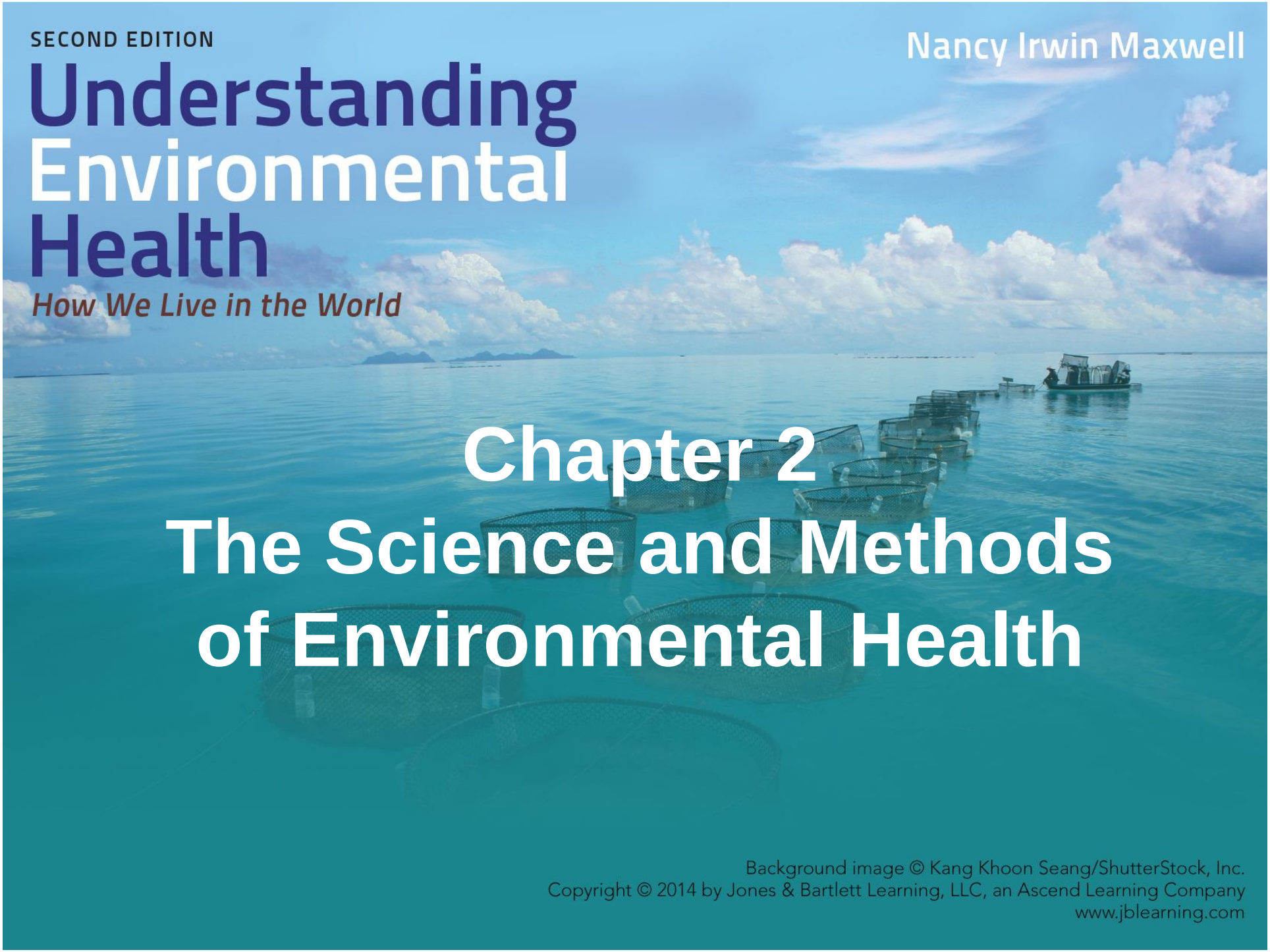

SECOND EDITION

Understanding Environmental Health

How We Live in the World

Nancy Irwin Maxwell

Chapter 2
The Science and Methods of Environmental Health

2.1 Understanding Environmental Hazards to Human Health

2.2 Responding to Environmental Hazards to Human Health

2.3 Precautionary Approaches in Environmental Health Policy

The Fate and Transport of Environmental Contaminants

Toxicology: The Science of Poisons

Exposure Assessment: An Applied Science

Epidemiology: A Quantitative Research Method

Community-Based Participatory Research

Introduction to fate and transport

- Key definitions
  - Fate: chemical or physical transformations of contaminants in the environment
  - Transport: movements of contaminants with or between environmental media

Physical-chemical properties

- Fate and transport of chemicals is affected by their physical-chemical properties.
  - Volatility
  - Aqueous solubility
  - Lipophilic tendency

Physical-chemical properties

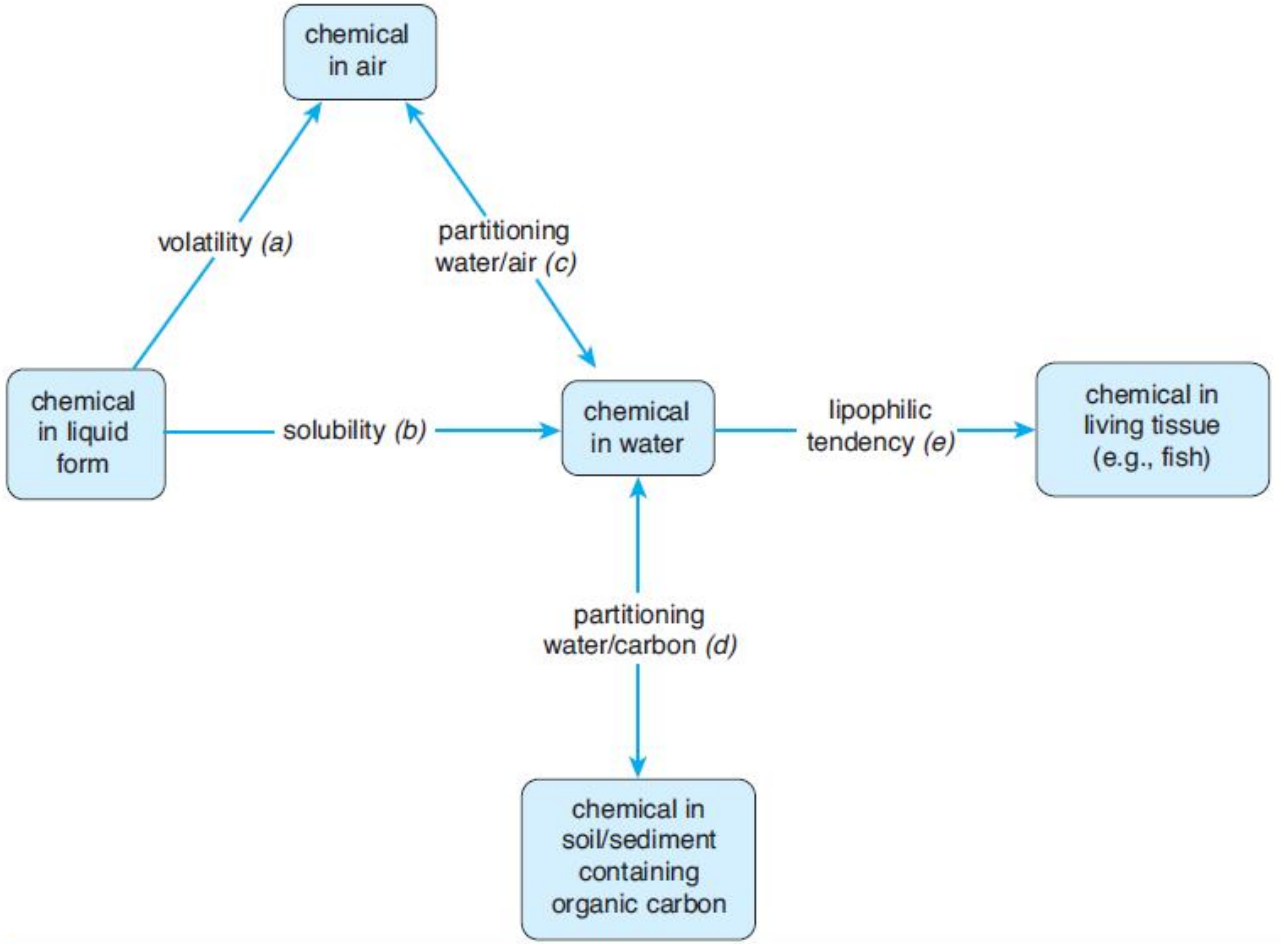

FIGURE 2.1 Physical–chemical properties of chemicals.

Physical-chemical properties

- Consequences of lipophilic tendency
  - Bioconcentration—movement into fatty tissues of organisms
  - Bioaccumulation—building up over time, in individual organism
  - Biomagnification—building up over time, across the levels in a food chain

Physical-chemical properties

- Generally, higher-molecular-weight chemicals are:
  - Less volatile and less water-soluble.
  - More lipophilic and more persistent.
- Persistence in environment
  - Quantified as a half-life in air, water, or soil
  - Affected by environmental conditions

The atmosphere

- Troposphere provides natural greenhouse effect
  - Earth absorbs energy from Sun; radiates some of this energy as heat
  - Trace gases in troposphere absorb this heat; re-radiate it back toward the earth
  - Natural greenhouse gases: water vapor, carbon dioxide (CO_2), methane (CH_4), nitrous oxide (N_2O), ozone (O_3)

The atmosphere

- Stratosphere provides protection from UV radiation
  - Includes a layer where concentration of ozone (O_3) is much higher
  - This ozone layer absorbs much of incoming ultraviolet radiation in sunlight

The atmosphere

- Global winds transport pollutants

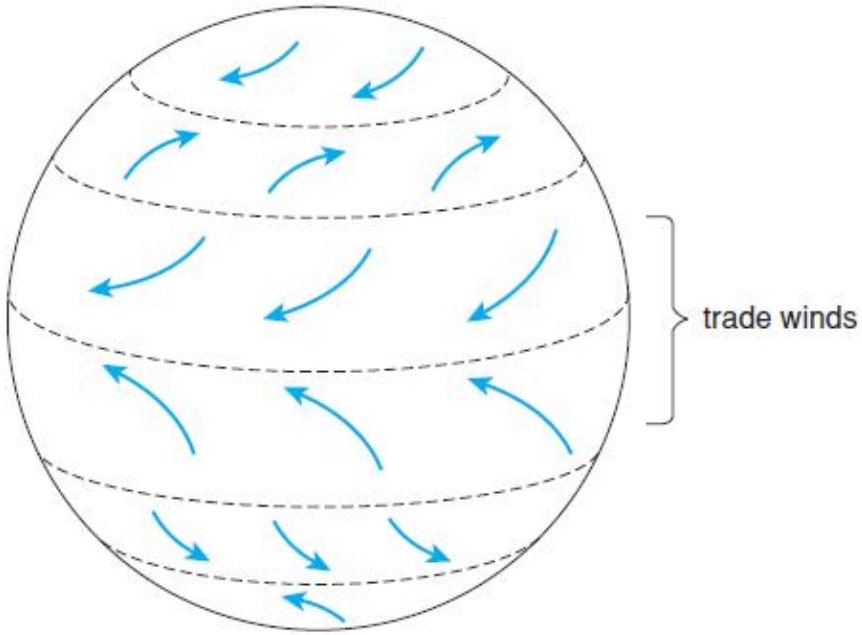

FIGURE 2.2 Global air circulation patterns.

The atmosphere

- Local atmospheric conditions
  - Normal: surface air, warmed by earth, rises; cooler, denser air above sinks; thus continuous mixing and low pollutant concentrations
  - Temperature inversion: cooler surface air trapped below warmer air above; thus little mixing and high pollutant concentrations at ground level

Water in the ambient environment

- Water in the global environment
  - Global hydrologic cycle connects water on local, global sales; see diagram →
  - Surface ocean currents transport pollutants globally
  - Deep ocean currents are driven by differences in density (thermohaline circulation)

Water in the ambient environment

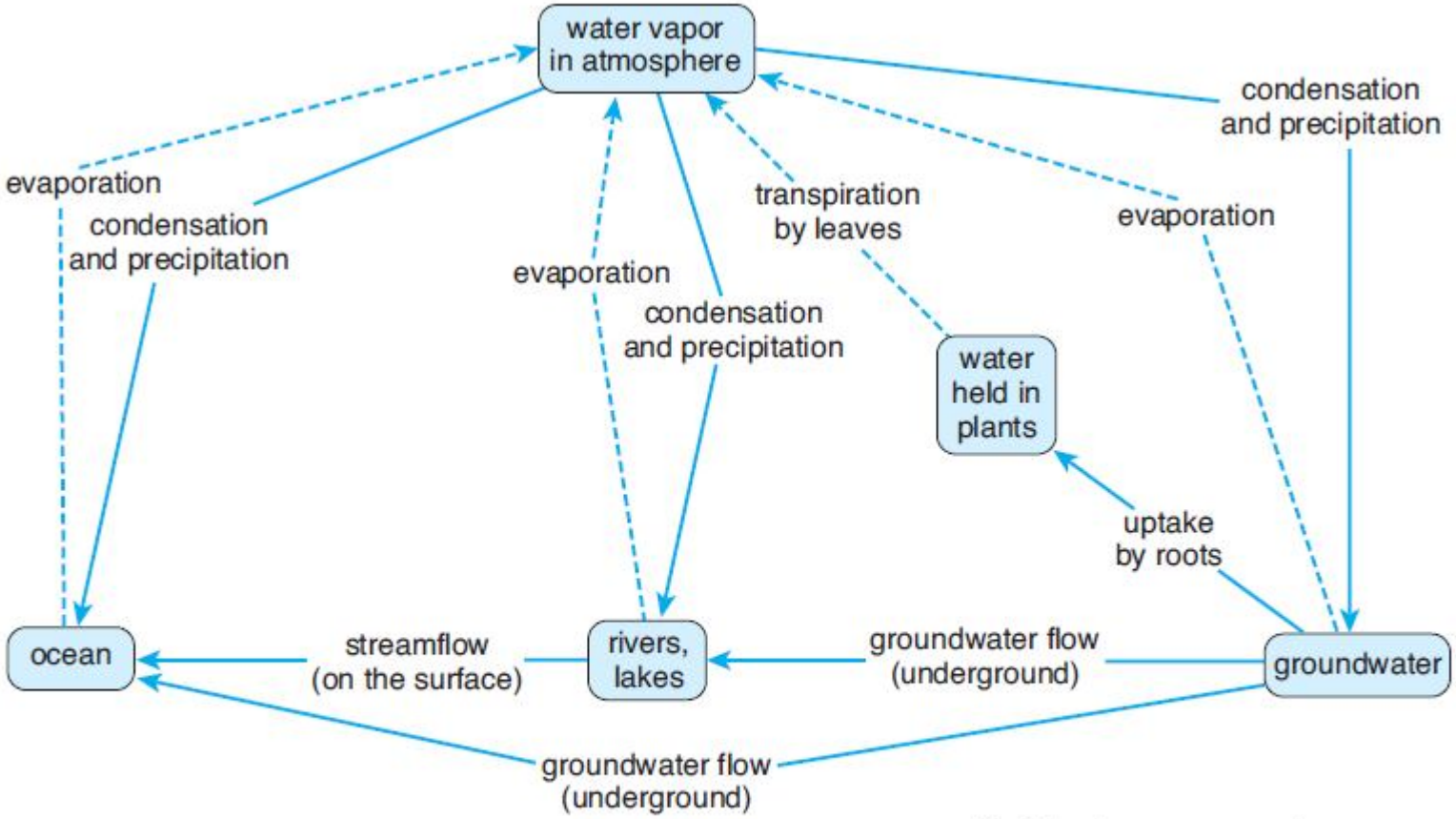

FIGURE 2.3 The hydrologic cycle.

Water in the ambient environment

- Fresh surface water
  - Drainage basin (or watershed): the area drained by a river and tributaries
- Groundwater
  - Aquifer: geologic material porous enough to hold and transmit water
  - Confined versus unconfined (water table) aquifer

Water in the ambient environment

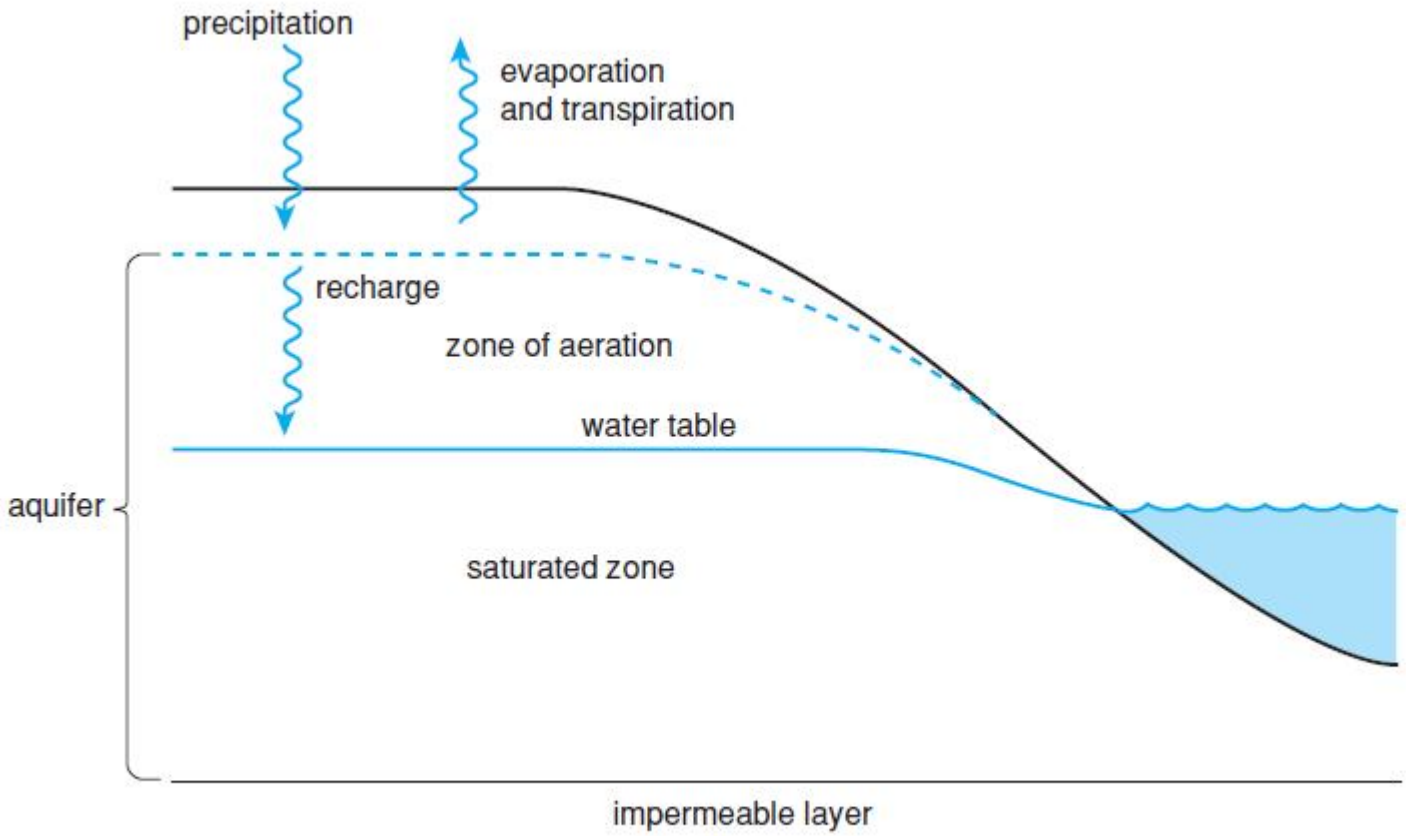

FIGURE 2.5 A water table aquifer.

Water in the ambient environment

- Water table: boundary between unsaturated and saturated zones
- Above the water table: zone of aeration
  - Water enters as precipitation, leaves by evaporation and transpiration
  - Water trickles downward to water table (recharge); water table rises and falls
  - Recharge can leach contaminants from wastes, becoming leachate

Water in the ambient environment

- Below the water table: saturated zone
  - Water can move in any direction
  - “Upgradient,” “downgradient”
- Well drilled into aquifer
  - In water table aquifer, water in well rises to level of water table
  - In confined aquifer, water is under pressure
    - Rises above top of aquifer
    - May rise above ground surface (artesian well)

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Introduction to toxicology: the science of poisons

- Toxicology—the science of the effects of toxic substances, and of their "fate and transport" in the body
- Major routes of exposure
  - Inhalation, ingestion, dermal contact
- Toxins versus toxicants

Exposure and dose

- The human envelope—boundary that separates the interior of the body from the exterior environment
- Exposure—contact with the human envelope
- Dose—a quantification of exposure

Disposition of chemicals in the body

- Toxicokinetics—the disposition of toxicants in the body
  - Absorption
  - Distribution
  - Metabolism
  - Storage
  - Excretion
- Toxicodynamics—effects in the body

Disposition of chemicals in the body

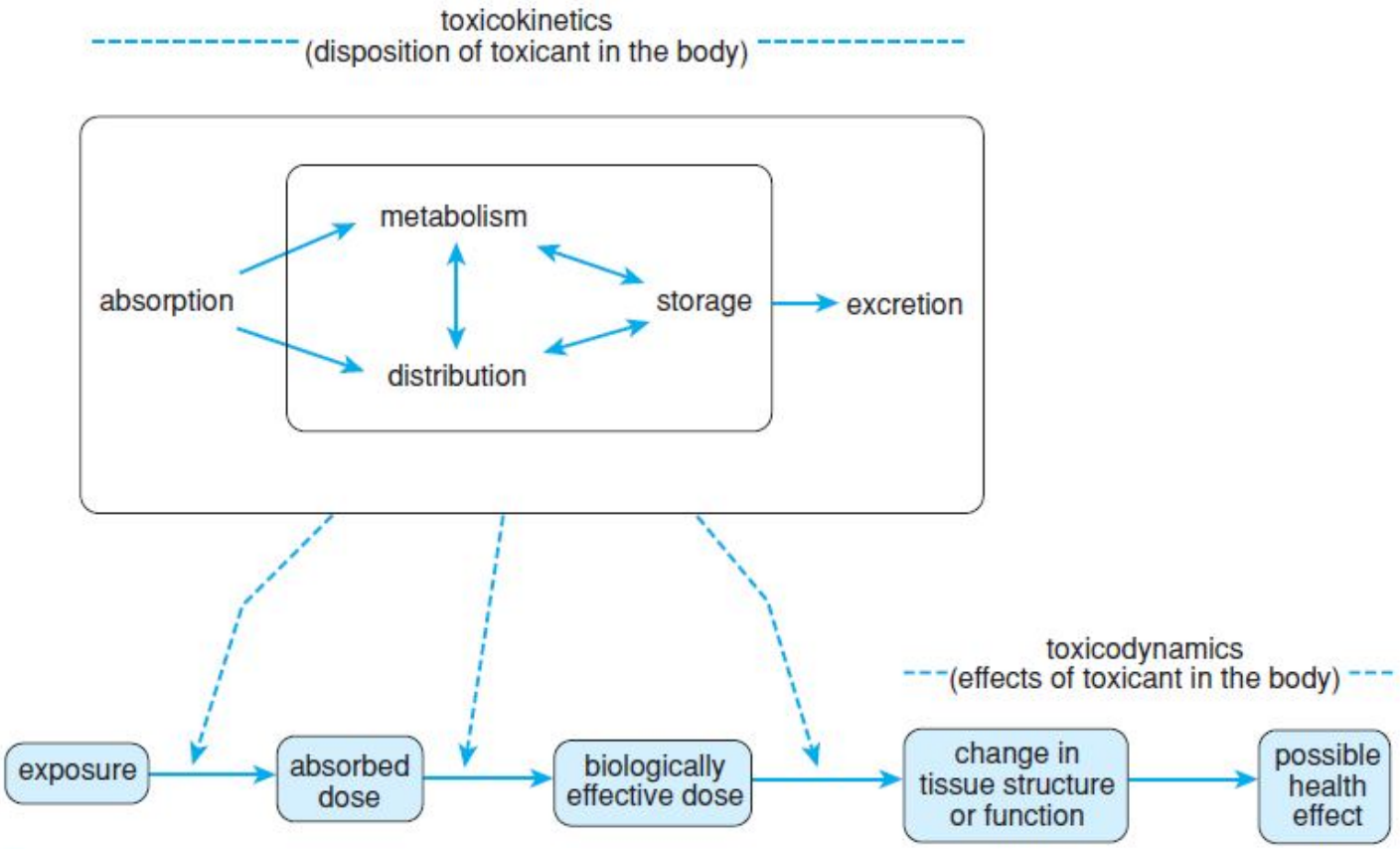


FIGURE 2.6 Disposition and effects of toxicants in the body.

Source: Special thanks to Wendy Heiger-Bernays and Michael McClean.

Disposition of chemicals in the body

- More on toxicokinetics
  - Body burden
  - Absorbed dose: quantity that passes through the human envelope
  - Biologically effective dose: quantity available to interact with a vulnerable tissue
  - Synergism, antagonism

Carcinogenesis

- Cancer: a disease in which cells multiply without restraint
  - Tumor invades tissue of origin
  - And metasticizes into other tissues
- Cancer results from an accumulation of mutations
  - Mutation: change to the DNA of a cell

Carcinogenesis

- Key mutations in carcinogenesis
  - Increase the activity of genes that instruct the cell to divide (oncogenes); or
  - Decrease the activity of genes that instruct the cell to stop dividing (tumor suppressor genes)
- Carcinogen: any agent that increases cancer risk at any stage in process

Carcinogenesis

- Simple view of stages in carcinogenesis
  - Initiation— initial mutation in a cell either
    - Enhances instructions to cell to divide; or
    - Dampens instructions to stop dividing
  - Promotion—initiated cell is stimulated to divide, becoming a benign tumor
  - Progression—mutations → cascading cell division → malignant tumor

Gene-environment interaction

- Models of gene-environment interaction
  - Genetic makeup increases exposure to environmental risk factor
  - Genetic makeup increases susceptibility to environmental risk factor
  - Genetic makeup and environmental factor are independent risk factors

The dose-response relationship

- Quantitative relationship between dose and effect (response)
  - Often summarized in graph
  - Dose on x-axis; response on y-axis
- Two key characteristics:
  - Slope (potency of effect)
  - Threshold (potential for safe dose)

The dose-response relationship

- A schematic representation

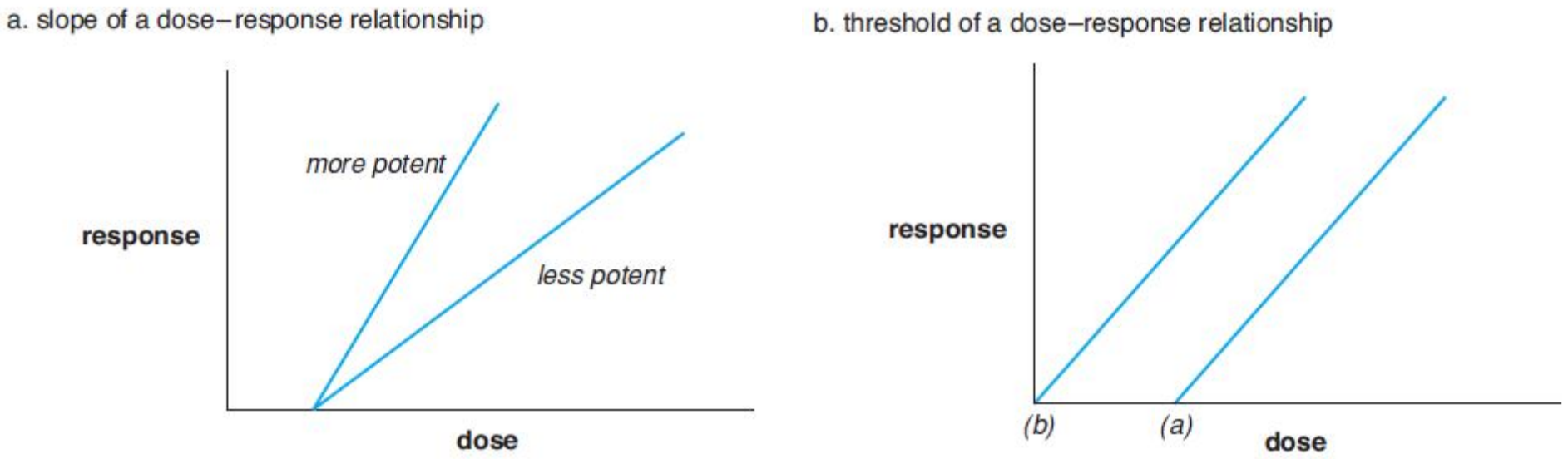


Figure 2.8 A schematic representation of the basic dose–response relationship.

The dose-response relationship

- A more realistic flattened *S*-shape

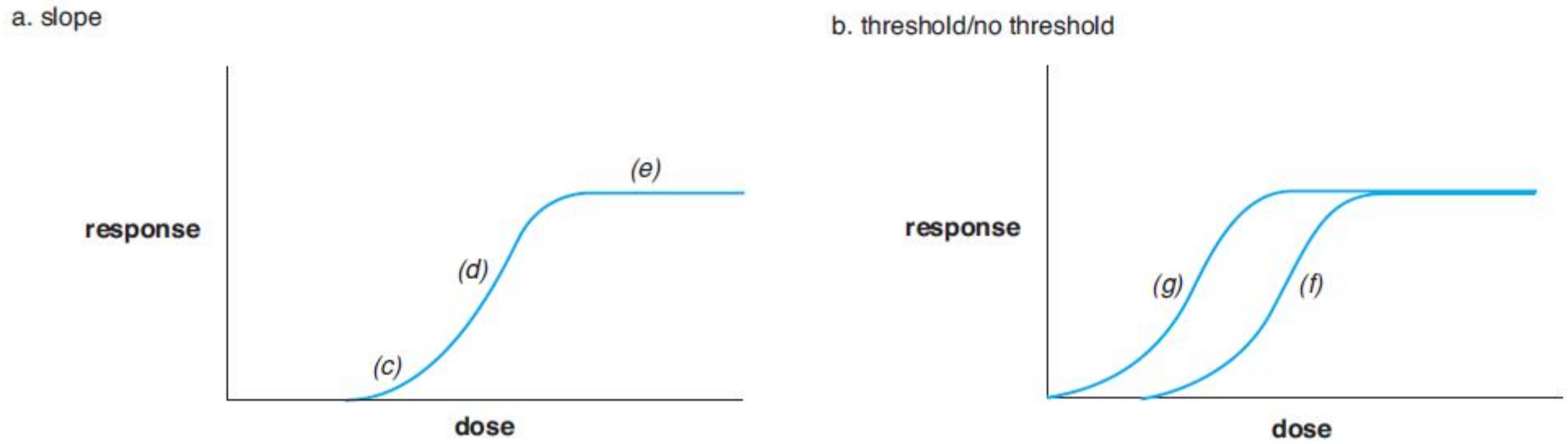


Figure 2.9 The dose–response curve.

Toxicity testing

- Regulatory toxicology
  - Tests chemicals' toxicity in living things
  - Done to support regulatory decision-making
- Preliminary testing
  - Test of mutagenicity in bacteria
  - Study of acute toxicity in rodents yields LD_{50}
  - Subchronic rodent bioassay (90 days)
    - Suggests doses for chronic bioassay
    - Identifies target organ and range of effects

Toxicity testing

- Chronic rodent bioassay (2 years)
  - 3 exposure levels, ideally including:
    - Dose high enough to test for cancer
    - Dose low enough to reveal no-effect level
  - Unexposed control group
  - Results used to create dose-response curves for various health effects

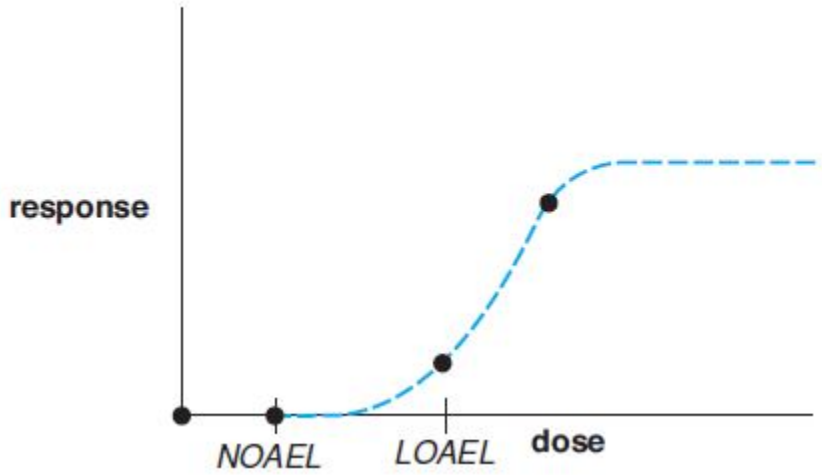
Toxicity testing

- Some doses are given special names
  - *Highest* non-zero dose at which *no* effect was observed = No Observed Adverse Effect level (NOAEL)
  - *Lowest* dose at which an effect *was* observed = Lowest Observed Adverse Effect Level (LOAEL)
- If a study shows both a NOAEL and a LOAEL, can infer that the threshold is between them

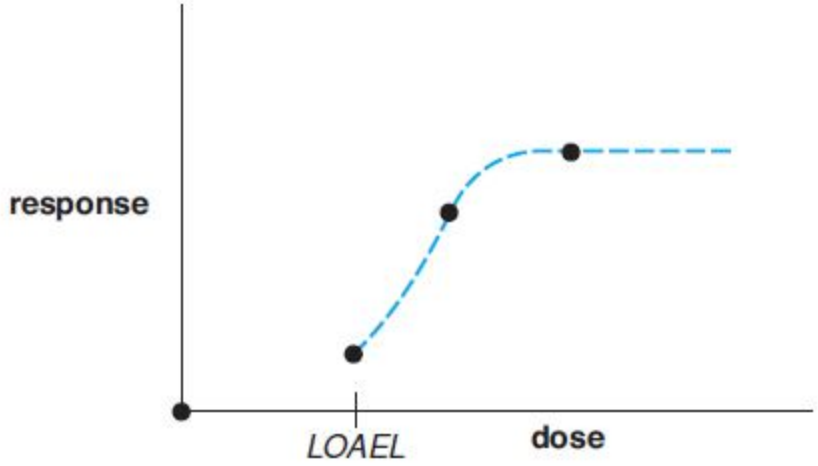
Toxicity testing

– Two dose-response curves

a. dose–response curve showing NOAEL and LOAEL



b. dose–response curve showing only LOAEL



Toxicity testing

- Dose-response curves developed for cancer and various non-cancer effects.
- Reproductive vs developmental effects:
  - *Reproductive* toxicity: effect on reproductive capacity of organism
  - *Developmental* toxicity: effect on developing organism, including teratogenesis

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Introduction to exposure assessment: an applied science

- Goal is to quantify exposure.
- Methods draw on understanding of both:
  - Environmental science (fate and transport of toxicants in environment)
  - Toxicology (fate and transport of toxicants in the body)

Completing the conceptual model of exposure

- Conceptual model of exposure begins with source of exposure . . .

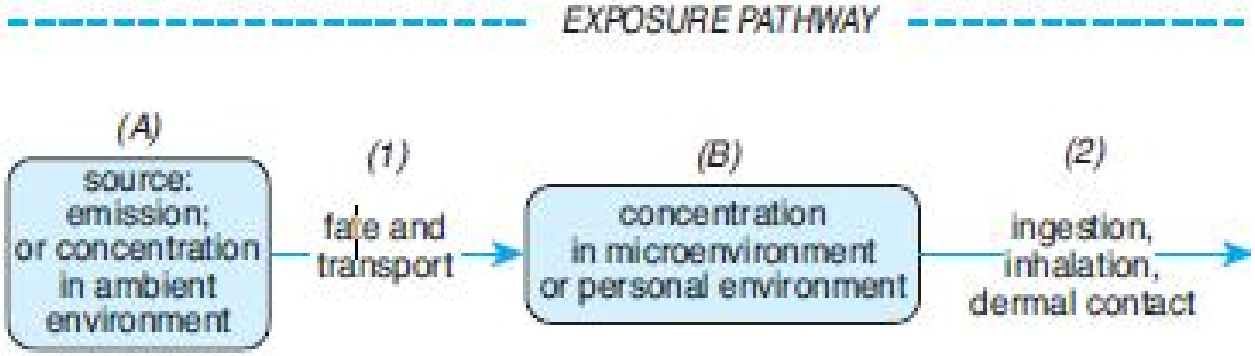

FIGURE 2.11 A conceptual model of fate and transport, exposure, dose, and effect.

Source: Special thanks to Wendy Heiger-Bernays and Michael McClean.

Completing the conceptual model of exposure

- . . . and concludes with toxicokinetics and effects in the body.

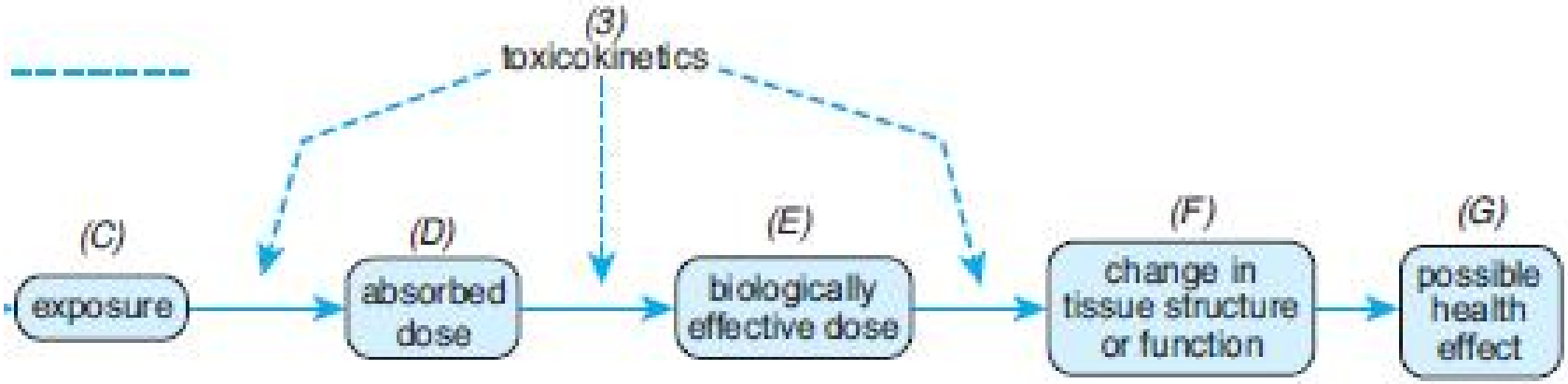

FIGURE 2.11 A conceptual model of fate and transport, exposure, dose, and effect.

Source: Special thanks to Wendy Heiger-Bernays and Michael McClean.

Quantifying exposure

- Translating event of exposure into a dose estimate.

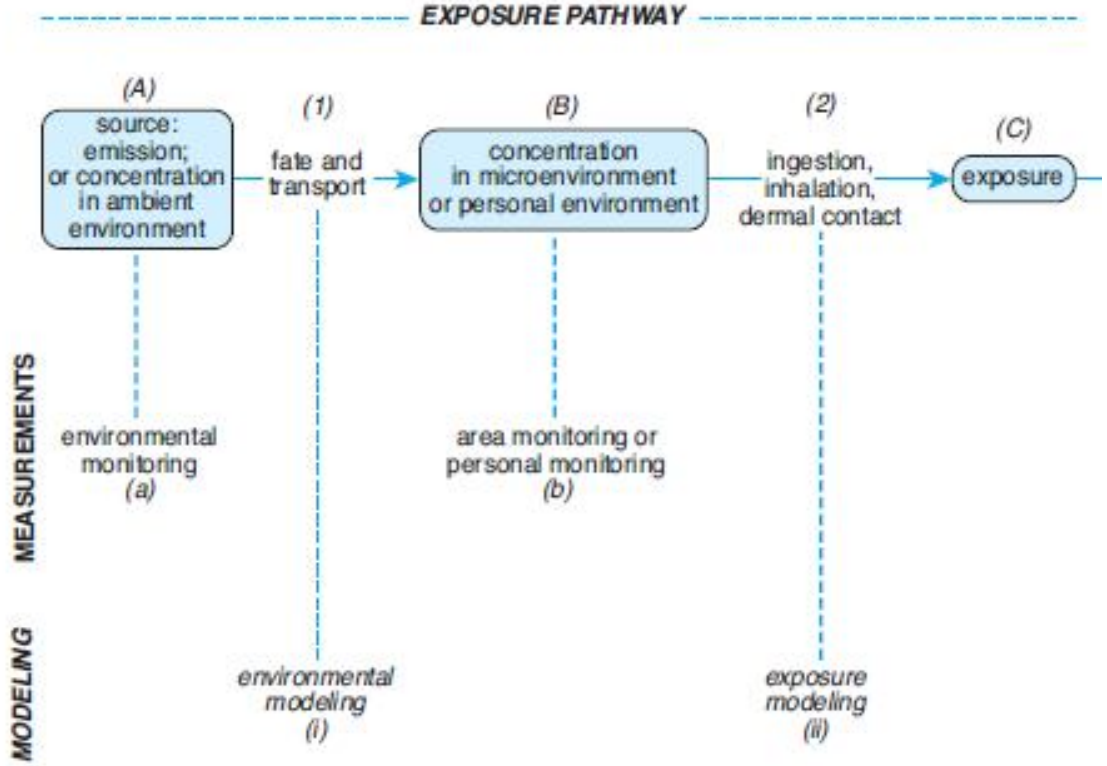

FIGURE 2.12 Measurement and modeling of fate and transport, exposure, dose, and effect.
Source: Special thanks to Wendy Heiger-Bernays and Michael McClean.

Quantifying exposure

- Tools for area monitoring and personal monitoring

(a)

(b)

Figure 2.13 Area monitoring: A filter inserted into the nozzle of a vacuum cleaner (a) collects dust to be analyzed in a laboratory. Personal monitoring: A portable sampling device (b) incorporates a pump that takes a continuous air sample near the subject's breathing zone; the device also collects a sample of particulate matter over the whole period.

Quantifying exposure

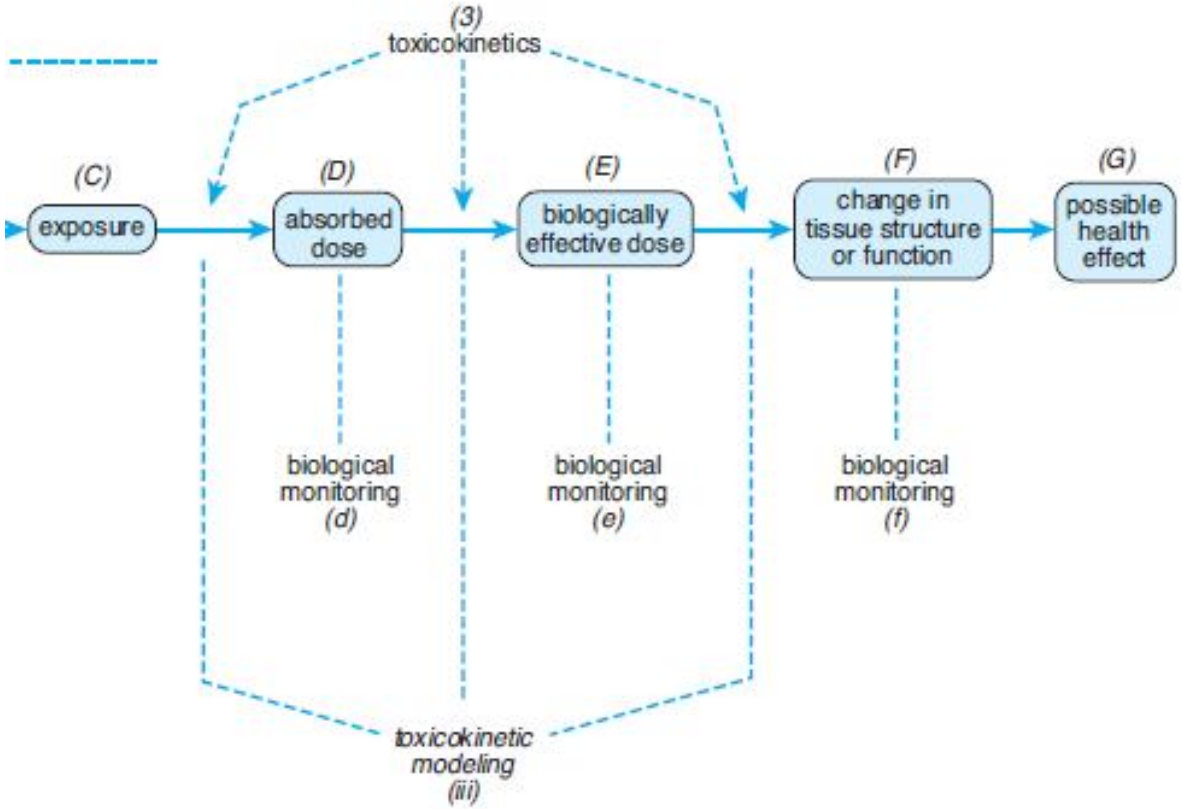

FIGURE 2.12 Measurement and modeling of fate and transport, exposure, dose, and effect.

Source: Special thanks to Wendy Heiger-Bernays and Michael McClean.

Quantifying exposure

- Units of absorbed dose: mg / (kg*day)
  - Mass of toxicant
  - Normalized to body weight
  - Averaged over time
- Other sources of exposure info
  - Questionnaires, diaries
  - Surrogate measures
  - Geographic information systems (GIS) →

FIGURE 2.14 This GIS map of a chemical plume in groundwater shows that private wells on nearby properties located upgradient of the source are unaffected by the contamination, whereas wells on more distant properties located downgradient are at risk.

Source: Courtesy of Verónica Vieira.

Quantifying exposure

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Epidemiology: A Quantitative Research Method

Community-Based Participatory Research

Epidemiology: a quantitative research method

- Documents the distribution of health and illness in populations.
- Links health outcomes to risk factors.
- Environmental epidemiology
  - Draws on toxicology and exposure assessment.
  - Strengths: in human beings; realistic exposures; meaningful outcomes

Key measures of health status of populations

- Incidence—new cases of disease during given time period
- Mortality—the incidence of death
- Prevalence—proportion of population with disease at given point in time
- Morbidity—a diseased (morbid) state
- Disability—a substantial limitation on a major age-appropriate life activity

Descriptive epidemiology

- Describes patterns of disease in populations.
- Case series—noteworthy set of cases
- Surveillance—tracks & compares disease rates across places, diseases, time
  - Surveillance biomonitoring—use of biomonitoring to document rates of exposure or disease in populations.

Descriptive epidemiology

- Crude incidence rate
  - Numerator: number of new cases in population during time period
  - Denominator: person-years at risk
  - Ex: 300 new cases in population of 100,000 over 10-year period → crude incidence rate of 0.0003 per year

Descriptive epidemiology

- Methodological challenge:
  - Many diseases occur at different rates in the two sexes or in different age groups.
  - Thus crude rate is affected by age distribution and M-F distribution.
  - Thus crude rates for different populations, or same population at different times, are not comparable.

Descriptive epidemiology

- Solution: standardization
  - Age: make populations comparable by using a third population as a reference
  - Sex: calculate rates separately for M and F
- Standardized rate (hypothetical rate)
  - overall rate of female breast cancer that would occur in Location A if it had the age distribution of the reference population

Descriptive epidemiology

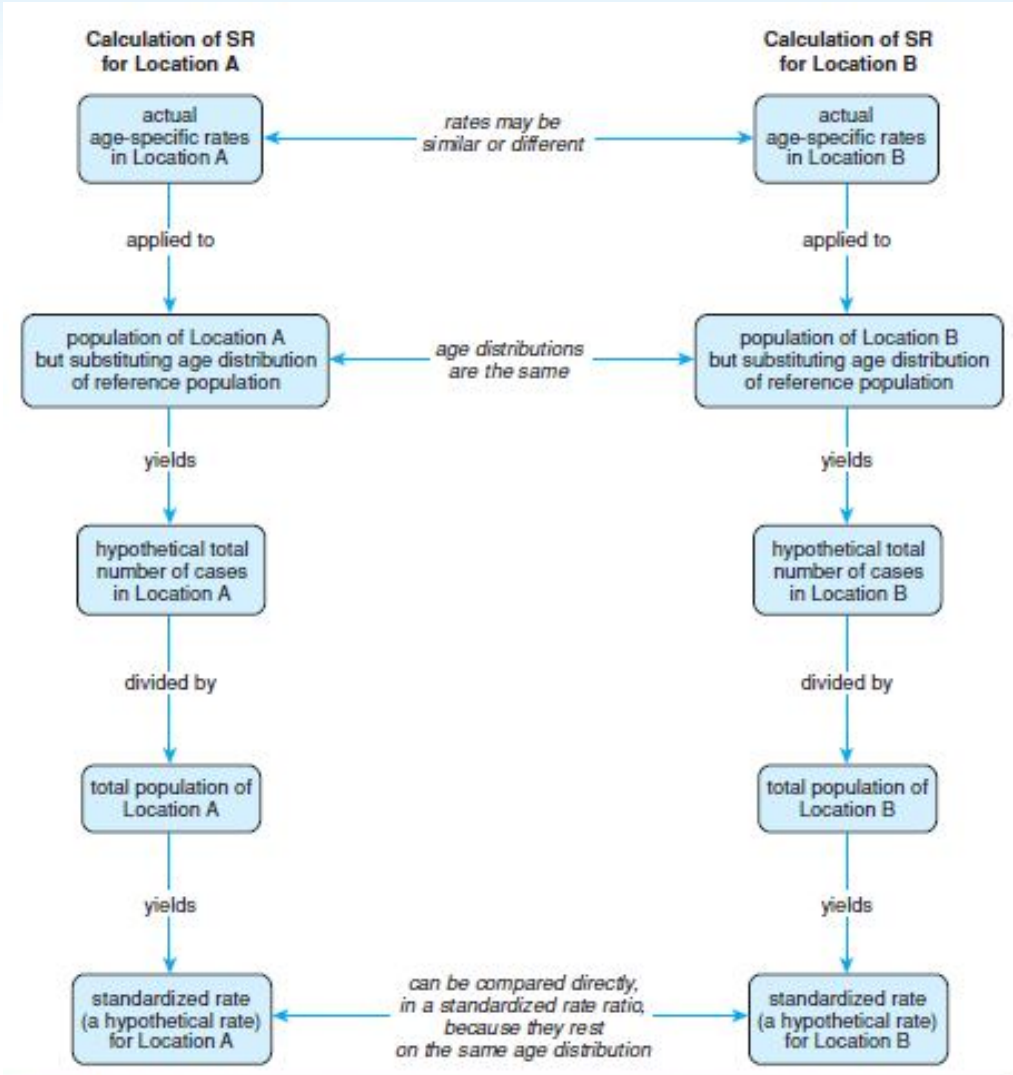

FIGURE 2.16 Standardized rate (SR) and standardized rate ratio (SRR).

Descriptive epidemiology

- Standardized rate ratio
  - Two standardized rates, calculated using the same reference population, can be compared directly in a ratio.
  - $SRR = SR_{\text{Location A}} \ / \ SR_{\text{Location B}}$
  - e.g., SRR of 1.3 means that the rate in Location A is <u>30% higher than the rate in Location B</u>

Descriptive epidemiology

- Standardized incidence ratio (actual excess)
  - SIR = actual cases / expected cases
  - Expected = the number of cases that would occur in population A, given its actual total population and actual age distribution, if the age-specific rates of the reference population were operating in Location A's population

Descriptive epidemiology

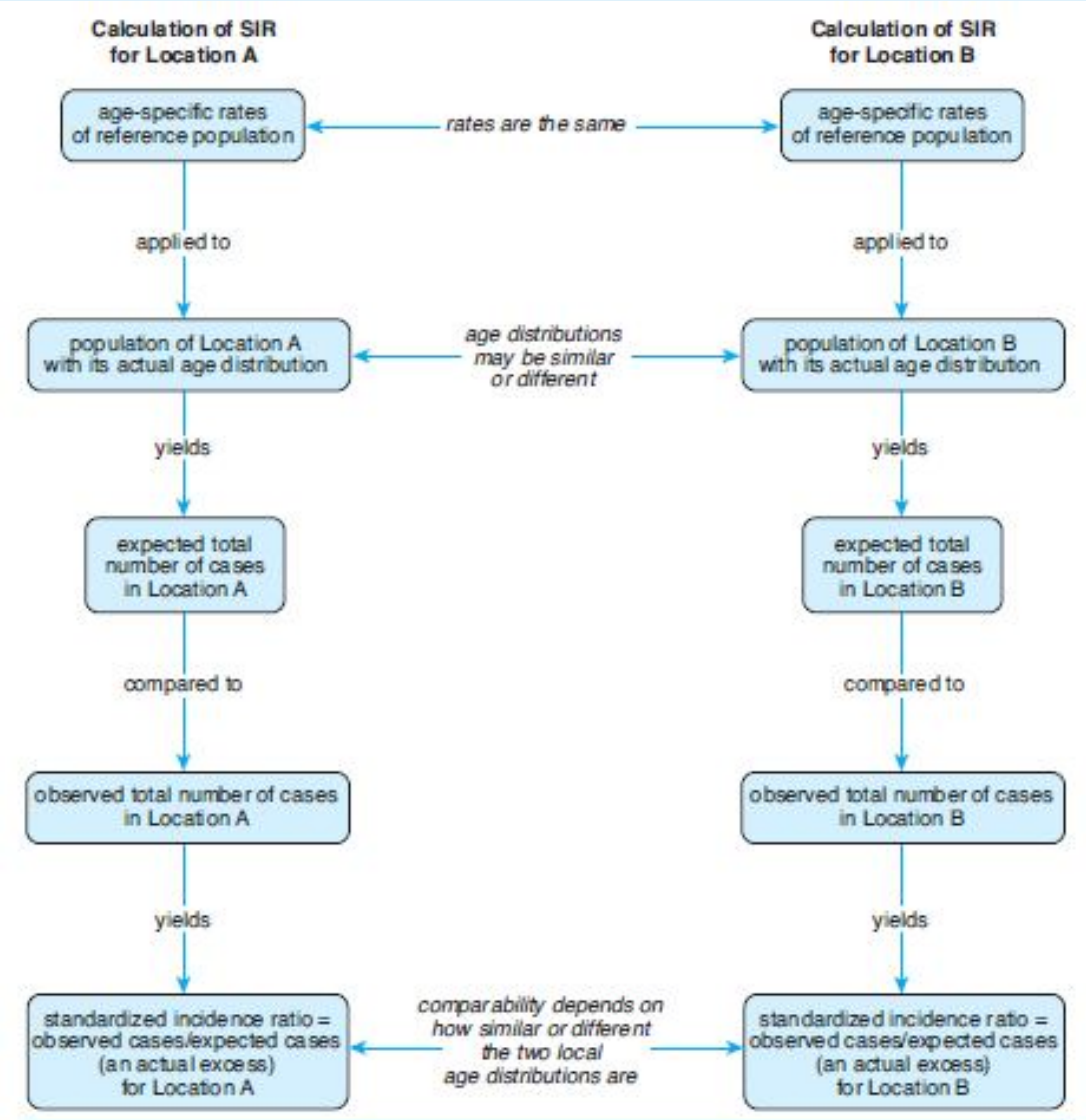

FIGURE 2.17 Standardized incidence ratio (SIR).

Descriptive epidemiology

- By convention, ratio multiplied by 100
  - Ratio of 1.3 → SIR of 130
- SIR of 130 means that the rate in Location A is 30% higher than expected, based on the reference population

- Recap: comparison of calculation of SRR and SIR →

Descriptive epidemiology

- SRR advantage
  - SRRs using same reference population are always comparable.
- SRR disadvantages
  - Depends on age-specific local rates: small n's are statistically unstable; and citizens can't get case counts.
  - Over time, reference population becomes dated; SRs calculated with new reference population cannot be compared to older SRs.

Descriptive epidemiology

- SIR disadvantage
  - Comparability of SIRs depends on how different local age distributions are; often insignificant effect, but must be assessed.
- SIR advantages
  - Does not use unstable local age-specific rates.
  - Citizens can obtain data needed to calculate.
  - Meaningful reference population built into calculation.

Observational and experimental study designs in epidemiology

- Evaluate associations between risk factors and health outcomes.
  - Observational vs. experimental
  - Group-level (always observational) vs. individual-level (observational or experimental)

Observational and experimental study designs in epidemiology

- Group-level observational studies (ecologic studies)
  - Document associations between characteristics of communities or groups
  - Cannot link exposure to outcome in same person
  - Subject to bias (ecologic fallacy)
  - Hypothesis-generating, not hypothesis-testing
  - Yet community-level factors may be important

Observational and experimental study designs in epidemiology

- Individual-level observational and experimental studies
  - Designed to test hypothesized association between exposure and outcome (analytic epidemiology).
  - Cross-sectional study—subjects classified on exposure and outcome; but exposure may not precede outcome.

Observational and experimental study designs in epidemiology

- Cohort study
  - Subjects selected according to exposure status.
  - Compared on disease status: other things being equal, are exposed more likely to be diseased?
  - Prospective vs retrospective; intervention studies
- Case-control study
  - Subjects selected according to disease status.
  - Compared on exposure status: other things being equal, are cases more likely than controls to have been exposed?

Observational and experimental study designs in epidemiology

- Evaluating individual-level studies
  - Finding due simply to chance?
  - Finding due to bias?
  - Finding due to confounding?
  - Effect modification?

Observational and experimental study designs in epidemiology

- Is association causal? Bradford Hill's criteria for use in evaluating causation[1]:
  - Strength of association
  - Consistency of findings
  - Appropriate temporal relationship
  - Dose-response relationship
  - Biological plausibility

Infectious disease epidemiology

- Methods emphasize mathematical modeling of transmission.
- Transmission affected by features of
  - The pathogen (e.g., its virulence)
  - The vector (e.g., mosquito vs bird)
  - Individual people (e.g., immune status)
  - Physical & social environment (e.g., nature / frequency of people's contact)

Infectious disease epidemiology

- Infectious disease in populations
  - Endemic—typically present at low to moderate level in a population
  - Epidemic—occurrence at unusually high rate in a population
  - Pandemic—global epidemic

Animal epidemiology

- Animals as sentinels for human disease risk[2]
  - E.g., “mad cow disease”
- Animals as surrogates for human research subjects[3,4,5]
  - E.g., in studies of residential exposures

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Community-Based Participatory Research

Community-based participatory research

- Roots in community activism
- Core principles[6]
  - Those affected by research should participate in it
  - Equitable sharing of power
  - Emphasis on practical solutions
- Tied to a specific community

2.1 Understanding Environmental Hazards to Human Health

2.2 Responding to Environmental Hazards to Human Health

2.3 Precautionary Approaches in Environmental Health Policy

Risk Assessment: A Regulatory Science

Risk Management: From Assessment to Action

Risk Communication: A Two-Way Street

Introduction to risk assessment, a regulatory science

- Why risk assessment?
  - Must sometimes take action without full scientific understanding of hazard.
  - Risk assessment sets default procedures for bridging gaps in scientific understanding.
  - Basic framework: evaluate exposure and toxicity; bring this information together to characterize health risk →

Introduction to risk assessment, a regulatory science

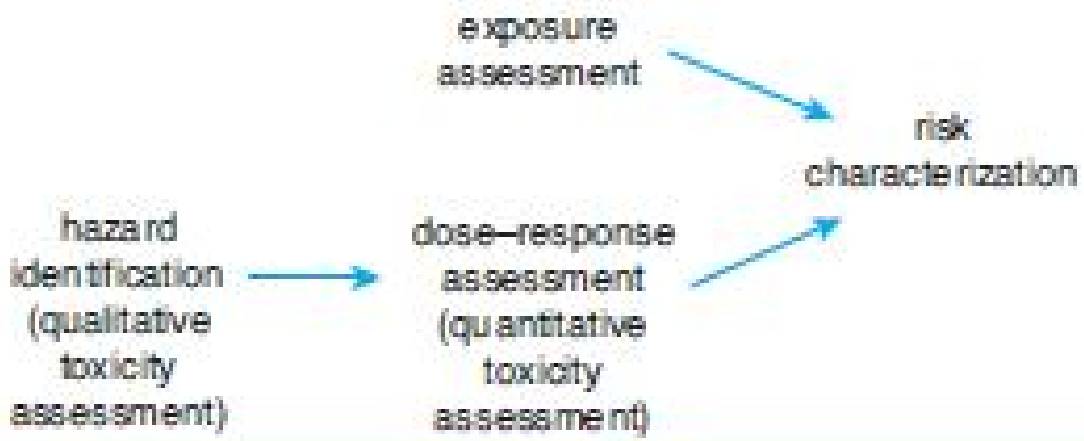

FIGURE 2.19 Basic framework of a risk assessment.

Risk assessment for a chemical

- A fundamental assumption in chemical risk assessment:
  - Noncancer effects have thresholds
  - Carcinogenicity has no threshold
- Therefore, key steps in risk assessment play out differently for cancer and noncancer effects.

Risk assessment for a chemical

- Assessment of noncancer hazard
  - Exposure assessment—measure or estimate dose in mg/(kg*day)
  - Hazard identification—establish range of noncancer effects; select one as basis
  - Dose-response assessment
    - Derive reference dose (RfD) in mg/(kg*day)—dose expected to have no adverse effects in sensitive people with lifelong exposure

Risk assessment for a chemical

- RfD derived from rodent NOAEL or LOAEL, by dividing it by uncertainty factors (to make RfD lower and thus more protective)

– Risk characterization:

- Hazard quotient (unitless) = actual or estimated dose / reference dose
- Hazard quotient >1.0 indicates potential for harm at actual or estimated dose

Risk assessment for a chemical

- Assessment of cancer risk
  - Exposure assessment—measure or estimate dose in mg/(kg*day)
  - Hazard identification—assess toxicant's potential to cause cancer in humans →

Risk assessment for a chemical

- Weight-of-the-evidence categories for carcinogenicity, as defined by IARC:
  - Group 1: Carcinogenic to humans
  - Group 2A: Probably carcinogenic to humans
  - Group 2B: Possibly carcinogenic to humans
  - Group 3: Not classifiable as to carcinogenicity to humans
  - Group 4: Probably not carcinogenic to humans

Risk assessment for a chemical

- Dose-response assessment
  - Derive cancer slope factor—estimate of potency (cancer risk per mg/(kg*day)
  - Derived from human or animal data using mathematical modeling
- Risk characterization
  - Incremental lifetime risk (probability) = dose * risk per unit dose

Risk assessment for a chemical

Table 2.5 The Four Major Steps in Risk Assessment as Applied to a Chemical

Step	Noncancer Effects	Cancer
Exposure assessment	Estimate doses at which populations of concern are exposed to the chemical	
Hazard identification	Identify noncancer effects	Assign weight-of-the-evidence classification
Dose–response assessment	Derive reference dose (mg/[kg × day]); assumes noncancer health effect has a threshold	Derive cancer slope factor (incremental risk per unit dose in mg/[kg × day]); assumes carcinogenic effect has no threshold
Risk characterization	Calculate hazard quotient (unitless)	Calculate incremental lifetime cancer risk (probability)

Risk assessment for a site

- Same four steps, but play out differently.
  - Hazard identification—characterize site contamination.
  - Exposure assessment—develop scenarios by which specific groups might be exposed to chemicals on the site; estimate doses.

Risk assessment for a site

- Dose-response assessment—for each chemical, obtain published reference dose and cancer slope factor; or develop these
- Risk characterization—for each exposure scenario and population,
  - Calculate hazard quotient for each chemical and sum across chemicals with similar toxic effect
  - Calculate incremental lifetime cancer risk for each chemical and sum across chemicals

Risk Assessment: A Regulatory Science

Risk Management: From Assessment to Action

Risk Communication: A Two-Way Street

Introduction to risk management: from assessment to action

- Risk management:
  - Actions taken, often by government agencies, to control or reduce environmental risks to human health.
  - Considers magnitude of the health risk, regulatory framework, technical options for controlling the hazard, costs, and social context including environmental justice[7,8].

Risk management for individual chemicals and sites

- Chemicals (e.g., in drinking water or workplace air)
  - Decisions about goals for standards
  - Decisions about feasible standards
- Contaminated sites
  - Complex: multiple chemicals, multiple media
  - Consider: toxicity, future uses of site, effectiveness of cleanup options, costs

Other examples of risk management

- Limits on emissions, requirements to treat wastes.
- Changes to industrial processes, isolation of a hazardous process in the workplace.
- Incentives for compliance, penalties for noncompliance.
- Publicly available information as incentive.
- Work of local health departments.

Risk Assessment: A Regulatory Science

Risk Management: From Assessment to Action

Risk Communication: A Two-Way Street

Risk communication about environmental health hazards

- Risk communication = exchange of information about a hazard between experts and those affected
- Public perception of environmental health risk as “hazard plus outrage”[9]
- Specific features of environmental hazards often generate outrage.

2.1 Understanding Environmental Hazards to Human Health

2.2 Responding to Environmental Hazards to Human Health

2.3 Precautionary Approaches in Environmental Health Policy

The Precautionary Principle

The Consensus Conference

The Health Impact Assessment

The precautionary principle

- Early warnings of serious harm from a substance or activity call for precautionary measures to be taken, before there is clear proof of harm.[10]
- Additional elements[11]:
  - Proponent bears burden of proof
  - Consider full range of alternatives
  - Open, democratic process

The precautionary principle

- Examples of precautionary approach
  - International agreements
    - Kyoto Protocol on global climate change
    - Montreal Protocol on ozone-depleting chemicals
  - US Toxic Substances Control Act
  - European Union's REACH program for new chemicals

The precautionary principle

- Some lost opportunities for precaution
  - Widespread, long-term use of asbestos
  - Large-scale development and use of synthetic organic chemicals
  - Depletion of global fisheries
  - Food industry practices that amplified “mad cow disease” and caused human illness

The Precautionary Principle

The Consensus Conference

The Health Impact Assessment

The consensus conference

- Danish-style consensus conference
  - Usually on complex issue; relevant to current policymaking
  - 3-day process:
    - A diverse group of citizens are briefed and then question panel of experts.
    - Citizens deliberate and prepare report.
  - Public participation in the development of scientific knowledge

The Precautionary Principle

The Consensus Conference

The Health Impact Assessment

The health impact assessment

- Assessment of likely population health impacts of a proposed policy or action before it is implemented.
  - Includes impacts on vulnerable subgroups.
  - Includes positive and negative impacts.
  - Seeks input from affected communities before decisions are made.

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