Lecture Abstract: September 30, 2003
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People are exposed to chemicals via many routes of exposure, including ingestion, inhalation, skin contact or mother-to-fetal transfer. The chemicals can be required dietary substances, or xenobiotics (i.e., foreign chemicals) such as drugs or environmental chemical pollutants. Substances that are fat soluble are most readily absorbed into the body, since they readily diffuse through the lipid layers of cell membranes. Indeed, fat soluble chemicals, particularly those that are chlorinated and do not readily decompose in the environment, tend to become gradually more concentrated as they work their way up through food chains. For every harmful chemical, a dose-response relationship exists. While it is relatively simple to graph dose-response relationships for drugs, it is typically very difficult to construct dose-response relationships for environmental chemicals that affect human populations, because knowledge of the actual dose of exposure to each person is often quite uncertain. In particular, the shape of the dose-response curve (i.e., between dose of chemical and adverse health effect) at the low end of the dose range is often uncertain; this is true because health effects at low doses are more rare, and thus statistical power is often limited. Toxicologists utilize dose-response curves to rank order chemicals in terms of their relative toxicity, and therefore their potential for adverse effects on human health. For example, the dose of a chemical that is lethal to 50% of mice exposed to that dose is known as the LD50 (i.e., lethal dose to 50% of animals). Compounds with very small LD50s, such as botulin toxin or the dioxins, are unusually hazardous.

Measurements of chemicals in blood can help unravel the past dose of exposure, particularly if one has knowledge of the half-life of that chemical in blood, i.e., the amount of time that it takes for the blood concentration to fall by 50%. Blood concentrations of chemicals fall due to either: a) movement of the chemical into other body tissues; b) urinary elimination of the substance; or c) metabolism of the chemical. The object of chemical metabolism, which is carried out primarily by the liver, but also by the gut mucosa, lung, skin and placenta, is to take fat soluble molecules and alter them so that they become more water soluble. Once water soluble, chemicals are eliminated more readily because they are more readily excreted in urine, bile or sweat, i.e., aqueous media. Metabolism is carried out in two phases, brilliantly named phase I and phase II. Phase I metabolism is primarily carried out by the so-called cytochrome P-450 system, an elaborate enzyme system located in the organs mentioned above. In essence, the P-450 enzymes add a hydroxyl group (-OH) to many types of chemicals, thereby making them slightly more water soluble. Phase II enzymes subsequently conjugate a water soluble molecule (e..g, a sugar) to that hydroxyl group, thus making the original chemical extremely water soluble. Chlorinated chemicals are not readily metabolized by these systems, and they therefore pose particular problems in the environmental health. Finally, the P-450 system can be induced or inhibited by substances such as drugs or dietary substances (e.g., in grapefruit juice), and can vary genetically; this contributes mightily to inter-individual variability in response that is the hallmark of exposures to chemicals in the environment.

Question: Chlorinated chemicals do not readily decompose in the environment. They are also relatively lipid soluble, accumulate in food chains, and are often exceedingly toxic. Some have suggested that the chorine industry should be banned or severely restricted because it regularly - sometimes inadvertently and sometimes intentionally - synthesizes chemicals that are highly toxic to human health.

Should the chlorine industry be banned? What are the pluses and minuses of doing so (or not doing so).