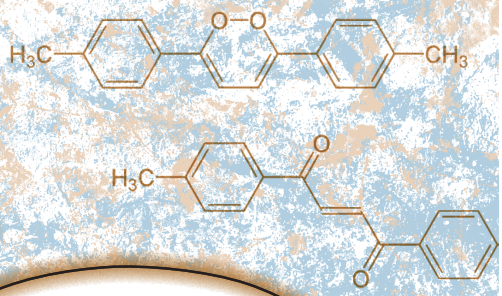
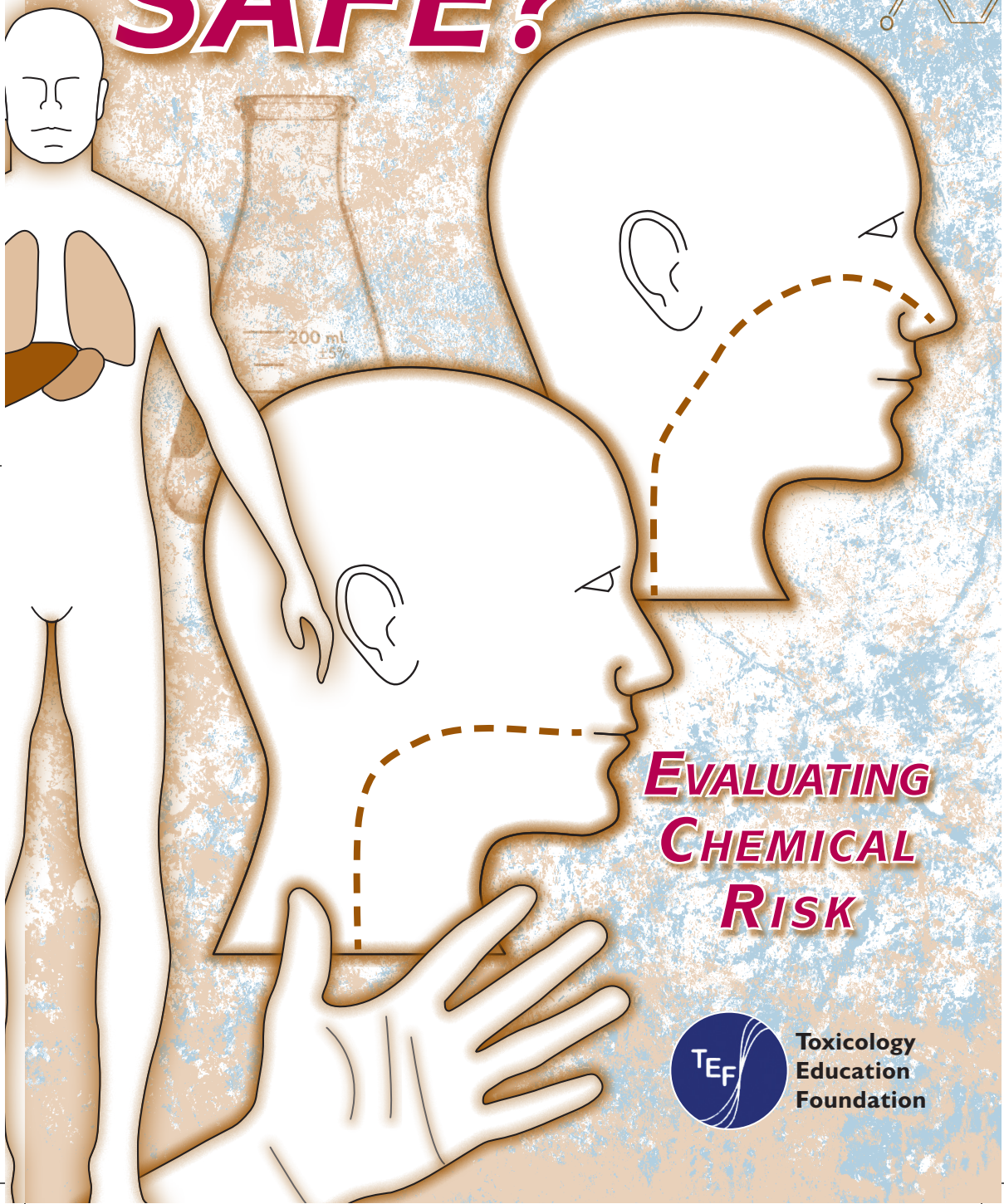
IS IT SAFE?





EVALUATING CHEMICAL RISK

Toxicology Education Foundation

IS IT SAFE?

EVALUATING CHEMICAL RISK

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INTRODUCTION

Every day there are news reports about the dangers of chemicals in our air, water or food. Often these chemicals have strange-sounding names, such as diethylhexyl phthalate. The reports may come from the traditional media, from bloggers, or from friends and relatives. How can you decide whether these chemicals really pose a danger? How can you make the choices that will best protect you and your family?

This primer is designed to help you answer these questions. It is divided into two parts. The first, "How do you know what the risk is?," describes a process, abbreviated as RITE, that can be used to assess risk. It is based on toxicology, the science used to evaluate the potential harmful effects of chemicals on humans. The second part, "How can you evaluate a report about risk?," provides strategies for using the basics of toxicology and the RITE process to evaluate media reports and assess claims about the dangers a chemical may pose.

HOW DO YOU KNOW WHAT THE RISK IS?

RITE

The key to assessing risk is to use the RITE approach. RITE is an abbreviation for **R**isk **I**s dependent on **T**oxicity and **E**xposure and so the first steps in understanding the RITE process are to learn how:

1. toxicity is defined and measured; and
2. exposure is defined and measured.

In brief, toxicity refers to harmful health effects that can be caused by chemicals or other agents. It depends on the type of agent, the dose of the agent and the characteristics of the individual exposed to the agent. These characteristics include age, sex, genetic make-up and state of health. Exposure, on the other hand, is the dose (the amount of the agent) that an individual experiences — by ingesting the agent, inhaling it or making skin contact with it. Exposure includes not only the dose, but also the route by which individuals are exposed, as well as how long and how often they are exposed.

RIToxicityE

Two concepts are critical to understanding toxicity. The first is that everything — people, trees, rocks, etc. — is made up of chemicals. There is nothing that is "chemical-free" despite what you might read in the media. The second is that all chemicals have the potential to cause toxicity when the dose is high enough. Although media headlines may refer to "toxic chemicals" as if they are a special category of chemicals, this is misleading. Chemicals cannot be divided into toxic and non-toxic; they are all potentially toxic and vary only in the types of effects they may cause and the dose at which these effects appear.

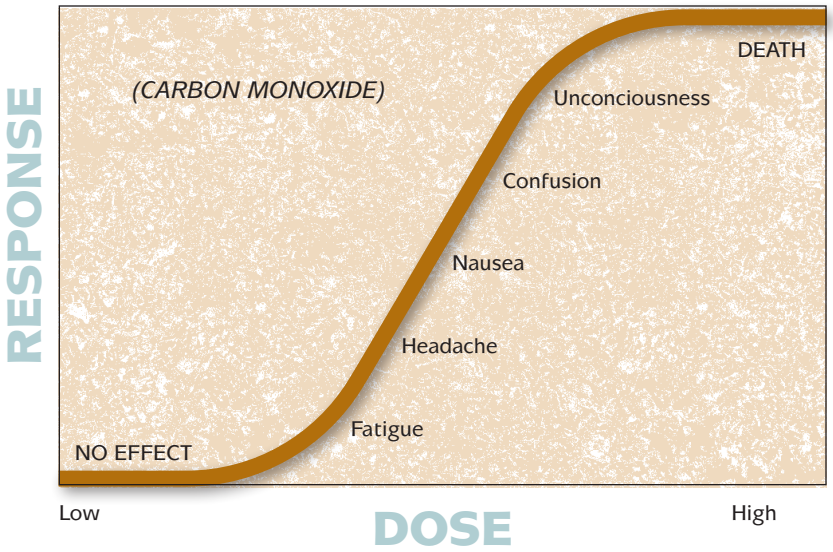
Since all chemicals are toxic, we distinguish the toxicity of one compared to another by its potency, which is measured by how large a dose of each is required to cause toxicity. A more potent agent causes toxicity at a lower dose. Because it is not acceptable to experiment on people, potency values are generally based on the results of studies on laboratory animals, such as rats and mice. In these studies, different doses, usually including quite high ones, are administered each day for up to a lifetime to different groups of animals and then the animals are examined for harmful effects.

Data from these studies are used to provide a picture of how toxicity varies with dose, a picture that is known as a dose response curve. There are two different types of dose response curves; one is used to assess the toxicity of chemicals that do not cause cancer — known as non-carcinogens — and the other to assess the toxicity of carcinogens.

Toxicity of Non-Carcinogens

The graph below, for non-carcinogens, shows how high a dose is required to cause effects and how the severity of the effects increases as the dose increases. An example of a dose response curve of this type is shown below for carbon monoxide.

DOSE RESPONSE FOR NON-CARCINOGENS



To estimate the potency of a chemical, the point on the curve that represents the highest dose that does not cause any effect is chosen. This is often known as a safe dose because harmful effects may occur if it is exceeded. The safe dose is generally determined from studies of laboratory animals, but what we really want to know is the safe dose for humans. Unfortunately, there is not enough known about the differences between laboratory animals and humans to calculate a precise safe dose for humans from studies on animals.

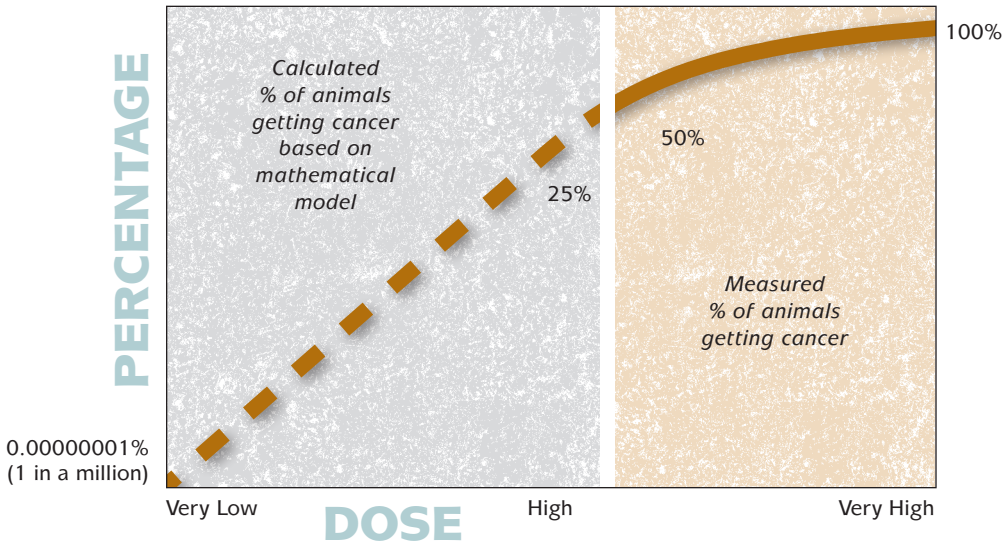
As a result, assumptions about the sensitivity of humans to the agent compared to that of animals and about the variability of humans compared to that of experimental animals have to be made. To be protective of human health, it is assumed that humans are much more sensitive than animals to all agents and that they vary much more in their response to chemicals than animals do. Using these protective assumptions, safe levels for non-carcinogenic chemicals are estimated. The levels calculated this way are intended to provide a sizeable margin of safety so that harmful effects are not likely to occur unless these values are exceeded by a large amount.

Toxicity of Carcinogens

A different type of dose response curve describes the toxicity of carcinogens. Instead of showing how the severity of the effect changes with dose, as we saw for non-carcinogenic agents, the curve for cancer shows how the percentage of animals getting cancer changes with dose. In addition, rather than assuming that there is a safe level, it is assumed that cancer can be caused by any amount of an agent — even a single molecule — and thus there is no safe level. Instead the potency of compounds thought to cause cancer is described by the dose estimated to cause a particular increase in the percentage of animals getting cancer; e.g., one additional cancer in one million exposed animals. The lower the dose required, the more potent the agent is.

The potency of a carcinogenic compound is based on toxicity data collected from studies of laboratory animals. However, because cancer is very rare at low doses, the animals have to be given very high doses of the chemical so a number of them will get cancer. These doses are much higher than those humans experience. Thus, to estimate cancer potency in humans, the high dose data is used to predict low dose values. This is done using a mathematical model as illustrated in the dose response curve below:

DOSE RESPONSE FOR CARCINOGENS



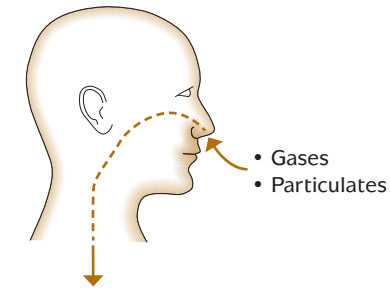
To be protective of the public, the model chosen is one that is thought to exaggerate the carcinogenic potency of the agent — most likely by a very large amount. Based on this model, the shape of the low dose part of the curve is determined and this information is then used to estimate the dose of cancer that can cause cancer in a very small fraction of the animals; e.g., one in a million. Thus, just as with non-carcinogens, large margins of safety are built into the way that toxicity values are calculated using data from animal experiments.

Summary

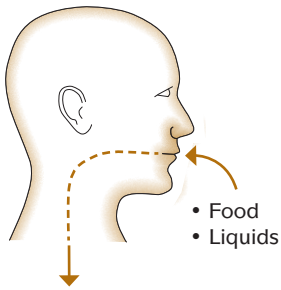
Toxicity is a fairly simple concept but the potency values that are generated to describe the toxicity of agents are complex because they cannot be measured directly in humans but instead must be based on data from studies of animals. Because toxicologists cannot precisely predict human responses from animal data, assumptions must be made to calculate human potency values; assumptions that incorporate margins of safety. Adding to the complexity is that agents that cause cancer and those that cause other types of effects are assessed differently; for the former the potency is measured as the percentage of animals or humans affected and for the latter it is expressed as a safe level.

RITExposure

Exposure is the amount (how much), duration (how long) and frequency (how often) of the dose that an individual experiences. For environmental exposures — as distinct from medical ones — the routes of exposure are: (1) ingestion for solids and liquids; (2) inhalation for gases and particulates; and (3) skin contact for all types of agents. While some agents can cause harm at the site of exposure; for example, the lung or skin, most cause effects only after they have been absorbed into the blood stream and carried throughout the body. In their travel through the body, they have the potential to affect all of the organs in the body — lung, liver, kidneys, heart, brain, etc.



INHALATION



INGESTION

SKIN CONTACT

While it would be ideal to know the dose of the agent that reaches the organ where harmful effects may occur, this is very difficult to determine. Therefore, exposure is usually measured as the dose that the individual comes into contact with — whether it is inhaled, ingested or results from skin contact.

Using Environmental Levels to Estimate Exposure

The most common method of estimating the exposure dose involves combining two different measures:

1. the concentration of the agent in the environmental medium under consideration; for example, the concentration in air for inhaled materials; and

2. the behavior of exposed individuals; for example, the amount of air inhaled by an individual each day as well as the frequency and duration of this exposure.

Thus, the following equation can be used to calculate daily exposure:

MEASURING EXPOSURE USING ENVIRONMENTAL LEVELS

Amount of chemical in air, food, water, etc. **X** Amount of air, food, water inhaled, ingested, etc. **=** Amount of exposure to chemical

As with toxicity assessments, exposure assessments are performed using assumptions that are intended to be protective of human health. For example, the amounts of the chemical in air used in the equation may be the highest value measured rather than an average. For another, the amounts of air inhaled may be high estimates. Multiplying these high values together in the equation leads to exposure values that are exaggerated and have large margins of safety.

Since long term effects are often of most concern, it is important to estimate not only the amount of exposure but also the duration and frequency of exposure. For most exposure

assessments, it is assumed that exposure doses are the same every day — usually for a lifetime. While this is true for laboratory studies on rodents since their daily intake can be carefully controlled, it is not likely for humans. For example, workers who are exposed to a particular chemical on the job are likely to be exposed only eight hours a day five days a week. In addition, people might exert themselves more at work and so inhale more air than when they are away from the job. Thus their exposures will vary over the course of the day and week and are likely to end once they retire.

One way to deal with this variability is to calculate an average exposure; for example, by combining the higher exposures during working hours with lesser exposures at other times. While this seems like a sensible solution, it may not provide the best values for calculating risk because toxicity may occur only after daily high exposures over a long time, and intermittent and/or limited time exposures may result in lower toxicity or no toxicity at all. Thus, it is important to understand the time course as well as the amount of the exposure in assessing risk.

Summary

The most common approach to assessing the amount and time course of exposure is based on knowledge of concentrations of chemicals in the environment; for example, air, and information about the amounts of this air that an individual takes in. Because both concentrations in the environment and daily intake vary over time, estimates of exposure using this approach are not very precise. In addition, the assumptions used in calculating exposures are protective in nature and so exposure estimates contain large margins of safety.

RiskITE

As mentioned previously, all chemicals have the potential for toxicity and can be distinguished from one another by the type of toxicity each produces and the dose required to produce this toxicity. Thus the first steps in characterizing the risk from a chemical are to determine:

1. the type of toxicity it produces; and
2. the dose at which the adverse effects occur.

To characterize the risk for a particular group of people, these must be combined with estimates of:

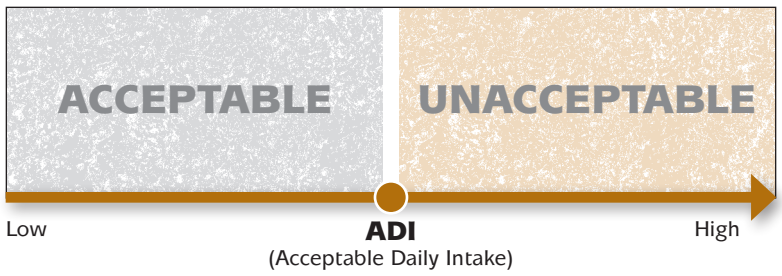
3. the dose to which this group is exposed.

As indicated in the section on toxicity, there are different methodologies for assessing non-carcinogenic and carcinogenic effects. As a result, characterizing the risk of each of these two types of toxicity is performed differently.

Characterizing Risk of Non-Carcinogens

For non-carcinogens, human exposures are compared to the safe dose, often known as the acceptable daily intake (ADI), a protective value calculated from the dose response curve. If the exposure is greater than the ADI, then the risk is considered unacceptable and actions to reduce the risk are often required. Because the ADI includes sizeble margins of safety, it is not possible to predict how large a dose above the ADI will be needed before toxic effects occur.

RISK CHARACTERIZATION FOR NON-CARCINOGENS

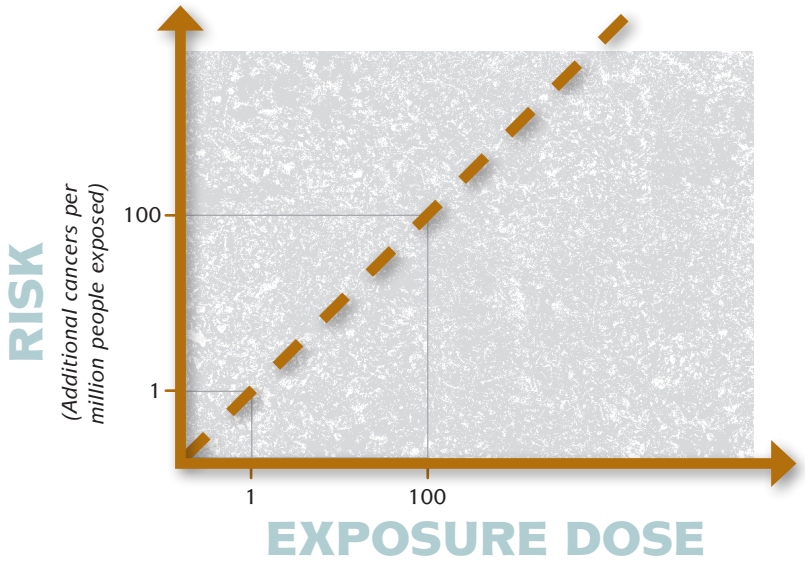


Characterizing Risk of Carcinogens

For carcinogens, the cancer potency (the dose calculated to produce a specific percentage of people with cancer, often one additional cancer in one million exposed individuals), is compared to the exposure dose of the population. The number of cancers produced in each million exposed individuals can then be calculated

by multiplying the exposure dose by the potency. For example, if the exposure dose is 100 times the dose producing one cancer in a million, then there will be an additional 100 cancers per 1 million individuals experiencing that exposure dose. This is illustrated in the following graph:

RISK CHARACTERIZATION FOR CARCINOGENS



Characterizing Risk Using Epidemiology

The above discussion applies to the most common type of risk characterization, that based on laboratory animal studies. However, risk can also be characterized using epidemiological evidence. This type of evidence has one advantage over animal studies; it applies directly to people since they are the ones being studied. No extrapolation from animals is needed. However, there are also a number of disadvantages of epidemiology. One is that it is difficult to separate out the effects of the chemical of concern from all of the other exposures (known as confounders) that people may experience in their daily lives. In addition, there is a large amount of uncertainty in exposure estimates because people move around and behave differently over time. A further limitation of epidemiology is that it

is not very successful at detecting effects that occur in only a small fraction of the population.

Because of all of these limitations, epidemiology is generally most useful in occupational exposure situations because exposures there are often much higher than those of the general population, exposure sources are well-defined, and the amounts of exposure much better known due to monitoring of the workplace environment. In addition, effects are often easier to detect since workers may have regular medical examinations. As a result, occupational epidemiology has allowed scientists to identify a number of chemicals, such as asbestos and lead, that pose serious risks, at least at high exposures.

Due to the problems in applying epidemiology to the general population, it is not surprising that many epidemiological claims based on one or a few studies have not been supported in further studies. Thus, epidemiological evidence is generally of limited usefulness in identifying toxic effects associated with an environmental exposure, and even less helpful in quantifying the risks of this exposure.

Summary

Risk characterizations are most often based on laboratory animal studies and involve a comparison of estimates of population exposure with acceptable intake values or acceptable risk values. For non-carcinogens, population exposures are compared to ADIs. The degree to which the ADI is exceeded is not proportional to the amount of risk so the ADI approach cannot provide an exact estimate of risk, only whether or not an exposure is greater than the acceptable value. For carcinogens, the exposure estimates are compared to doses estimated to produce one in a million risks and the results are often reported as the numbers of individuals per million who are estimated to get cancer from such exposures. Epidemiological studies may also be used to provide qualitative characterizations of risk although they have many limitations including variable and often poorly quantified exposure estimates, the presence of confounders, and the inability to detect effects occurring in small numbers of people.

HOW DO YOU EVALUATE A MEDIA REPORT ABOUT RISK?

ASSESSING THE QUALITY OF THE EVIDENCE

The first step in evaluating a media report about the risks of chemicals is to clearly identify the claim being made. While it is tempting to think that the headline of an article always summarizes the claim, this may not be the case, since headlines of media reports are generally written by someone other than the reporter. Because of space limitations and/or the desire to attract the reader's attention, the headline may be oversimplified and/or may emphasize the most dramatic interpretation of the claim. Thus, it is important to examine each article in detail rather than to rely on the headline.

Once you have identified the claim, the second step is to make an assessment of the quality of the evidence. Important characteristics that affect the quality of the evidence are: the consistency of the data, the source of the research cited, the type of study performed, and the completeness of the data. This assessment provides critical information that will help you decide if the evidence is of high enough quality that applying the RITE process will be useful in your evaluation of the claim.

How does the consistency of the data affect the quality of the evidence?

To evaluate consistency, start by carefully examining the media report to determine whether or not it indicates that there are other studies on this same topic in addition to the one described in the article. It would also be helpful to look at other media reports about this same claim to see if they might mention such studies. If none of the articles mention any other research on this claim, you should view it with a critical eye since only those results that have been reproduced by other scientists are considered valid.

If media reports do provide information about other research on this claim, are the results of the various studies consistent with one another? If not, the claim is considerably weakened. It is the way that the evidence fits together, rather than any one study, that guides scientists in assessing the quality of the claim.

How does the source of the research affect the quality of the evidence?

Determining the source of the evidence on which the claim is based can be very helpful in assessing its quality. The most credible source of evidence is research published in the scientific literature. Evidence based on press releases, research presented at a meeting, statements by groups or organizations, or personal experience are not nearly as credible. Although it may be tempting to rely on the last of these alternatives, personal experience, especially if it is the experience of someone you trust; e.g., a doctor, family member or friend, evidence of this type is rarely reliable. Individuals, even physicians, are often not aware of all of the possible factors that could explain effects that are observed. As a result, they may not be able to tell if there is a real connection between a chemical and an effect or if the apparent association is due to chance. Thus, claims based on sources other than scientific journal articles should be considered very skeptically.

How does the type of study affect the quality of the evidence?

Although scientific journals are the best sources, not all published evidence is equally helpful in evaluating a claim. For

example, studies of the effects of chemicals on cells or tissues in test tubes are not as useful as research on whole animals because chemicals administered directly to these cells or tissues in test tubes have not been processed by the body before reaching these cells. This is very important because body processes may change both the amount and the form of the chemical reaching the cell or tissue. In addition, cells in test tubes may react differently than those in the body, so it is impossible to know how the doses administered to the cells in the laboratory correspond in amount and effect to doses that reach these same cells in an animal or human who has experienced chemical exposure. As a result, such laboratory studies are of limited usefulness in assessing the risks to humans exposed to chemicals.

How does the completeness of the data affect the quality of the evidence?

Media reports about the risks of chemicals include a variety of claims. Often, the claim is that there is a risk because a scientific study links a chemical to a harmful effect. A headline of this type is "Chemical X Linked to Baldness, Study Shows" Other claims suggest that there is a risk because a chemical is present in the environment. A headline of this sort might read "Carcinogenic Chemical Found in Drinking Water". However, it is important to recognize: (1) that a link is not the same as a risk, and (2) the presence of a chemical is not equivalent to a risk.

In both of these cases, it is important to look not only at the quality of the study behind the report but also the completeness of the information that is provided. In particular, for you to assess whether or not there is a risk, you need to have information about both the amount of exposure humans are likely to experience and the amount of chemical needed to cause the toxicity mentioned in the headlines. If the exposures required to cause these effects are much higher than the ones humans experience, then there is little or no risk.

Other types of information, such as the route and duration of exposure, are also critical to your evaluation. If the appropriate toxicity, exposure and risk information are missing or incomplete it is difficult to successfully apply the RITE approach.

Summary

The answers to the questions posed in this section can be used to assess the quality of the evidence used to support a claim. They reveal that there are a small number of factors that can have a large impact on the quality of the evidence. The table below provides a summary of these factors and the impacts they have on quality. If the factors listed as leading to lower quality are present in a report they should make you very skeptical of the claim and suggest that applying the RITE approach is not worthwhile. However, if the factors listed in the left hand column are present, this suggests that the evidence in the report is of much higher quality and that applying the RITE approach will provide you with good guidance in assessing the claim.

EVALUATING THE QUALITY OF THE CLAIM

Factors Leading to Higher Quality	Factors Leading to Lower Quality
Multiple studies	Single study
Results consistent	Results inconsistent
Published in journal	Not published in journal
Based on experiments or epidemiology	Based on personal experience
Studies of whole animals	Studies of isolated cells or tissues
Evidence is thorough	Evidence is incomplete

EVALUATING THE SCIENTIFIC BASIS OF THE CLAIM USING RITE

Once you have clearly identified the claim and evaluated the quality of the evidence behind the claim, you are ready to evaluate the scientific basis of the claim using the RITE approach. As discussed earlier, applying the RITE approach depends on whether the:

1. claim is based on animal experimentation or epidemiological studies, and

2. claimed effects are carcinogenic or non-carcinogenic in nature.

Since the RITE approach is based on understanding exposure, toxicity and risk, this section will address the role each plays in evaluating the scientific evidence used to support the claim.

What does the exposure information tell you about the claim?

If the claim is based on laboratory studies, it can be assumed that the animals were exposed every day to the same dose for up to a lifetime. However, this is not true for epidemiological studies. In such studies, it is quite possible, for example, that the amount of human exposure was measured at only one time and there is no information about how long or how frequently the exposures occurred. Since most claims are about effects that occur after long term exposure, information about the duration and frequency of exposure is crucial and, in the absence of these critical data, the claim can not be validated.

Since the route of exposure can greatly affect the type of toxicity and the dose at which it may occur, a claim should specify the routes of exposure in the experimental or epidemiological studies. If the route of exposure in environmentally exposed humans is different from that in the studies supporting the claim, then the claim is considerably weakened.

What does the toxicity information tell you about the claim?

When animal studies are used as evidence of human toxicity, the toxic effects should be the same or very similar in both animals and humans. While this might seem obvious, some published claims have suggested that a specific effect in animals; e.g., a small reduction in the number of offspring, is evidence for a very broad range of reproductive effects in humans. The more dissimilar the effects are in animals from those claimed for humans, the less validity the claims have.

Similarly, when epidemiological studies are used to support a claim, the effects that were measured should be the same as the effects that are claimed. While it might seem that these would be identical, this is not always the case. In some instances, the study reports on a change in a chemical characteristic, such as a hormone level, and the claim is about some effect on human functioning, such as altered reproduction. Without evidence conclusively linking the chemical change to a harmful effect, the claim is not scientifically supported.

How can you evaluate risk characterizations based on animal evidence?

Reports about claims generally do not provide risk values; that is, the carcinogenic potency or the acceptable daily intake, that have been calculated for a chemical. However, these are often implicit in the media report. For example, a claim based on animal studies may include an estimate of the number of individuals who will contract cancer as a result of exposure to a chemical. From the RITE discussion, we know that this estimate is based on the cancer potency value and the size of the population. Similarly, a claim of non-carcinogenic effects based on animal studies may state that the exposure is a number of times higher than the acceptable value without explicitly specifying what the acceptable value is.

The RITE approach helps us to evaluate such reports. From RITE, we know that the calculation of carcinogenic potency is based on the results of high dose animal studies, results of questionable applicability to humans. Also, potency values are designed to be protective rather than predictive and so are likely to be greatly exaggerated. Combining such values with exposure values designed to be protective leads to estimates of human cancer risk that are likely to greatly overestimate the real risk.

Similarly, the acceptable daily intake (ADI) values are likely to significantly exaggerate the risks of non-carcinogens since these values include large margins of safety. Further, the ADI does not provide any estimate of the size of the risk at the ADI or at any value above it. Last, the exposure values used to calculate risks from non-carcinogens are protective in nature. Thus, a statement that human exposures exceed the ADI cannot be taken to mean that toxicity will occur. It is likely that human exposure doses will have to be much greater than the ADI before harmful effects can be expected.

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EVALUATING THE VALIDITY OF ANIMAL EVIDENCE FOR ASSESSING HUMAN RISK

Factors Increasing Validity	Factors Decreasing Validity
Similar effects in claim and in study results	Different effects in claim and in study results
Same routes of exposure in claim and in study results	Different routes of exposure in claim and in study results
Comparable exposures in claim and in study results	Claim based on high-dose animal studies

How can you evaluate risk characterizations based on epidemiology?

A different approach needs to be taken when evaluating risk claims based on evidence from epidemiological studies since neither cancer potency factors nor acceptable daily intakes are used. Instead, a comparison is drawn between the percentage of people who have been exposed to the chemical and show harmful effects and the percentage of those who have not been exposed to the chemical and show these same effects. The result of this comparison is often expressed as a risk ratio (the ratio of the percentage of the exposed population showing effects divided by the percentage of the unexposed population showing toxicity) Questions you should ask about such studies include:

1. are the people who were studied typical of the general population or are they special in some way?
2. has the study population been chosen at random?
3. how large is the study population?
4. have confounders (other possible causes for the toxicity) been taken into account?

If the people studied are special in some way; e.g., they are all nurses or a specific ethnicity, the results are not likely to mirror those for the general population. Also, if the subjects are not randomly selected; for example, include only volunteers, their

particular characteristics may influence the applicability of the study to the general population. Further, the size of the studied population is important; the smaller it is, the higher the probability that the results are due to chance rather than a real effect of the chemical.

Confounders are unmeasured characteristics of the exposed population that might affect the outcome of the study. Age, income, and smoking are a few of the most common confounders since they affect the risk of many diseases. If these factors are not taken into account when interpreting a study, the results are suspect. Thus, if confounders are not part of the epidemiological evidence, you should be skeptical of claims based on this evidence.

A last question is whether the study relies on the memories of the participants for estimates of exposure. If it does, this is likely to lead to significant uncertainties in exposure estimates and may introduce bias - such as people who have experienced harm being more likely to "remember" exposures. Clearly, the farther into the past recollections are gathered, the less reliable the study results.

EVALUATING THE VALIDITY OF EPIDEMIOLOGICAL STUDIES FOR ASSESSING HUMAN RISK

Factors Increasing Validity	Factors Decreasing Validity
Large study population	Small study population
Random selection of subjects	Non-random selection of subjects
Data based on direct observations	Data based on people's memories
Data well characterized	Data poorly characterized
Confounders taken into account	Confounders not taken into account

GLOSSARY

Absorption: the movement of an agent into the bloodstream after ingestion, inhalation or skin contact.

Acceptable Daily Intake: a protective estimate of the greatest amount of exposure that is likely to be without significant adverse effect.

Animal studies or animal experimentation: research on laboratory animals, often rodents (rats and mice), to understand the types of effects that agents cause and the doses needed to cause these effects.

Cancer: a disease characterized by abnormal and uncontrolled growth of cells.

Cancer potency value: a measure of how large a dose is needed to produce a specific number of cancers in a population.

Carcinogenicity: the ability of a substance to cause cancer.

Confounder: an agent, other than the one under study, that contributes to adverse effects, For example, secondhand cigarette smoke may be a confounder in studies of the effects of another environmental contaminant. If confounders are not taken into account, the conclusions of an epidemiological study may be incorrect.

Dose: a measure of the amount of substance administered to or taken up by an organism.

Dose-response curve: a pictorial representation of how an organism responds to exposure as the dose increases.

Effect: the response produced due to exposure to an agent.

Evidence: data collected scientifically. In risk assessment this includes both toxicity and exposure data.

Epidemiology: a study of the patterns of disease and the factors that may be associated with specific diseases

Exposure: the dose of an agent that an individual experiences - by ingestion, inhalation or skin contact. It includes the amount, the duration and frequency of this dose.

Extrapolation: using information from one situation to draw conclusions about another situation. For example, to estimate effects at low doses from studies performed at high doses.

Isolated cells or tissues: cells or tissues that have been removed from organisms and are studied in the laboratory.

Margin of safety: the difference between the dose that an individual experiences and the dose that can cause an adverse effect.

Non-carcinogen: a substance that causes adverse health effects other than cancer.

Occupational: pertaining to work or the work environment.

Potency: a measure of the magnitude of the dose needed to cause harm.

Risk: the possibility that a substance will cause harm.

Risk assessment: the process of estimating the type and size of risk to human health posed by exposures to chemicals or other agents.

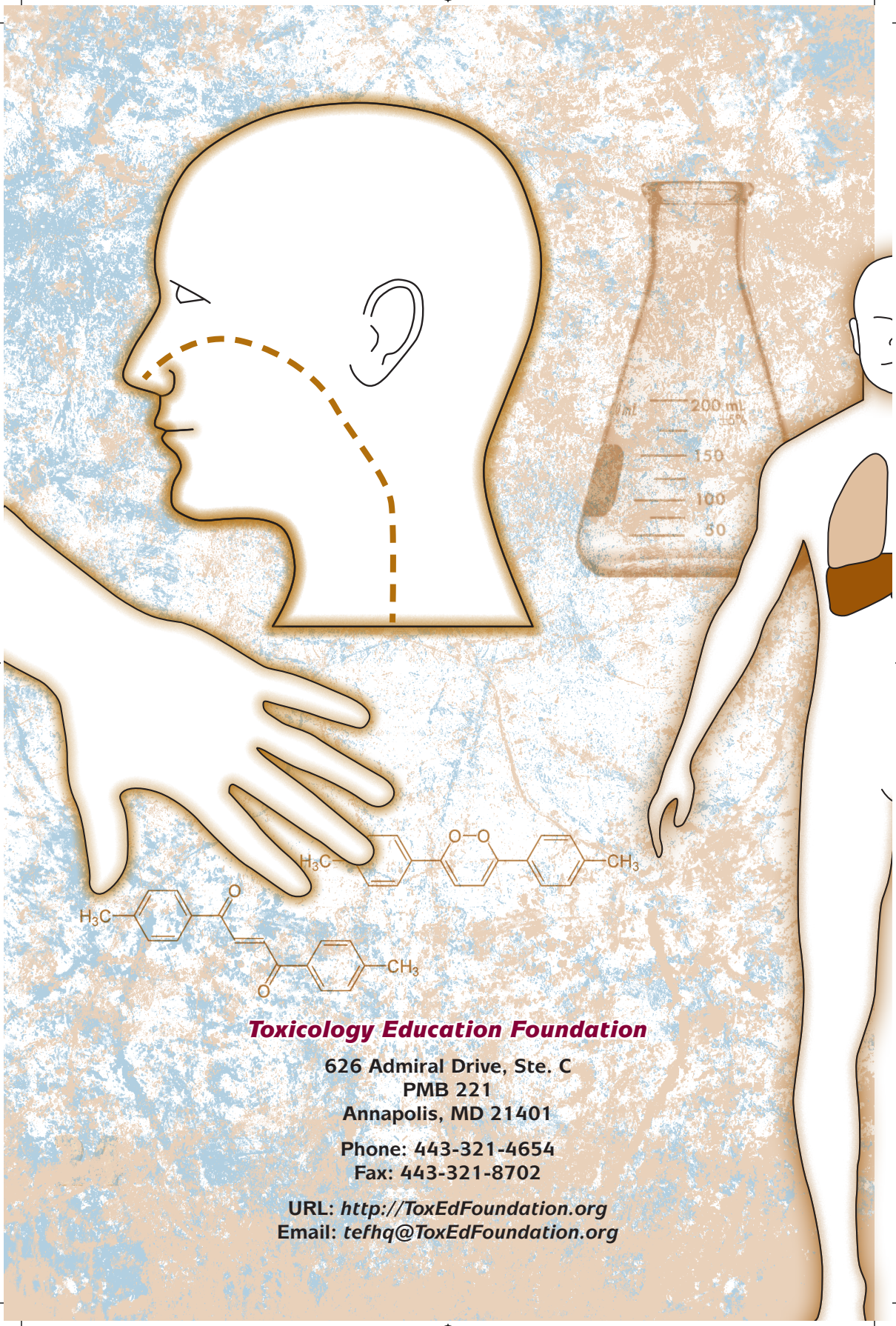
Risk ratio: the ratio of the risk (or incidence) of disease or death in the exposed population to the risk in the unexposed population. A risk ratio greater than 1.0 suggests that exposed individuals are at greater risk than those who are not exposed.

Safe dose: highest dose that is unlikely to cause an adverse effect

Toxicity: the potential of chemicals or other agents to cause harmful health effects.

Toxicology: the study of harmful interactions between chemical, physical, or biological agents and biological systems.

Validity: amount of confidence that the conclusions from a scientific study are accurate.



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