Commentary

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Determining Exposure and Biochemical Effects in Human Population Studies

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We all are surrounded by and exposed to many chemicals in our personal environment. These chemicals are either naturally occurring or man-made. Such exposures may have profound impact on our health, such as cigarette smoking, excessive alcohol consumption, and abuse of illicit and legal drugs, or they may be necessary for our survival, such as nutrients, disinfectants, fertilizers and fuels. However, this is not what will be discussed here. We are concerned about chemicals which have inadvertently contaminated the environment because of the way they were used and disposed of, such as pesticides and other industrial chemicals.

Of all the chemicals produced in industry, only some metals, halogenated compounds, plastics, and organotin compounds are persistent in the environment and in people. Most chemicals, unless present in large quantities, biodegrade and photodegrade rapidly in the environment. They are also rapidly metabolized and excreted by people. Therefore, unless exposure was relatively recent, it is not possible to measure such chemicals as mycotoxins, organophosphorus compounds, solvents, nitrosamines, and carbamates. It is not possible to estimate the past and present levels of exposure in people accurately. For a number of them, it has not been determined what the background levels might be in the general population.

When 100 blood and/or urine samples of people from the southeastern part of the United States were analyzed, 23% of these samples contained trace amounts of aflatoxin related materials (*1*). Similarly, Fine et al. (*2*) were able to measure trace amounts of nitrosamines in human blood. It is, therefore, conceivable that we all have trace amounts of all sorts of chemicals in our bodies. The more sophisticated our methods of analyses become, the more likely will it be to demonstrate the presence of such compounds.

Polycyclic aromatic hydrocarbons are present in soil and surface water, and with very sensitive methods, could probably also be determined in people. What is the significance of such levels and at what point do they cause an impact on human health? Only by comparing populations with high and low levels of these types of chemicals over extended periods of time will we be able to determine this. It will, however, not be possible to establish within a relatively uniformly exposed population what the health impact of such trace contamination might be.

Similarly, the biological systems that may be affected by undue chemical exposure, such as serum lipid levels, liver function tests, chromosomes, nerve conduction, reproduction, and immune response have not been extensively studied in the general population, and good baseline data for the general population are presently not available (*3*). Serum lipid levels are an exception. They have been determined in large samples of the general population under controlled laboratory conditions (*4*). In this study, information on confounding variables, such as height, weight, blood pressure, smoking, occupation and use of hormones was also collected, making this a very useful data base.

The data bases that are available primarily for pesticides and related compounds and their limitations will be discussed by Dr. Murphy.

Because some human samples, such as breast milk, are more easily available than others, they are sometimes suggested as media for monitoring purposes. That approach will be discussed later in this symposium (*5*).

At present, a single type of medium, such as

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milk, blood, saliva or sweat, gives us little information about body burdens of halogenated aromatic hydrocarbons. It is also not known, for instance, what a biologically significant concentration of these chemicals in breast milk is. One of the difficulties is the pronounced variation in the susceptibility to insult of the general population. In a cross-sectional study of workers exposed to kepone (*6*), mean kepone blood levels of workers with overt symptoms of poisoning were higher than of those who did not have overt symptoms of poisoning, but if the ranges were compared, a great overlap existed.

In recent studies, it has been found that both mean total DDT and PCB levels increase with age in serum (*7,8*) and in adipose tissue (*9*), suggesting that distribution of these compounds are affected by age, or that for certain xenobiotics, a steady state may not be reached during the average life time of humans. Furthermore, studies have been published showing that levels of chlorinated hydrocarbons are higher in adipose tissue and in other organs from patients with terminal cancer, hepatitis, and may be relatively high in stillborn infants (*10-12*). It cannot be concluded from such studies that a causal relationship exists between body burdens and disease. On the contrary, it must be determined how disease might influence body burdens. For this reason, the World Health Organization sponsored studies to determine the concentration of chlorinated hydrocarbon levels in adipose tissue in clinically well patients who came to surgery to have primary breast and colon cancers removed (*13*). The results reported thus far have involved small groups of patients and it is difficult to draw any conclusions from these reports. An increased concentration of organochlorine compounds in extracted lipids of malignant breast tissue was reported when these tissues were compared to adjacent apparently normal tissue, suggesting that some halogenated aromatic compounds are concentrated in malignant tissue. In contrast, in a recent study in rats, the concentration of polybrominated biphenyls (PBBs) in liver cancers were the same as in the surrounding normal liver tissue (*14*). In this study, exposure was stopped almost two years before the rats were killed. In the human situation, exposure probably occurred up to the time the tissue was obtained. Since the tissue concentrations of PBBs were higher in the rats, this may have affected tissue distribution, and different results may also be obtained for different compounds. Any generalizations at this point would be premature and additional well-designed studies are needed to elucidate these findings. Since these types of tissue analyses are time consuming and expensive, most reported studies have involved only few samples.

Metals, on the other hand, have been studied more extensively. Lead is probably the most studied in this respect, but even there, much is argued about permissible blood lead levels. Not much is known about chronic effects of lead on the kidneys (*15*), nor do we know how much more susceptible subpopulations, such as patients with sickle cell disease, might be to the toxic effects of lead (*16*). In many studies, particularly those affecting minerals and heavy metals in drinking water, speciation and bioavailability are usually not considered, making it impossible to draw comparisons between different studies (*17*).

When attempts are made to correlate tissue levels to symptoms and signs of illness, problems may arise from laboratory errors. These may be the result of specimen contamination or insufficient attention to quality assurance and control. Different laboratories may use different methods without interlaboratory comparisons. If attempts are made to compare results reported from such studies, data are often conflicting, resulting in much debate. Unfortunately, to measure chemicals in people, particularly when they are present in very low concentrations, is costly and time-consuming if it is done properly. For these reasons, shortcuts are often taken which produce questionable results. Unless all of these difficulties are properly addressed, namely, the development of baseline data, adequate standardization of methods to determine chemicals and biological effects, little useful progress will be made in those areas of occupational and environmental medicine which deal with health effects caused by chemical exposures.

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