



Issue Brief

MIXTURES & ENVIRONMENTAL CHEMICALS: A PERSPECTIVE ON RISK

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ISSUE SUMMARY

Humans encounter an ever-changing combination of natural and man-made chemicals at low levels, in normal, every day activities. This type of environmental exposure to mixtures of substances has raised the question: "Are low levels of these chemicals we encounter in our environment (either natural or man-made) causing harm?"

THE BOTTOM LINE

We are exposed to a number of natural and man-made chemicals simultaneously and continuously every day. It is no surprise that they can be detected in biomonitoring experiments, and this should not lead to undue concern. The presence of a substance that has adverse effects **at some level** does not imply that the presence of that chemical will lead to adverse effects **at all levels**. Potential toxicity must be considered in the context of the amount, route, duration and timing of exposure. For human health risks for chemical induced toxicity, evidence-based medicine and toxicology principles -- the true scientific consensus -- tell us that effects at high doses will not be realized at lower doses if the concentration falls below the target site threshold level. This principle applies just as much to "windows of susceptibility" during development as it does more broadly to all life stages.

OUR VIEW

Whether we are breathing air, which is composed of chemicals, or ingesting food, which is a complex mixture of chemicals, our bodies are absorbing a variety of chemicals every day. Scientists, physicians and others in related professions have long understood that the actions of life are chemical by their very nature. As we interact with our environment, we are exposed to many thousands of chemicals, both natural and synthetic. The specific chemicals vary from day to day depending on our environment and activity. Generally, if a chemical is taken in by the body, it is either used or changed into a new chemical that can be used (nutrient) or it is altered by systems in the body and sequestered or excreted as waste.

The increased sensitivity of analytical methods allows us to measure simultaneously more chemicals at lower concentrations in human tissues. This has led some to use the

term “chemical cocktail,” and to assert that the mere presence of chemicals in the body is harmful without regard for the amount of chemical being referred to or the frequency or duration of presence in the body.

“Dose makes the poison”

Our scientific understanding of how the body functions when exposed to environmental chemicals, and our knowledge based on current scientific methods for assessing harm posed by chemicals, indicates a large difference between low levels of exposure to chemicals and harm or disease resulting from exposure. Potential harm must be considered in the context of exposure and inherent toxicity of the chemical(s) -- the amount, route, duration and timing of exposure and toxicity. Both naturally occurring and environmental chemicals – can be toxic at some dose. Indeed, many “naturally occurring” chemicals are potent toxins. The quantity of exposure - the dose- is of utmost importance in determining potential risk. For example, one aspirin can be an effective therapeutic agent for a headache. Ingesting a full bottle of aspirin tablets will lead to toxicity. And taking an aspirin tablet and dividing into a hundred or a thousand equal parts, and then ingesting one of these small doses will not produce any effect whatsoever. This is a fundamental principle of biology and medicine and it applies to low level exposures to environmental chemicals, just as it applies to therapeutic agents and natural substances.

The human body is well equipped to manage low levels of chemicals. At low levels of many environmental chemicals, cells act to break down and excrete these substances as wastes, for example, as it disposes of alcohol. However, when any chemical is present or accumulates to a toxic level, harm can occur. The same would apply for mixtures of chemicals. The question is not simply one of whether chemicals, natural or man-made are present in the body (a question of exposure), or whether the chemical can cause harm (a question of the chemical’s inherent toxicity). Rather, it is the amount of those chemicals in the body relative to the amount that actually causes harm. In other words, the question is one of both exposure and toxicity.

Humans have always been exposed to low levels chemical mixtures since the dawn of human time. An apple is a mixture of more than 150 different chemical substances, and humans are exposed when they eat. Eating a fruit cocktail comprised of apples, bananas, strawberries, peaches, and pineapple, would lead to exposure to more than 400 different chemical agents.¹ These substances, like other chemicals in our environment, may enter the body through the normal processes of digestion and absorption.

Many of these substances could be detected in biomonitoring experiments. The US Centers for Disease Control and Prevention (CDC), in its US National Exposure Reports documents measuring a class of substances called isoflavonoids (derived mainly through ingestion of plants, such as soy) in urine of typical Americans². Even natural substances found in plants or foods can cause adverse health effects – at high enough exposure

¹ <http://www.ars-grin.gov/duke/>

² http://www.cdc.gov/exposurereport/results_07.htm

levels. Yet at low, environmentally-relevant exposure levels typically experienced in every day life, no effects are seen.

Therefore, it is the level and not the mere presence of any of the hundreds or thousands of chemicals in the body – regardless of their origin – that is important. This potential for harm relates to the concentrations of the chemicals in the body and their specific toxicity.

Evaluating Toxicity

The standard battery of toxicity tests employed by the chemical industry under TSCA for HPV chemicals (and harmonized internationally under OECD) includes specific tests on animals designed to address endpoints of concern to the health of humans, including children. This toxicity testing battery for industrial chemicals includes tests that have been specifically designed to evaluate endpoints that cover acute toxicity, hazards to development in the womb and to growth and reproduction, damage to cell components that could possibly trigger transformation into cancer later in life, and the potential of substances to produce adverse effects on all major organ systems, including the nervous system. This test battery specifically includes study designs to evaluate potential toxicity during the critical phases of development in utero and thus addresses concerns for any differential sensitivity of the developing organism during windows of development (these types of studies have been conducted routinely since the 1960s).

Under Responsible Care^{®3}, ACC's members go to great lengths to assure that the products they produce are safe for their intended uses. Responsible Care is a global initiative that is practiced currently in 52 countries, which share a common commitment to advancing the safe and secure management of chemical products and processes. To characterize potential risks, industry follows a tiered testing approach in which data are evaluated and decision criteria are applied to determine which specific type of tests should be conducted, and upon evaluation, whether or not to initiate further testing.

Evaluating Risk

To evaluate risk, the important question is whether chemicals present at given levels actually could cause harm. Risk is a function of both inherent toxicity and exposure. This approach, recommended by the National Research Council (NRC) (National Academy of Science) about 25 years ago, applies both to biomonitoring of individual substances as well as mixtures. The NRC's method, which has been widely adopted by scientific and

³ Since 1988, members of the American Chemistry Council (ACC) have significantly improved their environmental, health, safety and security performance through the Responsible Care[®] initiative. Participation in Responsible Care is mandatory for ACC member companies, all of which have made CEO-level commitments to uphold these program elements: Measuring and publicly reporting performance; Implementing the Responsible Care Security Code; Applying the modern Responsible Care management system to achieve and verify results; and Obtaining independent certification that a management system is in place and functions according to professional standards. See http://www.americanchemistry.com/s_responsiblecare/sec.asp?CID=1298&DID=4841.

regulatory bodies world-wide, entails four steps: hazard identification, dose-response assessment, exposure assessment, and risk characterization.⁴

Risk characterization is defined as "the process of estimating the incidence of a health effect under the various conditions of human exposure described in exposure assessment. It is performed by combining the exposure and dose-response assessments" (ibid). In other words, comparing actual human exposure to doses known to produce toxicity. Risk characterization is the most useful way to interpret information from biomonitoring.

Conclusion

Detection of numerous substances in biomonitoring a single individual is not unexpected, and should not in itself lead to undue concern. Exposure simultaneously to chemicals in our environment is normal, not an exception. There is no scientific basis to imply that the presence of an agent will lead to "toxicity" or "developmental toxicity" or "reproductive toxicity." The presence of a substance that has adverse effects **at some level** does not imply that the presence of that chemical will lead to adverse effects **at all levels**. Potential toxicity must be considered in the context of the amount, route, duration and timing of exposure. For human health risks for chemical induced toxicity, evidence-based medicine and toxicology principles -- the true scientific consensus -- tell us that effects at high doses will not be realized at lower doses if the concentration falls below the target site threshold level. This principle applies just as much to "windows of susceptibility" during development as it does more broadly to all life stages.

RESOURCES

Science-based info regarding Biomonitoring can be found at www.biomonitoringinfo.org, or visit www.americanchemistry.com/biomonitoring

Contaminant Concentrations

http://www.dec.state.ak.us/spar/csp/guidance/cont_concentrations.pdf

⁴ Hazard identification was defined as "the process of determining whether exposure to an agent can cause an increase in the incidence of a health condition," including "characterizing the nature and strength of the evidence of causation." Dose-response assessment was defined as "the process of characterizing the relation between the dose of an agent administered or received and the incidence of an adverse health effect ... as a function of human exposure to the agent," accounting for exposure intensity, age, sex, lifestyle, and other variables affecting human health responses to hazardous agents. Exposure assessment was defined as "the process of measuring or estimating the intensity, frequency, and duration of human exposures to an agent currently present in the environment or of estimating hypothetical exposures that might arise from the release of new chemicals into the environment. From "Issues in Risk Assessment (1993), NRC, http://books.nap.edu/openbook.php?record_id=2078&page=R1