inorganic materials is an important factor in iron bioavailability. From another perspective, studies in the laboratory of Alvin Crambliss have drawn attention to the use of iron by microbes in the soil and in our bodies. Iron is acquired by microbial organisms by the excretion of iron-specific complexing agents known as siderophores. Crambliss and colleagues have studied the kinetics and mechanisms of ligand-exchange reactions with iron complexes that are relevant to microbial iron transport. They have shown that metallic environmental pollutants such as aluminum can interfere with normal iron transport processes.

The MBC director, Celia Bonaventura, invites inquiries regarding the projects described above, potential animal models, or other aspects of the MBC. For more information or to receive the Center’s newsletter, ENVIRONs, write to MBC, Duke University School of the Environment Marine Laboratory, 135 Duke Marine Lab Road, Beaufort, NC 28516-9721.

Cyanide Exposure May Affect the Brain

Moderate, chronic exposure to cyanide, a commonly used industrial compound, may cause cellular damage and lesions to the brain, characteristic of what might be seen in Parkinson’s disease, animal studies supported by the NIEHS reveal. Cyanide is regularly used in the metal-processing industry. It is also present in cigarettes, as well as in the pits of apples, peaches, and apricots, but it is thought that the amounts of cyanide in these substances are generally too low to cause harm.

However, some industrial workers are typically exposed to cyanide on a regular, sustained basis, and some experts suspect this could alter brain function. Evidence from early animal studies suggest it may cause a loss of key brain chemicals.

Gary Isom and colleagues at Purdue University treated mice with moderate doses of cyanide twice a day for a week. Sixteen hours after the last dose was given, various measures of brain chemicals, blood, and behavior were taken and compared to the same measures in control mice. The researchers found that dopamine levels were significantly depleted in the treated mice due to a loss of brain cells. In some parts of the brain, dopamine levels declined by as much as 41%. Such changes did not occur in the controls.

Dopamine is a neurotransmitter that helps regulate movement. Accordingly, mice treated with cyanide for longer periods of time experienced noticeable motor control deficits, such as incoordination. These effects were not seen in mice only briefly exposed to the agent.

The mobility impairment seen in the cyanide-treated mice mimics, in part, some symptoms seen in Parkinson’s disease, leading the researchers to speculate that chronic exposure to elevated levels of cyanide may be a health hazard.

Validation of Alternative Methods

The NIEHS has established an ad hoc committee of staff from federal agencies that generate or use toxicity data for regulatory decisions. The committee will join the NIEHS in meeting the directive of the NIH Revitalization Act of 1993 to establish criteria for the validation and regulatory acceptance of alternative testing methods and to recommend a process through which scientifically validated alternative methods can be accepted for regulatory use. The panel has been designated the Interagency Coordinating Committee on the Validation of Alternative Methods, or ICCVAM.

In addition to the NIEHS, twelve other federal research and regulatory agencies have been invited to participate, including ATSDR, FDA, NIOSH and OSHA. The first meeting of the committee was in September, and it is anticipated that the group will meet monthly until completion of guidelines and recommendations on alternative methods.

William Stokes, a veterinarian on the NIEHS staff assigned to the alternative methods effort, noted that alternative methods, models, and approaches reduce the total number of animals required, incorporate refinements which result in the lessening of pain and distress to animals, and replace animals with nonanimal systems or replace one animal species with another, particularly if the substituted species is nonmammalian or invertebrate.

"The vast majority of proposed new testing methods, both animal and nonanimal, usually involve some aspect of refinement, reduction, or replacement," Stokes said.

The committee’s objective will be to develop uniform processes and criteria that will encourage the development of improved testing methods that will generate data more useful for risk assessment—lead to the scientific evaluation/validation of new alternative test methods, and increase the likelihood of regulatory acceptance of scientifically valid alternative test methods.