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# Politics, Perchlorate, And Public Health

*Chemical regulation is based on science, but that does not mean it is always logical. The way exposure limits have been determined for perchlorate in groundwater — initially associated with spilled rocket fuel but now found to be ubiquitous— shows how public health problems and the resources directed to address them are too often mismatched*

**GAIL CHARNLEY**

**B**alancing environmental risks with the resources needed to mitigate them has been creating controversy for decades. Most debates have concluded that our shared risk management resources are misdirected, producing calls for realignment. Industry complains that the enormous investments it makes in environmental protection are incommensurate with the nature and extent of the risks involved; consumers suffer. Agencies point out that their actions are dictated by statute and their attention directed by congressional appropriations; their hands are tied. Public health organizations argue that their efforts to characterize and combat clear threats are under-funded while agencies such as EPA receive huge budgets to chase much smaller problems. International organizations complain that the bourgeois West is preoccupied with minute, speculative risks while children in Africa die daily of malaria and malnutrition.

The reasons for continued resource misalignment are many. Members of Congress respond to public outcry involving alleged environmental threats in disproportion to their importance or relative risk; they wish to be re-elected. Regulatory agencies also respond to public outcry, whether or not citizens' concerns are scientifically warranted; agency appropriations must be justified. Research scientists and environmental activists perpetuate concerns about the problems they study; their continued funding depends on it. Meanwhile, although the quality of the environment in the United States continues to improve and the contribution of industrial chemical exposures to disease is small, surveys continue to report that the general public is skeptical of these improvements.

Although the public rightly perceives that there should be no monetary value placed on human life, the fact that there is a cost associated with implementing any

regulation intended to protect public health produces an implicit value on life. And because regulatory agencies generally must demonstrate to the Office of Management and Budget that their rules produce benefits that justify (although not necessarily exceed) the cost, agencies use various methods to monetize both benefits and costs. OMB economist John Morrall's comparison of the costs of regulations progresses from lows of \$0.1 million per statistical life saved for public health

regulations like childproof lighters and \$0.5 million for seatbelts, to \$50 million per life saved for EPA's drinking water regulations, to \$87,000 million for OSHA's restrictions on occupational exposure to formaldehyde, to \$100,000 million for EPA's solid waste disposal criteria. Tammy Tengs and coauthors have also shown that medical and safety interventions are generally more cost-effective than controls on chemical exposures. Comparisons such as these are often challenged, however, for failing to take into account benefits that cannot be quantified and for quantifying benefits that should not be quantified, such as the value of a life. Many environmental regulations are justified on the basis of justice, not efficiency.

Whether the benefits of chemical regulation tend to be justified or not, the scientific basis of many rules is not apparent. For example, despite the fact that we are exposed to many chemicals and other potentially toxic agents in

the environment, toxicity testing and chemical regulations generally focus on one chemical and one source at a time, often just in air, water, or food. This approach ignores the contribution of simultaneous exposures to the same substance from multiple sources, such as exposure to benzene from drinking water, tobacco smoke, household products, and automobile exhaust. Another example is methylmercury contamination of fish, which results from natural sources of mercury and from both U.S. and global industrial sources. Restricting mercury



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emissions from power plants that burn coal in the United States is a good idea, but will have little effect on our exposure to methylmercury from fish, which results primarily from natural and global sources. (SEE: "Is Mercury from Power Plants Poisoning Our Children?" by Gail Charnley, May/June 2005.)

Considering one chemical and one source at a time ignores the critical roles that social, behavioral, and environmental factors play in susceptibility to chemical exposures. It also ignores potential synergistic or antagonistic interactions among chemicals that could lead to under- or over-estimation of health risks (and regulatory benefits), respectively. Although evaluating the effects of one chemical in one environmental medium at a time may be illogical given real-world circumstances, regulators are constrained both by environmental statutes, which tend to address single environmental media, and by the limitations of our ability to understand and characterize the complex interactions among environmental, social, genetic, and other factors.

Focusing on chemicals and sources one at a time means that the potential contributions to health risks of similar chemicals in the background are generally ignored, leading to potential over- or underestimation of risk. An example is public concern about exposure to industrial hormonally active agents — so-called "endocrine disruptors" — which produced a huge investment in research and regulatory resources. These chemicals, which are capable of competing with the body's chemical messengers that control growth and development at the cellular level, occur at doses thousands of times lower than those of plant hormones with similar biological effects that occur naturally in the diet. Against the background of endogenous hormones, pharmaceutical hormones, and naturally occurring dietary hormones, it is unlikely that industrial hormonally active agents pose risks to health at current exposure levels. Indeed, the 1999 National Academy of Sciences report *Hormonally Active Agents in the Environment* found no evidence they are affecting human health.

Plants also contain varying levels of naturally occurring pesticides, but public and regulatory concern focuses only on trace lev-

els of synthetic pesticides. Plants use complex chemistry to defend themselves from insects, fungi, viruses, bacteria, and larger herbivores. A well characterized example of naturally occurring pesticides is the glycoalkaloids found in potatoes. The toxic effects of glycoalkaloids include nervous system toxicity, nausea, diarrhea, abdominal pain, and death in humans and birth defects in laboratory animals. Although synthetic pesticides have been subjected to extensive toxicological testing to meet EPA's requirements for registration, naturally occurring chemical pesticides are not systematically tested for toxic effects. Those natural pesticides that have been tested are just as capable of producing

toxicity in laboratory animals under experimental conditions as are synthetic pesticides. To be registered, synthetic pesticide products by law must have their risks well characterized and limited to negligible levels. The risks from naturally occurring pesticides are seldom characterized or limited by law. A 1996 National Academy of Sciences report concluded that "natural components of the diet may prove to be of greater concern than synthetic components."

The examples of natural versus synthetic pesticides and

hormonally active agents illustrate that considering potential risks to health from single substances against the background of similarly acting substances may serve to put those individual risks in context or, at the very least, to ground regulatory estimates of risk in truth. As discussed below, perchlorate is another example where background exposures should be considered when evaluating its potential health risk.



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One method that EPA uses to aggregate risks from groups of chemicals that share the same biological mode of action is referred to variously as "relative potency" or "toxic equivalency." For example, risks from exposure to multiple dioxin-like chemicals that act similarly at the cellular level are assessed by adding together the levels of exposure for each individual chemical adjusted by its relative potency, as determined by tests in laboratory animals. This basic approach is used to assess risks

## Steps To Reduce The Toxic Burden

from groups of organophosphate pesticides like chlorpyrifos and malathion, used agriculturally and in the home, and from polycyclic aromatic hydrocarbons, which are formed from combustion-related activities such as burning wood or grilling meat.

Although toxic equivalency approaches are applied to some groups of chemicals for the purpose of assessing risks and limiting exposures, not all groups of substances that share a biological mode of action are treated with the same logic. One substantially less logical example currently under dispute involves the groundwater contaminant perchlorate. Perchlorate is used in solid propellants for rockets, missiles, fireworks, and some munitions, but it also occurs naturally in the environment at low levels. Perchlorate exposure became a cause for concern when groundwater used for irrigation and potentially for drinking water in the vicinity of rocket fuel, defense, and aerospace plants was found to be contaminated with levels ten to thousands of times higher than what is now known to occur naturally in some areas. Perchlorate has the potential to interfere with normal thyroid gland function by virtue of its ability to block iodine uptake and lower thyroid hormone production. For that reason, perchlorate was used clinically in the past to treat over-active thyroid conditions.

Iodine is required for healthy thyroid function. People who have inadequate iodine in their diets can have low thyroid activity, which produces effects ranging from depression and fatigue to the formation of goiters, which are enlarged thyroid glands. Of particular concern is the important role that thyroid hormones play in successful neurologic development in the fetus and newborns. Inadequate maternal thyroid hormone levels during pregnancy can result in developmental delays, reduced cognitive function, and lower IQ after birth. In areas of the world where serious iodine deficiency is endemic, mental retardation and dwarfism are not uncommon. However, moderate iodine deficiency during pregnancy is adequately compensated for by the body and has no effect on children. Drinking water contaminated

The environmental movement started with factories belching black smoke and rivers on fire. Today the effects of pollution are more subtle. They are about loss of ecological functions and increased burden of non-infectious, chronic diseases such as asthma, cancer, neurological effects, or birth defects.

We could reduce the burden on health and the environment by switching to safer products and cleaner technologies. Both individuals and organizations have an interest in selecting products made with ingredients recognized as safe, and by methods that minimize pollution.

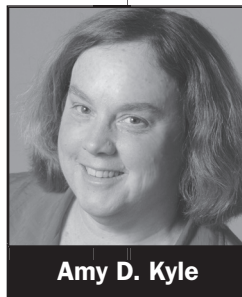
For example, the California legislature passed the Safe Cosmetics Act in 2005 to require product manufacturers to disclose ingredients that have been found to cause cancer or reproductive effects. The legislature decided that people should have the information necessary to choose cosmetics made without these toxic substances.

New scientific discoveries heighten the urgency of reducing exposure to toxic substances. We now know that very small exposures at the wrong time can be harmful. Early-life exposure to toxic chemicals can contribute to earlier or more severe manifestations of disease later in life. Even low doses at critical times can cause perturbations in human biology that contribute to disease. We understand that the developing child is sensitive to many compounds, particularly before birth, and that many substances cross the placenta to reach the fetus. We realize that genetic differences make some people highly sensitive to chemical effects.

To support decisions to switch to safer products and cleaner technologies, we need information about the relative toxicity and persistence of the chemicals we use and the wastes we produce. We need methods that can screen materials rapidly and provide information about their relative toxicity and persistence. This is in

contrast to the current focus in risk assessment on prolonged and intensive assessments of single chemicals, each considered independent of all others. While it may not be possible to achieve absolute safety, it is possible to make common sense choices for safer alternatives.

Updated methods for screening might include analysis of chemical



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structures to see if they resemble known toxics and use of targeted short-term assays to look for changes associated with adverse human health effects. New technologies, such as genomics and proteomics, show promise in looking for patterns

associated with toxicity, to allow comparison of compounds. This could also allow scientists to identify problematic chemicals that need more complete testing.

In the absence of action at the federal level, people in California and other states are working on straightforward ways to support a move to safer products and cleaner technologies. Earlier this year, the legislature passed the Healthy Californians Biomonitoring Act, which authorizes a program to find out what chemicals are being incorporated into the bodies of the state's residents. The legislature also passed a measure that gives the state authority to require manufacturers to provide methods to detect their products in human bodies and in the environment.

Though knowledge will never be complete, reducing the toxic load is a good thing. We can make better decisions now. In the last two years, Californians have taken major steps toward common sense strategies to reduce the burden of toxic and persistent chemicals.

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with perchlorate has not been directly shown to affect children; its potential effects are inferential. However, studies indicate that in areas where exposure to perchlorate from drinking water is high, adequate iodine intake compensates for any potential thyroid effects. Fortunately, iodine deficiency is rare in the United States, primarily because iodine is added to salt and other foods.

Perchlorate is only one of several substances that are considered goitrogens, or capable of interfering with normal thyroid function. A number of other goitrogens occur naturally in the diet or as environmental contaminants. Notable are two that act like perchlorate by inhibiting thyroid cell iodine uptake, nitrate and thiocyanate.

Nitrate is ubiquitous in food, occurring both naturally in many vegetables and as an intentionally added preservative in processed meats. Nitrate occurs naturally in soil and groundwater as a result of plant growth and decay and as a contaminant resulting from the use of nitrogen-containing fertilizers. Nitrate also is made normally in our bodies. Thiocyanate or its precursors occur naturally in many fruits and vegetables and in tobacco smoke. In regions of Africa where cassava is a dietary staple, the very high concentrations of thiocyanates in cassava can aggravate iodine deficiency and interfere with thyroid function in the fetus, producing serious malformations.

It is not possible to draw scientifically valid conclusions about the potential public health impact of perchlorate without considering simultaneous exposures to the very high levels of similar goitrogens in the diet and the level of dietary iodine. Studies have compared the relative abilities of perchlorate, nitrate, and thiocyanate to inhibit cellular iodine uptake. After adjustment for the length of time each substance spends in the body, perchlorate is half as potent as thiocyanate and 240 times as potent as nitrate. Current regulatory approaches ignore these differences.

The recent NAS report *Health Implications of Perchlorate Ingestion* recommends a "reference dose" of 0.0007 milligrams perchlorate per kilogram of body weight. An RfD is defined by EPA as an estimate of daily exposure that is likely to be without

an appreciable risk of adverse effects over a lifetime of exposure, including in sensitive individuals. RfDs are used to derive enforceable limits on exposure, such as maximum contaminant levels in drinking water. The RfD for perchlorate is based on its ability to inhibit iodine uptake by the thyroid gland, which is in itself not an adverse effect because of the body's ability to compensate continuously for normal levels of moderate inhibition, but was considered precautionary because it erred on the side of protecting human health. The committee that wrote the NAS report seems not to have considered simultaneous goitrogen exposures when it made its reference dose recommendation for

perchlorate, apparently because doing so was not included in the committee's mandate.

The reasoning used to develop an RfD for perchlorate is inconsistent with the reasoning used to develop RfDs for nitrates and thiocyanates. The RfD for nitrate is 1.6 milligrams per kilogram and that for cyanide (the active portion of thiocyanates) is 0.02 milligrams per kilogram. Taking into account relative potencies, the RfD for nitrate is 100 times higher and the RfD for cyanide is 50 times higher than the per-

chlorate RfD. Those differences could imply that perchlorate is 50 to 100 times safer than suggested by its RfD or that nitrate and thiocyanate are 50 to 100 times more dangerous than implied by their RfDs. For an adult in the United States eating a U.S. Department of Agriculture recommended diet, the average daily intake of nitrates and thiocyanates combined is equivalent to 0.5 milligrams — 1,000 times greater than the perchlorate RfD. We are either suffering dangerous hypothyroid conditions on an ongoing basis or perchlorate is not as dangerous as the NAS concluded. As there appears to be no epidemic of hypothyroidism attributable to goitrogens in the United States at present, any potential effects of low exposures to perchlorate are unlikely to be detectable against a natural goitrogen background exposure 1,000 times higher. Also undetectable would be the benefits of devoting significant resources to the reduction of low-level perchlorate exposure when it makes a vanishingly small contribution to our total daily goitrogen exposure.



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Of course, scientific “logic” may not be a prerequisite for chemical or any other type of regulation. Although agencies must demonstrate some logical basis for standard-setting or rulemaking, courts generally defer to agencies where technical issues are concerned. Agencies with a mission to protect public health and the environment are tasked to do just that, often taking precautionary measures based more on policy than science in order to fulfill that mission. The stovepipe nature of environmental statutes and EPA’s organizational structure prohibit scientific logic to a great extent. An August 2006 report from the EPA’s Inspector General’s Office, summarizing the results of 13 reports critical of the agency’s organizational structure, included the observation that “EPA might be missing an opportunity to be more effective because EPA bases its organizational structure on disparate environmental laws that do not consider that problems with the various media are interrelated.”

Nonetheless, not all statutes are silent on the subject of assessing health risks from aggregate or cumulative chemical exposures. For example, the Safe Drinking Water Act requires that sources of chemical exposures in addition to that being specifically regulated must be considered in standard-setting. EPA’s exposure limit for methylmercury in freshwater fish takes into account the fact that some of our exposure to methylmercury also comes from marine fish. The Food Quality Protection Act requires that, when evaluating risks from multiple commercial pesticides that share the same biological mode of toxicity, the agency must assess the cumulative risks from all sources (air, food, water) of all pesticides in the group.

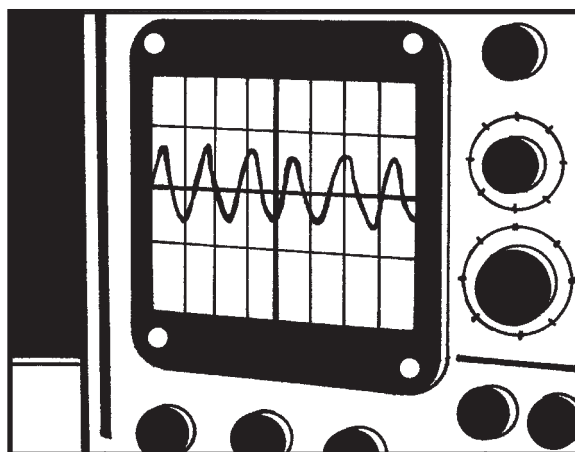
In its 2003 Framework for Cumulative Risk Assessment, EPA expresses the hope that attempts to focus on the combined effects of more than one agent or stressor may generate interest in a wider variety of nonchemical stressors than do traditional risk assessments. In other words, instead of focusing on the potential effects of individual chemical exposures in isolation, we

may start looking at public health in terms of the broader definition of environment. The World Health Organization defines environment as including “both the direct pathological effects of chemicals, radiation, and some biological agents, and the effects (often indirect) on health and well-being of the broad physical, psychological, social, and aesthetic environment which includes housing, urban development, land use and transport.”

The proportion of disease that is attributable to chemical exposures is relatively small against the backdrop of socioeconomic conditions, behavioral factors, psychological factors, infectious agents, nutrition, genetics, and other considerations. EPA acknowledges that “one of the greatest challenges to elucidating the connection between environmental exposure and disease is the fact that exposure to an environmental pollutant or stressor is rarely the sole cause of an adverse health outcome. . . . Other factors include, for example, diet, exercise, alcohol consumption, heredity, medications, and whether other diseases are present. . . . Also, different people have different vulnerabilities. . . . All

these factors make it difficult to establish a causal relationship between exposure to environmental pollutants and disease outcome.”

In view of our incomplete knowledge of the complex inter-relationships among multiple chemical and non-chemical, environmental and non-environmental stressors, a holistic approach to public health protection is a distant hope, probably dependent on the eventual decoding of the human genome and subsequent understanding of how molecular and cellular pathways can be perturbed in ways that lead to toxicity. While we eagerly anticipate that day, we can in the meantime evaluate health risks more holistically and with improved logic in the smaller spheres where it is currently possible to do so. Assessing and regulating the potential risks of industrial chemicals like perchlorate, other goitrogens, and hormonally active agents within the larger context of the naturally occurring backgrounds of both types of those substances would be a logical start. •



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