An Applied Approach to Epidemiology and Toxicology for Engineers

NIOSH Instructional Module

SHAPE

Safety/Health Awareness for Preventive Engineering

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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CDC

CENTERS FOR DISEASE CONTROL AND PREVENTION

AN APPLIED APPROACH TO EPIDEMIOLOGY AND TOXICOLOGY FOR ENGINEERS

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NIOSH Project Officer

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ABSTRACT

The five units of this course package provide the student with an introduction to the disciplines of epidemiology and toxicology with an emphasis on topics of special relevance to the engineer. The units are meant to be used sequentially. The sum of this experience is not intended to train epidemiologists or toxicologists but rather to acquaint the engineering student with the multidisciplinary context that exists in the pursuit of the relationships between health, occupation, and the environment.

Unit I
INTRODUCTION TO EPIDEMIOLOGY

PURPOSE

To introduce the participant to the basic concepts of epidemiology and to demonstrate its relevance to engineering.

OBJECTIVES:

To acquaint the student with:

1. The basic concepts of epidemiology
2. The sources of epidemiologic evidence
3. Types of epidemiologic study
4. Strengths and weaknesses of the epidemiologic approach

SPECIAL TERMS:

1. Epidemiology
2. Risk
3. Risk factor
4. Case control study
5. Cohort study
6. Relative risk
7. Ascertainment
8. Odds ratio
9. Prevalence
10. Incidence
11. Latency
12. Observation bias
13. Recall bias

INTRODUCTION

Epidemiology is a discipline within the health sciences that deals with the study of the occurrence of disease in human populations. The term is derived from the Greek words "Epi" (upon) and "Demos" (people) or diseases upon people. Whereas physicians are generally concerned with the ***single patient,*** epidemiologists are generally concerned with ***groups*** of people who share certain characteristics. A good example would be the interest epidemiologists show in characteristics associated with adverse health effects, e.g. smoking and lung cancer, asbestos exposure and asbestosis, or noise and hearing loss.

Epidemiology operates within the context of public health with a strong emphasis on the ***prevention*** of disease through the reduction of factors that may increase the likelihood that an individual or group will suffer a given disease. Implicit in the practice of epidemiology is the need for the different disciplines that may be required in studying the influence of occupation on human health.

DATA SOURCES

Epidemiologic data come from many different sources. Acquiring reliable, accurate, and complete data describing occupational health problems is a key concern of the epidemiologist. A primary and continuing problem is the ***ascertainment*** of occupational disease. Ascertainment is the identification of diseases that are, in this case, of occupational origin.

Occupational disease is not a new phenomenon. Ample historical evidence exists recounting the effects of lead poisoning, chronic respiratory problems associated with mining, and hazards of manufacturing including traumatic injury. For example, the first identification of an occupationally induced cancer is found in the work of Percival Pott who identified increased scrotal cancer among chimney sweeps in 18th century England. The ongoing tragedy of occupational disease can be seen in this excerpt taken from Adelaide Ross Smith's account of the work environment that women workers exposed to benzene encountered in 1928 in a small tin factory in New York.

> "There was direct ventilation of coated can covers. They emerged from the machine immediately after coating without having been heated and smelling directly of benzol... The eight coating machines consumed 45 to 50 gallons daily of a compound containing 75 percent of benzol. Adjoining the coating room and connected with it by a wide-open doorway was another room where paper gaskets were made...[A twenty-six-year-old woman] was employed for some months in the room adjoining the coating machines. She had always been well and was not bothered by the work until she became pregnant. Then she suffered from severe nausea and vomiting...Severe and prolonged nosebleeds were followed by bleeding from the gums and rectum and into the skin. She stopped work and improved... A premature child was born at seven months and three hours after delivery the mother died following severe uterine hemorrhage."[1]

Although it's been known for a long time that occupational exposures can induce human disease, as in the above example, the fact remains that diseases of occupational origin are ***underreported***. This can be attributed to three major factors. The first is that health professionals generally do not gather enough information concerning the patient's ***occupational history*** or the various jobs and duties carried out by the patient to possibly link employment with his/her symptoms.[2] The second is that many of the diseases associated with occupational causes could have been caused by other risk factors. Therefore, the occupationally caused case of lung cancer does not appear with some distinct marker to differentiate it from a lung tumor caused by personal risk factors such as smoking. Exceptions do, of course, exist: mesothelioma—a relatively rare cancer of the lining of the lung—generally only occurs with exposure to asbestos. A third factor, particularly for chronic diseases, is the long time interval that can exist between initial exposure to an occupational agent and the development of disease. This long time interval can make the recognition of the occupational origin of a disease quite difficult. This is in stark contrast to the relative ease of associating injuries with job-related causes.

Latency

Latency refers to the period of time that elapses between the first contact of a harmful agent and a host and the development of identifiable symptoms or disease. Latency may be as short as a few hours, the time required for photochemical smog to induce watery eyes. Or it may stretch to 20–30 years for a chronic condition such as asbestosis or malignant neoplasm of the lung. The association between a given exposure and a disease is all that more difficult because of the passage of time.

As we shall see in Unit III (Introduction to Toxicology and Risk Assessment), retrospective exposure status is a primary constraint of occupational epidemiology studies. It is exacerbated by the fact that many of the conditions currently under study are chronic disease conditions that may have long periods of latency.

TYPES OF STUDIES

Descriptive studies

The types of epidemiologic studies that attempt to note the number of cases of specific disease in a specific time period are generally known as ***descriptive studies.*** Descriptive studies attempt to provide investigators with information concerning the distribution of the disease in time and space as well as to identify attributes that may increase the chances of an individual contracting the disease. These attributes, called ***risk factors,*** include factors subject to change such as physical inactivity as well as and those that are immutable such as gender or age. For example, well-established risk factors for occupationally induced lung cancer include asbestos and coke oven emissions. Descriptive studies are also helpful in the ***formation of hypotheses*** regarding exposure and disease. Studies seeking to prove or disprove specific hypotheses are called ***analytic studies.***

Analytic studies

The two basic types of analytic studies are the ***case-control*** and ***cohort*** study. Each has their own strengths and weaknesses as well as different resource and time requirements. The cohort study involves the study of individuals classified by exposure characteristics, for example a group of welders. The study then follows the development of disease in the welders' group as well as in an unexposed comparison population. The measure that assesses the magnitude of association between the exposure and disease and that indicates the likelihood of developing the disease in the exposed group relative to the unexposed is the ***relative risk***. (See discussion of relative risk on pages I–6 to I–8.) A relative risk of 1.0 indicates no difference between the disease experience in the two groups. A relative risk of greater than 1.0 indicates a positive association between the exposure and the disease and an increased risk in those who are subject to the exposure.

In the case-control design, a group with a disease (cases) is compared with a selected group of nondiseased (control) individuals with respect to exposure. The relative risk in case-control studies can only be estimated as the incidence rate (see discussion below) among exposed individuals and cannot be calculated. The estimator used is the ***odds ratio***, which is the ratio of the odds of exposure among the cases to that among the controls.

The main difference between the case-control and the cohort type of study is that in the case-control format the investigator begins by classifying study subjects as to disease status. With the cohort study, the investigator begins by separating study subjects by exposure status. There are major resource consumption differences between the types of study. Cohort studies generally consume more resources and take longer to complete than do case-controls studies. The use of these analytic techniques will be covered in greater detail in Unit II (Analytic Epidemiology).

DETERMINING DISEASE FREQUENCY

A pressing challenge for epidemiologists interested in occupational health is to derive an accurate picture of disease frequency. This challenge is met by two broad types of measurement: prevalence and incidence.

Prevalence

Disease ***prevalence*** refers to the number of cases existing in the population. ***Point-prevalence*** identifies the prevalence estimated at a given time, e.g., the number of workers with abnormal chest films during a survey conducted in June 1987.

Prevalence is computed as the number of cases divided by the number of study subjects at a given point in time.

$$\text{Prevalence} = \frac{\text{number of persons with a disease}}{\text{total number in the study}}$$

Prevalence is thus not a true rate but really is a proportion, although the term prevalence rate is used fairly widely.

Incidence

Incidence, a true rate, refers to the number of new cases of a disease in a defined population in a given period of time. Thus the incidence rate can be expressed as:

$$\text{Incidence rate} = \frac{\text{number of new cases of disease during time period}}{\text{total number at risk}}$$

Central to epidemiology is the use of ***rates*** to express the health experience of populations. Rates are important because epidemiology is inherently a comparative discipline. An epidemiologist is constantly attempting to compare the disease experience of a study population with that of a comparison population. A rate is nothing more than a specialized proportion in which the counts of persons with a particular disease are placed over a denominator that is composed of people who are ***at risk,*** i.e., who have a chance of developing the disease. Men, for example, would not be included in the denominator used to calculate the prevalence or incidence of uterine cancer.

Relative risk

Because epidemiology is a comparative discipline, epidemiologists are interested in comparing the risk of a disease in people exposed to a particular agent with the disease experience of people not exposed to the agent. It is beneficial to have the results of such comparisons expressed as a single statistic that estimates the risk of developing a disease based on exposure status. This statistic is called the ***relative risk***. The classic formulation of this comparison can be expressed in a two-by-two table, so named because it has two rows and two columns (see Table I-1). The four cells, labeled a, b, c, and d, represent the number of people who have some level of exposure or the disease in question.

Table I-1
Generic Two-by-Two Table

	Disease		
Exposure	Yes	No	Total
Yes	a	b	a+b
No	c	d	c+d
Total	a+c	b+d	a+b+c+d

From this basic comparison flows the basis for the majority of epidemiologic comparisons. Inspection indicates that the cells of the table have the following attributes:

a = the number of exposed individuals who have the disease
b = the number exposed who do not have the disease
c = the number not exposed who have the disease
d = the number who are both not exposed and not diseased.

Once the basic structure of epidemiologic comparison is visualized, the calculation of the measures of association are relatively straightforward. The relative risk estimates the magnitude of an association between exposure and disease and the result indicates the likelihood of developing the disease in the exposed group in relation to those not exposed. This comparison directly forms a ratio of the incidence of the disease among the exposed group (a/a+b) to the incidence of disease among the unexposed group (c/c+d):

$$\text{Relative Risk} = \frac{\text{Incidence of the disease among exposed}}{\text{Incidence of the disease among unexposed}} \text{ or, } \frac{a/(a+b)}{c/(c+d)}$$

BIAS AND CONFOUNDING

Epidemiologists' studies attempt to identify associations between exposure or agents and disease. Factors that can interfere with visualizing these associations are of great interest to epidemiologists. ***Bias***, simply put, is the existence of some systematic error in the study results introduced by the design and or implementation of the study. Examples of some of the more common types of bias follow.

Selection bias

Selection bias results from using noncomparable selection criteria in enrolling participants in a study. The most common type of selection bias for the occupational epidemiologist is the ***healthy worker effect.*** This is a phenomenon that occurs when, for example, the all-causes mortality rate among a working population is lower than the all-causes mortality rate among a comparison population such as the general population than compared to the general population. To be included in the working population requires a certain level of mobility and health as contrasted with certain segments of the general population that may include the infirm and debilitated.

Observation bias

A second major form of bias is ***observation bias.*** Observation bias ensues when noncomparable information is received from the different groups in a study. This type of bias can have two components: principally ***interviewer bias*** and ***recall bias***. If an interviewer is aware of the case/control status of the informant, there may be a differential level of probing to elicit specific exposure information. Recall bias happens when the informant with a particular exposure or disease status is likely to remember and report experiences differently from those who are not affected. For instance, individuals living in a town of suspected environmental contamination may consciously or unconsciously overstate disease experience.

Confounding

Another possibility that could obscure the true relationship between an exposure and a disease is the existence of a third factor that is associated with the exposure and independently affects the risk of developing the disease. This third major form of bias is called ***confounding***. Confounding may produce a spurious result or obscure a real association. In most chronic respiratory disease studies, smoking (generally regarded as a potential confounder) is a personal risk factor that must be taken into account. The chronic respiratory conditions identified in the working population may not result from the occupational exposures but rather from the use of cigarettes. The confounder must be associated with the exposure and be a risk factor for the disease.

Control of confounding

A goal of epidemiologic inquiry, indeed of all science, is to control bias and confounding. Among strategies to minimize confounding are randomization and matching. Each attempts to allow the investigator to minimize confounding at either the design and/or analysis phase of the epidemiologic study. Randomization, which is difficult and in most occupational studies impossible to do, attempts to minimize confounding. Although randomization does not ensure that confounding will not take place, it does tend to distribute equally those factors that are potential confounders. Matching, another widely used strategy, allows study subjects to be, in some cases, paired according to the potential confounding variables such as age or sex. In general, information and selection bias are best handled by judiciously planning the study design. Confounding, however, can happen even in scrupulously planned studies and is generally addressed when analyzing the epidemiologic study.

MAGNITUDE OF OCCUPATIONAL DISEASE

The prevalence of occupational disease in the United States (see p. I-4) pose real challenges to the epidemiologist. How do we derive true estimates of this experience? If we begin with an estimate of the proportion of malignant neoplasms or cancers attributable to occupational exposures we can witness intense controversy. These estimates range from 3 to 38.5 percent, although consensus estimates generally range between 5 to 10 percent.[3] National estimates are sketchy even for events seemingly more amenable to mistake-free enumeration such as traumatic injury and job-related deaths.

For data collected at the state level, the ranges of estimates are even wider, the uncertainty greater. The Mount Sinai School of School of Medicine provided a report on occupational disease to the New York Legislature in 1987. Four data sources were used: worker compensation records, disease registries maintained by the state Department of Health, data from the U.S. Bureau of Labor Statistics (BLS) and extrapolations from California's physician reporting system. The investigators reported an almost complete absence of reliable data from these sources.[4] In fact, by employing the various sources of data, their estimates of the incident cases of occupational disease occurring in the State of New York on an annual basis ranged from 4,000 to 28,000 cases.

Other methods of estimating occupational disease have also been employed, most notably the use of death certificates[5] and the use of the Sentinel Health Event of Occupational Origin (SHE/O).[6] Death certificates, a favorite source of data for epidemiologists, are relatively easy to access, relatively cost efficient to use, and very complete in terms of coverage of the population. They are also plagued by problems involving the diagnosis and the industrial and occupational (I/O) information on the certificate. The I/O information is obtained from the decedent's survivor and entered on the death certificate. Most death certificates specifically call for information on the "occupation or industry performed during most of working life." Such a question discourages the respondent from only providing information on the last job held by the decedent, although this all too frequently happens. In most instances, the epidemiologist studying occupational disease is interested in the job performed for the longest period of time in trying to establish a link between work and health.

The SHE/O concept (jointly developed by Dr. David Rutstein of Harvard Medical School and the National Institute for Occupational Safety and Health (NIOSH)) attempts to expand on our ability to understand the patterns of work-related disease and to study those events most in need of attention.[7] For example, within the field of air transportation, crashes rather than successful flights are usually studied. In much the same way, Rutstein and colleagues developed a list of conditions thought to be primarily caused by occupational or man-made exposures. Such a list of conditions could then be used to screen death certificates or even hospital discharge data to identify cases of potential occupational origin. Such analyses have been performed at the state level with coordination from NIOSH.[8]

Death certificate studies and SHE/O investigations form a broad spectrum of epidemiologic analyses that, crudely defined, are concerned with understanding patterns of occupational disease. These activities are collectively known as ***health surveillance***. Surveillance is an important public health function that shapes the necessity for, and character of, intervention options once a health problem has been identified. Surveillance activities also assist in evaluating the effectiveness of any intervention measures that are implemented.[8]

Dr. Joseph Fraumeni headed a group at the National Cancer Institute that followed an interesting thread of surveillance work by analyzing mortality patterns of cancer mortality. The group, using the county as the unit of analysis, looked at noncancer causes of death experience of white and nonwhite populations. The results were mapped to display the distribution of mortality from pneumoconiosis due to silica and silicates. Clustering was apparent in two sections of the country: Appalachia, possibly as a result of anthracite coal mining operations, and the Far West, where hard rock, uranium, and other mining and smelting operations occur.[9] The data display standardized the age distribution of the county to the U.S. population in 1970 to remove the effects of age, a potential ***confounding*** variable. The distribution of pneumoconioses is known to vary directly with age, so that the effects of age must be controlled if we are to arrive at a true understanding of the distribution of the disease.

CONCLUSIONS

Concerns with the under reporting of occupational health problems continue. A review article by Landrigan and Baker points out that occupational disease is not fully recognized and that there is a consequent loss in the ability to prevent these conditions.[10]

Descriptive studies are useful in providing investigators with hypotheses between exposure and the development of disease. A ***hypothesis*** is nothing more than the formal statement of a presumed association between an exposure and a disease. The rigorous testing of hypotheses is reserved for the second major type of epidemiologic study, the ***analytic*** study.

REFERENCES

1. Smith, A.R, Chronic benzol poisoning among women industrial workers: A study of women exposed to benzol fumes in six factories. *J. Ind. Hyg.* 10:73-93. 1928. As cited in Checkoway, H., et al. Research Methods in Occupational Epidemiology. New York: Oxford University Press. 1989.
2. Goldman, R.H. and Peters, J.M. The occupational and environmental health history. *JAMA.* 246:2831-2836. 1981.
3. National Institute for Occupational Health and Safety and the Associations of Schools of Public Health. Proposed National Strategies for the Prevention of Leading Work-Related Diseases and Injuries. Part 1. Washington: ASPH. 1986.
4. Markowitz, S.B., Fischer, E., Fahs, M.C., et al. Occupational disease in New York State: A comprehensive examination. *Am. J. Indust. Med.* 16:417-35. 1989.
5. Office of Population Censuses and Surveys. Occupational Mortality-Decennial Supplement. London: Her Majesty's Stationery Office. 1978.
6. Kelley, B.C. and Gute, D.M. Surveillance Cooperative Agreement Between NIOSH and States (SCANS) Program-Rhode Island 1980-1982. Cincinnati: NIOSH. Feb. 1986.
7. Rutstein, D.D, Mullan, R., Frazier, T.M., et al. Sentinel health events (occupational): A basis for physician recognition and public health surveillance. *Am. J. Public Health.* 73:1054-1062. 1983.
8. Surveillance in occupational health and safety. *Am. J. Public Health.* 79:Supplement. Dec. 1989.
9. Mason, T.J., Fraumeni, J.F., Hoover, R., Blot, W.J. An Atlas of Mortality from Selected Diseases. Washington: U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. NIH Publication No. 81-2397. May 1981.
10. Landrigan, P.J., Baker, D.B. The recognition and control of occupational disease. *JAMA.* 266:676-680. 1991.

SUGGESTED AUDIO-VISUAL MATERIALS

1. Can't Take No More. Video produced by OSHA. 1970. Running time: 25 minutes.
2. Hard Metal Disease Series. Produced by the NBC Today Show. Running time: 75 minutes.

RESOURCE MATERIALS

Anderson, H.A. Evolution of environmental epidemiologic risk assessment. *Environ. Health Perspectives*. 62:389-392. 1985.

Bert, Joel L. Occupational Diseases. Instructional Module. Cincinnati: NIOSH. Order No. 88-79896. June 1989.

Checkoway, H., Pearce, N.E., and Crawford-Brown, D.J. Research Methods in Occupational Epidemiology. New York: Oxford University Press. 1989.

Goldman, R.H. and Peters, J.M. The occupational and environmental health history. *JAMA*. 246:2831-2836. 1981.

Goldsmith, J.R. Environmental Epidemiology: Epidemiological Investigation of Community Environmental Health Problems. Boca Raton: CRC Press. 1988.

Greenland, S., ed. Evolution of Epidemiological Ideas. Chestnut Hill, MA: Epidemiology Resources, Inc. 1987.

Kelley, B.C. and Gute, D.M. Surveillance Cooperative Agreement Between NIOSH and States (SCANS) Program. Rhode Island 1980-1982. Cincinnati: NIOSH. Feb. 1986.

Kopfler, F.C. and Craun, G. Environmental Epidemiology. Chelsea, MI: Lewis Publishers. 1986.

Levy, B.S. and Wegman, D.H. Occupational Health—Recognizing and Preventing Work-Related Disease. Boston: Little, Brown and Company. 1988.

McCunney, R.J. Health effects of work at wastewater treatment plants: A review of the literature with guidelines for medical surveillance. *Am. J. Ind. Med.* 9:271-279. 1986.

McCunney, R.J. ed. The occupational and environmental medicine report. Boston: OEM Health Information.

Monson, R.R. Occupational Epidemiology. Boca Raton: CRC Press, 1980.

Neutra, R.R. Epidemiology for and with a distrustful community. *Environ. Health Perspectives*. 62:393-397. 1985.

Office of Population Censuses and Surveys. Occupational Mortality, 1970-1972. London: Her Majesty's Stationery Office. 1978.

STUDY QUESTIONS

1. Compare and contrast the principal purposes of the descriptive and the analytic types of epidemiologic studies.
2. Why is it difficult to ascertain occupational disease?
3. What can you suggest as possible improvements in ascertaining of occupational/environmental disease? Hint: think about how the present knowledge of occupational/environmental diseases has been acquired.
4. The level of detection in many quantitative analyses for occupational and environmental contaminants has increased by orders of magnitude from parts-per-million to a state-of-the-art laboratory currently being able to quantitate at the parts-per-trillion level. What advantages are afforded the epidemiologist by this increase in precision? Any disadvantages?

Unit II
ANALYTIC EPIDEMIOLOGY

PURPOSE

To introduce the participant to the different types of analytic epidemiologic studies and to discuss the relative strength and weakness of each approach.

OBJECTIVES:

To acquaint the participant with:

1. The different types of analytic epidemiology studies
2. When to use certain study types
3. The limits of epidemiologic investigation
4. Key questions to ask when assessing any epidemiologic study

SPECIAL TERMS:

1. Hypothesis
2. Power
3. Causality
4. Retrospective
5. Prospective
6. Diagnostic criteria

HYPOTHESIS TESTING VERSUS HYPOTHESIS FORMATION

The principal difference between descriptive and analytic studies is that with the analytical type of study the investigator is attempting to ***test a hypothesis.*** With a ***descriptive*** study, the investigator is deriving or ***forming a hypothesis.*** If epidemiologic studies are conducted in series, each asking a more specific, more refined question, then it is possible to appreciate the flow from the descriptive to the analytic study format.

An epidemiologic hypothesis addresses the relationship between an agent or exposure and a host and the subsequent development of a disease of interest. An analytic study attempts to explain causal or preventative factors regarding the relationship between an exposure and a disease. The progression from hypothesis formation to hypothesis testing is a cardinal principle of the scientific method with a long tradition in epidemiology. Such a pattern can begin with clinical impressions of the distribution of disease. A good example of this was the initial point of investigation by a clinician linking angiosarcoma of the liver with the manufacture of vinyl chloride. This lead to gathering more data concerning its occurrence; supplementing this with either biologic, bioassay (animal study), or environmental laboratory data; and refining questions about this relationship into a specific hypothesis.

Example: The case of John Snow and the Broad Street pump handle

To further explicate the progression from hypothesis formation to hypothesis testing, the 19th century England activities of John Snow are instructive both for an understanding of the history of epidemiology and also for further appreciation of the development of a testable hypothesis.[1,2]

Snow was an English physician practicing in London during the 1840's and 1850's. Because of the recent availability of routinely collected population and mortality data, Snow was able to frame a hypothesis between the development of cholera (an infectious disease of great magnitude in 19th century England) and exposure to certain sources of drinking water. On the basis of these descriptive data, Snow postulated a hypothesis that cholera was transmitted by an unknown agent through contaminated water supplies. The causative agent for cholera was unknown at this time was because the germ theory of disease was in its infancy.

By consulting population and mortality data, Snow noted that death rates from cholera were particularly high in areas of London supplied with water from two companies: the Lambeth Company and the Southwark and Vauxhall Company.

Snow noted that between 1849 and 1854 when the Lambeth Company changed its source of drinking water pollution levels were lower. The rates of cholera declined in those areas of the city supplied by the Lambeth Company, whereas there was no change in those areas receiving water from Southwark and Vauxhall Company. The change in the source of drinking water for the Lambeth Company created a "natural experiment" between the sources of contaminated and uncontaminated drinking water. The "experiment" actually took shape when a virulent cholera epidemic struck London between August, 1853 and January, 1854. Snow was able to tabulate the number of cholera deaths occurring in areas supplied solely by each company and jointly by the two water companies (Table II-1). From Table II-2 it can be seen that the areas supplied solely by the Southwark and Vauxhall Company suffered much higher rates of cholera than did those areas supplied by the Lambeth Company. In fact, Snow noted no cases of cholera in these areas. For areas receiving water from both companies the rate of the disease was at a level between the two distinct areas.

Table II-1
Death Rates from Cholera, 1853-1854, According to Water Company Supplying Subdistrict of London*

Water company	Population in 1851	Cholera deaths in 1853-1854	Deaths per 100,000 living
Southwark and Vauxhall	167,654	192	114
Both companies	301,149	182	60
Lambeth	4,632	0	0

*Ref. 3, taken from Ref. 1.

Table II-2
Death Rates from Cholera in London, 1853-1854, According to Water Company Supplying Actual House*

Water company	Number of houses	Deaths from cholera	Deaths per 10,000 houses
Southwark and Vauxhall	40,046	1263	315
Lambeth	26,107	98	37
Rest of London	256,423	1422	59

*Ref. 3, taken from Ref. 1.

Snow's hypothesis that water quality determined susceptibility to cholera seems to have been borne out by his analysis according to the source of drinking water. He also realized that differences in geography might not be the only factor in determining the disease experience of the residents and that he would need to test his hypothesis further. He did this by actually determining the source of water supply for each house with a cholera death. The following data emerged (Table II-2).

These data show convincingly that water supplied by the Southwark and Vauxhall Company was responsible for the cholera outbreak in the affected areas. The hypothesis began with general observations regarding the distribution of cholera in London; the use of the subdistrict data contained in Table II-1 further refined the assumption that the drinking water source was tied to cholera outbreaks. This relationship was further pinpointed with the house- specific analysis.

Snow's own words summarize the elegance of the experiment:[3]

> "...In many cases a single house has a supply different from that on either side. Each company supplies both rich and poor, both large houses and small; there is no difference either in the condition or occupation of the persons receiving the water of different Companies. Now it must be evident that, if the diminution of cholera, in the districts partly supplied with the improved water (from Lambeth), depended on this supply, the houses receiving it would be the houses enjoying the whole benefit of the diminution of the malady, whilst the houses supplied with the water from the Battersea Fields (the Southwark and Vauxhall Company) would suffer the same mortality as they would if the improved supply did not exist at all. As there is no difference whatever, either in the houses or the people receiving the supply of the two Water Companies, or in any of the physical conditions with which they are surrounded, it is obvious that no experiment could have been devised which would more thoroughly test the effect of water supply on the progress of cholera that this, which circumstances placed ready made before the observer."

Snow's most important result

Snow's most important result was the formulation of a public health intervention. He was able to benefit from the existence of this natural experiment that allowed him to find further evidence in support of his hypothesis. Snow parlayed his understanding of the distribution of cholera into an effective public health ***intervention***. Interventions are steps taken by public health authorities to minimize risk to affected populations. Snow's intervention was as simple as it was effective. In an area supplied by a Southwark and Vauxhall water supply, Snow removed the pump handle from the implicated public well. This removal is accorded its place in history in a uniquely British manner—there is a pub named for the Broad Street pump!

The pattern and distribution of diseases of contemporary society, particularly in industrialized countries, make the job of the epidemiologist even more challenging. The problem framed for epidemiologists is that chronic diseases such as heart disease or cancer are multi-factorial in nature, i.e., there is more than one cause. This starkly contrasts with the infectious agents that usually cause a single identifiable disease. Major successes against these agents are largely attributable to the profound economic and social changes seen in Western Europe and the United States during the past century. Sanitary engineers, now known as environmental engineers, played a significant role in these advances by providing better housing, controlling human sewage and providing potable water of greater purity.

COHORT STUDY

The basic types of analytic study are the ***cohort*** and the ***case-control*** study. Each has its own strengths and weaknesses as well as different resource and time requirements. The cohort format generally provides the most intuitive and direct approach in assessing the relationship between health and disease. This flows from the manner in which study subjects are formed into groups and then, to as great as extent as possible, fully followed through time. The cohort format can capture all of the relevant person-time experience of the population under study.[4]. Cohort studies can be classified as prospective or retrospective, according to their temporal sequence, i.e., the starting point of the investigator. If the investigator begins currently and follows a defined population into the future, the study is classified as a ***prospective*** study. A prominent example of such a study is the Framingham Heart Study begun in 1948 to inquire into the etiology of cardiovascular disease. If, in contrast, the investigator begins to follow the disease experience of a cohort formed in the past and follows them towards the present, the study is classified as a ***retrospective*** or ***historical*** cohort study. This design is frequently used to study occupational populations. Carol Redmond's cohort study of long-term steel workers serves as an example.[5]

Cohort studies have a general set of defining characteristics: identifying a study population, or cohort, of persons exposed to the factors of interest; identifying a comparison population; following the cohort over time; and comparing the disease rates between the comparison and the cohort population.[4] The strengths and weaknesses of such studies can be concisely stated below:

Strengths of the cohort approach are that they:

- are particularly suited to the study of rare exposures,
- can examine multiple health effects from the same exposure, and
- can determine whether the exposure preceded the disease (Ref. 1, p.173).

Limitations of the cohort approach are that they:

- are inefficient for the study of rare (uncommon) exposures,
- can be resource intensive, particularly in the case of prospective designs, and,
- are limited by the availability of sufficient records for retrospective studies (Ref. 1, p. 173).

CASE-CONTROL STUDY

The entire cohort must be followed to determine both the exposure experience and the disease experience of the study population. This accounts for the relatively high cost of cohort studies. Often times, even in large cohorts, only a small proportion of the population actually develops the disease. The case-control format improves efficiency by beginning with a study population composed of individuals who have the disease (the cases) and then sampling from a larger group of people who do not have the disease (controls). In certain instances more than one case group or more than one control group is enumerated in the same study.

Measure of association

In a case-control study, the incidence of the disease among the exposed and the unexposed subjects generally can not be estimated. Therefore, the formula to calculate the relative risk for cohort data cannot be used directly. The relative risk can be estimated by using a formula that compares the ratio of the odds of exposure among the case group with that of a control group.

$$\text{Odds ratio} = \frac{\text{ratio of exposed among cases}}{\text{ratio of exposed among controls}} \quad \text{or} \quad \frac{a/c}{b/d} \quad \text{or} \quad \frac{ad}{bc}$$

An example taken from the work of Hayes et al.[6] will demonstrate the odds ratio in a quantitative fashion. They reported the results of a study that assessed the development of nasal cancer after formaldehyde exposure (Table II-3).

Table II-3
Exposure of Cases and Controls in a Study of Nasal Cancer and Formaldehyde Exposure*

Cohort	Exposed	Nonexposed	Total
Cases	31	60	91
Controls	34	161	195
Total	65	221	286

* Source: Ref.6.

This yields an odds of exposure among cases of a/b or 31/60, and an odds of exposure among controls of c/d or 34/161. The odds ratio can be estimated by applying the formula ad/bc or $(31 \times 161)/(60 \times 34)$ or 2.45. The interpretation of this value is straightforward--workers exposed to formaldehyde had 2.45 times the risk to develop nasal cancer than those not exposed to formaldehyde. Expressed another way, cases were 145 percent (2.45 minus the null value of 1.0) more likely to develop nasal cancer than those not exposed. Since the odds ratio is an estimate of the relative risk, both measures of association can be interpreted in the same manner. A relative risk or odds ratio ≥ 1.0 indicates a positive association (or an increased risk) among those exposed when compared with those not exposed to an agent. A relative risk of unity (or 1.0) indicates no association between the risk factor and the disease under study.

Strengths of the case-control design are that they:

- are relatively quick and inexpensive when compared with the cohort approach,
- are well suited for the study of diseases with a long latency,
- are well suited for the study of rare conditions because the disease of interest defines the case group, and
- can examine different possible causes for a single disease (Ref. 1, p.149).

The limitations of the case-control design are that they:

- are inefficient for the study of rare exposures,
- cannot compute incidence among the exposed and unexposed subjects,
- many times, cannot determine the temporal sequence of exposure and disease, and
- can be more prone to selection and information bias (Ref. 1, p.149).

DISTINGUISHING ASSOCIATION FROM CAUSATION

Epidemiology and toxicology can be useful in the inquiry into the relationship between human health and occupational risk factors. The ability of these disciplines to address specific occupational health topics is, however, inherently limited.

Epidemiological studies yield statistical associations between a disease and exposure. This is the first step followed by interpretation of the meaning of the relationships identified. An association may be artifactual, or spurious, noncausal, or causal. Causality is assumed when one or more factors are shown to contribute to the development of disease and removal will reduce the frequency of disease.

A useful construct to employ in assessing associations and causal relationships is abridged from a cogent essay by Hill.[7]

- Strength of association—how large is the measure of association?
- Consistency—does it agree with previously conducted studies?
- Specificity—is the effect specific to the agent?
- Temporal relationship—did the exposure precede the disease?
- Dose-response—is a gradient present?
- Biological plausibility—does the association make biological sense?

POWER

An important concept related to the interpretation of epidemiologic studies has to do with the size of the study population. An inherent attribute of all statistical inference is that the larger the study population the more stable are the estimates of effect that arise from the comparison. It holds that the conclusions and recommendations from studies suffering from small numbers will need to be more tentative. This is particularly true for the nonpositive study in which there is no effect between an exposure and a disease. In studies where no effect is found, the question becomes were there enough cases studied to yield a fair chance of the effect being detected if it is truly present? This attribute is known by statisticians and epidemiologists as the ***power*** of the study.

CONCLUSIONS

Epidemiology is an observational medical science that seeks to elucidate the cause(s) of disease. The success of the investigation is determined by the ability of the investigator to control a variety of biases and potential confounders that could distort the true relationship between an exposure and disease. Because society is increasingly concerned with achieving meaningful interventions concerning chronic diseases (with AIDS being a significant exception), epidemiology is being pushed to its limits in identifying possible causal factors.

REFERENCES

1. Hennekens, C.H. and Buring, J.E. Epidemiology in Medicine. Boston: Little Brown and Company. 1987.
2. Goldsmith, J.R. Environmental Epidemiology: Epidemiological Investigation of Community Environmental Health Problems. Boca Raton: CRC Press. 1985.
3. Snow, J. On the Mode of Communication of Cholera. London: Churchill. 1855.
4. Checkoway, H., Pearce, N.E,. and Crawford-Brown, D.J. Research Methods in Occupational Epidemiology. New York: Oxford University Press. 1989.
5. Redmond, C.K., Smith, E.M., Lloyd, J.W., and Rush, H.W. Long-term mortality study of steelworkers. III. Follow-up. *J. Occup. Med.* 11:513. 1969.
6. Hayes, R.B., Raatgever, J.W., de Bruyn, A., et al. Cancer of the nasal cavity and paranasal sinuses, and formaldehyde exposure. *Inter. J. Cancer.* 37:487-492. 1986.
7. Hill, A.B. The Environment and Disease: Association on Causation. In: Rothman, K., ed. Evolution of Epidemiologic Ideas. Chestnut Hill, MA: Epidemiology Resources, Inc. pp. 15-20. 1987.

RESOURCE MATERIALS

Ahlbom, A. Introduction to Modern Epidemiology. Chestnut Hill, MA: Epidemiology Resources, Inc. 1984.

Checkoway, H., Pearce, N.E., Crawford-Brown, D.J. Research Methods in Occupational Epidemiology. New York: Oxford University Press. 1989.

Friedman, G.D. Primer of Epidemiology. New York: McGraw-Hill Book Company. 1980.

Goldsmith, J.R. Environmental Epidemiology: Epidemiological Investigation of Community Environmental Health Problems. Boca Raton: CRC Press. 1985.

Greenland, S., ed. Evolution of Epidemiological Ideas. Chestnut Hill, MA: Epidemiology Resources, Inc. 1987.

Hennekens, C.H. and Buring, J.E. Epidemiology in Medicine. Boston: Little Brown and Company. 1987.

Monson, R.R. Occupational Epidemiology. Boca Raton: CRC Press. 1980.

STUDY QUESTIONS

1. What is the basic difference between analytic and descriptive epidemiology? Why is it important for a reader of an epidemiologic study to know which type of research he or she is reading?

2. Do we need to see clear results regarding the causation of a particular health effect linked to a particular agent before we mount an intervention meant to limit exposure to the agent? Can you suggest an example of where public health authorities have not waited before acting?

Unit III
INTRODUCTION TO TOXICOLOGY AND RISK ASSESSMENT

PURPOSE

To acquaint participants with an introduction to toxicology and to demonstrate the utility of basic precepts of the discipline. An important goal of the unit is to ensure an understanding of how toxicology can inform investigators of occupation and environmental health concerns.

OBJECTIVES:

To acquaint the student with:

1. Definitions of importance in toxicology
2. Differentiation between exposure and dose
3. How toxicology can contribute to the study of occupational and environmental health

SPECIAL TERMS:

1. Toxicology
2. Dose
3. Exposure
4. Target organ
5. Route of exposure
6. Body burden
7. Susceptibility
8. Synergistic
9. Potentiation
10. Ambient
11. Chronic
12. Acute
13. Latency
14. Metabolite
15. Dose-response
16. Risk assessment
17. Carcinogenesis
18. Threshold
19. LD_{50}
20. ED_{50}
21. Risk management
22. Teratogenesis
23. Mutagenesis

TOXICOLOGY

Toxicology is the science of poisons, i.e., the study of chemical or physical agents that produce adverse responses in biological systems.[1] Together with other scientific disciplines (such as epidemiology, the study of the cause and distribution of disease in human populations, and risk assessment), toxicology can be used to inquire into the relationship between an agent of interest and a group of people or a community. Of the many different types of toxicology (Table III-1), all types, or different applications of the science, start from a common nomenclature and set of cardinal principles.

Table III-1
Types of Toxicology*

Type	Purpose
Clinical toxicology	To determine the effects of chemical poisoning and the treatment of poisoned people
Descriptive toxicology	To test the toxicity of chemicals
Environmental toxicology	To determine the environmental fate of chemicals and their ecological and health effects
Forensic toxicology	To answer medicolegal questions about health effects
Industrial toxicology	To determine health effects of occupational exposures
Mechanistic toxicology	To describe the biochemical mechanisms that cause health effects
Regulatory toxicology	To assess the risk involved in marketing chemicals and products and establish their subsequent regulation by government agencies

*Adapted from Ref. 1, p. 8.

Of interest to the engineering student are the regulatory and environmental applications of the discipline. The former is of use in interpreting the setting of standards for allowable exposure levels of a given contaminant or agent in an ambient or occupational environment; the latter is of use in estimating the persistence and movement of an agent in a given environment. Both applications can be of direct use to risk assessment activities and both regulatory toxicology and environmental toxicology closely involve other branches of the discipline. The relationship is particularly close for the regulatory toxicologist who depends largely on the products of descriptive toxicology when making decisions on the risk posed by a specific agent.

KEY CONCEPTS

"All subjects are poisons; therefore there is none which is not a poison. The right dose differentiates a poison from a remedy." This quote is attributed to Paracelsus who lived from 1493–1541. It symbolizes a set of key concepts for understanding toxicologic data. Among chemical agents there is a wide spectrum of dose needed to produce some adverse health effect. Although dose and ***exposure*** are sometimes used interchangeably, this is technically incorrect. The dose is the concentration or amount of an agent that becomes biologically available to the body at an anatomic site or ***target organ***, and that is capable of

Dose

Exposure

inducing an adverse health effect. Exposure, on the other hand, represents the amount of the agent in the environment of concern. Exposure levels only translate to dose if the agent becomes available to the body through one of three principal ***routes of exposure:*** respiration, ingestion, or absorption through the skin. One can quickly surmise that although dose is the preferred measure, exposure is the only readily obtained measure involving community-wide exposure.

Returning to dose, toxicologists employ quantitative measures of toxicity or the ability of an agent to cause some health effect. Health effects can range from the minor, skin irritation, to the major, death. A standard measure of toxicology employs death as the outcome. The measure is the dosage of an agent needed to produce death in 50 percent of the treated animals (LD_{50}), or lethal dose.[1] The primary source of data for such measures are tests administered to laboratory animals, commonly the mouse and rat. Some chemicals considered extremely poisonous or toxic will achieve the LD_{50} with only a few micrograms of dose. Other agents will only cause harm if the host is challenged with large concentrations. The range of dose for some common agents is expressed in Table III-2. Note that most characterizations of dose are expressed as an amount expressed relative to body weight, e.g., in milligrams/kilograms of body weight of the test animal. The LD_{50} answers the question, "How toxic is the compound or agent?"

Table III-2
Approximate LD_{50}'s of Some Chemical Agents*

Agent	LD_{50} (mg/kg)
Ethyl alcohol	10,000
Sodium chloride	4,000
Morphine sulfate	900
Strychnine sulfate	2
Nicotine	1
Dioxin (TCDD)	0.001
Botulinum toxin	0.00001

*Adapted from Ref. 2, p. 12.

Toxicity is thus a relative concept depending on the type of agent and the amount of the agent (dose). Toxicologists classify agents as to their toxicity by arranging the universe of all potential agents into categories based on the results of laboratory tests similar in nature to the LD_{50} results. The LD_{50} has an analogue in the field of pharmacology where the effective dose for 50 percent of the test population, or ED_{50}, is routinely calculated for medicines. Categories for toxic agents range from practically nontoxic to extremely and supertoxic, each with relevant specific dosages. The important point is that toxicity is a continuum.

Agents may also be classified by many different attributes that may be even more useful in terms of assessing a community's experience, including:

- physical form (solid, liquid, or gas)
- specific target organ (e.g., grouping of all agents that affect the lung or kidney)
- use(s) of the agent(s) (pesticide, solvent, degreaser)
- health effect (cancer causing agent, chronic respiratory agent)
- labeling requirement (flammable? explosive? corrosive?)
- persistence in the environment (persisting for a long time in the environment or degraded or broken down by the action of the sun or water)

ROUTES OF EXPOSURE

The route of exposure is critical in the assessing community-wide environmental health problems. If an agent is known to exist in an environment, the critical question becomes, Is there a route or ***pathway*** of exposure that permits the agent to become biologically available to the host and that delivers the required dose to a target organ sufficient to engender a health effect? Although the primary routes of exposure are respiration, ingestion, and skin contact or absorption, another route results from either intended or unintended additives to or contaminants in the food chain. The significant routes of exposure for a given agent can change depending on the characteristics of the population being studied. For example, lead. Lead is of no biological use to the body; it is a poison with no redeeming physiological benefit. The principal routes of exposure for adults are different from those for young children. In children, lead is incorporated much more effectively through the gastrointestinal route with approximately 40 to 50 percent of all lead entering a child's body in this manner. Adults, in contrast, derive only approximately 10 percent of the total amount of lead in the body (or ***body burden***) in this manner. Lead exposure in adults is primarily through respiration of airborne lead; this accounts for approximately 90 percent of an adult's body burden. Absorption of inorganic lead through the skin, such as lead paint, is practically nonexistent. Skin absorption becomes more important when considering organic lead, such as contained in leaded gasoline.

Route of exposure is also important when assessing the degree to which animal data can be applied to human populations. Because the toxicity of a compound can be related to the manner in which exposure takes place, the same route of exposure must be used when applying animal results to human populations. For example, an agent that exercises its primary toxic effect through the lungs would elicit greater health effects if administered through the respiratory route than if painted on the skin of a test animal.

FACTORS THAT MODIFY TOXICITY

The ability of an agent to induce a health effect depends on the ability of the agent to reach a target organ in a sufficient concentration for a sufficient period of time to produce the adverse health effect. Characteristics of the host influence the degree to which adverse health effects will take place. These characteristics, under a general category of host ***susceptibility*** include such factors as age; preexisting disease; nutritional deficiencies; personal risk factors that may influence the toxic action of the agent, e.g. tobacco or alcohol consumption; or other factors that may modify toxicity. To visualize the concept of susceptibility consider that the same dose of an agent may well produce an adverse health effect in a child of 6 months and no adverse symptoms in a fully grown adult. Differences in physical size, surface area, respiration rate, consumption of food and water, maturity of the immune and metabolic systems, may all influence the toxic effect of a given agent.

The agent may also change in terms of its ability to cause harm. Changes in the physical characteristics of the agent may exert greater or less toxicity.

Another every-day problem, particularly in the review of community-wide exposures and in consideration of occupationally exposed populations, is the presence of mixtures. A useful checklist of factors that may modify community-wide response to toxic agents is presented below.

- Host factors
  - —age
  - —sex
  - —infectious disease history
  - —neuropsychological stress history
  - —physical activity level
  - —nutritional status
  - —toxic agent exposure history
  - —hobbies

- Environmental factors
  - —prevailing wind patterns
  - —geological structure
  - —hydrological structure
  - —presence or absence of additional environmental point source emitters

- Agent factors
  - —how is it distributed?
  - —physical form
  - —chemical form

Mixtures represent one or more agents in some combination. Traditionally, one of the most difficult parts of a toxicological review of human populations outside of a laboratory setting is the quantifying of either current or past exposure levels. This is particularly challenging when attempting to gauge the effects of more than one agent in the same population. Well-known gradients of increasing

risk with one or more agents exist for a variety of agents and disease. Two good examples of synergy are:

- increasing risks associated with asbestos exposure and smoking with reference to the expression of lung cancer and,
- risk of heart disease given the presence of elevated blood cholesterol, cigarette smoking, and uncontrolled hypertension.

Models for visualizing the effects of mixtures or the effects of multiple agents, are presented in Table III-3.

Table III-3
Models of Effects of Mixtures*

Model	Result
Additive effect	2 + 3 = 5
Synergistic effect	2 + 2 = 20
Potentiation	0 + 2 = 10
Antagonism	4 + 6 = 8

* Adapted from Ref. 2, p. 17.

An ***additive effect,*** the most common model, describes the cumulative effect of two substances (such as two organo-phosphate pesticides combining to increase a biologic indicator for the presence of pesticides, cholinesterase inhibition) by an additive amount. ***A synergistic effect,*** previously described, is present when combined agents yield greater than additive effects. An early classic study defined the risk of dying of lung cancer for nonsmokers not exposed to asbestos as 1.0, the risk for nonsmoking asbestos workers approximately 5.0, the risk in smokers not exposed to asbestos at roughly 10, and the risk for those exposed to asbestos ***and*** smoking over 50; clearly much greater than the additive model would suggest. ***Potentiation*** results when one agent alone will not induce a toxic effect but will increase the effect of another agent. Such an effect can be seen where the action of two pesticides, EPEN and malathion, is greater than the single effect of each agent in terms of cholinesterase inhibition. Pharmacologic potentiation can be seen in instances where the presence of alcohol can cause greater effects of a variety of over-the-counter and prescription drugs.

Antagonism occurs when two chemicals, administered together, interfere with each other's actions or one interferes with the action of the other chemical.

TOXIC EFFECTS OF ENVIRONMENTAL AGENTS

Two basic scenarios that will be encountered in evaluating community-wide patterns of exposure:

- low-dose, chronic exposure
- high-dose, acute exposure

Generally, low-dose, long-term exposures are found in the ***ambient*** or outdoor environment and represent the long-term or ***chronic*** exposure of community members to relatively low levels of environmental contaminants. This can be contrasted with the occupational environment in which the usual exposure scenario follows the high-dose, acute exposure path. Ambient environmental exposures can also follow this route as in the case of spills (ruptured tank car or truck) or large-scale incidents (Bhopal). Of great concern to a health specialist who will evaluate the possibility that a given exposure is responsible for a specific health effect is the estimate of exposure or dose that has occurred. Generally, an estimate of ***retrospective*** exposure, that which occurred in the past, is sought. Past exposure is of great interest because of the ***latency*** period—the time between the initial exposure to a toxic agent and the development of clinically recognizable disease.

The toxic effects of an agent can take many forms—from relatively minor, reversible conditions (upper airway irritation for example) to major, irreversible effects such death or permanent impairment. The toxic effect does not necessarily need to be produced by the agent to which the host is exposed. In the concern over the possibility that Alar—a growth regulator used primarily in apples—was associated with increasing cancer risk, it was not Alar that turned out to be the culprit. UDMH, a ***metabolite*** or compound formed through the break down products of Alar, was the stronger potential carcinogen. The lesson is clear; the specialist must be sure that the agent in its most toxic form is evaluated.

A greater variety of pathological end points are also coming under scrutiny. Such end points would include agents that can induce:

- carcinogenesis—the development of cancer,
- teratogenesis—induced birth defects developing between conception and birth, and
- mutagenesis—the ability of agents to cause changes in the genetic material in the nucleus of cells in ways that can be transmitted during cell division.

There is a growing interest in noncancer end points being used in studies seeking to characterize the possible health effects of a given compound. This does not mean to suggest that interest in cancer-causing substances is declining, rather, investigators and citizens are increasingly interested in ***adverse reproductive effects*** such as birth defects and other noncancer health effects.

SOURCES OF TOXICOLOGIC DATA

Toxicologic data are obtained from four principal sources. They are as follows:

- animal studies (bioassays)
- human populations (occupationally exposed)
- human populations (nonoccupationally exposed)
- in-vitro tests (e.g., Ames test)

In-vitro studies

In-vitro tests are usually less expensive than human or animal studies, and they generate results in a more timely manner. A weakness of the in-vitro tests is found in the assessment of whether a substance is a carcinogen. A positive result for one of these tests is actually a measure of mutagenicity and not carcinogenicity. In the Ames test, developed by Bruce Ames in 1966, a culture of a microorganism, ***Salmonella typhimurium,*** is challenged by a suspected carcinogen. A positive result indicates that the strain of microorganism yielded DNA alterations or altered gene expression after exposure to the suspected carcinogen. Although mutagenicity and carcinogenicity are closely linked, the finding of mutagenicity in a microorganism does not prove that this agent will cause cancer in humans. Ames and his co-workers have since gone on to question the very basis of using animals for human carcinogen testing,[4] a controversy outside the scope of this document.

Animal studies

The application of the findings of animal studies to human populations is called extrapolation. It is complicated by possible metabolic differences between the species of the test animal and humans and by other ways in which humans may detoxify carcinogens that animals will not. Two salient points must be recognized in animal testing: first, every substance that is tested does not cause cancer; second, for those substances that are confirmed or strongly suspected of causing human cancer, only a small fraction (two prominent examples being benzene and certain forms of arsenic) have not tested positive for cancer in animal studies.

Human population studies

Even data on human populations can present grave problems when assessing the likelihood of toxic effects of a given substance. Although human studies are the most expensive and time consuming form of gathering relevant data, human testing has the greatest value for inferring the potential for human health effects.

Three main problems merit discussion here The first is that because many human studies tend to have a small number of study subjects, results lack statistical power. Power can be thought of as the ability of a study to detect an effect between an agent and a host if the effect is truly present. Thus, for studies of small size, how does one interpret a negative study? Is the study negative because no effect was truly present or was it negative simply because the effect is too rare for the study to detect with any certainty. The second problem is that human studies are rarely unambiguous as to assessing the relationship between an agent and health effect. The finding of a causal relationship between an agent and a health effect is very rare. And third, extrapolation can also cause problems in human studies, usually when attempting to apply the results gained from an occupationally exposed population of workers to a population of community residents. The community resident population includes sub-populations with radically different host susceptibilities than the relatively healthy, younger, and more fit working population. In addition, the working population is usually exposed to higher doses of the agent than is the community population. Can we assume that these higher doses will translate into health effects at lower levels for the community population? Does a ***threshold*** exist for the compound of interest, that is, a dose level below which there will be no measurable health effects attributable to the agent? The concept of the threshold leads us to the subject of ***dose-response,*** which will serve to integrate much of the toxicologic material that we have covered.

DOSE-RESPONSE

A dose-response relationship is present between an agent and an effect (response) when, as the concentration of the agent at the reactive site increases, the probability that the effect or response in the host also increases. A characteristic dose-response curve is presented in Figure III-1.

A threshold would exist if there was a level of dose for which no apparent effect could be discerned as presented in Figure III-2.

This is a strongly debated topic for carcinogens. The regulatory community, in the interests of protecting the health of the public, usually assumes that no thresholds exist (for carcinogens) and performs its functions accordingly.

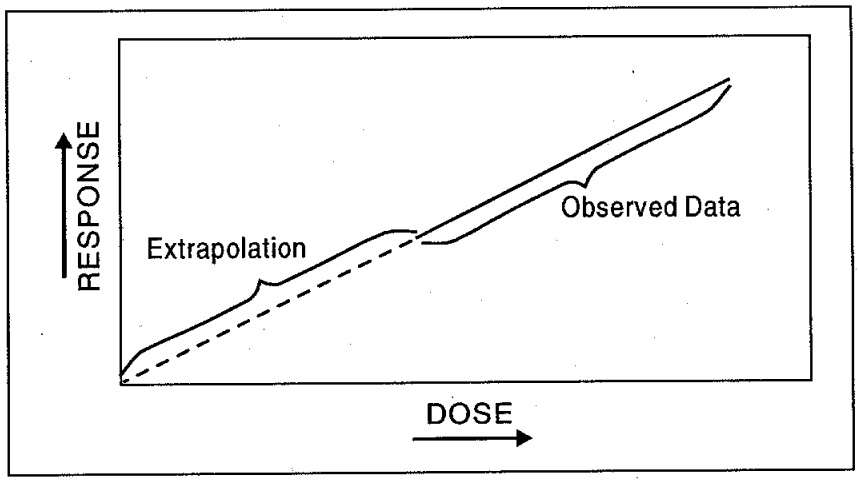

Figure III-1. Characteristic dose-response curve.

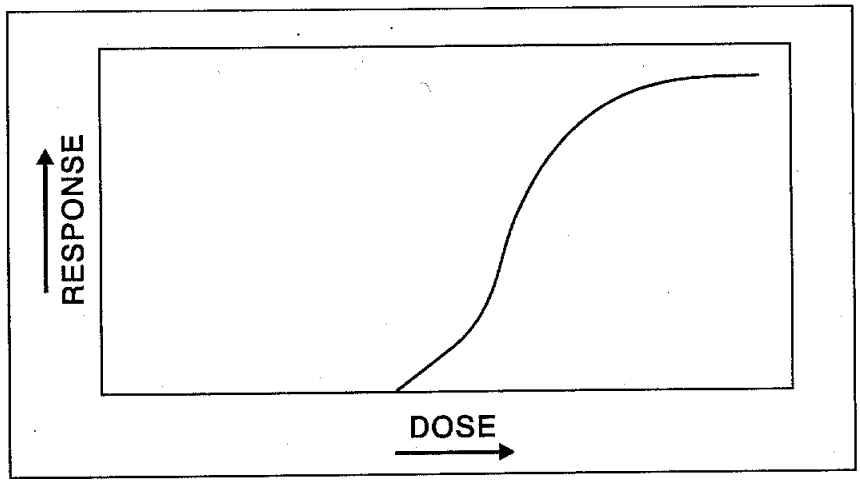

Figure III-2. Dose-response curve containing a threshold.

MERCURY IN LATEX PAINT CASE

In the case described below,[5] an epidemiologic health investigation emphasizes some concepts of importance in toxicology.

In August 1989 a previously healthy 4 year old boy in Michigan was diagnosed with acrodynia (or "pink disease"), a rare manifestation of childhood mercury poisoning. Symptoms of this condition include redness of the extremities, swelling, cramping, irritability, and low grade fever. A urine mercury level of 65 µg/dL was measured. Treatment with a chelating agent (a drug that fosters excretion of the mercury through the urine) was successful. Examination of his parents and two siblings found urine mercury levels greater than or approximately equal to his. The parents and siblings were asymptomatic.

The Michigan Department of Public Health (MDPH) identified inhalation of mercury-containing vapors from phenylmercuric acetate contained in latex paint as the probable route and source of mercury exposure for the family. Seventeen gallons of paint had been applied to the interior of the family's home during the first week of July. Samples of the paint contained between 930 and 955 ppm of mercury; the EPA limit for mercury as a preservative in interior paint is 300 ppm. The additive prolongs shelf-life of the product by acting as a fungicide and bactericide. During July, the house was air-conditioned and the windows were not open.

Commentary

By focussing on the ***agent*** (phenyl mercuric acetate), the ***host*** (the affected family), and the ***environment*** (the interior of the house) we can elucidate some important toxicologic principles.

Routes of exposure

The three principal ***routes of exposure*** for human populations are ***respiration***, ***ingestion***, and ***absorption.*** Each carries with it a characteristic efficiency for a particular contaminant. This changes by agent and by host. Here the primary route of exposure was respiration. The activity levels of children as well as basal breathing rates may have contributed to a greater requirement for air and thus to a potential for greater exposure.

Dose and target organ

The micro-environment also played a role in potentiating the disease. Two main factors likely accounted for greater ***doses*** being received by the host. The dose should not be confused with the interior air levels of mercury. The interior air levels represent ***exposure.*** Dose differs from exposure by being the concentration or amount of material biologically available to the body at the site of a target organ. A ***target organ*** is the is the preferred anatomical site of effect for a specified agent. (Some common agents and target organs are polychlorinated biphenyls (PCBs): adipose tissue; lead: the long bones—femur, tibia.) Disease can result when the concentration of the agent exceeds the ability of the body (specifically, the target organ) to handle the burden.

The dose received by the host, in the case, proved to be greater than the carrying capacity of the boy. The dose was increased by particular factors in the micro-environment. The two principal factors were the amount of paint applied (17 gallons) and the fact that the windows of the house were closed thus preventing dilution of interior air. Both factors likely conspired to increase the exposure: the concentration of the phenyl mercuric acetate in the interior air and the dose (the concentration of the phenyl mercuric acetate reaching target organs within the body).

Factors that modify toxicity

But why didn't all of the exposed individuals develop symptomatic disease? Many factors may modify toxicity in the host. Young age is clearly one factor. It influences bodyweight (which is correlated with the ability to tolerate a given dose of most toxicants), lung capacity (again influencing dose), and breathing rate and types of activities. Factors that modify toxicity for the agent, environment and host would include age, sex, activity engaged in, etc. An important concept to keep in mind is that the attributes of the agent, host, and environment are dynamic and that these changes must be carefully monitored to ensure maximal protection of the population's health.

CONCERNS ON ESTIMATION OF EXPOSURE/DOSE

Epidemiologists are very concerned about obtaining accurate measurements of exposure. In a toxicologic context, epidemiologists prefer to obtain a dose measurement. In most instances, the dose for free-living study populations involved in epidemiologic studies is impossible to obtain. In an environmental epidemiology example, investigators worked to uncover links between an increase childhood leukemia and water from two wells. Elaborate water distribution models were used to estimate availability of water from two suspect community wells shut down in 1979 after organic solvents were discovered in them. The task before the investigators was to estimate the exposures received from these well waters. For such retrospective exposure, the only method available was to estimate the proportion of water available to specific, small geographic areas of the town.[6] These data represent a proxy for dose in as much it is impossible to enrich these data with records of actual consumption either as obtained from study subjects directly or from water company records.

RISK ASSESSMENT

Another use for toxicologic data that has been receiving increasing scrutiny has to do with risk assessment studies. ***Risk assessment*** attempts to estimate the probability that an adverse health effect will occur. Information is gained from an array of sources, all of which bring with them characteristic strengths and weaknesses. Risk assessment can occur in two principal formats: ***qualitative risk assessment*** in which risks are compared between agents in a relative, nonquantitative manner, and ***quantitative risk assessment*** in which a numerical estimate of the risk of a specific agent is generated based on the findings of other studies. Decision makers usually access risk assessment data when pursuing a collateral policy objective, i.e., ***risk management***. Risk management is the process of arriving at a choice of possible interventions or no action at all based upon a review of the costs, benefits, and existing alternatives associated with a specific agent.

Steps of risk assessment

Risk assessment is generally composed of four specific steps[1]:

- Hazard identification: potential adverse human health effects identified from the existing toxicologic data base, which can comprise either human or animal data.

- Hazard evaluation: dose-response relationships, patterns of metabolism, and potency determined.
- Exposure evaluation: routes of likely human exposure (respiration, skin contact, ingestion) and the size of the affected population determined—with particular attention paid to special populations such as expectant mothers, infants, and the elderly.
- Risk estimation: probability or incidence of human health effects in a specific human population estimated, given certain assumptions regarding exposure and susceptibility of the hosts.

Uses of risk assessment

Risk assessment has many uses, particularly in the area of regulatory oversight of either occupational or environmental contaminants. The uses range from setting of standards or permissible levels for particular contaminants, to issuing health advisories concerning foods containing a specific exogenous substance, for example a residue of a pesticide or a heavy metal such as mercury or cadmium. The risk assessment that emerges, either qualitative or quantitative, is only as reliable as the data used to produce it. Sources of data for risk assessments include:

- animal studies (bioassays)
- human health studies (occupational and non-occupational exposures)
- human toxicologic studies that assess metabolic pathways, identify the target organ(s), and probe the existence of a dose-response relationship
- short-term tests, such as the Ames test, and other means of assessing mutagenicity.

Health end points assessed by these methods

Many health end points can be studied with risk methods. The most common is the development of of cancer ***carcinogenesis***. Cancer is a common end point given a high degree of regulatory interest but also because of the difficulties imposed by a chronic condition such as cancer in terms of providing adequate protection for the public. One attribute of carcinogenesis still debated is whether a ***threshold***, or a dose below which no health effect will occur, exists. It is obvious if one believes that no threshold exists for human health effects then the regulatory posture of government agencies with the responsibility of protecting the public's health would be to not allow additional identifiable exposure to a human carcinogen. Alternatively, if it is postulated that thresholds exist, it could be argued that the expense of totally removing a carcinogen from the food chain or ambient environment would not be justified.

Problems in interpretation

Risk assessments, in part owing to their stochastic properties as well as to the variety of data sources going into them, need to be interpreted with caution. Specific problems associated with risk assessment begin with scant information. No information ia available on possible health effects for 70 percent of the 67,000 chemicals in commerce in the United States. A complete health hazard assessment can be completed for less than 2 percent of chemicals used commercially.[7] In addition, profound metabolic differences may exist between humans and the variety of laboratory animals used in animal bioassay experiments such as rats, mice, guinea pigs, etc. With few exceptions, however, animal carcinogens generally prove to be human carcinogens as well. There also can be profound difficulties in estimating and making assumptions about patterns of exposure.

Differences in the risk assessment methods

At the heart of a controversy concerning the presence of Alar, a growth regulator, in apples and other fruits, were two substantially different risk assessments performed by two separate groups, the U.S. Environmental Protection Agency (EPA) and the Natural Resources Defense Fund (NRDC). The two risk estimates differed by a factor of 25; EPA estimated an additional 9 cancers per 1,000,000 exposed people whereas the NRDC estimated 240.[8]

The differences in these assessments resulted from:

- Disagreements concerning potency, i.e., the estimate of the number of cancers from a given dose. EPA claimed that NRDC's potency factor was not supported by peer review, and NRDC contended that the lower EPA potency factor was based on an incomplete study.

- Retrospective exposure, i.e., how many apples contained Alar and how many apples and units of juice are consumed by the American public, particularly by infants and children.

Differential consumption of juice was a key factor in altering the susceptibility of children. The NRDC contended that preschool children consumed almost 18 times as much apple juice (and the typical toddler more than 31 times as much), relative to his/her weight, than the average adult woman.[9,10] In addition, exposure to the carcinogen, (i.e., effect of Alar—the carcinogen of real interest in this case is UDMH, a human metabolite that is formed upon the absorption of Alar) may cause additional risks for children because of their physiological make-up. Children, because of their intense growth rates, exhibit much greater cell division than adults and also possess enzymatic and immune systems less fully developed than the same systems in mature adults. Both factors could increase the impact of exposure to carcinogens at a relatively early age.

Utility of risk assessment

Although great controversy can surround results of risk assessments, especially quantitative risk assessments, they are useful in particular applications. They can help establish priorities for regulatory action or interventions of any type. A uniform risk assessment performed across a range of substances can create a spectrum of the health risk to humans. The limits of risk assessment can be tested when government agencies (faced with the absence of other types of data and the need for action) must rely on risk assessment methods to establish health-based standards or guidelines to prevent of human exposure to hazardous substances. Because of risk assessment shortcomings and the desire for greater specificity in measuring exposure, increasing interest is shown in understanding pathologic changes at the molecular level with the hope that these investigators will permit toxicologic and epidemiologic analyses of greater accuracy and sensitivity.[11]

REFERENCES

1. Williams, P.L. and Burson, J.L., eds. Industrial Toxicology. New York: Van Nostrand Reinhold Company. 1985.
2. Klassen, C.D., Amdur, M.O., and Doull, J. Casarett and Doull's Toxicology. New York: Macmillan. 1986.
3. Hammond, E.C., Selikoff, I.J., and Seidman, H. Asbestos exposure, cigarette smoking and death rates. *Annals of the New York Academy of Sciences*. 330:473-490. December 14, 1979.
4. Marx, J. Animal carcinogen testing challenged. *Science*. 250:743-745. 1990.
5. Mercury exposure from interior latex pain—Michigan. *Morbidity and Mortality Weekly Report*. 39(8):125-126. Mar. 2, 1990.
6. Lagakos, S.W., Wessen, B., and Zelen, M. An analysis of contaminated wellwater and health effects in Woburn, Massachusetts. *J. Am. Statistical Assoc.* 81:583-614. 1986.
7. Conservation Foundation. State of the Environment—An Assessment at Mid-Decade. Washington: Conservation Foundation. 1984. As cited in: Disease Prevention/Health Promotion: The Facts. U.S. Department of Health and Human Services. Palo Alto: Bull Publishing Company. 1988.
8. Roberts, L. Alar: The numbers game. *Science*. 243:1343. 1989.
9. Natural Resources Defense Fund. Intolerable Risk: Pesticides in our Children's Food. Washington: Natural Resources Defense Fund. 1989.
10. Roberts, L. Pesticides and kids. *Science*. 243:1280-1281. Mar. 10, 1989.
11. Shields, P.G., and Harris, C.C. Molecular epidemiology and the genetics of environmental cancer. *JAMA*. 266:681-687. 1991.

RESOURCE MATERIALS

Cohrssen, J.J. and Covello, V.T. Risk Analysis: A Guide to Principles and Methods for Analyzing Health and Environmental Risks. Washington: U.S. Council on Environmental Quality, Executive Office of the President. 1989.

The Agency for Toxic Substances and Disease Registry has prepared a set of Case Studies in Environmental Medicine. These cases are prepared with reference to a single agent and present information concerning the toxicologic and epidemiologic properties of the agent, as well as discussing clinical management practices and strategies for control. These case studies can be obtained by contacting: Continuing Education Coordinator, Agency for Toxic Substances and Disease Registry, Division of Health Education, E33, 1600 Clifton Rd., Atlanta, GA 30333.

STUDY QUESTIONS

1. Comment on the following quotation from Paracelsus (1493–1541). "All subjects are poisons; there is none which is not a poison. The right dose differentiates a poison from a remedy."
2. Comment on the following observation. Toxicologic experimentation in the laboratory setting yields study results that are of demonstrably higher quality and utility than the results emanating from epidemiologic research conducted among human populations.

Unit IV
APPLYING THE PRINCIPLES: TWO CASE STUDIES —WASTEWATER TREATMENT WORKERS AND OCCUPATIONS EXPOSED TO LEAD

PURPOSE

To acquaint the participant with an overview of the health concerns of persons working in wastewater treatment plants and to evaluate the effects of lead. An introduction is given to the use of control technologies in terms of moderating risks to workers. The unit seeks to acquaint participants with the utility of the medical monitoring of working populations.

OBJECTIVES:

1. To outline the health risks posed to workers at wastewater treatment plants
2. To introduce the hierarchy of engineering controls within the context of work site interventions
3. To demonstrate the relevance of medical monitoring requirements

SPECIAL TERMS:

1. Medical surveillance
2. Hierarchy of controls
3. Wastewater treatment
4. Natural history of disease
5. Pica
6. Bioaccumulate

The first case study of this unit will look at the health concerns of wastewater treatment plant workers, a group in which the health risks are not commonly known. The second case study will emphasize the agent lead, for which there is an unequivocal record of toxicity.

WASTEWATER CASE STUDY

Treating wastewater to make it suitable for disposal or subsequent reuse requires a combination of physical, biological, and chemical processes. When these processes are not achieved in nature, they must be engineered in a wastewater treatment plant.[1] This unit will explore the specific health hazards posed to workers in such activities.

Characterization of wastewater

Human activities generate wastes that can be conveyed through the medium of water. Such mixtures can be characterized as:

- floating debris-oily residues
- suspended solids
- organic materials
- autotrophic plant nutrients
- bacteria and viruses
- heavy metals
- dissolved solids

These parameters help determine which design of a wastewater treatment plant may be most appropriate and efficient. Variations in these characteristics are also important in determining health risks to workers.

Increasing demand for wastewater treatment

Because the pressures of increased population and development in the United States and the presence of legislation such as the Federal Water Pollution Control Act of 1972, the number of wastewater treatment plants has increased. Unmet needs for wastewater treatment have received unparalleled interest as rate payers, particularly in coastal areas, are forced to invest in large infrastructure facilities or upgrade existing ones.

Health hazards from bacteria

A primary concern for workers is the spread of infectious disease from domestic wastewater, theprimary component of concern being human waste. Classic waterborne infectious diseases include cholera, salmonella, typhoid fever, shigella, and amoebic dysentery. Hepatitis, although most often spread by human contact, has also been spread via water.[2]

Exposure to these pathogens is most likely through inhalation of aerosols or direct hand-to-mouth contact. Absorption through intact skin is usually not a problem, and special care must be taken not to abrade or cut the skin. This would be an example of modified host susceptibility, as detailed in Unit III. The concentration and duration of exposure are also factors in determining transmission.

Health hazards from chlorination

Chlorine gas is toxic and it must be handled with care. Its odor threshold is about 3.5 ppm. Concentrations of 30 ppm or more induce coughing, and exposures of 40 to 60 ppm are dangerous, with 1,000 ppm being rapidly fatal. Because chlorine is heavier than air, it concentrates in lower portions of wastewater treatment plants.

Health hazards from sludge

The creation of sludge poses hazards mostly related from to unsafe conditions because of the presence of hydrogen sulfide (H_2S) and methane (CH_4). If the H_2S concentration exceeds 70 mg/m^3 (50 ppm), the area should be evacuated. The ability to detect hydrogen sulfide is made more difficult by the fact that concentrations of about 150 ppm quickly paralyzes the sense of smell. If workers smell the gas (a characteristic strong putrid odor) and then the smell ceases, the sense of smell may be accommodated and the workers should evacuate the area. Should any worker collapse, rescuers must wear a self-contained breathing apparatus.

H_2S is a highly toxic gas that can cause a range of health effects depending upon the concentration. Nausea, headache, shortness of breath, and eye and throat irritation predominate at the lower dose ranges of 0.003 to 11 mg/m^3. At higher levels, greater than 1,400 mg/m^3, death may be instantaneous.

Epidemiologic evidence of health hazards

The presence of human pathogens has prompted interest in whether wastewater treatment plant workers suffer health effects as a result of their employment. In the largest examination of 500 sewage treatment plant workers in Cincinnati, Chicago, and Memphis, no significant differences in illnesses rates, by city, were seen based on comparisons with control workers.[3] The controls selected were water treatment plant workers in Chicago, utility workers in Memphis, and highway maintenance workers in Cincinnati—comparable groups except for the exposure to the sewage treatment plant work environment.

In an attempt to quantify exposure to parasitic disease, stool samples of 125 sewer maintenance workers and highway workers were analyzed on a quarterly basis over a 1-year period.[4] No increase was seen in infections when the workers were compared with controls matched by age, race, and income.

MEDICAL SURVEILLANCE

Although the incidence of disease resulting from health hazards posed in wastewater treatment plantis not high, the potential is clear. A proposed medical surveillance plan would seek medical data that could lead to early identification of worker health problems. A ***hypothetical*** schedule of medical surveillance for these workers is outlined in Table IV-1.[2]

This presentation of medical monitoring for wastewater treatment workers does not include the overlay of regulation. In industries where workers are possibly exposed to harmful agents such as asbestos or lead, the Occupational Safety and Health Administration (OSHA) specifies medical tests and the intervals to conduct these tests. Strict guidelines also specify how the records and results are to be stored and how confidentiality of the records is to be maintained. The conceptual thrust is similar here; workers are to be monitored at regular intervals to ensure that developing health problems are identified as early as possible in the ***natural history*** of the disease. It follows that if a worker or community resident is identified with positive findings from an appropriate biological marker then that individual should be removed from the source of the agent to prevent the development of clinical disease. The use of medical monitoring will become clearer in the case study below that addresses possible intoxication from lead.

Table IV-1
Wastewater Treatment Plants: Medical Surveillance Methods*

Treatment process	Agent	Health effect	Method
Primary and secondary treatment	Domestic waste, including feces with: viruses, bacteria, fungus, worms, protozoa	GI infections Hepatitis	Medical history Hepatitis antigen Baseline liver functions
	Industrial waste/heavy metals	Kidney disease	Medical history Baseline renal functions Blood chemistry
		Anemia	Blood count
Chlorination	Chlorine gas	Pulmonary and mucous membrane irritation	Medical history
Sludge treatment	Methane Hydrogen sulfide Pathogens present in domestic waste Oxides of metals	Asphyxiation Respiratory arrest GI infections	Medical history

*Adapted from Ref. 2.

LEAD CASE STUDY

Lead is a well-recognized human toxicant, exerting its influence in both environmental and occupational settings. Lead is a naturally occurring element with many industrial applications—applications ranging from additives to paint to use in "home" or folk remedies. In many instances, attributes of lead make its use well-suited for industrial function without a full appreciation of the health risks.

In the United States, adult body burdens of this ubiquitous element have fallen from 16 µg/dL to an average of approximately 7 µg/dL. This decline is encouraging and most likely due the result of removing lead from gasoline, which began in the mid-1970's. The principal routes of exposure presented by leaded gasoline are through inhaling lead-containing fumes or by ingesting lead-containing particles that settle out of contaminated air onto soil. Similar reductions were also recorded for children throughout the 1970's and 1980's. A 1990 report of a long-term epidemiologic study identified toxic effects, most particularly affecting neurobehavioral development, being recorded at levels of lead exposure that were previously though to be "safe."[5]

Such evaluations of the toxicity of lead add urgency to the deliberations of such agencies as the U.S. Centers for Disease Control and Prevention (CDC). The CDC has lowered the guideline for medical intervention for children: from 25 µg/dL blood lead level to 10 µg/dL. CDC guidelines serve as reference points for the lead poisoning prevention programs mounted by state and local health departments across the country.

It is estimated that approximately 1 million U.S. workers employed in over 100 occupations may be exposed to lead.[6] These occupations include the obvious ones such as lead smelters and refiners, and miners extracting lead, as well as those occupations not as closely tied to lead including auto repairers, particularly radiator repair operatives,[7] and construction workers.

Pathway of exposure

The lead found in all adults is primarily from man-made sources. It confers no biological advantage to human hosts. The principal environmental sources of lead are paint, auto exhaust, food, and water.[6] For children the primary sources are lead paint chips, lead dust, and contaminated food and drink. The principal routes of exposure for inorganic lead is through inhalation and ingestion. Organic lead, such as found in leaded gasoline, can be readily adsorbed through the skin. Although the hazard emanating from leaded gasoline has been greatly abated given the forced reduction of lead from U.S. gasoline stocks, this potential for exposure still persists in foreign stocks.

In adult workers, the main route of exposure is through inhalation or respiration. This is because of the tremendous volume of air inspired daily by the average adult (approximately 10,000 to 20,000 l/day).[8] Such volumes of air allow toxicants present even at relatively low concentrations to exert toxic effects once they become biologically available. The lung is also relatively efficient at capturing inspired lead particles and making them biologically available. Adults may also ingest lead, particularly through contamination on objects placed in the mouth such as food, cigarettes, pipes, pencil, etc.

In children, the relative importance of the routes of exposure are essentially reversed. Children, because of behavioral characteristics and proximity to potential lead sources, are placed at greater risk as a result of ingestion. The classic pathway is for the toddler to mouth an object, throw it to the floor, and return it to his/her mouth. The moistened object at this juncture carries with it any dust or contaminants it has come in contact with.

Pica

Children also engage in a behavior known as ***pica*** or the repetitive eating of non-food items. The stereotypical source of lead exposure has been eating chips of leaded paint. These chips, because of their bright primary colors, are visually stimulating to the child and possess a sweet taste that encourages further consumption. Hungry children will exhibit greater amounts of pica. Malnourishment can also account for greater harm to these children who lack sufficient stores of calcium and iron compared to children who have adequate amounts of these nutrients. In other words, at similar dose levels, the health effects attributable to lead exposure will be more severe for a population of malnourished children than for those having adequate nutrition. The reason is that lead competes for the same binding or receptor sites that iron and calcium do.

Biologic action

Once lead has been presented to the body in a biologically available form, it is absorbed and distributed. The amount absorbed varies with the pathway of exposure. Inhaled lead making its way to the respiratory tract is very efficiently absorbed. Ingested lead is not as efficiently absorbed; approximately only 10 to 15 percent of such lead is absorbed.[6] Host characteristics also influence the amount of lead absorbed. For example, the percentage of lead absorbed from the GI tract in pregnant women and children can approach 50 percent. Similar increases in absorption efficiency can be seen in individuals who exhibit the dietary deficiencies described above.

Having entered circulating blood, lead is distributed among three compartments: blood, soft tissue (kidney, bone marrow, liver, and brain) and mineralizing tissue (bones and teeth).[6] Needleman et al.[5] capitalized on this property when they chose the shed teeth of children as their means of measuring lead levels in study subjects. The biologic fate of lead in each compartment varies greatly. In single-exposure studies with adults, lead has a half-life in blood of approximately 25 days; in soft tissue, approximately 40 days; and in bone, more than 25 years.[6]

The level of lead in bone is further subdivided into a labile portion and central core pool. The labile portion exists in some rough equilibrium with circulating blood; this accounts for the "bounce-back" phenomenon that can be noted when treating workers for elevated blood lead levels with chelating agents, which scavenge for lead as well as other minerals found present in the body.[9] After the initial course of treatment with chelating agent, the patient's blood lead level decreases, but upon re-test, goes back to a level that is lower than the pretreatment level, but still elevated. The reason for this elevation is found in the labile stores of lead in bone being mobilized to seek a new equilibrium in circulating blood. A subsequent course of chelating drug treatment is usually prescribed in this situation to return the worker to lower levels of blood lead. Similarly, lead can be mobilized from bone in women as a result of the stresses of pregnancy. Such lead can pass through the barrier presented by the placenta surrounding the developing fetus. This can translate into infants being born with elevated blood leads as a result of retrospective maternal exposure.

Lead is an insidious agent for a number of reasons; of particular concern its ability to ***bioaccumulate***. Bioaccumulation is the ability of an agent to be stored within the human body. With lead, the preferential storage is in long bones. In similar ways, other environmental agents can bioaccumulate, e.g., the storage of polychlorinated biphenyls in adipose tissue. This property of bioaccumulation makes it possible to receive toxic levels of lead in a chronic, as opposed to an acute, fashion. When small amounts of lead are absorbed faster than the body can rid itself of them, body burdens (that carry with them deleterious effects) are gradually built-up.

Health effects

The severity of the effects of lead depend on the level of dose. The most common way to measure dose is to examine circulating blood and to determine blood lead levels, expressed as μg/dL. The organ system most sensitive to the effects of lead is the central nervous system (CNS).

- Study results indicate that measurable deficits in cognitive development may result from prenatal and postnatal blood lead levels as low as 10 µg/dL.[10]

- Losses in hearing acuity and accompanying development delays (as measured by the first date of sitting up, walking, and speaking) have been noted in work carried out with results from National Health and Nutrition Examinations Survey (NHANES).[11] This finding is mentioned as an example of the postulated set of sensitive end points that may be affected by lead exposure. Such data have caused the advisory level of concern for blood lead levels in children to be lowered (see Table IV-2).

In Table IV-2 it is evident that differing regulatory agencies set different levels of concern depending on the population of interest and duration of exposure.

Table IV-2
Summary of Standards and Regulations for Lead*

Agency**	Focus	Level	Comments
CDC	Blood	10 µg/dL	Advisory; level of concern
OSHA	Air	50 µg Pb/m^3	Regulation; PEL@ over 8-hour workday
OSHA	Blood	60 µg/dL	Regulation; medical removal from exposure
FDA	Food	100 µg Pb/day	Advisory
CPSC	Paint	600 ppm (0.06%)	Regulation; by dry weight

*Adapted from Ref. 6.
**CDC = Centers for Disease Control and Prevention; CPSC = Consumer Product Safety Commission; FDA = Food and Drug Administration; OSHA = Occupational Safety and Health Administration.
@PEL (Permissible Exposure Limit) = highest level of lead in air, averaged over an 8-hour workday, to which a worker may be exposed.

Children exposed to lead suffered greater, persistent neurologic impacts, such as decreases in I.Q. and relative failure to complete high school, than did less exposed children from the same neighborhoods.[5] Occupational exposures can manifest themselves in the classic presentation of "wrist drop" in which voluntary movement of the hand is compromised. This effect generally presents as a late sign of lead intoxication among workers.

Hematologic effects of lead are generally represented by anemia. Anemia reflects the absence of the oxygen-carrying faction of blood cells, hemoglobin. Because anemia is only evident after significant exposure, it cannot be taken as early warning sign of exposure to lead. In fact, many early signs of lead exposure are very nonspecific (fatigue, irritability, occasional abdominal discomfort) and are easily overlooked. Lead also exerts toxic effects on renal and reproductive systems. One particularly disquieting feature of lead intoxication is that lead readily crosses the placenta thus exposing the developing fetus to whatever levels of lead are in the mother's circulating blood. The normal changes and stress of pregnancy can mobilize maternal lead stores in bone and induce increases in circulating maternal blood. Given the insidious nature of lead intoxication, the health of workers can be best advanced through primary prevention--minimizing exposures.

HIERARCHY OF CONTROL

How to control exposure of working and community populations is well within the professional practice of engineers. Prevention specialists, when addressing the control of workplace hazards, usually express the available options as a ***hierarchy of control.*** The ordered nature of a hierarchy is emphasized in that there are ways of ensuring greater levels of protection for working populations. These options generally present themselves, from top to bottom, as:

1. changing the industrial process or the materials used so as to reduce toxicity and exposure resulting from the process;

2. isolating the source and installing engineering controls such as ventilation systems, noise baffles, and air filtration systems;

3. using administrative controls to limit the amount of exposure and, hopefully, dose a worker receives; and

4. requiring workers to use personal protective equipment to forestall exposure.

The hierarchical nature of these options quickly becomes evident to the observer. Obviously using personal protective equipment (respirators, breathing devices, goggles, hearing protection) is only as effective as the integrity and availability of such equipment, the workers' knowledge regarding the proper way to use such equipment, and workers' actual use of the equipment according to accepted methods.

Convenience of use, job performance/productivity issues, and lack of priority placed on compliance in the workplace can pose significant problems.

Personal protective equipment has been shown to offer levels of protection that are unequal, highly variable, and substantially lower than those predicted from laboratory measurements.[12] Their effectiveness is tied to proper training and maintenance of equipment both of which can be deficient. For example,one of the most frequent cause of OSHA citations for health inspections is the failure of employer respirator programs. Personal protective equipment is also burdensome on employees; it can be hot, heavy, and interfere with job-related communication. On the other hand, engineering controls are less subject to human error, and they can affect multiple pathways of exposure simultaneously.

Substituting less toxic raw materials or redesigning a work process to minimize or eliminate toxic products or by-products is obviously at the top of the hierarchy. Substitution can be complicated by hazards from unknown qualities in the replacement substance. For example, carbon tetrachloride, which had been used as a substitute for petroleum naphtha, is now widely recognized as toxic itself, and some of the substitutes for carbon tetrachloride are suspected of causing adverse health effects.[12] Predicting the cost of implementing engineering controls is also difficult. Engineering controls can appear to be more costly than alternatives because of the difficulty in measuring the positive impacts engineering controls can have on productivity and the relative decreases in absenteeism.

This unit would not be complete without making a strong plea for the placing of the strongest emphasis on the prevention of exposure before some intervention or risk management action is required. Preventing exposure is paramount, either by substituting less toxic materials or by eliminating the contaminant from the reaction or process.

This plea is underscored by three examples of wholly avoidable lead intoxication. Of particular concern are two examples arising in working populations engaged in the renovation of bridges. The first episode occurred in 1979 and resulted in the intoxication of both workers and abutting community residents due to removal of lead-based paint from a bridge.[13] Adhering to improved work practices could have ameliorated the problem. This break down in prevention was ironically largely duplicated 9 years later with the same deleterious results.[14] The wisdom of educating employers and workers as to how a hazard such as lead can be successfully abated can only be reiterated here.

The risks of haphazard abatement work practices can also be seen in a case report of a Victorian farmhouse in which household occupants became lead poisoned.[15] This case occurred in an upper-level socioeconomic status area—thus not conforming to the stereotype that lead poisoning is an urban problem.

REFERENCES

1. Salvato, J.A. Environmental Engineering and Sanitation. New York: Wiley-Interscience. 1982.
2. McCunney, R.J. Health effects of work at wastewater treatment plants: A review of the literature with guidelines for medical surveillance. *Am. J. Ind. Med.* 9:271-279. 1986.
3. Pahren H. and Jakubowski, W., eds. Wastewater Aerosols and Disease, Proceedings of a Symposium. Cincinnati: U.S. Environmental Protection Agency. Publication No. EPA-600/9-80-028. 1980.
4. Clark, C.S., Linnemann, C.C., Clark, J.G., and Gartside, P.S. Enteric parasites in workers occupationally exposed to sewage. *J. Occup. Med.* 26:273-274. 1984.
5. Needleman, H.L. Schell, A., Bellinger, D., Leviton, A., and Allred, E.N. The long-term effect of exposure to lead in childhood. An eleven-year follow-up report. *New England J. Med.* 322:83-88. 1990.
6. Agency for Toxic Substances and Disease Registry, U.S. Public Health Service. Case Studies in Environmental Medicine. Atlanta: ATSDR No.1. June 1990.
7. Goldman, R.H., Baker, E.L., Hannan, M., and Kamerow, D.B. Lead poisoning in automobile radiator mechanics. *New England J. Med.* 317:214-218. 1987.
8. Samet, J.M., and Utell, M.J. The environment and the lung. *JAMA*. 266:670-675. 1991.
9. Rempel, D. The lead-exposed worker. *JAMA*. 262:532-534. 1989.
10. Bellinger, D., Leviton, A., Waternaux, C., Needleman, H., and Rabinowitz, M. Longitudinal analyses of prenatal and postnatal lead exposure and early cognitive development. *New England J. Med.* 316:1037-1043. 1987.
11. Schwartz, J. and Otto, D. Blood lead hearing thresholds, neurobehavioral development in children and youth. *Arch. Environ. Health.* 42:153-157. 1987.
12. Office of Technology Assessment. Preventing Illness and Injury in the Workplace. Washington: GPO. April 1985.
13. Landrigan, P.J., Baker, E.L., Himmelstein, J.S., Stein, G.F., Weddig, J.P., and Straub, W.E. Exposure to lead from the Mystic River Bridge: The dilemma of deleading. *New England J. Med.* 306:673-676. 1982.
14. Himmelstein, J., Wolfson, M., Pransky, G., Morse, D., Ross, A., and Gill, J. Lead poisoning in bridge demolition workers–Massachusetts. *Morbidity and Mortality Weekly Report.* 38: 688-694. 1989.
15. Marino, P.E., Landrigan, P.J., Graef, J., Nussbaum, A., Bayan, G., Boch, K., and Boch, S. A case report of lead paint poisoning during renovation of a Victorian farmhouse. *Am. J. Public Health.* 80:1183-1185. 1990.

STUDY QUESTIONS

1. Think of an industry other than wastewater treatment that could benefit from a hierarchy of controls? Explain why?
2. Why would confidentiality of a worker's medical results be a legal and ethical problem?

Unit V
HAZARDOUS WASTE: OVERLAP BETWEEN OCCUPATIONAL AND ENVIRONMENTAL HEALTH

PURPOSE

To acquaint participants with the way in which hazardous waste problems have both an environmental and occupational focus. The need for an interdisciplinary team of specialists in addressing the resulting problems of hazard identification, risk management, and risk abatement will be demonstrated in a case involving polychlorinated biphenyls (PCBs).

OBJECTIVES:

1. To demonstrate the interrelationship between occupational and environmental health
2. To demonstrate multiple routes of exposure for the same agent
3. To demonstrate multiple routes of exposure for the same agent

SPECIAL TERMS:

1. Chloracne
2. Polychlorinated biphenyls (PCBs)

INTRODUCTION

In the United States in 1989, approximately 225 to 275 million tons of hazardous waste were generated.[1] This translates into approximately 1 ton of hazardous waste generated for each person in the country per year. According to the National Solid Waste Management Association about 90 percent of the hazardous waste is produced by about 14,000 large-quantity generators; 685 are chemical manufacturers. Hazardous materials include items ranging from aerosol hair sprays and cleaning compounds, to battery acid and gases.[2]

The Toxic Substances Control Act (1971) (TSCA); the Resource Conservation and Recovery Act (1976) (RCRA); the Comprehensive Environmental Response, Compensation, and Liability Act (1980) (CERCLA); and the Superfund Amendments and Reauthorization Act (1986) (SARA) are examples of major legislation passed at the Federal level that strictly define how hazardous wastes must be controlled from "cradle to grave" and how illegal hazardous waste sites must be remediated.[3] Where states pass requirements that are either consistent with or more stringent than Federal hazardous waste standards the U.S. Environmental Protection Agency (EPA) may authorize state agencies to administer their own programs. Currently, 41 states have exercised this option.

Much attention has been focussed on the oversight and progress achieved in abating existing hazardous waste sites, particularly those classified under the Superfund's National Priority List (NPL) program. Inclusion on this list indicates that the EPA has evaluated the site by a set of criteria designed to estimate potential threat to human health through the application of concepts of epidemiology, toxicology, and other relevant environmental health science disciplines. In 1991, EPA identified 1211 final and proposed NPL sites. The potential for human exposure is clear.

The characterization of a substance or material as hazardous requires epidemiologic, toxicologic, and exposure data to classify the agent into an appropriate category. To explore this topic further we shall consider polychlorinated biphenyls (PCBs). This example will also highlight another important concept—the interconnectedness of occupational and environmental health problems. In reality, many environmental problems have occupational antecedents. A factor complicating this realization is the separate scientific, technical, and regulatory mechanisms that confront occupational and environmental problems.

Occupational health circumscribes exposures and attendant health effects suffered in the workplace. Environmental health addresses human health concerns arising from contaminants in the ambient environment. The example presented in this unit, PCBs, represents the fluidity between these two areas of interest given the existence of both occupational and food chain exposures. The former American College of Occupational Medicine, as a symbol of the growing interest in drawing occupational and environmental health professionals together, has changed its name to the American College of Occupational and Environmental Medicine.

POLYCHLORINATED BIPHENYLS

Polychlorinated biphenyls (PCBs) are a group of chemical compounds based on a biphenyl ring structure. The number of chlorine atoms hung from this ring impart distinctive qualities to the 209 possible isomers. PCBs, as with other halogenated aromatic compounds, are highly lipophilic—an important point when we address the human metabolism of PCBs. They are relatively immiscible in aqueous solutions; this is also an important quality to keep in mind when we discuss the environmental fate and transport of PCBs in the ambient environment.

Historical patterns of use

Although PCBs were first synthesized in 1881, the full economic potential of the compounds remained unrealized until Monsanto Inc., began to manufacture them for industrial use in the early 1930's. PCBs were attractive for industrial purposes because of certain physical characteristics including their resistance to combustion, possession of high electrical resistance, and relative inertness to most chemical reactions. These qualities made them ideal for many industrial applications including their use in electrical capacitors and transformers. Other examples of use included such industries as dye manufacturers,herbicide makers, paper manufacturing, rubber companies and textile flameproofing.

Environmental contamination

PCBs are virtually ubiquitous in the United States and in the rest of the world. Hundreds of thousands of tons of PCBs have been manufactured in the United States. The persistence of these compounds can be quickly realized when it is observed that of the total of 627,000 tons of PCBs manufactured in the United States only approximately 39 percent of this amount is considered to be degraded.[4] Degradation does not guarantee safety in that possible chemical end points of degrading are certain dioxins and furans each of which carry certain health risks. The amount of PCBs available to the environment is also expressed in the environmental monitoring levels reported for these compounds. PCBs have been identified in municipal wastewater and sewage sludge, in many large lakes (Great Lakes, etc.), and in many large rivers (e.g., Hudson River). Levels as high as 2.8 million ng/l have been discovered in the Hudson River.[5] This level of contamination may be unusual although rivers near industrial sources of PCBs typically show considerable levels of contamination.

Disposal methods

Until recently, the usual methods for disposing of PCB wastes were landfilling, incineration, and ocean dumping. These practices also account for the wide distribution of these compounds. Today, in the United States, EPA only approves high-temperature incineration for PCBs. Destruction rates of > 99.99% have been achieved for certain technologies in test situations. A continuing concern is the field reliability of the technology and the effectiveness of environmental monitors to offer acceptable levels of protection to an increasingly skeptical public.

Bioaccumulation and human metabolism

Environmental accumulation via the food chain is considered to be the major source of exposure for in the United States. Historically, occupational exposures were another route of major concern; however, in 1976, the EPA, acting under the guidelines of TSCA, banned the manufacture of PCBs in the United States. Humans, at the top of the food chain, consume other species that are high in other competitive food chains and that are subject to PCB contamination through food chain exposure. Many fish, both freshwater and marine, show a marked ability to ***bioaccumulate*** PCBs. Bioaccumulation represents the ability to store increasingly larger amounts of a certain substance within the body based on cumulative exposures occurring over time. Such a buildup is predicated on the fact that excretion occurs at a slower rate than the buildup of the substance in the target organ. PCBs, due to their lipophilic qualities, are preferentially stored by both fish and humans in adipose tissue. Just as PCBs can bioaccumulate in lower order species, such as birds and fish, these compounds also can be stored in humans exposed either occupationally or through the food chain.

Health effects

A variety of possible human health effects attributable to PCB exposure have been suggested. These range from carcinogenicity, to adverse reproductive outcome, to a characteristic skin lesion occurring in certain high-dose, acute-exposure situations. This lesion is called ***chloracne***. The first of two incidents, both involving Asian populations, occurred in Japan in 1968; the second, in Taiwan in 1979. Both involved large-scale human exposure via contaminated rice cooking oil. Initially, at both outbreaks it was thought that PCBs were the dominant agent responsible for the health effects in question. Upon re-analysis, however, in addition to PCBs being clearly found to be present, other perhaps even more toxic compounds (including polychlorinated dibenzofuran [PCDFs] and polychlorinated quarterphenyls [PCQs]) were noted in both of the rice oils.[6] The PCDFs are formed from PCBs only at very high temperatures. The common symptoms in both study populations were dark brown pigmentation of the nails, distinctive hair follicles, acne-like skin eruptions, pigmentation of skin, numbness in limbs, swelling of upper eye lids, and increased eye discharge.

Although acute exposure can produce such well- documented health effects, long-term consequences of exposure for chronic disease remain more problematic. In animals, PCBs appear to be carcinogenic, particularly for hepatic (liver) tumors in rats. In humans, the results are more difficult to interpret as a result of generally small, inconclusive studies lacking sufficient numbers of study subjects (power) to be truly informative. The characterization of other possible health effects leads to the finding that PCBs are associated with neurotoxicity.

Labeling convention

A four-digit number following the trade name (Aroclor) is governed by the following convention: the first two digits are assigned to represent the 12 carbon atoms (thereby identifying the appropriate biphenyl structure) and the final two digits are used to represent the approximate percentage of chlorine by weight in the PCB blend.[7] As a general rule of thumb, as chlorine content increases, environmental persistence also increases. For most industrial applications in and around New Bedford, Massachusetts, Aroclor 1242 was of the greatest interest because it was the blend of PCBs most widely used.

NEW BEDFORD, MASSACHUSETTS CASE STUDY

In 1977 the EPA discovered widespread PCB environmental contamination of the New Bedford Harbor and the Acushnet River estuary. Near the harbor and estuary were factories producing electrical capacitors. This led to gross levels of PCB contamination from direct discharge of factory waste. The sediments underlying the entire New Bedford Harbor contained elevated levels of PCBs with concentrations ranging from a few parts per million (ppm) to well over 100,000 ppm. Such contamination, as expected, exerts a burden upon the species occupying this ecosystem. Raised levels of PCB were identified in many marine species: five different fin species had levels higher than 5.0 ppm (safe level for human consumption as set by the U.S. Food and Drug Administration). The levels in fish were highest in those species known to be bottom feeders. Concentrations in lobsters were found to be even higher than the fin species. Particularly elevated in lobsters was the main detoxifying organ, the liver, popularly known as "tomalley."

In response to these findings, the Massachusetts Department of Public Health (MDPH) promulgated regulations to close the contaminated area to commercial fishing in September 1979. It must be emphasized that this closure affected only those specific portions of the harbor and estuary found to be contaminated and not the customary fishing grounds of the active ocean-going fishing fleet that uses New Bedford as its home port. The MDPH action was predicated on the belief that closing the harbor to commercial fishing and lobstering would reduce the potential for human exposure to PCBs through the food chain. This action was called for as a result of the widespread scale of PCB contamination from discharges (some governed by state regulatory permits, some not) into the harbor and estuary. Throughout the New Bedford area other sources of contamination other than direct discharge also existed. A continuing source of potential population exposure to PCBs is the burning of electrical transformers that contain PCBs. The storage of capacitors containing PCBs around the New Bedford manufacturing facilities represents such potential exposure. Waste oils containing PCBs were used by New Bedford and other communities to oil local roadways for dust control. The municipal wastewater treatment plant also has measurable levels of PCBs as a result of some difficult-to-monitor discharges of PCBs to municipal sewers. Other areas of PCB contamination included soil sediments from factory sites as well as abutting areas.

The worksites where this contamination emanated from were of concern. Air levels of PCBs within one of the plants in 1977 ranged from 0.17 to 1.26 mg/m^3 (OSHA exposure standard for Aroclor 1254 is 1 mg/m^3). One published study of electrical capacitor workers at a site other than in New Bedford indicated the presence of microsomal enzyme induction, the long-term consequences of which are unclear.[8] Suggestions have also been raised concerning the relationship between PCB exposure and increases in blood pressure, but difficulties have been found in identifying a discrete cause for this phenomena.[9]

What is clear is that the occupational antecedent, the production of electrical capacitors for an extended period of time near the estuary and harbor, has led to gross levels of contamination and a major remediation problem. Estimates for possible clean-up scenarios for the harbor range in the tens to hundreds of millions of dollars. Based on concerns for the nonoccupationally exposed population of the Greater New Bedford area, the MDPH in conjunction with the U.S. Centers for Disease Control launched a health study in 1984 to establish whether residents were being exposed to PCBs through the food chain. The study was conducted in two phases. The first was to describe the distribution of PCB levels for the Greater New Bedford area and to identify a group of individuals sufficient in size for a second series of analyses, that was designed to inquire into the possible health effects of PCB exposure. The study concluded in 1987. Of 840 randomly selected residents, only 1.3 percent had serum PCB levels greater than 30 ppb, the level set as the bench mark for inclusion in the second phase of the study. Even after alternative means of identifying more heavily exposed subjects was pursued through alternative methods (e.g. actively soliciting individuals who maintained active fishing and lobstering licenses), it was deemed impossible to continue with the second phase of the study.[10]

The subjects did exhibit some unequivocal patterns of similarity. Age and PCB level were directly associated; the older a subject was, the higher the PCB level. Individuals (both males and females) who reported eating fish caught from the harbor had higher PCB levels than those who ate less or who reported not eating harbor fish. Based on these findings the MDPH believed it prudent to maintain the fishing ban even though the levels of PCB found in the New Bedford population were relatively unremarkable. The only individuals found to exhibit relatively high levels had acquired this exposure through an occupational source as a result of employment in one of the capacitor manufacturing facilities.

CONCLUSIONS

The example indicates the delicate relationship between occupational and environmental health problems. One of the more challenging aspects of conducting the health study of the Greater New Bedford area residents was accounting for the dual sources of possible exposure--occupational and food chain. The study also demonstrated the need for an interdisciplinary team of specialists to address occupational/environmental health questions. Analyses of both occupational and environmental health manpower forecast the need for more trained personnel in these areas.[11,12]

REFERENCES

1. Wenzt, C.A. Hazardous Waste Management. New York: McGraw-Hill. 1989.
2. Title 49, Code of Federal Regulations, pt. 172. As cited in: Boske, L.B. and Hadden, S.G. Hauling hazardous materials:The regulatory picture. *Health and Environ. Dig.* 2(12):1-3. Jan. 1989.
3. Dawson, G.W. and Mercer, R.A. Hazardous Waste Site Management. New York: John Wiley & Sons. 1986.
4. Erickson, M.D. Analytical Chemistry of PCBs. Boca Raton: Lewis Publishers. 1991.
5. Evans, M.S. Toxic Contaminants and Ecosystem Health: A Great Lakes Focus. New York: Wiley & Sons. 1988.
6. Hsu, Shu-Tao, et al. Discovery and epidemiology of PCB poisoning in Taiwan: A four-year follow up. *Environ. Health Perspectives.* 59:5-10. 1985.
7. Weaver, G. PCB contamination in and around New Bedford, Mass. *Environ. Sci. Technol.* 18:22A-27A. 1984.
8. Lawton, R.W., Ross, M., Feingold, J., and Brown, J.F. Effects of PCB exposure--biochemical and hematological findings in capacitor workers. *Environ. Health Perspectives.* 60:165-184. 1985.
9. Kreiss, K. Studies on populations exposed to polychlorinated biphenyls. *Environ. Health Perspectives.* 60:193-199. 1985.
10. Massachusetts Department of Public Health, Massachusetts Health Research Institute, and the U.S. Centers for Disease Control. The Greater New Bedford PCB Health Effects Study, 1984-1987. Boston: Massachusetts Department of Public Health. 1987.
11. Institute of Medicine. Role of the Primary Care Physician in Occupational and Environmental Medicine. Washington: The National Academy Press. 1988.
12. Sexton, K. and Perlin, S.A. The federal environmental workforce in the United States. *Am. J. Public Health.* 80:913-920. 1990.

SUGGESTED AUDIO-VISUAL MATERIALS

1. "Who's Killing Calvert City?" Frontline, PBS Video, 1989. Running time: 58 minutes.

STUDY QUESTIONS

1. What would your opinion be of the environmental situation in New Bedford if you were a resident of the area? Would it be different if you worked at one of the capacitor plants?
2. Why is the public relatively accepting of certain levels of exposure that take place in a work setting but relatively unaccepting of the same exposure taking place in a community setting?

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GLOSSARY

ACUTE: short-term exposure (contrast with chronic).

AMBIENT: outdoor environment as contrasted with environments defined by a structure.

ANALYTIC EPIDEMIOLOGY: a class of epidemiologic studies attempting to test a hypothesis between an exposure and a disease (contrast with Descriptive Epidemiology).

ASCERTAINMENT: the recognition of an accurate count of a specific disease, in this case particularly focussing on those of environmental and occupational origin.

BIAS: any systematic error interfering with the estimate of association that may exist between an exposure and a disease.

BIOACCUMULATE: the ability of certain compounds to accumulate in the body usually at specific target organs.

BODY BURDEN: the total amount of an agent absorbed in the body.

CASE-CONTROL STUDY: a type of analytic epidemiology study in which the relative exposure experience of individuals with a specified disease (cases) are compared with a group of disease-free individuals (controls).

CAUSALITY: the ability to ascribe an etiologic relationship between an agent and a health outcome.

CHLORACNE: a dermatologic condition arising from exposure to PCBs marked by cystic acne.

CHRONIC: long-term exposure (contrast with acute).

COHORT STUDY: a type of analytic epidemiologic study in which a group of disease-free individuals is formed and followed either retrospectively or prospectively and the disease experience of the cohort is evaluated relative to exposure status.

DESCRIPTIVE EPIDEMIOLOGY: a class of epidemiologic studies attempting to characterize the distribution of a disease in either time, space, or by presence of selected risk factors. Primarily employed as a vehicle to contribute to the formation of hypotheses that are then evaluated via analytic epidemiologic studies (contrast with analytic epidemiology).

DIAGNOSTIC CRITERIA: criteria setting forth in clear, consistent, and unambiguous terms the definition of a case for inclusion in epidemiologic studies.

DOSE: the amount of an agent interacting with the target organ or tissue.

DOSE-RESPONSE: a relationship involving an increase in effect on health outcome for each increase in dose of the etiologic agent.

ED_{50}: the dose at which 50 percent of the study population experiences the effectiveness of a particular agent, usually a drug.

EPIDEMIOLOGY: the study of the etiology of disease in human populations.

ETIOLOGY: the cause of specific diseases.

EXPOSURE: the amount of an agent coming into contact with a host.

HIERARCHY OF CONTROLS: a concept of controls or levels of protection instituted in workplaces to prevent workers from receiving toxic doses of agents.

HYPOTHESIS: a formalized inference about the relationship between an exposure and a disease.

INCIDENCE: the number of new cases of a specified disease developing in a given geographic area over a specific interval of time (contrast with prevalence).

LD_{50}: the dose at which death is caused in 50 percent of the animal study population.

LATENCY: the time lapsing between first exposure and the clinical presentation of a health outcome or disease.

MEDICAL SURVEILLANCE: the use of regular, uniform medical tests to produce a cumulative history of workers with the intent of detecting either physiologic or symptomatic changes brought about by workplace exposure so that meaningful interventions can be mounted.

METABOLITE: compound formed within the host as a result of metabolic action.

MUTAGENESIS: the ability of agents to cause changes in the genetic material in the nucleus of cells in ways that can be transmitted during cell division.

NATURAL HISTORY OF DISEASE: the clinical picture of how a disease presents itself.

ODDS RATIO: the ratio of the odds of exposure among the cases to that among the controls.

PICA: eating of nonfood items

POLYCHLORINATED BIPHENYLS: a class of carbon compounds noted for their industrial utility that have been banned because of possible health effects and environmental persistence.

POTENCY: the level at which toxic doses are produced.

POTENTIATION: when one agent will not induce a toxic effect in isolation but will increase the effect of another agent.

POWER: the ability of a given epidemiologic study to detect an effect between exposure and disease if it is present.

PREVALENCE: the number of cases of a given disease in a specified geographic area for a given period of time (contrast with incidence).

PROSPECTIVE: looking forward in time.

QUALITATIVE RISK ASSESSMENT: the specification of risk in cases where quantification is not possible but where the weight of evidence derived from available data indicates the possibility of health effects.

QUANTITATIVE RISK ASSESSMENT: the specification of risk through quantitative methods usually in the form of the risk of an event per 100,000 population.

RELATIVE RISK: the relative disease experience of exposed individuals as contrasted with those unexposed to the agent of interest.

RETROSPECTIVE: looking back in time.

RISK: the chance of contracting a specific disease.

RISK FACTOR: factors either alterable (cigarette smoking, seat-belt use) or unalterable (age, race) that influence the risk of developing a specific disease.

RISK MANAGEMENT: the process of arriving at a choice of possible interventions, or no action at all, based on a review of the cost, benefits, and existing alternatives associated with a specific agent.

ROUTE OF EXPOSURE: a pathway or route through which an agent can interact with a human host, commonly via respiration, digestion, or dermal contact.

TARGET ORGAN: an organ serving as a receptor for an agent once it is absorbed into the body.

TERATOGENESIS: the inducement of birth defects during the development between conception and birth.

THRESHOLD: a point in the dose-response curve at which for each and every increase in dose there is a corresponding increase in health effect.

TOXICOLOGY: the science of poisons, i.e., the study of chemical or physical agents that produce adverse responses in biological systems.

SUSCEPTIBILITY: factor(s) rendering individuals or populations at greater risk of suffering a health effect, e.g., unimmunized individuals are more susceptible to certain infectious diseases.

SYNERGISTIC: greater than additive effects.

WASTEWATER TREATMENT: the process of removing unwanted or objectionable materials from water that may include the unit operations of screening, sedimentation, oxidation, disinfection, and other advanced methods.

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