BREAKFAST FOR THE BRAIN©

An Educational Outreach Program of the Massachusetts Society for Medical Research, Inc.

Breakfast for the Brain© is a school-year e-mail service for science educators and others on topics in life science, biomedical research, and biotechnology, published by the Massachusetts Society for Medical Research, Inc.

Subscription to **Breakfast for the Brain**© is free to K-12 educators throughout the Northeastern U.S. (New England and New York) and to employees of MSMR member institutions. Others may subscribe at the rate of $100 annually. See **MANAGING YOUR SUBSCRIPTION** below for further information.

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JANUARY 2002 – VOLUME 1 - TOXICOLOGY

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WELCOME MESSSAGE & INTRODUCTION TO VOLUME 1

Welcome to the debut issue of **Breakfast for the Brain**©, the newest educational outreach initiative of the Massachusetts Society for Medical Research, Inc.!

Breakfast for the Brain© is a school-year e-mail service (September through June) for science educators and others on topics in life science, biomedical research, and biotechnology. Topics change monthly and reflect current issues and areas of research in the life sciences. **Breakfast for the Brain**® features a topical article delivered on the first weekday morning of each month, followed by lesson plans, background facts and information, classroom activities, puzzles and games, announcements, and other items related to the topic delivered subsequently on varying mornings throughout the month. While topics focus on issues and events in biomedicine and biological science, **Breakfast for the Brain**® strives to be cross-curricular and to relate these issues and events to curricula and events in non-science, as well as science, disciplines.

To achieve these goals and make **Breakfast for the Brain®** a welcome addition to the classroom, subscribers are encouraged to actively participate in the content and format of this unique medium with insights, tried-and-true lesson plans, and other valuable input. Make suggestions for future topics and features you'd like to see covered in **Breakfast for the Brain®**. We will incorporate your feedback into the format through the **Open Forum** section of the newsletter.

Introduction to Volume 1 - Toxicology

Personal health and safety are a priority for each of us. Many of us take for granted the safety of our medications and consumer products, highlighting how safe these have become for their intended use. When they are accidentally misused, we have confidence that our poison control centers can help us prevent tragedy.

How the safety of the products and drugs we use is determined is the business of the science of toxicology. As with other fields of biomedical and biological science, the use of animal models is a critical tool in the experimental armament of a toxicologist for assessing the risks associated with the chemicals we use. And like other areas biomedicine and biology, the pursuit of alternatives to animal research is a priority for toxicology professionals.

This first volume of **Breakfast for the Brain®** offers an introduction to this complex and fascinating field of science.

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MSMR INFORMATION & ANNOUNCEMENTS

The mission of the Massachusetts Society for Medical Research, Inc. (MSMR) is to promote and enhance biomedical and biological research, including the proper care and use of animals, for the improved health and well-being of people, animals, and the environment. In furtherance of this mission, the goal of the MSMR is to improve basic literacy in and enthusiasm for life science among the public, the media, and especially future generations of citizens and scientists.

The MSMR offers a full-range of programs and materials to classroom educators on topics in biomedical science, biotechnology, and the use of animals in research and testing. Most of the MSMR's outreach programs and materials are available free of charge to K-12 educators throughout the Northeast (New England and New York). To request a copy of the MSMR's catalogue of programs and materials, send an e-mail request to Leslie Nader, Ph.D., *Vice President for Education*, at lnader@concentric.net.

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NOTABLE QUOTE

"BAN IT NOW! Dihydrogen monoxide is colorless, odorless, tasteless and kills uncounted thousands of people every year. Most of these deaths are caused by accidental inhalation of dihydrogen monoxide, but the dangers of dihydrogen monoxide do not end there. Quantities of dihydrogen monoxide have been found in almost every stream, lake, and reservoir in America today. The pollution is global, and the contaminant has even been found in Antarctic ice. Companies dump waste dihydrogen monoxide into rivers and the ocean, and nothing can be done to stop them because this practice is still legal."

- Adapted from winning 1997 science fair project by Nathan Zohner, a 14-year-old student at Eagle Rock Junior High School in Idaho Falls.

Source: <http://urbanlegends.about.com>

Note: Another name for dihydrogen monoxide is H_2O (or good old water).

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TOXICOLOGY ... is the study of the qualitative and quantitative effects of chemicals on living systems.

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FEATURE ARTICLE

A Primer on Toxicology

Each of us is concerned to some degree about the effects of chemicals on people, animals, and the environment. We know that some chemicals can have severely adverse impacts -- for example, the many deaths from methyl isocyanate in Bhopal, India, or the birth defects in children whose mothers took thalidomide during pregnancy. We are also aware of environmental contaminants that affect public health, such as the effects on our children of lead in soil and drinking water. How concerned should we be about the countless small exposures to chemicals we experience each day? This is the business of toxicology.

What substances are toxic?

Any substance can be toxic. The higher the exposure to any substance, the greater the chance of an adverse effect. One example is sodium chloride, or table salt. Although essential to life, children have died from eating salt and many adults suffer from hypertension, which is associated with too much salt in the diet.

A number of vitamins are toxic at high doses. Vitamin D, in fact, is classed as a highly toxic substance and only tiny amounts are needed for proper nutrition. Many foods and beverages actually contain chemicals that could be toxic if you ate very large quantities. Carrots, for example, contain arsenic. Many plants produce toxins and many spiders, snakes and insects produce venoms that contain powerful toxins. Certain bacteria also produce toxins, e.g., the *Botulinus* toxin found in improperly preserved foods.

How does a substance exert a toxic effect?

The mechanisms for toxicity vary widely. Some chemicals disrupt the body's ability to use oxygen. In cyanide poisoning, for example, oxygen can get to tissue cells, but cannot be used once it arrives. The *Botulinus* toxin interferes with the transmission of nerve impulses which can lead to paralysis of respiration.

How does exposure occur?

Before a toxic effect can occur, there must be exposure. A toxic substance may enter the body through the mouth, lung, or skin. Once ingested, a chemical may be absorbed across the wall of the gastrointestinal tract into the bloodstream. Most of a chemical absorbed in this way is carried first to the liver. The liver biotransforms the chemical into a less -- or sometimes more – toxic form.

Unless a substance is injected directly into the body, the lung is usually the most rapid means of entry into the bloodstream. For example, gaseous anesthetics act very rapidly. And inhaled toxins, such as the fumes released by burning plastics, can have rapid and catastrophic effects.

Skin is usually a defense against toxic substances, but it can also be a point of entry. For example, the pesticide parathion is absorbed through the skin into the bloodstream. In a recent case, a scientist was poisoned by mercury absorbed through laboratory gloves.

The effects of a toxin will depend on the dose and how the body responds to the dose. Some substances are poorly absorbed by the body and may be excreted rapidly, while others may be stored and build up in tissues over time.

Why and how are animals used in toxicology?

Animals are used as models to predict the effects of human exposure to a chemical. Once toxicity is determined in animals, low risk products may receive approval by regulatory agencies for consumer purchase. Many chemicals or chemical formulations (e.g., herbicides, veterinary drugs and animal feed

additives) are not tested in people, but animal (in vivo) test results are used to predict the effect of accidental human exposure or misuse.

At the early stages of drug development, pharmacokinetic studies in animal models determine the absorption, distribution, metabolism, and elimination (ADME) of a potential new drug. These studies can only be conducted in intact, living organisms and yield information critical for designing further toxicology studies and human clinical trials. Other animal studies used in toxicology include lifetime toxicity and carcinogenicity studies, which determine toxicity and cancer-causing potential of a chemical over the lifetime of an animal; developmental toxicity studies, to determine the effects of chemicals on a developing fetus; and neurotoxicity studies, which determine the effects of a chemical on the nervous system. Most of these studies are conducted in rodent species.

In general, animal-based toxicology studies help determine the hazard potential of a chemical by defining how it might injure people and other animals. These studies, in combination with non-animal tests and other related information, are used by regulatory agencies to perform risk assessment to determine whether the benefit of a particular drug or product is worth the potential risk.

What factors influence how toxic a chemical will be?

A wide variety of factors influences chemical toxicity. A chemical may be very toxic to one species but have little effect on another. The toxicity of dioxin, for example, varies greatly among species, being highly toxic in guinea pigs and only slightly toxic to hamsters. Within a single species, individual differences make some individuals more resistant and some more susceptible to chemical toxicity. Some people, for example, may react to food additives such as sulfites or MSG. The gender of the animal can affect sensitivity as well. Women are more susceptible to alcohol than men. Age can also affect toxicity. Babies and small children have less well developed immune systems and higher respiration rates than adults, making them generally more susceptible.

Nutrition can also affect susceptibility. Mice fed a well-balanced, but low-calorie diet, have been shown to develop fewer cancers and other diseases than do overweight mice.

How the body metabolizes a chemical also affects toxicity. The liver typically metabolizes substances into less toxic forms, but it can sometimes make a chemical more toxic. This is true of some environmental carcinogens, which are not carcinogenic in and of themselves, but become so when processed by the liver.

Many other factors also affect toxicity. Elemental mercury (such as that found in thermometers) is less toxic than mercury in compound form. By the same token, barium is a toxic heavy metal, yet barium sulfate, which used in x-ray diagnosis, is fairly innocuous because it is so insoluble that it is not absorbed across the wall of the gastrointestinal tract.

How do combinations of chemicals interact in the body?

This is an area of ongoing concern and study by toxicologists because we are typically exposed to many chemicals rather than just one. Most commonly, the effect of multiple exposures is additive. Sometimes, a second chemical can *antagonize* (or diminish) the action of another -- such an antagonist may be an appropriate antidote. One example is the use of excess oxygen as a treatment for carbon monoxide poisoning. The interaction of most concern is *synergism*, in which one chemical enhances the toxicity of another. An example is radon exposure and smoking. A smoker exposed to radon is much more susceptible to lung cancer than a non-smoker.

The major concern with exposure to many chemicals at the same time is predicting the net effect. This is a subject toxicologists will be struggling with for many years to come.

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CHEMICAL TOXICITY… <u>NOT</u> a Simple Picture

Aspirin... has a complex range of effects. It is a pain reliever, and reduces fever and inflammation, among other things. Aspirin is also a stomach irritant, and may have adverse effects in pregnant women during the third trimester.

Atropine... is a supertoxic chemical produced in the deadly nightshade plant. It is also an antidote for organophosphate pesticides and for nerve gas poisoning.

***Botulinus* toxin**... is the most acutely toxic chemical known. It has also been used to treat muscle spasms.

Thalidomide... produces serious birth defects in humans. Yet it is also a potent immune response-modifying drug, and is being studied for use as an immunosuppressant in organ transplant recipients and as a drug for ameliorating many AIDS-related conditions.

Vitamin A... is an essential nutrient. It is also a human teratogen (causes birth defects) at high doses.

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CONNECTION

Environmental Toxicity

Toxic chemicals can build up through the food chain. When chemicals do not break down easily, they may be ingested at safe levels by organisms low on the food chain, but build up in higher feeders. A rodent may not be harmed by an insecticide, but a bird of prey that feeds on the rodent may accumulate the chemical in its body. And products such as mercuric compounds in water systems can build up in fish and then accumulate to even higher levels in birds and mammals (including people) that eat the fish.

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CONNECTION

Risk vs. Benefit

Toxicity can vary from species to species, and even among individuals of the same species. This causes a problem, for example, when strains of bacteria develop resistance to certain antibiotics or when some people develop side effects to drugs. Drug side effects demonstrate the evaluation of risk vs. benefit. In other words, do the benefits of disease control outweigh the disadvantage of adverse side effects in some people? Similar risk-benefit analysis is used in many of our daily personal decisions.

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CONNECTION

Risk Assessment

There is no way to eliminate the risk involved with exposure to synthetic and natural chemicals. However, toxicologists working with government regulators have developed means to assess risk.

Risk assessment is a process in which the toxicity of chemicals in animals and other models, as well as the level of human exposure, is examined. From this evaluation is calculated a "safe dose" of the compound. Risk assessment is used to set standards (levels that should not be exceeded) -- for example, the level of pesticide residue on fresh fruits and vegetables.

The risk assessment process is deliberately conservative – when definite answers are not known, worst case assumptions are made to ensure that even very sensitive people would not be harmed by a standard exposure.

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PROFESSIONAL RESOURCES & OPPORTUNITIES

School Nurses Pushing for Healthier Schools, Role of Toxicology Addressed

Every school day, parents send their children to school with the hopes that they will be healthy and safe and will receive an education. A variety of environmental risks may be posed in some schools that can make them potentially unsafe and unhealthy, and hinder children's ability to learn. The American Nurses

Association has updated its educational package on healthier schools. Written primarily for school nurses, "Safe Workplaces and Healthy Learning Places: Environmentally Healthy Schools" touches on a range of subjects -- including children's special vulnerabilities to environmental risks, indoor air quality, pesticides, and environmentally preferable products. This independent study module (ISM) provides a brief overview of some of the key environmental health risks associated with schools. Information is presented about the environmental exposures, signs and symptoms of toxicity, and the nurse's role as an agent of change to help encourage and produce healthy and safe schools. Children's special vulnerabilities are described, as well as child-specific information regarding the toxicity associated with exposures. **Contact**: Hope Hall, American Nurses Association, tel. 202-651-7027, e-mail hhall@ana.org, or download the full report at http://nursingworld.org/mods/ mod250/cesafull.htm.

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OPEN FORUM

Contribute! Send comments, questions, interesting Web sites, lesson plans, or articles that you would like to share with other educators to Leslie Nader, Ph.D., *Editor*, **Breakfast for the Brain©**, at lnader@concentric.net. Subscriber feedback will be included through the **Open Forum** section of **Breakfast for the Brain©**, as well as guest articles, and other venues.

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Look for the next issue of **Breakfast for the Brain©**, Volume 1 - **Toxicology**, later this week.

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