthma and are exposed to air pollution) with the odds of developing the disease among unexposed people (those who develop asthma but are not exposed to air pollution). If the odds ratio is equal to 1.0, it means that there is *no association* between the exposure and disease. In other words, the exposure does not increase or decrease the odds of developing the disease. If the odds ratio is less than 1.0, it means that the exposure is protective and *decreases* the odds of developing the disease whereas if the odds ratio is greater than 1.0, it means that the exposure is a risk factor and *increases* the odds of developing the disease.

Suppose, for example, that a case-control study of air pollution and childhood asthma finds an odds ratio of 2.0. This finding means that children who are exposed to air pollution have 2.0 times the odds of developing asthma as compared to children who are not exposed to air pollution. Even when the odds ratio indicates that an association is present, we cannot automatically conclude that the exposure *caused* the disease. The assessment of causation is a separate process that considers strength of the study methods and other sources of information.

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Why do we do it?

Fish studies

by Mark E. Hahn, PhD

Question: Why do we spend money and time studying a species like zebrafish? How is this research relevant to human health?
Answer:
Zebrafish are considered a useful model system for studying biological processes relevant to human health. Model systems make it easier for scientists to answer questions about biology. Much of our understanding of how our bodies work has been obtained by studying model systems such as yeast, fruit flies, mice, and zebrafish (to name just a few).

Zebrafish have several characteristics that make them a good model for human biology, and especially for studying the processes involved in embryonic and fetal development—the transformation of a single-cell fertilized embryo to a fully formed adult with a variety of cell and tissue types.

Question: Why is the zebrafish a useful and important model system?
Answer

- Fish and humans are vertebrate animals that share most genes and develop similarly, so results obtained in zebrafish are likely to be applicable to humans as well.
- Zebrafish possess most genes linked to human genetic diseases and can often be made to reproduce those diseases, allowing therapies to be tested. Examples of human diseases modeled in zebrafish include blood diseases such as anemia, cancers including leukemia and melanoma, and a variety of birth defects.

- Zebrafish embryos develop outside of the mother, and more quickly than mammals, allowing experiments to be done more easily.
- Zebrafish embryos are transparent, so scientists can observe how they develop under a microscope.
- Zebrafish embryos can be easily manipulated in the laboratory to tag specific genes or cells with fluorescent markers, or to inactivate specific genes. This helps scientists to better understand their function.
- Zebrafish embryos are small and can be grown in small volumes, making them especially useful for large experiments in which chemicals are tested on thousands of embryos to see if they are helpful or harmful to development.
- In contrast to experiments done using cells in culture, the zebrafish embryo is an *in vivo* (living organism) system that maintains all the complexity of complete living organisms, and thus is better able to reproduce biological processes that involve multiple tissues or cell types.

Because the zebrafish is such a good model for studying normal biological processes, it is also a good model for studying how chemicals can interfere with those processes to cause toxicity. Thus, zebrafish are widely used to test chemicals to see if they are safe and to see whether humans will develop diseases later in life if they are exposed to chemicals when they are young.

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What is it, and **How** and **why** do we do it?

Risk assessment

By Wendy Heiger-Bernays, PhD

Question: What is Risk Assessment?
Answer:
Risk assessment is a decision-making tool that is used to answer questions about the chances or likelihood of developing illness from exposure to environmental stressors. These stressors include toxic chemicals, disease-causing organisms (like salmonella in food), radiation, heat, and noise. We focus here on chemicals, and we use polychlorinated biphenyls (PCBs) as example, but the same basic four-part approach is used for all stressors:

- Hazard identification - whether there is scientific evidence that PCBs can cause harm to people;

- Exposure assessment - who is exposed to the PCBs, how they are exposed and how much PCBs get into the body from the exposure – also called the dose of PCBs;
- Dose-response assessment – the dose of PCBs that is "safe" and;
- Risk characterization - a comparison of the estimated exposure to the dose that is considered "safe."

Risk is never calculated as "zero" – there is always some risk IF exposure to the chemical occurs.

Question: What is risk assessment used for?
Answer:
Risk assessment is used by the US Environmental Protection Agency (US EPA), states and other regulatory bodies to set allowable levels of toxic chemicals in food, water, air, and consumer products. Risk assessment is also used to make decisions about how much contamination needs to be cleaned up at hazardous waste sites. Risk assessments have been used to set allowable fish consumption guidelines, drinking water guidelines and drinking water standards for the per- and polyfluorinated alkyl substances (PFAS).

Question: Why is there criticism of risk assessment-based guidelines and standards*?*
Answer:
There are valid criticisms of risk assessment, which include that:

- Risk assessments focus on single chemicals and not mixtures (with very few exceptions), and; people are exposed to multiple chemicals and other stressors simultaneously and the current risk assessment approaches do not take these into account in the development of risk-based standards and guidelines;
- Dose response does not account for short exposures over time (such as the impact of endocrine disruptors), and; it is not sufficiently sensitive to study very subtle and biologically relevant effects that have been documented by scientists, such as those on the development of children's brains, immune system and metabolic effects in children that result from maternal exposures. Traditional methods do not capture these effects in a way that allows the science to be used in the risk assessment.
- In a "risk/benefit" analysis, regulatory authorities may decide that there is "acceptable" risk – this is the amount of health risk that is allowed. This is a risk management decision – not based on science or health, but based on societal, political and economic decisions.

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