



UNITED NATIONS ENVIRONMENT PROGRAMME
INTERNATIONAL LABOUR ORGANISATION
WORLD HEALTH ORGANIZATION

INTERNATIONAL PROGRAMME ON CHEMICAL SAFETY

Environmental Health Criteria 214

HUMAN EXPOSURE ASSESSMENT

This report contains the collective views of an international group of experts and does not necessarily represent the decisions or the stated policy of the United Nations Environment Programme, the International Labour Organization, or the World Health Organization.

First draft prepared by Dr D. L. MacIntosh, University of Georgia, Athens, GA, USA and Professor J. D. Spengler, Harvard University, Boston, MA, USA

Published under the joint sponsorship of the United Nations Environment Programme, the International Labour Organization, and the World Health Organization, and produced within the framework of the Inter-Organization Programme for the Sound Management of Chemicals.

World Health Organization
Geneva, 2000

The International Programme on Chemical Safety (IPCS), established in 1980, is a joint venture of the United Nations Environment Programme (UNEP), the International Labour Organization (ILO), and the World Health Organization (WHO). The overall objectives of the IPCS are to establish the scientific basis for assessment of the risk to human health and the environment from exposure to chemicals, through international peer review processes, as a prerequisite for the promotion of chemical safety, and to provide technical assistance in strengthening national capacities for the

sound management of chemicals.

The Inter-Organization Programme for the Sound Management of Chemicals (IOMC) was established in 1995 by UNEP, ILO, the Food and Agriculture Organization of the United Nations, WHO, the United Nations Industrial Development Organization, the United Nations Institute for Training and Research, and the Organisation for Economic Co-operation and Development (Participating Organizations), following recommendations made by the 1992 UN Conference on Environment and Development to strengthen cooperation and increase coordination in the field of chemical safety. The purpose of the IOMC is to promote coordination of the policies and activities pursued by the Participating Organizations, jointly or separately, to achieve the sound management of chemicals in relation to human health and the environment.

WHO Library Cataloguing-in-Publication Data

Human exposure assessment.

(Environmental health criteria ; 214)

1.Environmental monitoring - methods 2.Environmental exposure
3.Models, theoretical 4.Data collection - methods
5.Toxicity tests
I.International Programme on Chemical Safety II.Series

ISBN 92 4 157214 0
ISSN 0250-863X

(NLM Classification: QT 162)

The World Health Organization welcomes requests for permission to reproduce or translate its publications, in part or in full. Applications and enquiries should be addressed to the Office of Publications, World Health Organization, Geneva, Switzerland, which will be glad to provide the latest information on any changes made to the text, plans for new editions, and reprints and translations already available.

(c) World Health Organization 2000

Publications of the World Health Organization enjoy copyright protection in accordance with the provisions of Protocol 2 of the Universal Copyright Convention. All rights reserved.

The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of the Secretariat of the World Health Organization concerning the legal status of any country, territory, city, or area or of its authorities, or concerning the delimitation of its frontiers or boundaries.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by the World Health Organization in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

CONTENTS

ENVIRONMENTAL HEALTH CRITERIA FOR HUMAN EXPOSURE ASSESSMENT

PREAMBLE

ABBREVIATIONS

FOREWORD

1. DEFINING EXPOSURE

1.1. Introduction

1.2. Defining exposure

1.2.1. Exposure and exposure concentration

1.2.2. Exposure estimation by integration and averaging

1.2.3. Exposure measurements and models

1.2.4. Exposure in the context of an environmental health paradigm

1.3. Elements of exposure assessment

1.4. Approaches to quantitative exposure assessment

1.5. Linking exposure events and dose events

1.6. Summary

2. USES OF HUMAN EXPOSURE INFORMATION

2.1. Introduction

2.2. Human exposure information in environmental epidemiology

2.3. Human exposure information in risk assessment

2.3.1. Risk allocation for population subgroups or activities

2.3.2. Population at higher or highest risk

2.4. Human exposure information in risk management

2.5. Human exposure information in status and trend analysis

2.6. Summary

3. STRATEGIES AND DESIGN FOR EXPOSURE STUDIES

3.1. Introduction

3.2. Study design

3.3. Sampling and generalization

3.4. Types of study design

3.4.1. Comprehensive samples

3.4.2. Probability samples

3.4.3. Other sample types

3.5. Exposure assessment approaches

3.5.1. Direct approaches to exposure assessment

3.5.1.1 Personal monitoring of inhalation exposures

3.5.1.2 Personal monitoring of dietary exposures

3.5.1.3 Personal monitoring of dermal absorption exposures

3.5.2. Indirect approaches to exposure assessment

3.5.2.1 Environmental monitoring

3.5.2.2 Models as an indirect approach to assessing exposure

3.5.2.3 Questionnaires as an indirect approach to assessing exposure

3.6. Summary

4. STATISTICAL METHODS IN EXPOSURE ASSESSMENT

4.1. Introduction

4.2. Descriptive statistics

4.2.1. Numerical summaries

4.2.2. Graphical summaries

4.2.2.1 Histograms

4.2.2.2 Cumulative frequency diagrams

4.2.2.3 Box plots

4.2.2.4 Quantile-quantile plots

4.2.2.5 Scatter plots

4.3. Probability distributions

4.3.1. Normal distribution

4.3.2. Lognormal distribution

4.3.3. Binomial distribution

4.3.4. Poisson distribution

4.4. Parametric inferential statistics

4.4.1. Estimation

4.4.2. Measurement error and reliability

4.4.3. Hypothesis testing and two-sample problems

4.4.4. Statistical models

4.4.4.1 Analysis of variance and linear regression

4.4.4.2 Logistic regression

4.4.5. Sample size determination

4.5. Non-parametric inferential statistics

4.6. Other topics

4.7. Summary

5. HUMAN TIME-USE PATTERNS AND EXPOSURE ASSESSMENT

5.1. Introduction

5.2. Methods

5.2.1. Activity pattern concepts

5.2.1.1 Time allocation parameters

5.2.1.2 Microenvironment parameters

5.2.1.3 Intensity of contact

5.2.2. Surrogates of time-activity patterns

5.2.3. Data collection methods

5.3. Potential limitations

5.3.1. Activity representativeness

5.3.2. Validity and reliability

5.3.3. Inter- and intra-person variability

5.4. Summary

6. HUMAN EXPOSURE AND DOSE MODELLING

6.1. Introduction

6.2. General types of exposure model

6.3. Environmental media and exposure media

6.4. Single-medium models

6.4.1. Outdoor and indoor air

6.4.2. Potable water

6.4.3. Surface waters

6.4.4. Groundwater

6.4.5. Soil

6.5. Multiple-media modelling

6.5.1. Inter-media transfer factors

6.5.1.1 Diffusive partition coefficients

6.5.1.2 Advective partition coefficients

6.5.2. Exposure factors

6.5.3. Multiple-media/multiple-pathway models

6.6. Probabilistic exposure models

6.6.1. Variability

- [6.6.2. Uncertainty](#)
- [6.6.3. Implementing probabilistic exposure models](#)
- [6.7. A generalized dose model](#)
- [6.8. Physiologically based pharmacokinetic models](#)
- [6.9. Validation and generalization](#)
- [6.10. Summary](#)

[7. MEASURING HUMAN EXPOSURES TO CHEMICALS IN AIR, WATER AND FOOD](#)

- [7.1. Introduction](#)
- [7.2. Air monitoring](#)
 - [7.2.1. Gases and vapours](#)
 - [7.2.1.1 Passive samplers](#)
 - [7.2.1.2 Active samplers](#)
 - [7.2.1.3 Direct-reading instruments](#)
 - [7.2.2. Aerosols](#)
 - [7.2.3. Semivolatile compounds](#)
 - [7.2.4. Reactive gas monitoring](#)
- [7.3. Water](#)
 - [7.3.1. Factors influencing water quality](#)
 - [7.3.2. Water quality monitoring strategies](#)
 - [7.3.3. Sample collection](#)
- [7.4. Assessing exposures through food](#)
 - [7.4.1. Duplicate diet surveys](#)
 - [7.4.2. Market basket or total diet surveys](#)
 - [7.4.3. Food consumption](#)
 - [7.4.3.1 Food diaries](#)
 - [7.4.3.2 24-h recall](#)
 - [7.4.3.3 Food frequency questionnaires](#)
 - [7.4.3.4 Meal-based diet history](#)
 - [7.4.3.5 Food habit questionnaires](#)
 - [7.4.4. Contaminants in food](#)
- [7.5. Summary](#)

[8. MEASURING HUMAN EXPOSURE TO CHEMICAL CONTAMINANTS IN SOIL AND SETTLED DUST](#)

- [8.1. Introduction](#)
- [8.2. Selected sampling methods](#)
 - [8.2.1. Soil](#)
 - [8.2.1.1 Surface soil collection](#)
 - [8.2.1.2 Soil contact and intake measurements](#)
 - [8.2.2. Settled dust](#)
 - [8.2.2.1 Wipe sampling methods](#)
 - [8.2.2.2 Vacuum methods](#)
 - [8.2.2.3 Sedimentation methods](#)
- [8.3. Sampling design considerations](#)
 - [8.3.1. Concentration and loading](#)
 - [8.3.2. Collection efficiency](#)
- [8.4. Sampling strategies](#)
- [8.5. Summary](#)

[9. MEASURING BIOLOGICAL HUMAN EXPOSURE AGENTS IN AIR AND DUST](#)

- [9.1. Introduction](#)
- [9.2. House dust mites](#)
 - [9.2.1. Air sampling for house dust mites](#)
 - [9.2.2. Dust sampling for house dust mites](#)
 - [9.2.3. Available methods of analysis for house dust mites](#)
 - [9.2.3.1 Mite counts](#)

- 9.2.3.2 [Immunochemical assays of dust mite allergens](#)
 - 9.2.3.3 [Guanine determination](#)
 - 9.2.4. [Mite allergens](#)
 - 9.3. [Allergens from pets and cockroaches](#)
 - 9.3.1. [Air sampling for allergens from pets and cockroaches](#)
 - 9.3.2. [Dust sampling for allergens from pets and cockroaches](#)
 - 9.3.3. [Available methods of analysis](#)
 - 9.3.4. [Typical allergen concentrations](#)
 - 9.4. [Fungi](#)
 - 9.4.1. [Air sampling for fungi](#)
 - 9.4.2. [Settled dust for fungi](#)
 - 9.4.3. [Available methods of analysis for fungi in air](#)
 - 9.4.3.1 [Total counts of viable and non-viable fungal particles](#)
 - 9.4.4. [General considerations for fungi](#)
 - 9.5. [Bacteria \(including actinomycetes\)](#)
 - 9.5.1. [Air sampling for bacteria](#)
 - 9.5.2. [Dust sampling for bacteria](#)
 - 9.5.3. [Available methods of analysis for bacteria](#)
 - 9.5.3.1 [Total count of viable and non-viable bacteria](#)
 - 9.5.3.2 [Viable bacteria](#)
 - 9.5.3.3 [Endotoxins](#)
 - 9.6. [Pollen](#)
 - 9.6.1. [Air sampling for pollen](#)
 - 9.6.2. [Dust sampling for pollen](#)
 - 9.6.3. [Available methods of analysis for pollen in air](#)
 - 9.6.4. [General considerations for pollen sampling](#)
 - 9.7. [Summary](#)
10. [ASSESSING EXPOSURES WITH BIOLOGICAL MARKERS](#)
- 10.1. [Introduction](#)
 - 10.2. [General characteristics](#)
 - 10.3. [Considerations for use in environmental exposure assessment](#)
 - 10.3.1. [Toxicokinetics and toxicodynamics](#)
 - 10.3.2. [Biological variability](#)
 - 10.3.3. [Validation of biological markers](#)
 - 10.3.4. [Normative data](#)
 - 10.4. [Advantages of biological markers for exposure assessment](#)
 - 10.4.1. [Characterizing inter-individual variability](#)
 - 10.4.2. [Efficacy of use](#)
 - 10.4.3. [Internal exposure sources](#)
 - 10.5. [Limitations of biological markers for exposure assessment](#)
 - 10.5.1. [Source identification](#)
 - 10.5.2. [Biological variability and altered exposure response](#)
 - 10.5.3. [Participant burden](#)
 - 10.5.4. [Biosafety](#)
 - 10.6. [Media available for use](#)
 - 10.6.1. [Blood](#)
 - 10.6.2. [Urine](#)
 - 10.6.3. [Exhaled breath](#)
 - 10.6.4. [Saliva](#)
 - 10.6.5. [Keratinized tissue \(hair and nails\)](#)
 - 10.6.6. [Ossified tissue](#)
 - 10.6.6.1 [Teeth](#)
 - 10.6.6.2 [Bone](#)

- 10.6.7. Breast milk
- 10.6.8. Adipose tissue
- 10.6.9. Faeces
- 10.6.10. Other media
- 10.7. Summary

11. QUALITY ASSURANCE IN EXPOSURE STUDIES

- 11.1. Introduction
- 11.2. Quality assurance and quality control
- 11.3. Elements of a quality assurance programme
- 11.4. Quality assurance programme
 - 11.4.1. Organization and personnel
 - 11.4.2. Record-keeping and data recording
 - 11.4.3. Study plan and standard operating procedures
 - 11.4.4. Collection of samples
 - 11.4.5. Equipment maintenance and calibration
 - 11.4.6. Internal audit and corrective action
- 11.5. Quality control/quality assurance for sample measurement
 - 11.5.1. Method selection and validation
 - 11.5.1.1 Accuracy
 - 11.5.1.2 Precision
 - 11.5.1.3 Sensitivity
 - 11.5.1.4 Detection limits
 - 11.5.2. Internal quality control
 - 11.5.2.1 Control charts
 - 11.5.3. External quality control
 - 11.5.4. Reference materials
- 11.6. Quality assurance and control issues in population-based studies
- 11.7. Summary

12. EXAMPLES AND CASE STUDIES OF EXPOSURE STUDIES

- 12.1. Introduction
- 12.2. Exposure studies
- 12.3. Air pollution exposure studies
 - 12.3.1. Particle studies
 - 12.3.2. Carbon monoxide
 - 12.3.3. Nitrogen dioxide
 - 12.3.4. Ozone
 - 12.3.5. Combined exposure studies
 - 12.3.6. Assessing ambient pollution impacts indoors
 - 12.3.7. Volatile organic compounds
 - 12.3.8. Commuter exposures
- 12.4. Exposures and biomarkers
 - 12.4.1. Exposure to lead and cadmium
 - 12.4.2. Exposure to furans, dioxins and polychlorinated biphenyls
 - 12.4.3. Exposure to volatile organic compounds and urinary metabolites
- 12.5. Exposure to contaminants in drinking-water
- 12.6. Exposure to microbes
- 12.7. Exposure studies and risk assessment
 - 12.7.1. The German Environmental Survey
 - 12.7.2. The National Human Exposure Assessment Survey
 - 12.7.3. Windsor, Canada exposure and risk study
 - 12.7.4. Pesticide exposure study
 - 12.7.5. Czech study of air pollution impact on human health

REFERENCES

RÉSUMÉ

RESUMEN

NOTE TO READERS OF THE CRITERIA MONOGRAPHS

Every effort has been made to present information in the criteria monographs as accurately as possible without unduly delaying their publication. In the interest of all users of the Environmental Health Criteria monographs, readers are requested to communicate any errors that may have occurred to the Director of the International Programme on Chemical Safety, World Health Organization, Geneva, Switzerland, in order that they may be included in corrigenda.

* * *

A detailed data profile and a legal file can be obtained from the International Register of Potentially Toxic Chemicals, Case postale 356, 1219 Châtelaine, Geneva, Switzerland (telephone no. + 41 22 - 9799111, fax no. + 41 22 - 7973460, E-mail irptc@unep.ch).

* * *

This publication was made possible by grant number 5 U01 ES02617-15 from the National Institute of Environmental Health Sciences, National Institutes of Health, USA, and by financial support from the European Commission.

Environmental Health Criteria

PREAMBLE

Objectives

In 1973 the WHO Environmental Health Criteria Programme was initiated with the following objectives:

- (i) to assess information on the relationship between exposure to environmental pollutants and human health, and to provide guidelines for setting exposure limits;
- (ii) to identify new or potential pollutants;
- (iii) to identify gaps in knowledge concerning the health effects of pollutants;

- (iv) to promote the harmonization of toxicological and epidemiological methods in order to have internationally comparable results.

The first Environmental Health Criteria (EHC) monograph, on mercury, was published in 1976 and since that time an ever-increasing number of assessments of chemicals and of physical effects have been produced. In addition, many EHC monographs have been devoted to evaluating toxicological methodology, e.g., for genetic, neurotoxic, teratogenic and nephrotoxic effects. Other publications have been concerned with epidemiological guidelines, evaluation of short-term tests for carcinogens, biomarkers, effects on the elderly and so forth.

Since its inauguration the EHC Programme has widened its scope, and the importance of environmental effects, in addition to health effects, has been increasingly emphasized in the total evaluation of chemicals.

The original impetus for the Programme came from World Health Assembly resolutions and the recommendations of the 1972 UN Conference on the Human Environment. Subsequently the work became an integral part of the International Programme on Chemical Safety (IPCS), a cooperative programme of UNEP, ILO and WHO. In this manner, with the strong support of the new partners, the importance of occupational health and environmental effects was fully recognized. The EHC monographs have become widely established, used and recognized throughout the world.

The recommendations of the 1992 UN Conference on Environment and Development and the subsequent establishment of the Intergovernmental Forum on Chemical Safety with the priorities for action in the six programme areas of Chapter 19, Agenda 21, all lend further weight to the need for EHC assessments of the risks of chemicals.

Scope

The criteria monographs are intended to provide critical reviews on the effect on human health and the environment of chemicals and of combinations of chemicals and physical and biological agents. As such, they include and review studies that are of direct relevance for the evaluation. However, they do not describe every study carried out. Worldwide data are used and are quoted from original studies, not from abstracts or reviews. Both published and unpublished reports are considered and it is incumbent on the authors to assess all the articles cited in the references. Preference is always given to published data. Unpublished data are only used when relevant published data are absent or when they are pivotal to the risk assessment. A detailed policy statement is available that describes the procedures used for unpublished proprietary data so that this information can be used in the evaluation without compromising its confidential nature (WHO (1990) Revised Guidelines for the Preparation of Environmental Health Criteria Monographs. PCS/90.69, Geneva, World Health Organization).

In the evaluation of human health risks, sound human data, whenever available, are preferred to animal data. Animal and *in vitro* studies provide support and are used mainly to supply evidence missing from human studies. It is mandatory that research on human subjects is conducted in full accord with ethical principles,

including the provisions of the Helsinki Declaration.

The EHC monographs are intended to assist national and international authorities in making risk assessments and subsequent risk management decisions. They represent a thorough evaluation of risks and are not, in any sense, recommendations for regulation or standard setting. These latter are the exclusive purview of national and regional governments.

Content

The layout of EHC monographs for chemicals is outlined below.

- * Summary -- a review of the salient facts and the risk evaluation of the chemical
- * Identity -- physical and chemical properties, analytical methods
- * Sources of exposure
- * Environmental transport, distribution and transformation
- * Environmental levels and human exposure
- * Kinetics and metabolism in laboratory animals and humans
- * Effects on laboratory mammals and *in vitro* test systems
- * Effects on humans
- * Effects on other organisms in the laboratory and field
- * Evaluation of human health risks and effects on the environment
- * Conclusions and recommendations for protection of human health and the environment
- * Further research
- * Previous evaluations by international bodies, e.g., IARC, JECFA, JMPR

Selection of chemicals

Since the inception of the EHC Programme, the IPCS has organized meetings of scientists to establish lists of priority chemicals for subsequent evaluation. Such meetings have been held in: Ispra, Italy, 1980; Oxford, United Kingdom, 1984; Berlin, Germany, 1987; and North Carolina, USA, 1995. The selection of chemicals has been based on the following criteria: the existence of scientific evidence that the substance presents a hazard to human health and/or the environment; the possible use, persistence, accumulation or degradation of the substance shows that there may be significant human or environmental exposure; the size and nature of populations at risk (both human and other species) and risks for environment; international concern, i.e. the substance is of major interest to several countries; adequate data on the hazards are available.

If an EHC monograph is proposed for a chemical not on the priority list, the IPCS Secretariat consults with the Cooperating

Organizations and all the Participating Institutions before embarking on the preparation of the monograph.

Procedures

The order of procedures that result in the publication of an EHC monograph is shown in the flow chart. A designated staff member of IPCS, responsible for the scientific quality of the document, serves as Responsible Officer (RO). The IPCS Editor is responsible for layout and language. The first draft, prepared by consultants or, more usually, staff from an IPCS Participating Institution, is based initially on data provided from the International Register of Potentially Toxic Chemicals, and reference data bases such as Medline and Toxline.

The draft document, when received by the RO, may require an initial review by a small panel of experts to determine its scientific quality and objectivity. Once the RO finds the document acceptable as a first draft, it is distributed, in its unedited form, to well over 150 EHC contact points throughout the world who are asked to comment on its completeness and accuracy and, where necessary, provide

additional material. The contact points, usually designated by governments, may be Participating Institutions, IPCS Focal Points, or individual scientists known for their particular expertise. Generally some four months are allowed before the comments are considered by the RO and author(s). A second draft incorporating comments received and approved by the Director, IPCS, is then distributed to Task Group members, who carry out the peer review, at least six weeks before their meeting.

The Task Group members serve as individual scientists, not as representatives of any organization, government or industry. Their function is to evaluate the accuracy, significance and relevance of the information in the document and to assess the health and environmental risks from exposure to the chemical. A summary and recommendations for further research and improved safety aspects are also required. The composition of the Task Group is dictated by the range of expertise required for the subject of the meeting and by the need for a balanced geographical distribution.

The three cooperating organizations of the IPCS recognize the important role played by nongovernmental organizations. Representatives from relevant national and international associations may be invited to join the Task Group as observers. While observers may provide a valuable contribution to the process, they can only speak at the invitation of the Chairperson. Observers do not participate in the final evaluation of the chemical; this is the sole responsibility of the Task Group members. When the Task Group considers it to be appropriate, it may meet *in camera*.

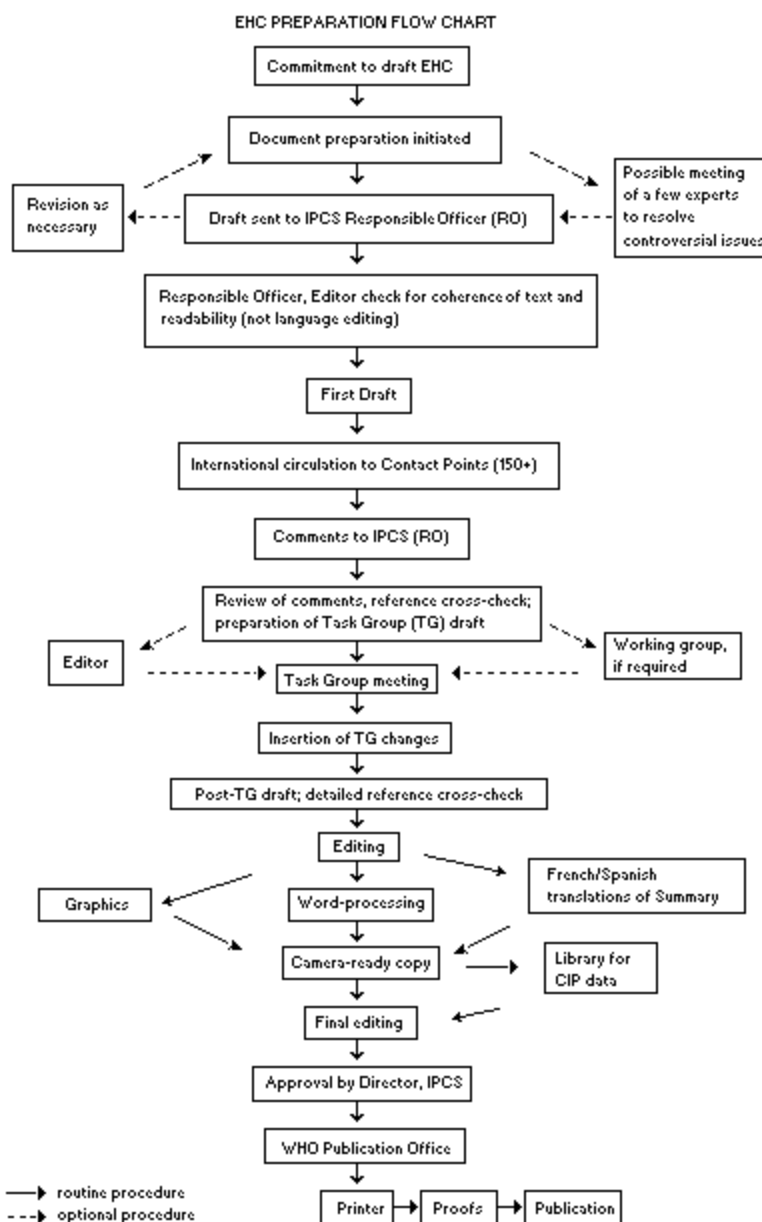
All individuals who as authors, consultants or advisers participate in the preparation of the EHC monograph must, in addition to serving in their personal capacity as scientists, inform the RO if at any time a conflict of interest, whether actual or potential, could be perceived in their work. They are required to sign a conflict of interest statement. Such a procedure ensures the transparency and probity of the process.

When the Task Group has completed its review and the RO is

satisfied as to the scientific correctness and completeness of the document, it then goes for language editing, reference checking, and preparation of camera-ready copy. After approval by the Director, IPCS, the monograph is submitted to the WHO Office of Publications for printing. At this time a copy of the final draft is sent to the Chairperson and Rapporteur of the Task Group to check for any errors.

It is accepted that the following criteria should initiate the updating of an EHC monograph: new data are available that would substantially change the evaluation; there is public concern for health or environmental effects of the agent because of greater exposure; an appreciable time period has elapsed since the last evaluation.

All Participating Institutions are informed, through the EHC progress report, of the authors and institutions proposed for the drafting of the documents. A comprehensive file of all comments received on drafts of each EHC monograph is maintained and is available on request. The Chairpersons of Task Groups are briefed before each meeting on their role and responsibility in ensuring that these rules are followed.



WHO TASK GROUP ON HUMAN EXPOSURE ASSESSMENT

Members

Dr J. Alexander, Department of Environmental Medicine, National Institute of Public Health, Folkehelse, Torshov, Oslo, Norway

Dr M. Berglund, Institute of Environmental Medicine, Division of Metals and Health, Karolinska Institute, Stockholm, Sweden

Dr M. Dellarco, US Environmental Protection Agency, Washington, DC, USA

Mrs B. Genthe, Environmentek, CSIR, Stellenbosch, South Africa

Dr L. Gil, Department of Biochemistry, University of Chile - Faculty of Medicine, Casilla, Santiago, Chile

Dr S. Goto, Department of Community Environmental Sciences,
Institute of Public Health, Minato-ku, Tokyo, Japan

Professor M. Jantunen, Department of Environmental Hygiene and
Toxicology, National Public Health Institute, Kuopio, Finland

Dr N. Künzli, Department of Environment and Health, Institute of
Social and Preventive Medicine, University of Basel, Basel,
Switzerland

Dr D. MacIntosh, Environmental Health Science, University of
Georgia, Athens, GA, USA

Dr M. Morandi, Environmental Sciences, Houston School of Public
Health, Houston Health Science Center, University of Texas,
Houston, TX, USA

Dr S. Pavittranon, National Institute of Health, Department of
Medical Sciences, Bamrasnaradura Hospital, Nonthari, Thailand

Dr N. Rees, Risk Assessment, Management and International
Coordination Branch, Ministry of Agriculture, Fisheries and Food,
London, United Kingdom

Dr B. Schoket, Department of Biochemistry, National Institute of
Environmental Health, "Fodor József" National Public Health
Centre, Budapest, Hungary

Dr L. Sheldon, US Environmental Protection Agency, National
Research Laboratory, Research Triangle Park, NC, USA

Professor J. D. Spengler, School of Public Health, Harvard
University, Boston, MA, USA

Dr P. Straehl, Swiss Federal Agency for Environment, Forestry and
Landscape, Swiss Department of the Interior, Bern, Switzerland

Observers

Mrs S. Munn, European Commission, European Chemicals Bureau,
Environment Institute, Ispra (VA), Italy

Secretariat

Mr C. Corvalan, Office of Global and Integrated Environmental
Health, World Health Organization, Geneva, Switzerland

Dr K. Gutschmidt, International Programme on Chemical Safety,
World Health Organization, Geneva, Switzerland

Dr M. Krzyzanowski, European Centre for Environment and
Health, World Health Organization, Regional Office for Europe,
Bilthoven Division, De Bilt, Netherlands

Dr G. Moy, Food Safety, World Health Organization, Geneva,
Switzerland

Dr H. Tamashiro, Office of Global and Integrated Environmental
Health, World Health Organization, Geneva, Switzerland

Dr M. Younes, International Programme on Chemical Safety,
World Health Organization, Geneva, Switzerland

ENVIRONMENTAL HEALTH CRITERIA FOR HUMAN EXPOSURE ASSESSMENT

A Task Group on the Environmental Health Criteria for Human Exposure Assessment met in Glion-sur-Montreux, Switzerland, from 16 to 20 February 1998. Dr M. Younes, IPCS, welcomed the participants on behalf of the Manager, IPCS, and the three IPCS cooperating organizations (UNEP/ILO/WHO). The Task Group reviewed and revised the final draft of the monograph. In preparation for the final draft a review meeting was held at the National Institute of Health Sciences (NIHS), Tokyo, from 17 to 19 July 1996.

The first draft was prepared by Dr D. L. MacIntosh, University of Georgia, USA and Professor J. D. Spengler, Harvard University, USA.

Dr K. Gutschmidt was responsible officer in IPCS for the overall scientific content of the monograph and the organization for the meetings, and Ms K. Lyle (Sheffield, United Kingdom) was responsible for the technical editing of the monograph.

The efforts of all who helped in the preparation and finalization of the monograph are gratefully acknowledged.

ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
ADD	average daily dose
AI	acceptance intervals
ALAD	Delta-aminolaevulinic acid dehydratase
AMIS	Air Monitoring Information System
ANOVA	analysis of variance
AOAC	Association of Official Analytical Chemists
ASTM	American Society for Testing of Materials
CDF	chlorinated dibenzofurans; cumulative distribution function
CFU	colony-forming units
CI	confidence interval
DG18	dichloran 18% diglycerol agar
DVM	dust vacuum method
EDTA	ethylenediamine tetra-acetic acid
ELISA	enzyme-linked immunosorbent assays
EPS	extracellular polysaccharides
ETS	environmental tobacco smoke (exposure)
EU	endotoxin unit
FDA	US Food and Drug Administration
FFQ	food frequency questionnaire
GEMS	Global Environment Monitoring System
GerES	German Environmental Survey
GM	geometric mean
GSD	geometric standard deviation
HEAL	Human Exposure Assessment Location
HPLC	high-pressure liquid chromatography
HUD	US Department of Housing and Urban Development
IAEA	International Atomic Energy Agency
IAQ	internal air quality
ISEA	International Society of Exposure Analysis
ISO	International Organization for Standardization

LADD	lifetime average daily dose
LAL	<i>Limulus</i> amoebocyte lysate
LOD	limit of detection
LOQ	limit of quantification
LWW	Lioy-Weisel-Wainman
MAD	maximum allowable deviations
MCS	multiple chemical sensitivity
MDL	method detection limit
MEA	malt extract agar
NAAQS	National Ambient Air Quality Standard
NHEXAS	National Human Exposure Assessment Survey
NIOSH	National Institute for Occupational Safety and Health
NTA	nitriloacetic acid
OR	odds ratio
PAH	polycyclic aromatic hydrocarbons
PBPK	physiologically based pharmacokinetic (method)
PCB	polychlorinated biphenyls
PCDD	polychlorinated dibenzo- <i>p</i> -dioxin
PCP	pentachlorophenol
PDF	probability distribution function
PEM	personal exposure monitor
PM _n	particulate matter with aerodynamic diameter < <i>n</i> μm
PTEAM	particle total exposure assessment methodology
QA	quality assurance
QC	quality control
RAST	radioallergosorbent tests
RIA	radioimmunoassay
RSP	respirable particulate matter
SAM	stationary outdoor monitor
SBS	sick building syndrome
SD	standard deviation
SEM	scanning electron microscope
SIM	stationary indoor monitor
SOP	standard operating procedure
SVOC	semivolatile organic compound
TCCD	2,3,7,8-tetrachloro dibenzo- <i>p</i> -dioxin
TDS	US FDA Total Diet Study
TEQ	TCCD toxic equivalents
TSP	total suspended particulates
TWI	tolerable weekly intake
UNEP	United Nations Environment Programme
VOC	volatile organic compound
XRF	X-ray fluorescence

FOREWORD

The International Programme on Chemical Safety (IPCS), launched in 1980, is a joint collaborative programme of the International Labor Organization (ILO), the United Nations Environment Programme (UNEP), and the World Health Organization (WHO); WHO is the Administrating Organization of the Programme. The two main roles of the IPCS are to establish the scientific health and environmental risk assessment basis for safe use of chemicals (*normative function*) and to strengthen national capabilities for chemical safety (*technical cooperation*). In the field of methodology, the work of the IPCS aims at promoting the development, improvement, validation, harmonization and use of generally acceptable, scientifically sound methodologies for the evaluation of risks to human health and the environment from exposure to chemicals. The work encompasses the development of

Environmental Health Criteria monographs on general principles of various areas of risk assessment covering various aspects related to risk assessment such as, in this publication, on exposure assessment.

The WHO and the World Meteorological Organization coordinate the assessment of climate, urban air and water pollution, and health status of populations. These measures provide the indicator of trends and status.

Until 1995, the basic source for internationally comparable urban air pollution data was the Global Environment Monitoring System (GEMS/Air) of UNEP and WHO. Started in 1974, shortly after the Stockholm Environment Conference, GEMS had built up a system that collected comparable ambient air pollution data in about 50 cities of 35 countries, varied in geography and income (UNEP/WHO, 1988, 1992). Typically, sulfur dioxide and total suspended particulates (TSP) had been monitored in three stations of each city, one each in industrial, commercial, and residential zones. Later, GEMS also collected monitoring data for carbon monoxide, nitrogen dioxide, and lead, and made emissions estimates for all five pollutants. The results were published periodically by GEMS, and also often appeared in other periodic international data sets, such as those of the World Bank (World Bank, 1992), the World Resources Institute (World Resources Institute, 1992), the United Nations (UN ESCAP, 1990) and UNEP itself (UNEP, 1991).

More recently, WHO created with the Air Management Information System (AMIS) the successor of GEMS/Air. Like GEMS/Air, AMIS provides air quality data for major and megacities. Data on sulfur dioxide, nitrogen dioxide, carbon monoxide, ozone, black smoke, suspended particulate matter, PM_{10} , lead and others are available. AMIS also includes information on air quality management (WHO, 1997).

Much of what is known about contaminants in food, soils, water and air has become available through WHO and UNEP publications. For more than 20 years WHO/UNEP has been promoting an appreciation for improved assessments of human exposures through training sessions, workshops, demonstration projects, and published methodologies and reports. Through a series of WHO-sponsored studies in every populated continent, the principles of human exposure assessment have been illustrated for indoor and outdoor air pollutants, food contamination and water. In 1984, after some background reports (e.g., UNEP/WHO, 1982), WHO and UNEP conducted the Human Exposure Assessment Location (HEAL) Project, which facilitates research and information sharing among 10-15 institutions worldwide concerned with exposure assessment for a limited number of pollutants (Ozolins, 1989). Unfortunately, although providing important functions, the HEAL project has not had the mandate or anything approaching the resources required to actually make comparable international estimates of population exposures. HEAL projects, for the most part, have investigated exposures to conventional inorganic air pollutants such as carbon monoxide, nitrogen dioxide and general undifferentiated particle mass where inhalation is the primary route of exposures. However, the HEAL programme does offer examples of lead, cadmium and pesticide studies which illustrate multiple exposure pathways and demonstrate the necessity of extensive analytical training and quality programmes. An analytical quality control programme which involved all participating laboratories enabled reliable international comparisons of exposure despite differences in methodologies applied by the different

laboratories.

Preceding this criteria document the UNEP, FAO and WHO have been actively advancing the concepts and methodologies for human exposures. GEMS/Air, GEMS/Water and GEMS/Food are establishing the uniformity among data collected worldwide to establish national and international status and trends. These efforts, together with others, such as the Codex Committee on Pesticide Residues, the several Joint FAO/WHO Consultations on food consumption, pesticide residues, veterinary drugs, additives and chemical contaminants, have been developing the basis of quantitative assessment of human exposures and risk. Table 38 (pg. 279) provides a listing of pertinent publications related to assessment of air, water and food contamination.

Scope

This current criteria document on human exposure assessment presents in one publication the concepts, rationale, and statistical and procedural methodologies for human exposure assessment. The underpinnings of exposure assessment are the basic environmental and biological measurements found in the more familiar specialties of air and water pollution and food and soil sciences. Therefore, throughout this document readers are referred to other publications for technical details on instrumental and laboratory methods. This criteria document is intended for the community of scientific investigators inquiring about the human health consequences of contaminants in our environment. As such, this text will be of interest to physical scientists, engineers and epidemiologists. It is intended also for those professions involved in devising, evaluating and implementing policy with respect to managing the quality of environmental health, inclusive of air, water, food and soil. By necessity environment is defined broadly to include place, media, and activities where we humans encounter contaminants.

Of primary concern in this document are those environmental contaminants that exist in various media as a consequence of direct or indirect human intention. We have included some biological agents that are "natural" but, through actions of irritation and allergy, can contribute to or cause morbidity and mortality as a result of inadequate building design and maintenance. We recognize that viral, bacterial and other biological agents in air, food, soil and water contribute significantly to the burden of disease worldwide. However, in the context of environmental exposure assessment the focus is on chemical contaminants and a few specific allergens that might contribute directly to disease or, in combination with biopathogens, alter susceptibility and expression of disease.

To say that exposure assessment of environmental contaminants is exclusive of any population or location is, in principle, a contradiction. There are practical considerations, however, for identifying the industrial workplace as a separate domain. Administratively, many nations handle occupational health and safety concerns separately from the environment. The management of workplace hazards through well-established industrial hygiene practices of source control, ventilation and worker protection are widely recognized. This separation of workplace exposures from the general environmental exposure focus in this document is not hard and fast. Occupationally acquired contaminants can expose family members not working in the specific industry. Industrial control strategies that

increase ventilation can adversely affect the neighbouring community. In many societies, commercial and residential use of property are integrated. Family operated business along congested streets means that contaminants generated in outdoors, indoors and workplaces are intermingled. Even where commercial and residential property are distinct, chemical and biological contaminants can lead to non-worker exposures.

Information on human exposures has a well-recognized role as a corollary to epidemiology. But it is more than this, because understanding human exposures to environmental contaminants is fundamental to public policy. The adequacy of environmental mitigation strategies is predicated on improving or safeguarding human and ecological health. The public mandate for and acceptance of controls on emissions is first based on sensory awareness of pollution. Irritated airways, foul-smelling exhaust, obscuring plumes, oil slicks on water, dirty and foul-tasting water, and medical waste and debris on beaches are readily interpreted as transgressions against us and threaten commonly shared natural resources. As we enter the twenty-first century, we recognize that we, humans have had profound but often subtle impacts on the chemistry of the biosphere and lithosphere. Metals, organic compounds, particulate matter, and photochemically produced gases are widely dispersed, recognizing no geographic or political boundaries. Global markets, urbanization, and increased mobility have environmental contamination as a consequence.

Assessing the quantities and distribution of potentially harmful contaminant exposures to human populations is a critical component of risk management. As long as disease prevention and health promotion are the principal tenets of public health, then assessing the levels of contaminant exposures in environmental and biological samples will be necessary.

This book presents the methodologies for surveying exposures, analysing data and integrating findings with the ongoing national and global debate defining natural limits to human behaviour. It serves the cross-disciplinary needs of environmental managers, risk assessors and epidemiologists to learn something about the design, conduct, interpretation and value of human exposure studies of multimedia environmental contaminants. For investigators considering exposure studies, this book guides them to contemporary information on measurement of analysis methods and strategies.

In Chapter 1 of the document the basic terms and concepts used in exposure assessment are defined. Similar understanding of terms used commonly among health assessors working in the different fields of air, water, soil and food sciences is a critical starting point in defining the emerging specialist area of exposure assessment. Application of exposure research and routine assessments to the information needs of risk managers, policy-makers and epidemiologists is established in Chapter 2. Discussion of these information needs is developed in Chapter 3, which presents the objectives for various study designs.

Chapter 4 covers basic statistical concepts used in exposure assessment. The intent is to inform the reader of how statistical analysis is vital to all components of an exposure assessment. By examples and references the reader is directed to more substantial texts on study design, data analysis, modelling and quality control.

Chapter 5 is devoted to a component of exposure assessment related to the collection and interpretation of human activity patterns. Information on how, where and when people contact potentially contaminant media is useful for data interpretation, establishing risk scenarios and identifying activities, locations and populations at differential risk. The emphasis here is primarily related to air pollution exposure studies. In the conduct of total multimedia exposure investigations or modelling analogous information is needed for the ingestion of water and food, as well as for dermal contact.

Chapter 6 extends the concepts of the preceding chapters in discussing models for human exposure assessment. The data requirements for various pathways and various modelling approaches are presented.

Chapter 7 separates the conceptual first half of the text from the pragmatic guidelines offered in the rest of the document. The chapter contains a discussion of air monitoring, water monitoring and food sampling. These particular fields are rather well developed

individually, if not well integrated into multimedia studies. The reader is referred to many other resources that can guide the investigator to details on instruments, sampling methods and laboratory analysis.

In Chapter 8, proportionally more emphasis is placed on soil and settled dust sampling. Again, the laboratory methods for metals, organics and various chemical compounds are readily available in the published literature. This chapter, then, focuses on relatively new sampling techniques to quantify in a standardized way the contaminant levels in soil and settled dust.

In Chapter 9, on microbiological agents, assessment techniques for commonly encountered allergens, mycotoxins, fungal and pollen spores, microbiological bacteria and endotoxins are presented. These agents have been included because of their imputed contribution to respiratory disease and potential interactions with chemical pollutants. There is growing recognition that exposure to these agents in schools, homes, hospitals and office buildings constitutes a specific risk to atopic, asthmatic and compromised individuals.

The use of biomarkers for exposure assessments is presented in Chapter 10. Biological samples derived from human tissue or fluids have been used as markers of both effects as well as exposure (dose) to a variety of occupational and environmental contaminants. The chapter describes the applications of biomarkers in exposure studies.

The quality assurance (QA) activities that should be considered in conducting and evaluating exposure studies are addressed in Chapter 11. Contributors to this document intended to impart their experiences to improve future exposure study. It is emphasized that QA aspects must be considered in all components of exposure studies, to enhance comparability and interpretation.

Chapter 12 presents brief synopses of exposure studies. Selections illustrate a variety of study designs with different objectives and target pollutants and populations. Relatively more emphasis has been given to particles and passive exposure to cigarette smoke. The evidence is that cigarette consumption has increased almost worldwide, suggesting that greater attention be given to

characterizing and reducing exposures to non-smokers, in particular, infants and young children. Epidemiological studies conducted over the last 15 years indicate that ambient particulate matter is adversely affecting human health at levels well below many of the established standards. Exposure assessment along with toxicology and epidemiology will be needed to answer many of the remaining unresolved issues about ambient and indoor suspended particles.

Other studies summarized show how exposure assessment is supportive of epidemiology and risk management. The reader should recognize that Chapter 12 is not comprehensive but is intended to help educate the research community and others about the application, use and limitations of exposure assessment methodologies.

1. DEFINING EXPOSURE

1.1 Introduction

People are exposed to a variety of potentially harmful agents in the air they breathe, the liquids they drink, the food they eat, the surfaces they touch and the products they use. An important aspect of public health protection is the prevention or reduction of exposures to environmental agents that contribute, either directly or indirectly, to increased rates of premature death, disease, discomfort or disability. It is usually not possible, however, to measure the effectiveness of mitigation strategies directly in terms of prevented disease, reduced premature death, or avoided dysfunction. Instead, measurement or estimation of actual human exposure, coupled with appropriate assumptions about associated health effects or safety limits (e.g., acceptable daily intake, tolerable daily intake), is the standard method used for determining whether intervention is necessary to protect and promote public health, which forms of intervention will be most effective in meeting public health goals, and whether past intervention efforts have been successful (Ott & Roberts, 1998).

The purpose of this chapter is to define the concept of exposure, and the direct and indirect method of exposure assessment. A brief discussion of exposure in the environmental health paradigm and its relationship to dose is presented.

1.2 Defining exposure

Exposure is defined as contact over time and space between a person and one or more biological, chemical or physical agents (US NRC, 1991a). Exposure assessment is to identify and define the exposures that occur, or are anticipated to occur, in human populations (IPCS, 1993). This can be a complex endeavour requiring analysis of many different aspects of the contact between people and hazardous substances (see Table 1). Although exposure is a well-established concept familiar to all environmental health scientists, its meaning often varies depending on the context of the discussion. It is important however, that exposure and related terms be defined precisely. In the following sections, we describe and define important exposure-related terms used in this document. The definitions are consistent with the US EPA's Exposure Assessment Guidelines and related WHO publications (WHO, 1987, 1996a; US EPA, 1992a; IPCS, 1994). It is important to recognize, however, that terminology and definitions vary among organizations and nations. Thus, the reader is advised to concentrate on the concepts, rather than the specific terms, as they represent the crux of exposure

assessment.

Table 1. Different aspects of the contact between people and pollution that are potentially important in exposure analysis (Sexton et al., 1995b)

Agent(s)	biological, chemical, physical, single agent, multiple agents, mixtures
Source(s)	anthropogenic/non-anthropogenic, area/point, stationary/mobile, indoor/outdoor
Transport/carrier medium	air, water, soil, dust, food, product/item
Exposure pathways(s)	eating contaminated food, breathing contaminated workplace air touching residential surface
Exposure concentration	mg/kg (food), mg/litre (water), $\mu\text{g}/\text{m}^3$ (air), $\mu\text{g}/\text{cm}^2$ contaminated surface), % by weight, fibres/ m^3 (air)
Exposure route(s)	inhalation, dermal contact, ingestion, multiple routes
Exposure duration	seconds, minutes, hours, days, weeks, months, years, lifetime
Exposure frequency	continuous, intermittent, cyclic, random, rare
Exposure setting(s)	occupational/non-occupational, residential/non-residential, indoors/outdoors
Exposed population	general population, population subgroups, individuals
Geographic scope	site/source specific, local, regional, national, international, global
Time frame	past, present, future, trends

1.2.1 Exposure and exposure concentration

Exposure, as defined earlier, is the contact of a biological, chemical, or physical agent with the outer part of the human body, such as the skin, mouth or nostrils. Although there are many instances where contact occurs with an undiluted chemical (e.g., use of degreasing chemicals for cleaning hands), contact more often occurs with a carrier medium (air, water, food, dust or soil) that contains dilute amounts of the agent. "Exposure concentration" (e.g., mg/litre, mg/kg, $\mu\text{g}/\text{m}^3$) is defined as the concentration of an environmental agent in the carrier medium at the point of contact with the body.

1.2.2 Exposure estimation by integration and averaging

A minimal description of exposure for a particular route must

include exposure concentration and the duration of contact. If the exposure concentration is integrated over the duration of contact (Table 2), the area under the resulting curve is the magnitude of the exposure in units of concentration multiplied by time (e.g., mg/litre·day, mg/kg·day, $\mu\text{g}/\text{m}^3\cdot\text{h}$). This is the method of choice to describe and estimate short-term doses, where integration times are of the order of minutes, hours or days.

Over periods of months, years or decades, exposures to most environmental agents occur intermittently rather than continuously. Yet long-term health effects, such as cancer, are customarily evaluated based on an average dose over the period of interest (typically years), rather than as a series of intermittent exposures. Consequently, long-term doses are usually estimated by summing doses across discrete exposure episodes and then calculating an average dose for the period of interest (e.g., year, lifetime). Although the integration approach can also be used to estimate long-term exposures or doses, its application to time periods longer than about a week is usually difficult and inconvenient.

1.2.3 Exposure measurements and models

Direct measurements are the only way to establish unequivocally whether and to what extent individuals are exposed to specific environmental agents. But it is neither affordable nor technically feasible to measure exposures for everyone in all populations of interest. Models, which are mathematical abstractions of physical reality, may obviate the need for such extensive monitoring programmes by providing estimates of population exposures (and doses) that are based on a smaller number of representative measurements (Fig. 1). The challenge is to develop appropriate and robust models that allow for extrapolation from relatively few measurements to estimates of exposures and doses for a much larger population (US NRC, 1991b).

For relatively small groups, measurements or estimates can be made for some or all of the individuals separately, and then combined as necessary to estimate the exposure (or dose) distribution. For larger groups, exposure models and statistics can sometimes be used to derive an estimate of the distribution of population exposures, depending on the quantity and quality of existing data. Monte Carlo and other statistical techniques are increasingly being used to generate and analyse exposure distributions for large groups (US EPA, 1992a).

1.2.4 Exposure in the context of an environmental health paradigm

The presence of hazardous substances in our environment does not necessarily imply a risk to human health or to the ecosystem. Exposure is an integral and necessary component in a sequence of events having potential health consequences. An expanded and more detailed version

Table 2. Mathematical expressions for some important exposure-related and dose-related events

Exposure

$$E = \int_{t_1}^{t_2} C(t) dt$$

Potential dose for intake processes

$$D_{\text{applied}} = \alpha \int_{t_1}^{t_2} C(t) IR(t) dt$$

Applied dose

$$D_{\text{potential}} = \int_{t_1}^{t_2} C(t) IR(t) dt$$

Internal dose

$$D_{\text{internal}} = D_{\text{applied}} \int_{t_1}^{t_2} f(t) dt$$

E, magnitude of exposure; $t_2 - t_1$, exposure duration; α , availability factor; C(t), exposure concentration as a function of time; IR, ingestion or inhalation rate; f(t), nonlinear absorption function (Sexton et al., 1995a)

of the environmental health paradigm also showing the role of exposure is depicted in Fig. 2. The role of exposure assessment in the risk assessment framework applied by EU and US EPA is shown in Fig. 3.

The release of an agent into the environment, its ensuing transport, transformation and fate in various environmental media, and its ultimate contact with people are critical events in understanding how and why exposures occur. Definitions for key events in the continuum are summarized below. They were compiled from three sources: Ott (1990); US EPA (1992a); Sexton et al. (1995a).

- * *Sources*. The point or area of origin for an environmental agent is known as a source. Agents are released into the environment from a wide variety of sources, which are often categorized as *primary sources* including point sources (e.g., incinerator) versus area sources (e.g., urban runoff), stationary sources (e.g., refinery) versus mobile sources (e.g., automobile) and anthropogenic sources (e.g., landfill) versus non-anthropogenic sources (e.g., natural vegetation) and *secondary sources* including condensation of vapours into particles and chemical reactions of precursors producing new pollutants.
- * *Exposure pathway*. An exposure pathway is the physical course taken by an agent as it moves from a source to a point of contact with a person. The substance present in the media is quantified as its concentration.

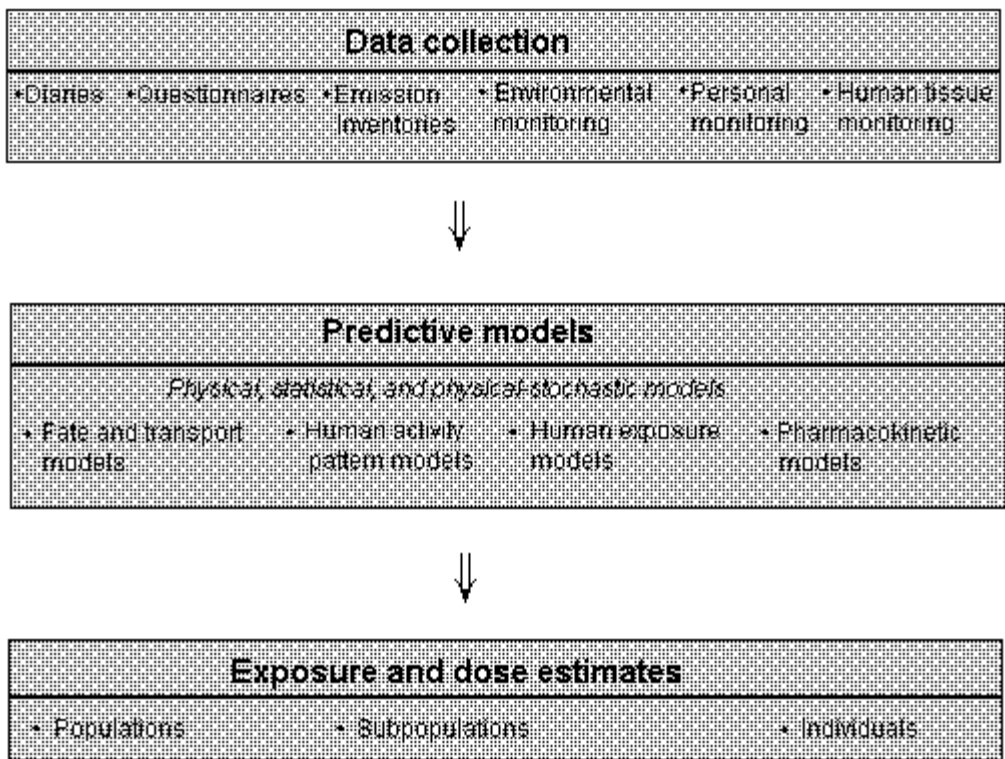


Fig. 1. The relationship among data collection, predictive models, and exposure and dose estimates (Sexton et al., 1995b)

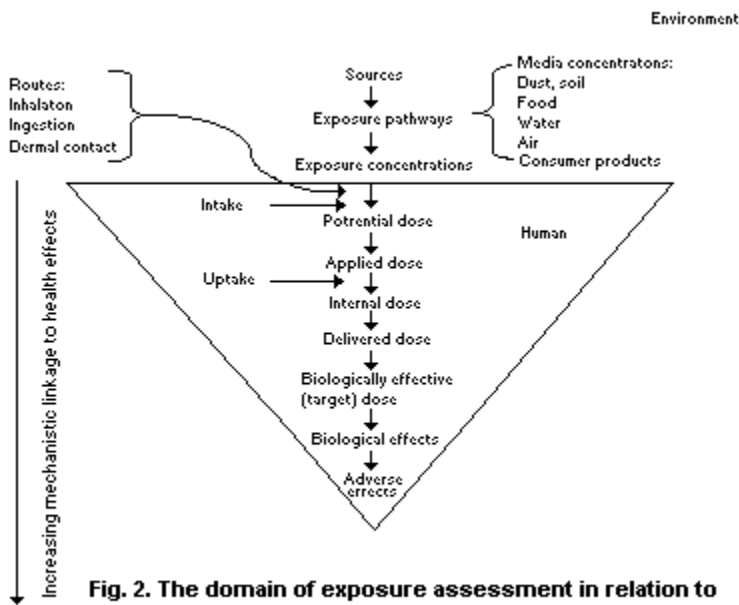


Fig. 2. The domain of exposure assessment in relation to an environmental health paradigm (adapted from IPCS, 1993; Sexton et al., 1995a)

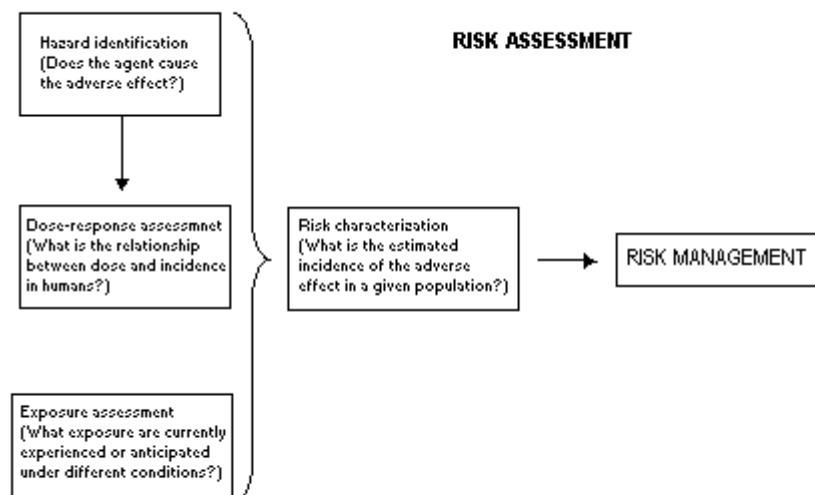


Fig. 3. Elements of risk assessment (modified from US NRC, 1983)

- * *Exposure concentration.* As discussed in 1.2.1, exposure is the concentration of an agent in a carrier medium at the point of contact with the outer boundary of the human body. The concentration is the amount (mass) of a substance or contaminant that is present in a medium such as air, water, food or soil expressed per volume or mass. Assessments are often not at exposure or exposure concentration, since that information alone is not very useful unless it is converted to dose or risk. Assessments therefore usually estimate how much of an agent is expected to enter the body. This transfer of an environmental agent from the exterior to the interior of the body can occur by either or both of two basic processes: intake and uptake.
- * *Exposure route.* Exposure route denotes the different ways the substance may enter the body. The route may be dermal, ingestion or inhalation.
- * *Intake.* Intake is associated with ingestion and inhalation routes of exposure. The agent, which is likely to be part of a carrier medium (air, water, soil, dust, food), enters the body by bulk transport, usually through the nose or mouth. The amount of the agent that crosses the boundary per unit time can be referred to as the "intake rate", which is the product of the exposure concentration times the rate of either ingestion or inhalation. For inhalation, intake may be calculated for any time period. For ingestion, intake is usually expressed as the amount of food or water consumed times the pollutant concentration in that medium during a certain time period.
- * *Uptake.* Uptake is associated with the dermal route of exposure, as well as with ingestion and inhalation after intake has occurred. The agent, as with intake, is likely to be part of a carrier medium (e.g., water, soil, consumer product), but enters the body by crossing an absorption barrier, such as the skin, respiratory tract or gastrointestinal tract. The rates of bulk transport across the absorption barriers are generally not the same for the agent and

the carrier medium. The amount of the agent that crosses the barrier per unit time can be referred to as the *uptake rate*. This rate is a function of the exposure concentration, as well as of the permeability and surface area of the exposed barrier. The uptake rate is also called a *flux*.

- * *Dose*. Once the agent enters the body by either intake or uptake, it is described as a dose. Several different types of dose are relevant to exposure estimation. All these different dose measures are approximations of the target or biological effective dose.
 - *Potential (administered) dose*. Potential or administered dose is the amount of the agent that is actually ingested, inhaled or applied to the skin. The concept of potential dose is straightforward for inhalation and ingestion, where it is analogous to the dose administered in a dose-response experiment. For the dermal route, however, it is important to keep in mind that potential (or administered) dose refers to the amount of the agent, whether in pure form or as part of a carrier medium, that is applied to the surface of the skin. In cases where the agent is in diluted form as part of a carrier medium, not all of the potential dose will actually be touching the skin.
 - *Applied dose*. Applied dose is the amount of the agent directly in contact with the body's absorption barriers, such as the skin, respiratory tract and gastrointestinal tract, and therefore available for absorption. Information is rarely available on applied dose, so it is calculated from potential dose based on factors such as bioavailability (Fig. 2).
 - *Internal (absorbed) dose*. The amount of the agent absorbed, and therefore available to undergo metabolism, transport, storage or elimination, is referred to as the *internal* or *absorbed* dose (Fig. 2). Bioavailability has been used to describe absorbed dose.
 - *Delivered dose*. The delivered dose is the portion of the internal (absorbed) dose that reaches a tissue of interest.
 - *Biologically effective (target) dose*. The biologically effective dose is the portion of the delivered dose that reaches the site or sites of toxic action.

The link, if any, between biologically effective (target) dose and subsequent disease or illness depends on the relationship between dose and response (e.g., shape of the dose-response curve), underlying pharmacodynamic mechanisms (e.g., compensation, damage, repair), and important susceptibility factors (e.g., health status, nutrition, stress, genetic predisposition).

- * *Biological effect*. A measurable response to dose in a molecule, cell or tissue is termed a biological effect. The significance of a biological effect, whether it is an indicator or a precursor for subsequent adverse health effects, may not be known.
- * *Adverse effect*. A biological effect that causes change in morphology, physiology, growth, development or life span which results in impairment of functional capacity to compensate for

additional stress or increase in susceptibility to the harmful effects of other environmental influences (IPCS, 1994).

1.3 Elements of exposure assessment

Assessing human exposure to an environmental agent involves the qualitative description and the quantitative estimation of the agent's contact with (exposure) and entry into (dose) the body. Although no two exposure assessments are exactly the same, all have several common elements: the number of people exposed at specific concentrations for the time period of interest; the resulting dose; and the contribution

of important sources, pathways and behavioural factors to exposure or dose. A list of the types of estimates that might comprise a comprehensive exposure assessment could include the following (as described in part by Brown (1987) and Sexton et al. (1995a)):

* *Exposure*

- routes, pathways and frequencies
- duration of interest (short-term, long-term, intermittent or peak exposures)
- distribution (e.g., mean, variance, 90th percentile) -- population, important subpopulations (e.g., more exposed, more susceptible)
- individuals -- average, upper tail of distribution, most exposed in population.

* *Dose*

- link with exposures
- distribution (e.g., mean, variance, 90th percentile) -- population important subpopulations (e.g., higher doses, more susceptible)
- individuals -- average, upper tail of distribution, highest dose in population.

* *Causes*

- relative contribution of important sources
- relative contribution of important environmental media
- contribution of important exposure pathways
- relative contribution of important routes of exposure.

* *Variability*

- within individuals (e.g., changes in exposure from day to day for the same person)
- between individuals (e.g., differences in exposure on the same day for two different people)
- between groups (e.g., different socio-economic classes or residential locations)
- over time (e.g., changes in exposure from one season to another)
- across space (e.g., changes in exposure/dose from one region of a city, country to another).

* *Uncertainty*

- lack of data (e.g., statistical error in measurements, model parameters, etc.; misidentification of hazards and causal pathways)
- lack of understanding (e.g., mistakes in functional form of models, misuses of proxy data from analogous contexts).

Although comprehensive exposure assessments could be considered

the ideal, they are very costly; decisions therefore need to be made on the most important elements for inclusion. For any study, the purpose must first be defined. Possible purposes include environmental epidemiology, risk assessment, risk management or status and trend analysis (see Chapter 2). The data elements and measuring approaches

that are needed for this purpose are then determined. Table 3 summarizes the basic information that is required for each study. It should be mentioned that different elements of the exposure assessment framework might be selected to meet different study requirements.

Table 3. Basic information needed for exposure assessments in different contexts

	Information required
Risk assessment	Point estimates or distributions of exposure and dose Duration of exposure and dose
Risk management (conducted once hazard is identified)	Pollutant source contributing to exposure and dose Personal activities contributing to exposure and dose Effectiveness of intervention measures
Status and trend	Change of exposure and dose of populations over time
Epidemiology	Individual and population exposures and doses, exposure dose categories

1.4 Approaches to quantitative exposure assessment

Quantitative estimation of exposure is often the central feature of assessment activities. The quantitative estimation of exposure can be approached in two general ways: *direct assessment*, including point-of-contact measurements and biological indicators of exposure; and *indirect assessment*, including environmental monitoring, modelling, questionnaires (US NRC, 1991b) (see Chapter 3.5). These two generic approaches to quantitative estimation of exposure are independent and complementary. Each relies on different kinds of data and has different strengths and weaknesses. It is potentially useful, therefore, to employ multiple approaches as a way of checking the robustness of results. Among other factors, the choice of which method to use will depend on the purpose of the assessment and the availability of suitable methods, measurements and models.

Direct approaches for air, water and food include personal air monitors, measurements of water at the point of use and measurement of the food being consumed. Indirect approaches include microenvironmental air monitoring and measurements of the water supply and food supply (contents of a typical food basket, for instance).

Exposure models are constructed to assess or predict personal

exposures or population exposure distributions from indirect measurements and other relevant information.

Measures of contaminants in biological material (biomarkers) afford a direct measure of exposure modified by and integrated over some time in the past which depends on physiological factors that control metabolism and excretion. Such measures give no direct information about the exposure pathways. Examples of the type of biomarkers measured in human material that can be used for reconstructing internal dose and their relevance to exposure assessment are discussed in Chapter 10.

1.5 Linking exposure events and dose events

The schematic framework in Fig. 2 shows how the interrelationships among significant exposure- and dose-related events in the paradigm can be conceived.

It is important to keep in mind that, although events along the continuum are correlated, the relative position of a particular individual within a distribution may change dramatically from one event to the next as the agent or its metabolite/derivative moves through the various stages from exposure concentration to biologically effective dose.

To make realistic estimates for a specific event (e.g., an internal dose), it is necessary to have at least one of two types of information: measurements of the event itself (e.g., internal dose), or measurements of an earlier (e.g., potential dose) or later (e.g., delivered dose) event in the continuum. It is also necessary to understand the critical intervening mechanisms and processes (e.g., pharmacokinetics) that govern the relationship between the event measured and the event of interest (e.g., internal dose). Unless such data are on hand, extrapolating from one event to another, moving either from exposure to dose (downwards in Fig. 2) or from dose to exposure (upwards in Fig. 2) is problematic.

Suitable data and adequate understanding are seldom, if ever, available to describe and estimate all of the significant events for the groups and individuals of interest. Generally speaking, measurement of exposure concentration and delivered dose (*body burden*) is in many cases relatively straightforward, whereas measurement of potential (administered) dose and internal (absorbed) dose is usually possible only with substantially greater effort. Measurement of biologically effective (target) dose may also be possible in some cases, although it is usually impossible to measure the applied dose.

This situation presents us with a conundrum. We would like to have realistic estimates of exposure concentrations of an agent for all important pathways, and the resulting biologically effective dose. Typically, however, if relevant data are available at all, they are

related to exposure concentrations for one pathway or route of exposure. In the few cases where data on dose are also available, these data usually reflect delivered dose (body burden) rather than biologically effective dose. Even if suitable measurements of both exposure concentration and delivered or target dose are on hand, the absence of pharmacokinetic understanding to relate these measurements to each other, as well as to other significant events along the

continuum, seriously impairs efforts to establish the link between exposure and dose.

We are thus left with a situation in which we can measure specific events on either side of the body's absorption boundaries, but we can relate them to each other only by using a series of unsubstantiated assumptions. Yet it is this relationship between exposure and dose that is critical to, for example, establishing cause and effect relationships between exposure and diseases.

1.6 Summary

Exposure requires the occurrence of the presence of an environmental toxicant at a particular point in space and time; and the presence of a person or persons at the same location and time. In addition, the amount which comes in contact with the outer boundary of the human body is required.

As the intrinsic value of exposure-related information has become recognized, "exposure analysis" has emerged as an important field of scientific investigation, complementing such traditional public health disciplines as epidemiology and toxicology, and is an essential component in informed environmental health decision-making (Goldman et al., 1992; Sexton et al., 1992, 1994; Wagener et al., 1995).

2. USES OF HUMAN EXPOSURE INFORMATION

2.1 Introduction

Exposure assessments collect data on the route magnitude, duration, frequency and distributions of exposures to hazardous agents for individuals and populations. Human exposure data have been used for the evaluation and protection of environmental health in four interrelated disciplines: epidemiology, risk assessment, risk management, and status and trends analysis. The fundamental goal of exposure assessment studies is to reduce the uncertainty of the exposure estimates that are used within each discipline to make public policy decisions or reach research conclusions.

Epidemiology is the examination of the link between human exposures and health outcomes (Sexton et al., 1992). *Risk assessment* is the estimation of the likelihood, magnitude and uncertainty of population health risks associated with exposures. In contrast, *risk management* is the determination of the source and level of health risks and which health risks are acceptable and what to do about them. Status and trends analysis comprises the evaluation of historical patterns, current status and possible future changes in human exposures.

The purpose of this chapter is to describe the disciplines from environmental epidemiology through risk assessment. It also describes how human exposure assessment data are used in each of these disciplines

2.2 Human exposure information in environmental epidemiology

Epidemiology is the study of the determinants and distribution of health status (or health-related events) in human populations. Environmental epidemiology searches for statistical associations between environmental exposures and adverse health effects (presumed)

to be caused by such exposures. It is a scientific tool that can sometimes detect environmentally induced health effects in populations, and it may offer opportunities to link actual exposures with adverse health outcomes (US NRC, 1991c, 1994; Matanoski et al., 1992; Beaglehole et al., 1993).

Exposure assessment methods can be used for identifying and defining the low or high exposure groups. They can also be used for devising more accurate exposure data from measured environmental contaminant levels and personal questionnaire or time-activity diary data, or estimating population exposure differences between days of high and low pollution, or between high and low pollution in communities using measured environmental and population behavioural data (see also Chapters 3 and 5).

In particular, to establish long-term health effects of "low dose" environmental exposures, epidemiological methods are the predominant, if not only, tools at hand for health-effect assessment. However, the excess risk of most environmentally related health effects is small, with relative risks and odds ratios usually being less than 2 across the observed range of exposure experienced by populations. Furthermore, there are usually no "non-exposed" comparison groups, and the factors contributing to the development of diseases are numerous. As a consequence, environmental epidemiology faces considerable methodological challenges. Adequate exposure assessment is one key issue, as well as the need for studies conducted with large populations.

2.3 Human exposure information in risk assessment

Risk assessment is a formalized process for estimating the magnitude, likelihood and uncertainty of environmentally induced health effects in populations. Exposure assessment (e.g., exposure concentrations and related dose for specific pathways) and effects assessment (i.e., hazard identification, dose-response evaluation) are integral parts of the risk assessment process. The goal is to use the best available information and knowledge to estimate health risks for the subject population, important subgroups within the population (e.g., children, pregnant women and the elderly), and individuals in the middle and at the "high end" of the exposure distribution (US NRC, 1983; Graham et al., 1992; Sexton et al., 1992).

Environmental health policy decisions should be based on established links among emission sources, human exposures and adverse health effects. The chain of events depicted in Fig. 4 is an "environmental health paradigm": a simplified representation of the key steps between emission of toxic agents into the environment and the final outcome as potential disease or dysfunction in humans. This sequential series of events serves as a useful framework for understanding and evaluating environmental health risks (Sexton, 1992; Sexton et al., 1992, 1993). It is directly related to the risk assessment process.

* *Exposure assessment* in the risk assessment framework focuses on the initial portion of the environmental health paradigm: from sources, to environmental concentrations, to exposure, to dose. The major goal of exposure assessment is to develop a qualitative and quantitative description of the environmental agent's contact with (exposure) and entry into (dose) the human body. Emphasis is placed on estimating the magnitude, duration and frequency of exposures,

as well as estimating the number of people exposed to various concentrations of the agent in question (US NRC, 1983, 1991a; Callahan & Bryan, 1994).

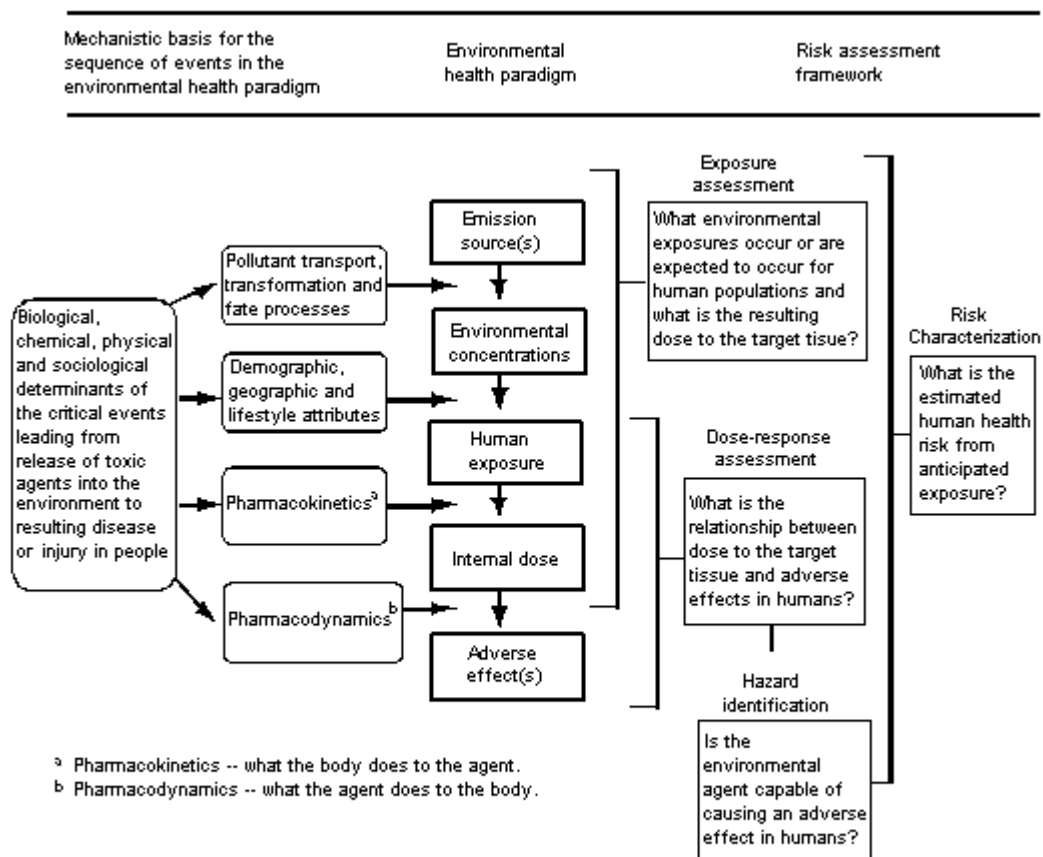


Fig. 4. An environmental health paradigm and its relationship to the risk assessment framework (Sexton et al., 1995c)

- * *Effects assessment* examines the latter portion of the events continuum: from dose to adverse health effects (Fig. 4). The goals are to determine the intrinsic hazards associated with the agent (hazard identification) and to quantify the relationship between dose to the target tissue and related harmful outcomes (dose-response/effect assessment). The overlap between exposure assessment and effects assessment reflects the importance of the exposure-dose relationship to both activities (Sexton et al., 1992).
- * *Risk characterization* is the last phase of the risk assessment process. The results of the actual exposure assessment and the effects assessments are combined to estimate the human health risks from the exposures.

Systemic (non-cancer) toxicants are usually assumed to have thresholds below which no effects occur. For these toxicants, safety assessments are performed with establishment of *tolerable intakes* (IPCS, 1993) or *reference concentrations/doses* (USEPA). From these, guidelines are derived and standards designed to protect public health. Ambient concentration standards, and workplace personal exposure limits, are often established at or below threshold levels

determined as part of the risk assessment process. Although these standards are set with safety margins, exposures that exceed these reference levels raise concerns about potentially elevated health risks for the exposed population (Fig. 5a).

Quantitative risk assessment for carcinogens is a well established, albeit controversial, procedure. As part of the guidelines developed by the WHO, it is common practice to extrapolate from high to low dose by assuming a linear, non-threshold model for carcinogenicity. Under this assumption, cancer risk for individuals can be estimated directly from the exposure or dose distribution, and the number of excess cancer cases (i.e., the increase above background rates) in the exposed population can usually be estimated by multiplying the average dose by both the total number of people exposed and the dose-response slope factor (Fig. 5b). Although individual risk is assumed to increase with increasing exposure and dose all along the distribution, exposures of concern are typically defined to be those above some minimal level of risk (e.g., WHO considers this to be a 1 in 10^5 or 10^6 excess lifetime risk of developing cancer). Unit cancer risk numbers are given in inverse concentration units for food, water and air as $(\text{ppm})^{-1}$, $(\text{ppb})^{-1}$ or $\text{mg}^{-1}\text{m}^{-3}$. Expressed in inverse dose units ($\text{mg kg}^{-1}\text{day}^{-1}$), the cancer slope risk factor is multiplied by ingestion or inhalation rates and adjusted for body weight. Individual cancer risk is calculated by assuming a lifetime of exposure at a given level of contamination. When exposure data are available, it is then possible to approximate the cancer risk of the typical or average person in the population or one who might be at maximum risk due to a greater level of exposure.

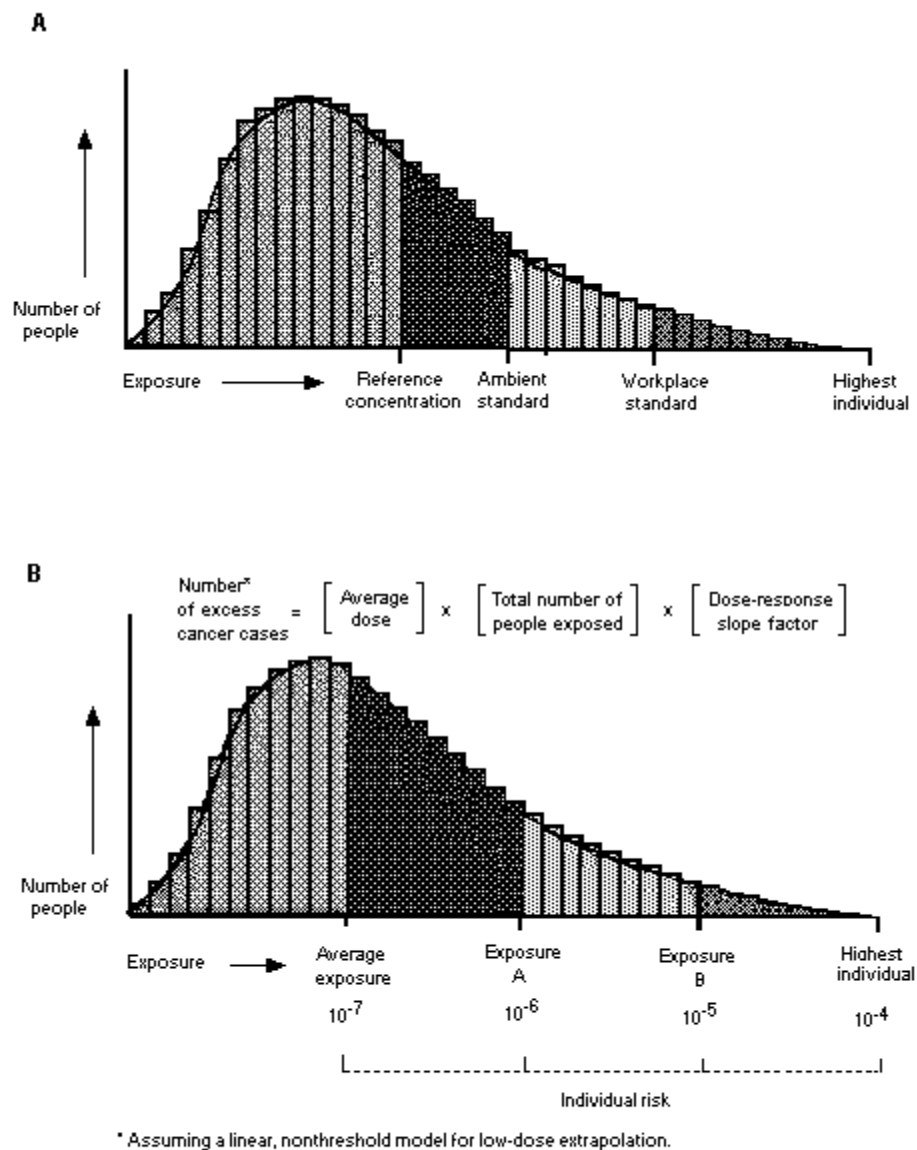


Fig. 5. Human exposure distributions for (A) a hypothetical systemic (non-cancer) toxicant and (B) a hypothetical carcinogen (Sexton et al., 1993)

In regulatory applications of risk assessments, exposure estimates are often constructed using existing data or single point measurements to estimate the risk of a facility, hazardous waste site or chemical waste site, or even the use of a chemical product. This approach can result in large errors in the exposure assessment and hence the risk assessment. Exposure assessment studies are used to obtain a more accurate determination of the exposure associated with a health impact outcome of concern. Population-based risk assessments benefit from the use of population-based measurements derived from surveys or models (see Chapter 3) to estimate the distribution of health effect outcomes in the total exposed population over a specified time period.

2.3.1 Risk allocation for population subgroups or activities

Exposure studies may also be conducted to provide more realistic and location-specific information for use in human health risk assessments. Measurement data on pollutant concentrations and exposure factors, such as contact rates, can be used instead of relying on assumed "default" values for an "averaged" or representative individual. An example of an exposure study designed to collect data for the purpose of allocating risk to locations, sources and activities is the Windsor Air Quality Study conducted in Windsor, Ontario, Canada (Bell et al., 1994).

The Windsor Air Quality Study was designed to investigate the Windsor airshed characteristics with respect to airborne toxic compounds and to determine personal inhalation exposures to these compounds. Data were then used as inputs for a multimedia assessment of risk due to total pollutant exposure. The air quality study examined just one aspect, the inhalation route. It was designed to separately attribute risk to several airborne contaminants by indoor and outdoor locations. Statistical analysis and inference were used to impute source contributions to population risk (i.e., the waste incinerator across the river in Detroit, Michigan, USA) for selected volatile organic compounds (VOCs), carbonyls and trace metals (see Table 4) based on microenvironmental and personal measurements and time activity patterns. In general, air quality was determined to be relatively poor in recreation halls, new office buildings, cars and garages when compared to outdoor air quality standards and criteria. Although high contaminant concentrations were detected in various microenvironments, population exposures (defined as the product of concentration and time) were relatively low because the study subjects did not spend any appreciable time in those microenvironments. This point is illustrated in Fig. 6. For all of the VOCs, the highest concentrations were measured during the commuting periods, with comparable concentrations being measured indoors at the office and home and the lowest outdoors (Table 3). When time in each microenvironment is considered, exposure in the home accounted for over 70% of the total exposure profile for that individual.

Table 4. Target analytes in the Windsor air quality study

Volatile organic compounds

Propane, chloromethane, 2-methylpropane, chloroethene, 1,3-butadiene, butane, 2-methylbutane, pentane, isoprene, 1,1-dichloroethene, dichloromethane, allyl ch hexane trichloromethane, 1,2-dichloroethane, 1,1,1-trichloroethane, benzene, tetrachloromethane, xylenes, styrene, o-xylene, 1,1,2,2-tetrachloroethane, nonan 1,3,5-trimethylbenzene, 1,2,4-trimethylbenzene, 1,4-dichlorobenzene; decane, 1,2-dichlorobenzene, undecane, 1,2,4-trichlorobenzene, dodecane, tridecane

Carbonyls

Formaldehyde, acetaldehyde, acrolein, acetone, propionaldehyde, crotonaldehyde, ethyl ketone, benzaldehyde, isovaleraldehyde, 2-pentanone, valeraldehyde, o-tol m-tolualdehyde, p-tolualdehyde, methyl isobutyl ketone, hexanal, 2,5-dimethylb

Trace metals

Beryllium, chromium, manganese, nickel, arsenic, selenium, cadmium, lead

Results of the study emphasize the importance of exposure assessments for policy decisions. For this community, changes in lifestyle, consumer product formulations, cleaning of indoor air and increased ventilation would probably have more impact on reducing health risks from exposures to VOCs than reliance on government-mandated abatement strategies for ambient sources.

2.3.2 Population at higher or highest risk

Risk assessment may be used to identify and evaluate those populations, subpopulations and individuals at potentially greater risk so that, if warranted, appropriate mitigation actions can be implemented. Individuals and groups are deemed to be at potentially higher risk because they are exposed to high concentrations of hazardous pollutants (Sexton et al., 1993). Individuals and groups can also be at increased risk because they are more susceptible to the adverse effects of a given exposure. Among the potential causes of enhanced susceptibility are inherent genetic variability, age, gender, pre-existing disease (e.g., diabetes, asthma), inadequate diet, environmental or lifestyle factors (e.g., smoking), stress and inadequate access to health care. As far as possible, it is important to identify these susceptible individuals and groups so that we can understand their exposures and take account of this information in assessing and managing risks. Exposure and risk information for susceptible populations is critical since health standards and regulations are often developed with the intent of protecting these individuals.

Exposure studies provide valuable information for the risk assessment by quantifying the distribution of exposures in a population and identifying those subpopulations or individuals who have the highest exposures. Information is also gathered on characteristics of the populations and factors that could contribute to elevated exposures. In these studies, measures of central tendency, such as the median and average, along with expressions of variability, such as the standard deviation, are commonly used to describe the distribution of exposures for a population (Fig. 7). Often, the relative position of an individual or group in the exposure distribution is of primary interest to the exposure assessor. Among the most frequently used descriptors for individual and subgroup exposures are values near the middle of the distribution, values above the 90th percentile and values at the extreme upper end, such as for the most exposed person in the population. Exposure studies that are targeted on susceptible populations are used with the same type of inputs in risk assessment for these groups.

2.4 Human exposure information in risk management

Risk management decisions carried out by policy-makers are of four basic types: priority setting, selection of the most cost-effective method to prevent or reduce unacceptable risks, setting and evaluating compliance with standards or guidelines, and the evaluation of the success of risk mitigation efforts. Exposure information is crucial to these decisions. In addition to data on exposures and related health effects, decision-makers also must account for the economic, engineering, legal, social and political aspects of the problem (Burke et al., 1992; Sexton et al., 1992).

Conceptually, as shown in Fig. 8, estimating and prioritizing health risks are seemingly straightforward. Risk is a combination of effects estimates, where "highest" priorities can be thought of as those that entail both "high" toxicity for the agent of interest (adverse effects are likely to occur in humans at relatively low exposures or doses), and "high" exposures for the population, subpopulation or individuals of interest (exposures or doses are above a health-based standard). Conversely, "lowest" priority risks involve "low" toxicity and "low" exposures. "Medium" priority risks are those for which either toxicity or exposure is "low" while the other is "high" (Sexton, 1993). The Windsor Air Quality Study, for example, showed that incinerator emissions contributed little to total human exposure for VOCs. Despite the fact that the pollutants were of high toxicity, incinerator emissions were considered to be of relatively low risk to the population. In contrast, studies show that second-hand smoke has both high toxicity and high human exposures, and should therefore be identified as a high priority risk.

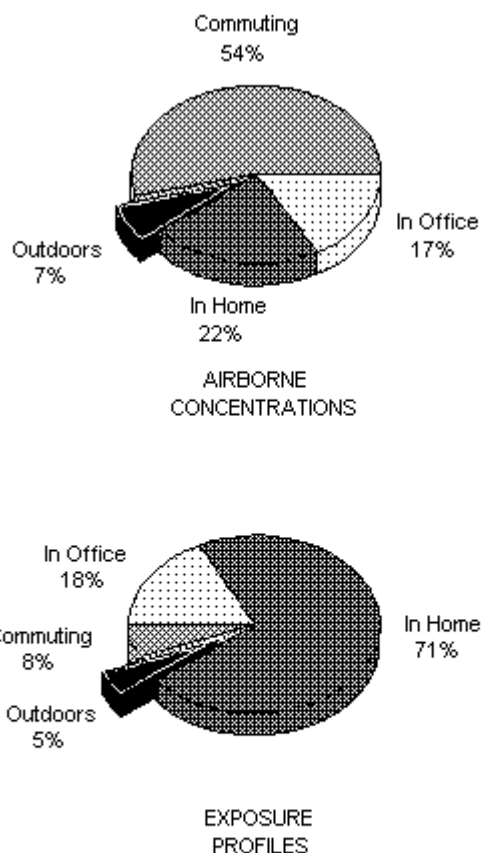


Fig. 6. Airborne concentrations and exposures to VOCs by location/activity. Exposure is the product of the average airborne concentrations measured in an environment and the average time a person spends in that environment (Bell et al., 1994)

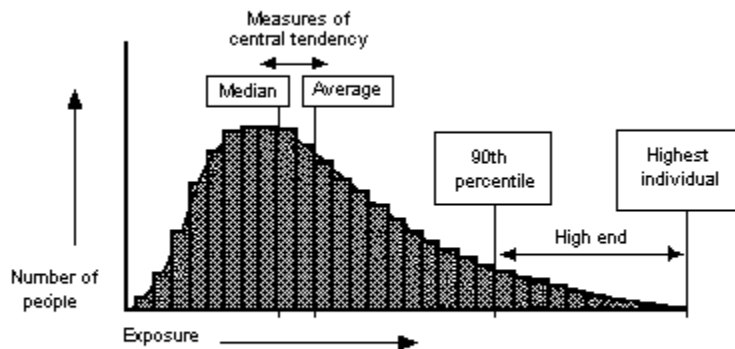


Fig. 7. Common descriptors for human exposures to environmental agents (Sexton et al., 1993)

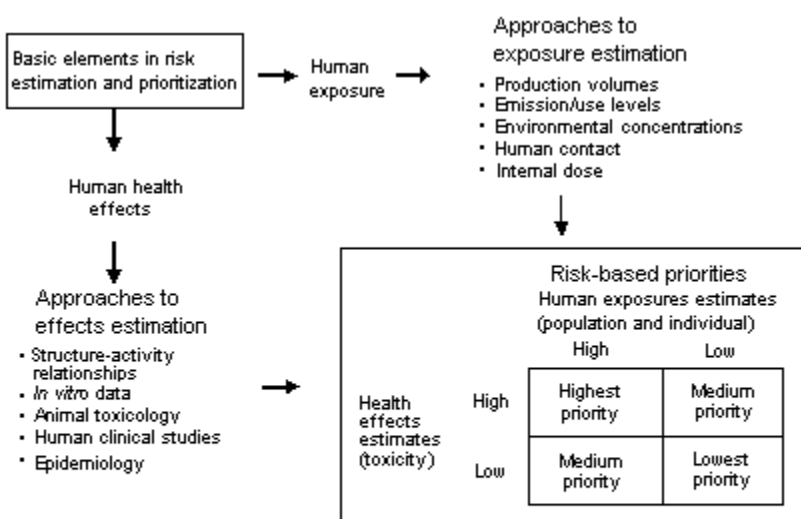


Fig. 8. Basic elements in the estimation and prioritization of environmental health risks (Sexton, 1993)

Risk mitigation proceeds from first determining that an exposure is a hazard (risk assessment) to identifying and quantifying the route and the environmental pathways for a contaminant. Where a contaminant has multiple sources or routes of exposure, relative contributions to individual and population risk must be determined. Exposure assessments are crucial for developing this information, and may rely on both measurements and modelling. Once this information is obtained, then effort can be directed toward the most effective mitigation strategies.

In fact, intervention studies are implicitly or explicitly predicated on the sequence of risk assessment and mitigation. Intervention at the source, transmission or receptor (receiving person) is intended to reduce the effect or risk of an effect. Prohibiting smoking in public buildings or sections of restaurants is designed to separate sources from receptors. Specific ventilation

requirements for operating theatres or isolation rooms of infectious patients are designed to dilute potential contaminants and pathogens. On a larger scale, substitution of cleaner fuels (e.g., reformulated or unleaded gasoline, cleaner coal, low-sulfur oil, natural gas) radiation of food or ozonation of drinking-water are examples of risk mitigation interventions based on the assumption that contaminant reductions experienced in the environmental media will result in a corresponding reduction in actual exposures and hence risk. It is essential, then, to understand the efficacy of mitigation strategies with respect to their effect on human exposures.

The combined use of total exposure assessment for air, receptor-source modelling and economic principles can assist environmental policy and regulation in developing risk mitigation strategies. The hybridization of these well-developed models can be used to assist in the identification of priority sources to target regulatory programmes, and in the development of cost-effective strategies for air pollution control to bring about the greatest and earliest reduction in pollutant exposures.

Epidemiological information about the health effects of relatively low levels of air pollutants now raises controversial policy issues for risk management. On the one hand, the economic consequences of these health effects may be substantial; on the other hand, for some pollutants, control measures may become very expensive. For pollutants such as VOCs, for example, exposure monitoring rather than ambient air monitoring may lead to more rapid and cost-effective risk reduction policies.

Developed countries have experimented with regulatory reforms that include emission trading. Basically, the concept calls for emission reduction at one source to be credited to the emission levels at another source. These trading schemes are based on the assumption that equal mass emission reduction of a pollutant would result in equal health or ecological benefits. Thinking in terms of total exposure assessment reorients the relative importance of sources and their impacts on different populations. Accordingly, control options for reducing exposures can be broadened (Smith, 1995).

2.5 Human exposure information in status and trend analysis

Evaluating the current status of exposures and doses in the context of historical trends is an important tool for both risk assessment and risk management. In many cases it requires collecting exposure data over a relatively long period of time (e.g., 5-20 years). This can only be done through an exposure assessment study and often when the contaminant has a long residence time in the environment or biological tissue. If concentrations of a contaminant exhibit high variability in environmental media, the study may require relatively large sample sizes, the use of probability samples and/or extensive follow-up to observe trends. Data on status and trends can be invaluable for identifying new or emerging problems, recognizing the relative importance of emission sources and exposure pathways, assessing the effectiveness of pollution controls, distinguishing opportunities for epidemiological research and predicting future changes in exposures and effects (Goldman et al., 1992; Sexton et al., 1992).

Exposure studies may be conducted to document the status and

trends of human exposure (e.g., Kemper, 1993; Noren, 1993). A good example of a study designed for this purpose is the German Environmental Survey (GerES). The nationwide representative survey was conducted for the first time in 1985-1986, on behalf of the Federal Ministry for the Environment, Nature Conservation and Reactor Safety. In 1990-1991 the survey was repeated in West Germany (the FRG before reunification) and in 1991-1992 it was extended to East Germany (former GDR) (Krause et al., 1992; Schulz et al., 1995).

The purpose of the survey was to establish a representative database on the body burden of the general population. Biological monitoring was used to characterize exposure to pollutants (predominantly heavy metals). In addition, the occurrence of a number of pollutants in the domestic area likely to contribute to total exposure (house dust and drinking-water) was studied. The design of the study is summarized as follows:

- * *Population samples.* Cross-sectional samples using a stratified two-step random sampling procedure according to the size of the community, gender and age. The final set included 2731 West Germans in 1985-1986 and 4287 adults from East and West Germany in 1990-1992 (aged 25-79 years). In addition about 700 children (aged 6-14 years) living in the same households were included in 1990-1992.
- * *Human biomonitoring.* Analysis of blood (lead, cadmium, copper, mercury), spot urine (arsenic, cadmium, copper, chromium, mercury) and scalp hair (aluminium, barium, cadmium, chromium, copper, magnesium, phosphorus, lead, strontium and zinc).
- * *Questionnaires.* Questions about social factors, smoking habits, potential sources of exposure in the domestic, working, and general environment, and nutritional behaviour.
- * *Domestic environment.* Concentration of trace elements in dust deposit indoors, in vacuum cleaner bags (pentachlorophenol [PCP], lindane and pyrethroids) and in household tap water; determination of VOCs in homes of a subsample of 479 participants (passive sampling) in 1985-1986.
- * *Personal sampling.* Determination of VOCs by personal sampling using a subsample of 113 people in 1991.
- * *Dietary intake.* A 24-h duplicate study in 1990-1992 with a subsample of 318 people.

Characteristics of the frequency distributions (percentiles) and other statistical parameters of the concentration of elements and pollutants in the different media were calculated. As an example, the concentrations of elements and compounds in blood and urine of the German adult population analysed in 1990-1992 are shown in Table 5. The 1990-1991 and 1991-1992 surveys showed differences between East and West Germany. The mercury concentrations in blood and urine as well as the cadmium, chromium and copper concentrations in urine were significantly higher ($p < 0.001$) in East Germany than in West Germany. The blood lead level was identical in both study populations (geometric mean 45 $\mu\text{g/litre}$).

The comparison of the results for the biological, personal and microenvironmental exposure measurements taken in East Germany in

1985-1986 and in 1990-1992 permits an analysis of trends over time. The success of abatement measures could be shown in a number of cases: the reduction of lead concentrations in petrol and of industrial cadmium emissions resulted in decreased lead and cadmium concentrations in the blood of the general population. The ban on PCP led to a decrease of PCP in house dust. The results of the GerES have provided a useful set of reference data to characterize and to assess exposures of the general population. They have also been useful for a number of risk assessments, for example the role of copper in drinking-water and liver cirrhosis in early childhood, and presence of mercury in amalgam fillings.

2.6 Summary

The specifics of any particular exposure analysis hinge on its intended use or uses. For example, the pertinent aspects of exposure to be considered, the nature of the information required and the necessary quantity and quality of the data will depend on whether the exposure assessment is being conducted in the context of an epidemiological investigation (Matanoski et al., 1992), risk assessment (Graham et al., 1992), risk management (Burke et al., 1992) or status and trend analysis (Goldman et al., 1992) (see also Chapter 1, Table 1).

Table 5. Elements and compounds in blood and urine of the German population (Krause et al., 1992)

	QL	N	<QL	10	50	90	95
Blood							
Lead (µg/litre)	15	3966	61	24.0	45.3	86.8	105.
Cadmium (µg/litre)	0.1	3965	231	0.1	0.3	1.9	2.6
Copper (mg/litre)	0.1	3968	0	0.8	0.9	1.2	1.3
Mercury (µg/litre)	0.2	3958	632	<0.2	0.6	1.6	2.1
Urine							
Arsenic (µg/litre)	0.6	4001	210	1.8	7.1	19.8	29.9
Arsenic (µg/g creatinine)		4001		1.4	4.9	15.3	24.1
Cadmium (µg/litre)	0.1	4002	150	0.1	0.3	0.9	1.3
Cadmium (µg/g creatinine)		4002		0.1	0.2	0.7	0.9
Chromium (µg/litre)	0.2	4002	1716	0.15	0.2	0.4	0.6
Chromium (µg/g creatinine)		4002		0.0	0.1	0.3	0.5
Copper (µg/litre)	1.1	4002	20	4.5	9.7	18.7	22.9
Copper (µg/g creatinine)		4002		3.5	6.7	13.1	17.7
Mercury (µg/litre)	0.2	4002	785	<0.2	0.5	2.6	3.9
Mercury (µg/g creatinine)		4002		0.1	0.4	1.6	2.2
Nicotine (µg/litre)	5	3750	1566	<5	9.3	1438	2431
Nicotine (µg/g creatinine)		3748		1.3	7.0	1003	1636
Cotinine (µg/litre)	5	3800	1813	<5	5.6	2037	2681
Cotinine (µg/g creatinine)		3798		1.3	4.9	1396	1940
Creatinine (mg/100 ml)	0	4002		0.7	1.5	2.5	2.9

Annotations: QL = quantification limit, N = sample size, n < QL = number of values, MAX = maximum value, AM = arithmetic mean, GM = geometric mean.

Source: UBA, WaBoLu, Environmental Survey 1990-1992, Federal Republic of Germany

Knowledge of human exposures to environmental contaminants is an important component of environmental epidemiology, risk assessment, risk management and status and trends analysis. Exposure information provides the critical link between sources of contaminants, their presence in the environment and potential human health effects. This information, if used in the context of environmental management predicated on human risk reduction, will facilitate selection and analysis of strategies other than the traditional "command and control" approach. Most of the environmental management structures around the world rely directly on the measured contaminants in various media to judge quality, infer risk and interpret compliance. Even in these cases, exposure information can evaluate the effectiveness of protecting segments of population more susceptible or at higher risk.

It is this direct connection that makes exposure measures invaluable for evaluation of environmental health impacts on a local, regional and global scale.

3. STRATEGIES AND DESIGN FOR EXPOSURE STUDIES

3.1 Introduction

Accurate estimates of human exposure to environmental contaminants are necessary for a realistic appraisal of the risks these pollutants pose and for the design and implementation of strategies to control and limit those risks. Three aspects of exposure are important for determining related health consequences:

- * *Magnitude*: What is the pollutant concentration?
- * *Duration*: How long does the exposure last?
- * *Frequency*: How often do exposures occur?

The design of an exposure study specifies the procedures that will be used to answer these three questions.

In this chapter, strategies and designs for exposure studies are discussed with emphasis on their relative advantages and disadvantages. The brief discussion of study design presented in Chapter 1 is expanded upon here in terms of fundamental types of generic study designs and approaches to assessing human exposure to chemicals in the environment. Statistical considerations for study design are presented in Chapter 4. The reader is referred to subsequent chapters for details on implementing exposure study designs through modelling (Chapter 6), monitoring of environmental media (Chapters 7, 8 and 9) and monitoring of biological tissue (Chapter 10).

3.2 Study design

A good study design is the most important element of any exposure study. A flow chart that includes critical elements is shown in Fig. 9. First the purpose of the study is defined: epidemiology, risk assessment, risk management or analyses of status and trends (see also Chapter 2). Within this context, specific study objectives are formulated. Often studies have several objectives, which must be

prioritized to ensure that the primary objective is fulfilled. Study parameters must be selected that are consistent with the objective. A study design is formulated which links objectives to measurement parameters in a cost-effective manner. Two critical and often overlooked elements of the study design are development of a statistical analysis plan and quality assurance (QA) objectives. For general population studies, methods for measurement and analysis of contaminants in collected environmental or biological samples must be sufficiently sensitive to determine their concentration at typical ambient levels. For multimedia studies, method detection limits must be consistent across media. The study design is not complete until a pilot study has been conducted to evaluate sample and field study procedures.

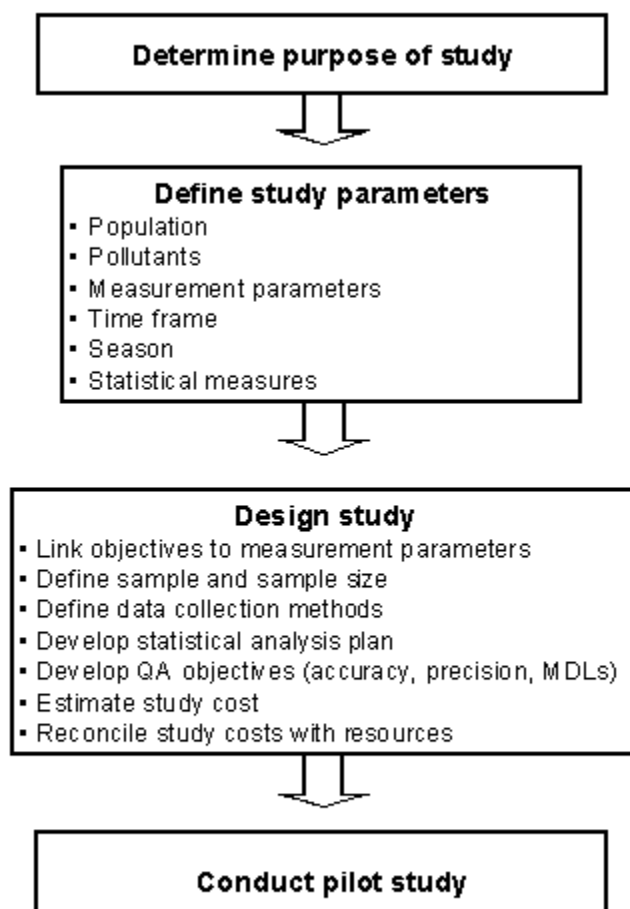


Fig. 9. Critical elements of a human exposure assessment study

3.3 Sampling and generalization

Decisions on population sampling strategies involve consideration both of the populations that are available and of the types of measurements needed. Of prime consideration are the people, place and time (i.e., individuals, locations, sampling period or conditions) from which exposure samples are to be collected. Also, it is important to determine if the estimates to be derived from the proposed sample could be generalized to a wider population of interest. For example, consider an exposure assessment study from a sample population of a

small town in southwestern Australia. The many potential populations of interest which this sample might generalize include: all people living in that town; people living in a small southwestern Australia town; people living in southwestern Australia; people living in Australia; people living in any small town; people in general. In this case, the sample population is not likely to provide a representative sample of the latter two populations.

The appropriateness of the generalization is determined by considering if the sample is randomly selected in such a way as to be representative of the larger population of interest (Whitmore, 1988). This randomization is in terms of the distribution of the collected data. For continuous outcomes, the percentages of key attributes, such as demographic factors, should be similar between the sample and the population. However, when this is not possible, owing to limited funding for example, a descriptive study (described below) can provide credible data, although the extent to which these can be generalized is limited.

3.4 Types of study design

Once the population is defined, then the attention shifts to sampling strategies; in particular, comprehensive samples, probability samples, and other types of samples. A *comprehensive sample* includes all members of the selected population. In a *probability sample* each member has a known likelihood of being selected. *Simple random sampling* is a special case where each member of the population has an equal probability of being selected. Other types of study groups are selected on the basis of other characteristics, such as availability or convenience.

3.4.1 Comprehensive samples

Complete populations can be used to collect a full picture of the process being studied, especially when the total population is relatively small such as families in a neighbourhood. In these cases, an exhaustive collection of measurements is taken from every potential subject, and the completed data describe the situation exactly. There is no sample variability except through the methods and procedures used for measurement and monitoring. The main reasons for studies of this nature are either a small population size, a need for a complete evaluation of the problem, high potential risk, high variability among units or legal requirements. The advantages of this type of study are

that a complete description of the exposure is given, and there is no need for generalization because all potential subjects are covered. The disadvantage of this approach, if the population is large, lies in the expense: all individuals in all locations must be monitored at all times.

3.4.2 Probability samples

Surveys consist of a random sampling of subjects from the population of interest. This approach aims to remove selection bias and is useful for generalizing results beyond the study sample. It is important to distinguish that "random" does not translate to "haphazard". A truly random sample is independent of human judgement. Every unit in the total population has a known above-zero likelihood of being included in the sample. Effective study design allows researchers to draw statistically valid inferences about the general

population that the sample is designed to represent (Kish, 1965). For these studies, one needs to (Sexton & Ryan, 1988):

- * choose a population for investigation
- * choose an appropriate unit for sampling and analysis (e.g., person, household, neighbourhood, city, etc.)
- * stratify as appropriate
- * choose a sampling strategy (e.g., simple random sampling, multistage sampling).

The results of a probability survey can be used to make general statements about the population under investigation. The advantages include having results that represent the population, taking into account the possible error due to sampling. The disadvantages of this scheme lie in the complicated sample selection, difficulty in maintaining compliance from participants and the potentially complex statistical analysis. In addition, randomized surveys of insufficient sample size may miss rare hazardous events or small populations with high exposure or risk.

Sampling strategies for survey studies include randomization methods for choosing subjects to enroll in the study. Simple random sampling is a scheme in which all sampling units of the same size have equal probability of being selected. It can be difficult to implement but relatively easy to generalize. Simple random sampling presents logistic and fiscal constraints when considered for exposure surveys that are large in geographic scope. For example, a national survey of 5000 personal exposures to respirable particulate matter that utilizes simple random sampling may result in individuals selected from 1000 cities and towns. The travel and site preparation costs of such a design may not be feasible in many situations.

A variety of alternatives to simple random sampling exist that may be used to provide practical and efficient samples of large populations (Callahan et al., 1995). *Stratified sampling* may be used to obtain more precise survey results if exposures are more homogeneous within strata than between them. Possible strata include urban, suburban and rural populations, or occupationally exposed and non-occupationally exposed individuals.

Oversampling of target populations or contaminants also may yield substantial increases in the precision of results. Because the individuals anticipated to have the highest exposures to a particular pollutant may be rare in the population being studied, oversampling can be considered to obtain more precise estimates of exposure. Before committing substantial resources to oversampling, special care must be taken to ensure that assumptions or data used to support a rationale for selecting the oversampled population are accurate; otherwise erroneous oversampling may decrease the precision of the study results (Callahan et al., 1995).

Multistage sampling designs utilize clusters of sampling units thereby limiting sampling locations to manageable areas. Depending on the scope of the study, the stages of probability sampling necessary may include:

- * selection of primary sampling unit (e.g., a city)

- * selection of sample area segments (e.g., blocks within the city)
- * selection of sample housing units within sample segments (e.g., residences within the blocks)
- * selection of sample individuals within sample housing units
- * selection of sample time points within the monitoring period (Callahan et al., 1995).

The optimal degree of clustering depends on the variability of the survey variables between and within the clusters and the costs of fieldwork relative to sample collection and analysis costs. Although details of this approach are beyond the scope of this chapter, it should be recognized that cluster sampling introduces correlation among the sample individuals that affects the validity of the survey estimates. Thus, tradeoffs between increased sample size achieved through clustering and loss of validity must be considered carefully. Details of multistage and cluster sampling may be found in Hansen et al. (1953), Kish (1965), Cochran (1977), Kalton (1983), Kollander (1993) and Callahan et al. (1995).

One concern with survey studies is maintaining participation of subjects who did not initially volunteer. Another issue, which is more conceptual, is subject selection for the more complex sampling strategies. In particular, stratification factors need to be carefully chosen so that potential confounders can be determined and the

adjustments can be made from the resultant effects. Important considerations for the design of population-based (e.g., national or regional) exposure surveys, including response rates and confounders, are discussed by Whitmore (1988) and Callahan et al. (1995).

3.4.3 Other sample types

Non-probability sample studies ("anecdotal studies") may consist of selecting a sample based on the self-reporting of conditions, such as complaint cases for "sick building" syndrome. Data collected in this manner are potentially subject to biased reporting. It is difficult to generalize results unless causal relationships are very strong or unless there is little reason to believe that a confounder or an unmeasured significant factor is relevant. In general, such studies are used for description or exploration of a given situation. In particular, they can be used to evaluate the variability of outcomes and explore unknown situations for further explanatory study. When choosing subjects, it is useful to focus on variability in the expected outcome and also on the likelihood of completing the study. It is also helpful to focus on a simple, preferably dichotomous, hypothesis. Extensive validation will be necessary before accepting or rejecting the hypothesis since the generalization of the results is uncertain.

The advantages of targeted anecdotal studies are the inexpensive and quick ways in which they aid in the design of future studies. For example, when exploring protocols, determining stratification variables, potential biases and confounders, and identifying the units of analysis, the use of cooperative volunteers can simplify field operations. The uncertainty of the results of these studies is due to potential biases from the non-random and possibly non-representative

sample (i.e., responder bias). Since the population in such non-probability sample studies is often made up of volunteers, there is usually some factor present which distinguishes them from those who do not choose to participate. This factor could influence the results; in particular, those who participate may tend to consider themselves strongly affected or not affected by the pollutant being studied and may alter their responses or behaviours as a result. This phenomenon is a special case of responder bias, often termed *self-selection bias*. Also, a poorly designed study can fail to control for temporal and spatial variability, as well as meteorological, site and source bias. This bias is a result of a single, "random-day", or grab sampling and single-location sampling, which decreases the potential for generalization.

Controlled experiments are useful to examine a few factors and to study their influence on the resulting exposure. The use of randomization and control ensures that the effects are real and not the result of confounding causes, incorrectly measured variables or missing variables. Examples include chamber studies and other situations where the investigator has control over most of the environmental factors.

3.5 Exposure assessment approaches

As discussed in Chapter 1, strategies for assessing environmental exposure can be categorized as one of two general approaches; direct or indirect. *Direct* approaches include personal exposure monitoring and biological markers of exposure. *Indirect* approaches include environmental sampling, combined with exposure factor information, modelling and questionnaires.

3.5.1 Direct approaches to exposure assessment

Direct measures of exposure include samples collected at the interface between an exposure medium and the human body, e.g., at the breathing zone in the case of air pollutant exposure, or samples of biological tissue in which concentrations of target pollutants can be quantitated. Measurements in food or drinking-water (duplicate portions) which are ingested could also be viewed as a direct way of assessing exposure through these media. Thus, direct approaches to exposure assessment include personal exposure monitoring and biological markers of exposure. Personal monitoring methods are discussed below, and the subject of biomarkers of exposure is presented in detail in Chapter 10.

Personal monitoring of exposure to environmental contaminants refers to collection of samples at the interface between the exposure medium and the human receptor (e.g., the breathing zone). Personal monitoring approaches are summarized in Table 6. Personal monitors make it possible to measure exposures for an identified subset of the general population. Moreover, if study participants maintain records of their activities, then locations where highest exposure concentrations occur as well as the nature of emission sources can often be inferred. Personal monitoring can be done for all potential exposure media (e.g., air, water, soil, food) and pollutants of interest. Although available, personal monitoring methods may not be employed in a particular investigation due to study design, time or expense considerations. The principal limitation on the use of personal monitoring for exposure assessment is the availability of sample collection methods that are sensitive, easy to operate, able to

provide sufficient time resolution, free from interferences and cost-effective. Consideration should be given to the likelihood that the inconvenience of complying with personal monitoring protocols may alter the normal behaviour of the study participants. For example, participants tend to wear personal air monitors on days that they do not go to work. In duplicate portion studies, participants may not provide equal portions of expensive or well-liked foods, leading to underestimation of intake. Approaches to personal monitoring of inhalation, dietary and dermal exposures are discussed below.

Table 6. Summary of personal monitoring approaches

Exposure route	Media	Environmental sample	Biological sample
Inhalation	air	personal monitor	breath urine
Ingestion	water	tap water	blood
Ingestion	food	duplicate portion	faeces breast milk
Dermal	soil/dust	dermal patch	others

3.5.1.1 Personal monitoring of inhalation exposures

Personal monitoring of human exposure to air pollutants requires that study participants transport their sample collection device with them at all times during the assessment period. Examples include a diffusion tube used for passive sampling of gases, such as VOCs, or a filter with a battery-operated pump for active sampling of aerosols and their components (ACGIH, 1995).

Personal air monitors can be grouped into two general categories: *integrated samplers* that collect the pollutant over a specified time period and then are returned to the laboratory for analysis, and *continuous samplers* that use a self-contained analytical system to measure and record the pollutant concentration on the spot. Instruments in both categories can be either active or passive. *Active monitors* use a pump and a power source to move air past a collector or sensor. *Passive monitors* depend on diffusion to bring the pollutants into contact with the collector or sensor. Additional information may be found in Chapter 7 and ACGIH (1995).

As Wallace & Ott (1982) pointed out, the direct measurement of exposures using personal monitors raises several methodological issues. Personal monitoring studies are complex, expensive, time consuming and labour intensive. Other challenges include selection and recruitment of representative subjects; distribution, maintenance and retrieval of many monitors; laboratory analysis of many air samples returned from monitors in the field or calibration and validation of many real-time monitors; and the transcription and statistical analysis of data on pollutant concentrations and time-activity patterns.

3.5.1.2 Personal monitoring of dietary exposures

Exposures to contaminants in food may be directly measured by collecting meals as prepared for consumption by members of the study population; such samples are often termed duplicate portion samples. Duplicate portion study designs provide food samples as actually consumed, rather than samples of unprepared, individual food items that are typical of surveillance approaches to characterizing dietary exposures (US NRC, 1993). This distinction is important because the method by which food is prepared for consumption (e.g., washed, washed and cooked, or commercially processed) can influence contaminant residues. In addition, some pollutants can be generated during cooking, for example, benzo [a]pyrene (Waldman et al., 1991a) and heterocyclic amines (Skog et al., 1998). Thus, residue levels measured in duplicate portion samples are likely to more accurately reflect personal dietary ingestion exposures than raw agricultural commodities and other foods collected at the producer, processor or distributor level. Depending on the objectives of the study, water may also be included as part of the duplicate portion sample.

Duplicate portion study designs use either collection of individual servings or meals or composite samples. In studies of this type, participants are often monitored over one or more days, and the duplicate portion samples are collected daily over the monitoring period. The former affords a detailed examination of contaminant levels in specific commodities or foods comprised of several commodities; however, the analytical chemistry costs associated with this degree of temporal resolution may be prohibitive. Composite samples provide an integrated measure of dietary exposure and provide an efficient means for characterizing total dietary exposures. Both collection schemes require a high level of effort from study participants, and the complex food matrices may present analytical chemistry challenges.

Duplicate portion studies require a high degree of participation by the study respondents, because they are primarily responsible for preparation and storage of an additional serving of every food or meal consumed over the monitoring period. This burden makes it difficult to collect representative samples of all foods consumed by the respondent, especially when food is relatively expensive or scarce or is consumed outside the home. Respondent burden also makes it difficult to conduct studies of chronic dietary exposures using the duplicate portion approach. Additional information on assessment of dietary exposure, including both direct and indirect approaches, may be found in Chapter 7.4 as well as WHO (1985a, 1995c); EC (1997a).

3.5.1.3 Personal monitoring of dermal absorption exposures

Personal monitoring of dermal exposure is used for those situations where a pollutant comes in contact with the skin and intake occurs via absorption through the skin. Dermal patches and skin wipe samples are used to evaluate exposures for residues adhering to the surface of the skin (US EPA 1992b; Fenske, 1993; Geno et al., 1996;

Shealy et al., 1997). These methods have typically been used for industrial hygiene assessments where very high exposures are expected. Dermal patches and skin wipe samples have been used to characterize transfer of pesticide residues from soil and grass to skin as well as spot concentrations of residues on skin (Fenske et al., 1991). Dermal absorption can also occur during bathing, showering or swimming. In this case, the contaminant is in the water and exposure occurs when

the water contacts the skin. Dermal exposure in this situation is defined as the concentration of the contaminant in the water and the duration of contact.

3.5.2 Indirect approaches to exposure assessment

Indirect measures of exposure include estimates derived from environmental monitoring (i.e., measurements made in locations frequented by the study participants), models and questionnaires.

3.5.2.1 Environmental monitoring

Indirect estimates of exposure may be made by combining measurements of pollutant concentrations at fixed sites with information on rates of contact with these media recorded in data logs and diaries or time-activity surveys. Examples include air pollutant concentrations in specific areas combined with time budget records (see Chapter 5), food contaminant data combined with information on dietary patterns (see Chapter 7.4 for details), and pollutant concentrations on skin combined with data on frequency and duration of hand-to-mouth contact. Although collection of environmental, time-activity and questionnaire data needed for this exposure assessment approach is simpler than for personal monitoring, it is still invasive and laborious, and may lead to selection bias.

Microenvironmental monitoring is a special case of environmental monitoring in which the location where measurements are made is considered to be homogeneous with respect to concentrations of the target pollutants over the averaging time of interest. The concept of a microenvironment has been widely applied in air pollution exposure assessments. Examples of potentially important micro-environments used for air pollution exposure assessment are listed in Table 7. The general form of the equation used to calculate time-weighted integrated exposure from micro environmental monitoring data is

$$E = \frac{1}{T} \sum C_{ijk} t_k \quad (3.1)$$

where E is the time-weighted integrated exposure (e.g., mg/m³), C is the concentration (e.g., mg/m³), t is the unit time (e.g., minute), T is the total elapsed time (e.g., minutes). The subscripts i , j and k denote the medium, the pathway and the microenvironment respectively (Duan, 1982). The most important assumptions inherent in this model are:

- * The concentration C_j in microenvironment j is assumed to be constant during the time that person i is there.
- * The concentration C_j within microenvironment j and the time that person i spends there are assumed to be independent events.
- * The number of microenvironments necessary to characterize personal exposure adequately is assumed to be small.

The concept of a time-weighted integrated exposure is illustrated in Fig. 10. A unit width is indicated on the j axis for each of five microenvironments: indoors at home, indoors at work, indoors in other

locations, in transit, and outdoors. The concentration of respirable particles (RSP) is displayed on the y axis, and the fraction of time that person i spends in each microenvironment over the 24-h period is plotted on the t axis. Even though the RSP concentration was low inside the home, it contributed significantly to the time-weighted exposure because this person spent 18 out of 24 h there. Conversely, the RSP concentration outdoors made only a minor contribution because this person was outdoors less than half an hour during the 24-h period.

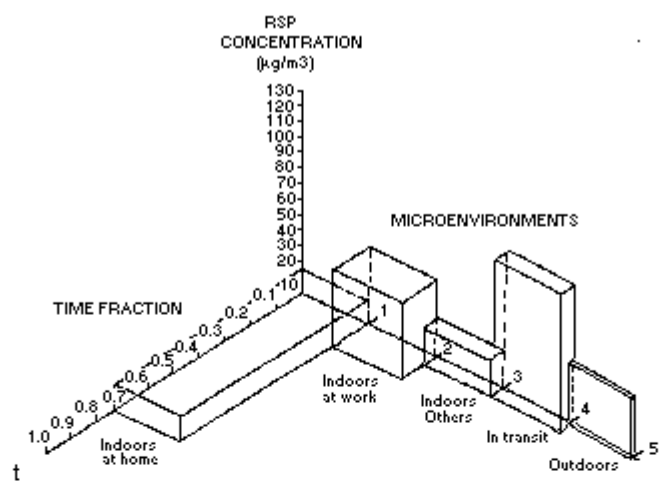
Indirect monitoring of ingestion exposures via hand-to-mouth contact may be obtained by collection of dermal wipe samples. However as indicated above, the use of this method has been limited to date. A drawback of the dermal wipe approach is that the integration time may be highly variable among subjects owing to variations in frequency of hand and body-washing, making interpretation of the results difficult (Fenske, 1993). Information on rates of contact between the contaminated skin and mouth is also required to complete the exposure assessment. A discussion of these types of data may be found in Chapter 5.

Given the diversity of microenvironments that people move through each day (see Table 7), application of the indirect approach to exposure assessment is not straightforward. Its utility depends on identification of and sampling in the microenvironments with the greatest potential to influence human exposure. The costs and practical difficulties of monitoring in all, or even most, of the locations where people are likely to spend their time limits the scope of indirect measurements.

Table 7. Potentially important microenvironments for air pollution exposure

Microenvironments	Comments
<u>Outdoors</u>	
Urban	metropolitan areas where air pollution levels are high as stationary sources
Suburban	small- to medium-sized cities where air pollution levels are high, although transport of urban pollution can affect 1
Rural	agricultural communities and small towns with few major air pollution sources; Air pollution levels tend to be low, although transport of local air quality under certain conditions
<u>Indoors-occupational</u>	
Industrial	manufacturing and production processes, such as those in plants, and smelters
Non-industrial	primarily service industries where workers are not involved in manufacturing processes, such as insurance companies, law offices, and
<u>Indoors-Non-occupational</u>	
Residential	single-family houses, apartments, mobile homes, condominiums
Commercial	restaurants, retail stores, banks, supermarkets

Public	post offices, courthouses, sports arenas, convention hall
Institutional	schools, hospitals, convalescent homes
<u>Indoors-Transportation</u>	
Private	automobiles, private aeroplanes
Public	buses, subways, trains, commercial aeroplanes



Microenvironment type	RSP concentration (C_j , $\mu\text{g}/\text{m}^3$)	Time fraction ^a (t_{ij})	$C_j \times t_{ij}$ ($\mu\text{g}/\text{m}^3$)	Microenvironment contribution to (%) ^b
Indoors at home	15	0.75	11.25	47
Indoors at work	50	0.15	7.5	31
Indoors, other	25	0.04	1.00	4
In transit	90	0.04	3.60	15
Outdoors	40	0.02	0.80	3

$$E_i = \sum C_j \times t_{ij} = 24.15 \mu\text{g}/\text{m}^3$$

^a Fraction of 24 h spent in each environment

^b Percentage that each microenvironment contributes to the 24 h, time-weighted, integrated exposure (E_i).

Fig. 10. Examples of the relative contributions from specific microenvironments to an individual's time-weighted, integrated exposure to RSP. From: Sexton & Ryan (1988)

3.5.2.2 Models as an indirect approach to assessing exposure

The microenvironmental exposure equation describes a model commonly used for assessment of air pollutant exposure. More generally, models are useful tools for quantifying the relationship between pollutant exposure and important explanatory variables, as well as for expanding existing exposure information to estimation of exposures of new populations and subgroups, and future exposure scenarios. Validated exposure models reduce the need for expensive

measurement programmes. The challenge is to develop exposure databases and models that allow maximum extrapolation from minimum measurements or costs. Such models need to reflect the structures of the physical environments and human activities of interest in exposure assessment.

In addition to the essentially physical (deterministic) exposure models, physical-stochastic (probabilistic) and statistical (regression) models are used. The former type is particularly useful for population exposure distribution assessments, the latter requires less supporting information but cannot be used for extrapolation outside of the study population. Exposure models are discussed in detail in Chapter 6.

3.5.2.3 Questionnaires as an indirect approach to assessing exposure

Questionnaires typically provide qualitative, often retrospective, information. They may be used to categorize respondents into two or more groups with respect to potential exposure (e.g., exposed or unexposed, high exposure or low exposure) and are commonly used for this purpose in epidemiological studies. As noted earlier, questionnaires may also be used to aid in interpretation of personal and environmental monitoring results. A *priori* knowledge of the determinants of the exposure of interest is required to develop effective questionnaires relevant to exposure assessment (e.g., high formaldehyde exposure for workers in a certain industry, or high carbon monoxide and lead exposure for traffic policemen, bus drivers and road toll collectors). Most often the information necessary to develop questionnaires is obtained from previous studies that utilized environmental measurements, models or biological monitoring to measure exposure. In many cases, basic socio-demographic questionnaire data may provide extremely valuable information as they might be strong surrogates of exposure. It has long been known that rates of disease differ in social strata. In addition, it is readily apparent in many countries that the physical characteristics of one's residential environment are linked to income level. For lead exposure, differences in exposure among groups defined by income and social status have been demonstrated. Phoon et al. (1990) have shown that diet and job category were the most important predictors of blood lead levels among men in Singapore. In the USA, elevated blood lead levels have been linked to children who live in older, inner-city housing, particularly properties in poor repair (MMWR, 1997). Homes in these areas are more likely to have been painted with leaded paints (pre-1950) and have higher concentrations of lead in soil owing to deposition of emissions from leaded gasoline prior to the 1970s. Haan et al. (1987) found an increased risk of death among people living in a poverty area in the USA as compared to an adjacent non-poverty area, even after adjusting for differences in smoking, race, baseline health status, access to medical care, employment status, marital status, depression, sleep patterns and body mass index. These results suggest that sociophysical aspects of the environment, such as increased exposure to contaminants from poorer housing, may be important contributors to the association between socio-economic status and excess death rates.

3.6 Summary

A good study design is the most important element of any exposure assessment. It includes the purpose and objectives of the investigation as well as relevant methods for sampling, measurements, statistical analyses, and quality assurance. Methods for

characterizing the magnitude, duration and time patterns of human contact with environmental contaminants may follow a direct approach or an indirect approach. Direct approaches to exposure assessment include point-of-contact measurements and measures of biological markers of exposure. Indirect approaches include environmental monitoring, modelling and questionnaires. These approaches may be employed in various types of exposure studies that are typified by the manner in which the study population is selected; for example, comprehensive studies that include all members of the study population, descriptive studies consisting of a non-probability sample, or surveys based on a randomly selected, representative sample of individuals.

4. STATISTICAL METHODS IN EXPOSURE ASSESSMENT

4.1 Introduction

Statistics is a necessary and critical tool in exposure assessment studies. Statistics can be employed at each stage of the exposure assessment study. At the planning stage, statistics aids in selection of study design and determination of the amount and form of data to collect. After the data are collected, statistical description of the results helps understanding of the basic characteristics of exposure and its determinants. Statistics is also essential during final analysis of the data for hypothesis testing, characterizing exposure through various routes and media, and exploring relationships between ideal measurements (e.g., exact lung uptake) and feasible measurements (e.g., ambient, indoor, or personal measures). Furthermore, statistical inference allows one to generalize the observations derived from a sample to a wider population from which the sample was drawn. Finally, as noted in Chapter 11, statistics play an important role in quality assurance (QA) programmes.

Selected applications of descriptive and inferential statistics in exposure assessment studies are discussed in the following sections. This chapter is not a substitute for a course in statistical methods, but is intended to provide a brief review and useful references. Widely available statistical software for personal computers can be used to perform data processing and necessary calculations. One example of such packages is the statistical programme Epi Info developed for and distributed by WHO (Dean et al., 1995).

Throughout the chapter, data collected as part of a lead exposure study performed in Malta and Mexico (WHO, 1985b) (Table 8) will be used to illustrate some key statistical concepts and methods. The purpose of this study was to investigate the relative importance of lead exposure via different routes of exposure. Blood lead concentrations were considered to be an indicator of lead uptake from all exposure routes, whereas faeces lead concentrations were considered to represent exposure via ingestion. In the course of this study, blood lead and faeces lead measurements were obtained from 36 and 19 individuals in Malta and Mexico, respectively.

4.2 Descriptive statistics

Descriptive statistics summarize data in a simple manner to discern key points about the collected information. We typically assume that the collected data are a sample from a larger population of possible measurements and that the sample is representative of the

population. The sample consists of the individual observations from the study population, with multiple variables or covariates recorded for each observation. *Univariate methods* examine the distribution of a single variable; *multivariate methods* describe relationships among two or more variables. That is, if we consider a single observation and know the value of one variable, multivariate methods indicate what

Table 8. Blood lead (PbB) and faeces lead (PbF) data from sample populations in Malta and Mexico. Source: WHO, 1985b

Number	Malta		Mexico	
	PbB ($\mu\text{g/litre}$)	PbF ($\mu\text{g/g}$)	PbF ($\mu\text{g/litre}$)	PbB ($\mu\text{g/g}$)
1	171	2.9	239	6.3
2	270	30.5	263	4.2
3	198	5.6	198	5.7
4	122	3.8	163	5.3
5	96	16.6	217	4.3
6	385	35.5	188	4.7
7	359	49.6	190	3.3
8	267	6.8	248	5.2
9	261	8.1	225	4.5
10	301	25.6	152	3.4
11	202	7.7	177	5.9
12	222	32.3	157	3.8
13	339	10.9	297	5.3
14	156	5.7	144	3.6
15	262	18.7	257	9.8
16	290	16.5	131	4.8
17	158	4.9	187	5.1
18	343	37.8	168	3.2
19	228	9.1	112	2.8
20	256	14.1		
21	270	9.9		
22	245	4.9		
23	337	14.3		
24	362	19.2		
25	155	4.9		
26	194	9		
27	206	6.7		
28	276	12.4		
29	222	11.2		
30	214	21.3		
31	248	7.8		
32	283	17.8		
33	215	10.9		
34	279	14.9		
35	229	8.6		
36	127	17.3		

Table 8. (continued)

Number	Malta		Mexico	
	PbB ($\mu\text{g/litre}$)	PbF ($\mu\text{g/g}$)	PbF ($\mu\text{g/litre}$)	PbB ($\mu\text{g/g}$)

	PbB ($\mu\text{g/litre}$)	PbF ($\mu\text{g/g}$)	PbF ($\mu\text{g/litre}$)	PbB ($\mu\text{g/g}$)
Median	246.5	11.1	188	4.7
Mean	243	14.8	195.4	4.8
Standard deviation	70.9	10.8	49.5	1.6
Standard error	11.8	1.8	11.4	0.4
Minimum	96	2.9	112	2.8
Maximum	385	49.6	297	9.8
Range	289	46.7	185	7

we can infer about the other variables. Both numerical and graphical techniques may be used to characterize the sample and any relevant subsets, and to obtain preliminary results from the study.

4.2.1 Numerical summaries

Numerical approaches include calculating descriptive statistics that describe the distribution of a variable (e.g., blood lead concentrations) in terms of central tendency and dispersion as well as descriptions of associations between pairs of variables. Other numerical descriptive measures can be used to describe points in the distribution (e.g., percentiles). Each of these descriptive statistics is described below and where appropriate the formulas used to calculate them are provided in Table 9.

Standard measures of central tendency include the *sample median* (i.e., midpoint observation) and *sample mean* (i.e., average). Referring to the lower half of Table 8, note that the median blood lead concentration for the Maltese study population was 246.5 $\mu\text{g/litre}$, intermediate between the eighteenth and nineteenth observations. Thus, 50% of the individuals in this sample had a blood level less than 246.5 $\mu\text{g/litre}$ and 50% had a greater blood lead concentration. The sample mean blood lead concentration in the Maltese population was 243 $\mu\text{g/litre}$ compared to 195.4 $\mu\text{g/litre}$ in Mexico, indicating that blood lead levels were higher in the Maltese population. Methods for assigning confidence levels to statements such as this are described in Section 4.4. The sample mean is more precise for estimating the average of the distribution, but it is sensitive to measurement imprecision, errors and extreme values. Although the sample median is less precise for estimating the average, it is more robust with respect to errors in the data. Therefore, when outliers or extreme values are present, or when possible errors and contamination in the observed data are suspected, the median is likely to be a better descriptor of central tendency than the mean.

Table 8. Formulas for selected descriptive statistics

Sample mean

$$\bar{X} = \frac{\sum_{i=1}^n X_i}{n} \quad (\text{Equation 4.1})$$

Sample variance

$$s^2 = \frac{1}{n-1} \sum_{i=1}^n (x_i - \bar{x})^2 \quad (\text{Equation 4.2})$$

Sample standard deviation

$$s = \sqrt{s^2} \quad (\text{Equation 4.3})$$

Sample range

$$\text{range} = \text{maximum} - \text{minimum} \quad (\text{Equation 4.4})$$

Correlation coefficient

$$r = \frac{\sum_{i=1}^n (x_i - \bar{x})(y_i - \bar{y})}{\sqrt{\left[\sum_{i=1}^n (x_i - \bar{x})^2 \right] \left[\sum_{i=1}^n (y_i - \bar{y})^2 \right]}} \quad (\text{Equation 4.5})$$

Standard measures of dispersion include the sample variance, the sample standard deviation and the sample range (formulas in Table 9). These measures describe the spread of the observations. Examination of Table 8 reveals that blood lead concentrations are more variable in the Maltese sample population (standard deviation = 70.9 µg/litre, range = 289 µg/litre) than that in Mexico (standard deviation = 49.5 µg/litre, range = 185 µg/litre). Measures of dispersion are useful for characterizing the degree of variability of a given measure among the members of a study population. As we will see later in this chapter, dispersion is also a key component of some study design issues.

The concept of sample percentile is an important aspect of exposure assessment. A sample percentile for a variable in a data set is the value of the data such that at least $p\%$ are at or below this value, and $(1 - p)\%$ are at or above this value. A percentile is determined by first ordering the sample (i.e., rank from lowest to

highest) and then identifying the observation that corresponds with the desired fraction of the data set. In the case of blood lead concentrations measured in the Maltese sample population, 283 µg/litre is the 75th percentile since it is the 27th of 36th rank-ordered

values in the data set. Graphical representation of percentiles is discussed in the next section.

Multivariate summary statistics allow one to evaluate relationships between or among different variables. Most of these examine correlation (the strength of the linear relationship) between variables, where the direction and magnitude of the relationship, or association, is described by the correlation coefficient (r). The correlation coefficient ranges from -1 to +1, where negative values indicate an inverse relationship between two variables, positive values indicate a direct relationship, and values near zero, whether negative or positive, indicate a weak relationship. In the example case, the correlation between blood lead and faeces lead in the Maltese study population is 0.57, indicating these biomarkers of lead exposure have a moderate to strong positive association.

4.2.2 Graphical summaries

Graphical summaries of data provide illustrative information about the distribution of the observed values and associations between variables. Graphical presentations of data can suggest the shape of the distribution and aid in exploring hypothesized relationships between factors included in the study. In many situations and for many exposure analysts, graphical summaries of data convey information more readily than numerical summaries. Fundamental graphical presentation methods are described here. A description of advanced visualization methods may be found in Cleveland (1993) and Tufte (1983, 1997).

4.2.2.1 Histograms

Histograms are bar charts used to illustrate the relative frequency of values or ranges of values within an exposure metric. Observations are assigned to ranges of the data, and the height of the bar represents the frequency of observations in that range. It is important to note that the choice of ranges can be arbitrary, resulting in many possible different pictures of the results. A histogram of the Maltese blood lead data is shown in Fig. 11. Here, the data were grouped into bins with interval ranges of 25 $\mu\text{g/litre}$. Blood lead concentrations between 200-225 $\mu\text{g/litre}$ and 275-300 $\mu\text{g/litre}$ were observed the most often. Histograms can be used to illustrate absolute or relative frequency.

4.2.2.2 Cumulative frequency diagrams

Cumulative frequency or probability diagrams can be used to graphically express percentiles of a distribution. A cumulative probability chart for the Maltese blood lead data is shown in Fig. 12. The value associated with a given percentile, or vice versa, can easily be determined from such a figure.

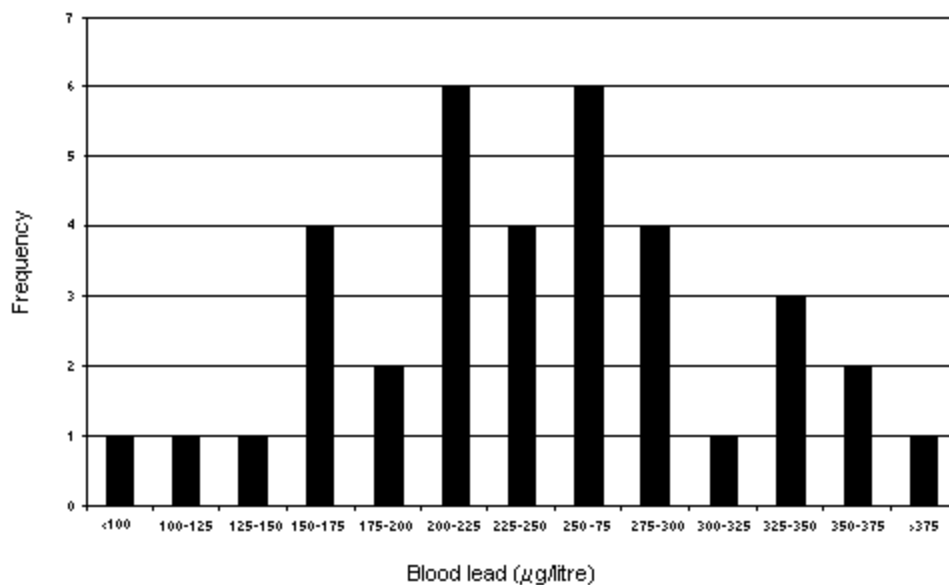


Fig. 11. Histogram displaying Maltese blood lead data (WHO, 1985b)

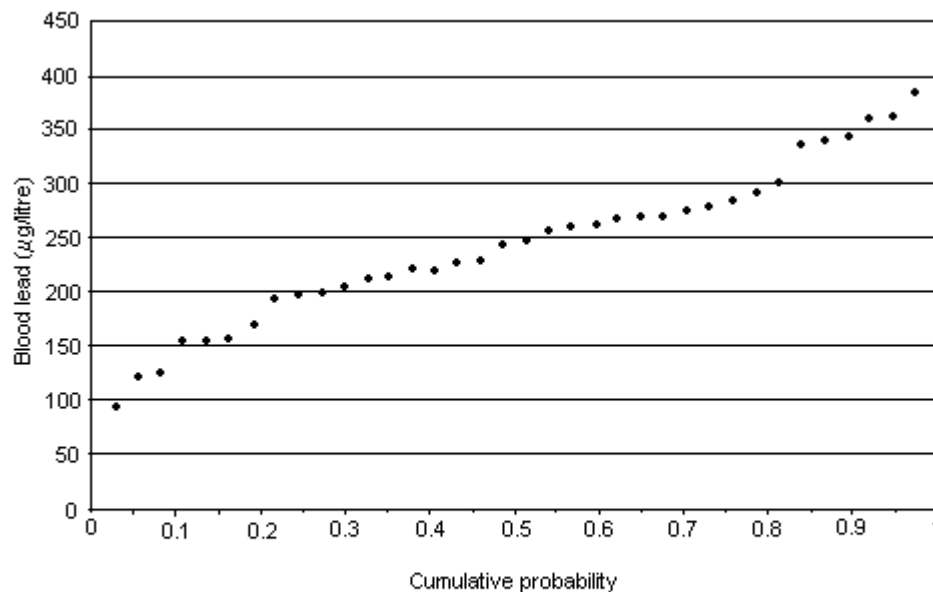


Fig. 12. Cumulative probability chart of Maltese data (WHO, 1985b)

4.2.2.3 Box plots

A box plot is another approach for graphically describing the distribution of a measurements in an exposure study. Some details of box plots vary among users; however, all of them display the sample median, mean, 25th percentile and 75th percentile. Selected other values, such as 10th and 90th percentiles or 5th and 95th percentiles as well as the extremes (i.e., the minimum and maximum) of the distribution are displayed, too. Fig. 13 shows box plots of the blood

lead measurements from the Maltese and Mexican sample populations. The bottom and top horizontal lines of each box denote the interquartile range (i.e., the 25th and 75th percentiles) and the solid horizontal line across the centre indicates the sample median. The dotted line across the box indicates the mean of the distribution. The whiskers on the boxes in Fig. 12 extend to the 10th and 90th percentiles of the distributions, and the open circles denote all observations beyond those percentiles. As illustrated here, box plots are a convenient method for displaying information on the central tendency, dispersion, symmetry and tails of an exposure measure.

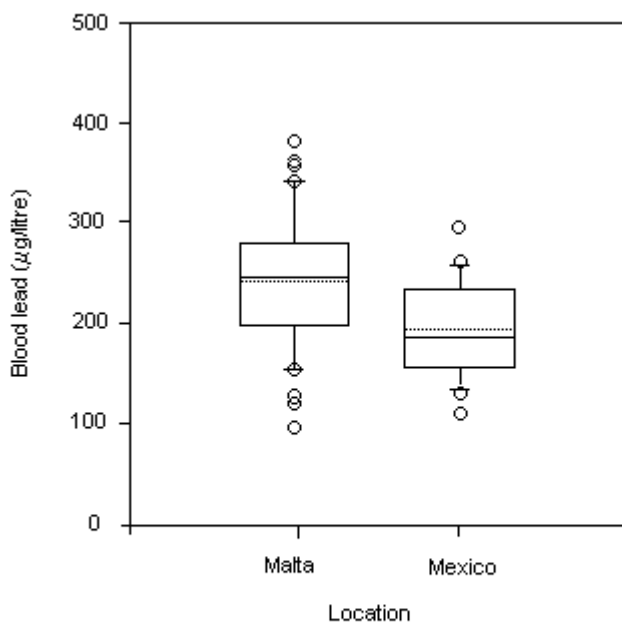


Fig. 13. Box plots displaying distribution of blood levels in Malta and Mexico (WHO, 1985b)

4.2.2.4 Quantile-quantile plots

Quantile-quantile plots can be used to compare the distribution of a variable with a different sample or a known distribution. Exposure measures are commonly compared to the normal or lognormal distribution (see section 4.3) for purposes of evaluating whether the normality assumptions inherent in numerous statistical inference methods are met. While a discussion of probability distributions and statistical inference methods is reserved for later in the chapter, a quantile-quantile plot is shown in Fig. 14. Here, the Maltese blood lead data are plotted against the standard normal distribution (see section 4.3). This special form of quantile-quantile plot is known as a *normal probability chart*. Data that form an approximately straight line on such a chart are approximately normally distributed. Data that do not form a straight line follow a non-normal probability distribution.

4.2.2.5 Scatter plots

Scatter plots display the relationship between two exposure variables measured from the same unit of observation (e.g., a person or location). Scatter plots are useful for graphically illustrating associations that are summarized numerically by correlation coefficients. Possible results include noticeable linear or non-linear trends, the absence of trend (a big "cloud") or a general trend with some observations as outliers. *Outliers* are observations that do not follow the trends of the rest of the data and can strongly affect estimates of associations by masking real effects. Outliers can be the result of measurement error, human error or a correct but abnormal observation. Regardless, all potential outliers should be checked for accuracy and corrected or removed if this is justifiable. Fig. 15 contains a scatter plot of blood lead and faeces lead measurements made concurrently on the Maltese sample population. Note that the plot indicates a positive association between the two measurements, but that the relationship is not 1 : 1, i.e., a unit change in blood lead levels is not accompanied by a constant change in blood faeces concentrations. This observation is consistent with the correlation coefficient between these measures of 0.57 that was noted in the previous section.

4.3 Probability distributions

Most exposure measurements can be considered random variables; that is, the different values obtained for a measurement of a given type are a function of a set of causative variables that may or may not be known to the analyst (Ott, 1995). Statistics allows for analysis of random variables by incorporation of variation through probability. This addition of variation allows for the generalization of results to populations larger or different than the sample under consideration.

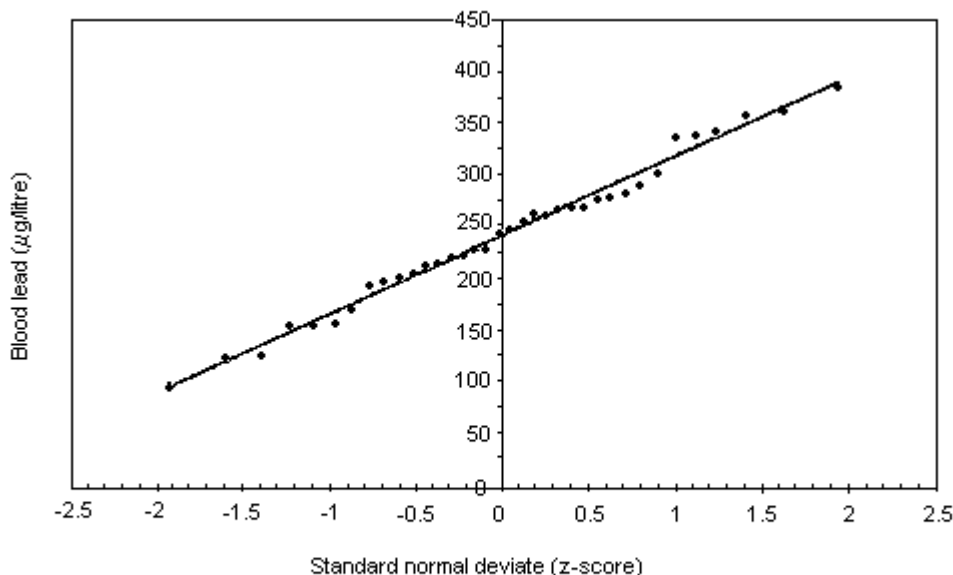


Fig. 14. Quantile-quantile plot. Maltese blood data plotted against the normal probability distribution (WHO, 1985b)

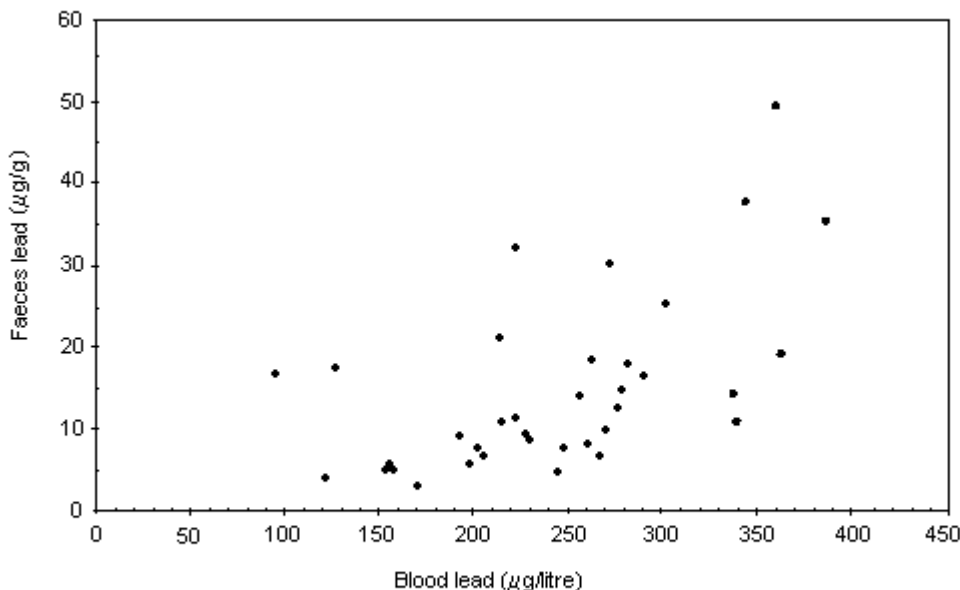


Fig. 15. Scatter plot of blood lead and faeces lead data from Malta (WHO, 1985b)

Continuous probability distributions are described by their probability density function (PDF), which provides the probability of an outcome taking values in a small interval, and by their cumulative distribution function (CDF), which describes the probability of an outcome being less than a particular value. The PDF and CDF are directly analogous to the concepts of a histogram and cumulative probability distribution discussed in Section 4.2.

Probability models are used to make statements such as, "The probability that the daily maximum ozone concentration will be greater than 120 ng/litre today is 0.08." Such estimates can be based upon empirical evidence (i.e., by looking at the number of observed concentrations greater than 120 ng/litre in comparison with the total number of observed concentrations) or by choosing a distribution and parameters that describe the observed data. An example of the latter would be to model the distribution of blood lead levels in Maltese subjects as normally distributed with a mean of 243 µg/litre and standard deviation of 70.9 µg/litre and to use the properties of the distribution to estimate the probability. The amount of confidence in the accuracy of the estimates is related to the amount of data available and the sampling scheme used to collect the data, as well as the degree to which the mathematical distribution fits the observed data.

Two standard distributions commonly used in exposure assessment for modelling continuous outcomes are the *normal* and the *lognormal* distributions. The *binomial* and *Poisson* distributions are often used in exposure studies as well. Many other probability distributions are available which have more flexibility (Johnson & Kotz, 1970a,b), but these four are frequently used and thus warrant attention here.

4.3.1 Normal distribution

The normal distribution, also known as the *Gaussian distribution*, is one of the most important statistical distributions. It is characterized by a symmetric, bell-shaped frequency distribution and is commonly used as a basis for analysis of environmental exposure data. Usually, a random variable (X) that follows a normal distribution with mean μ and variance ρ^2 is denoted by $X \sim N(\mu, \rho^2)$. The probability density function of the normal distribution with parameters μ and ρ^2 is given in Table 10.

Since the cumulative distribution function cannot be integrated in a closed form, the best we can do is to numerically compute the integral. The values $\mu = 0$ and $\rho = 1$ specify the *standard normal distribution*. The values of the CDF for the standard normal distribution have been tabulated and are available from most statistical textbooks and computer packages. The capital letter Z is

usually reserved to denote a standard normal random variable, i.e., $Z \sim N(0,1)$. The normal distribution ranges from positive infinity to negative infinity and is symmetric. Equation 4.7 can be used to transform any normal random variable X to a standard normal random variable (Table 10). Standardized normal random variables are useful for computing the probability of an event occurring, e.g., the likelihood that someone in Malta has a blood lead concentration greater than 384 $\mu\text{g/litre}$. Assuming the Maltese blood lead data presented earlier are representative of the general population and the blood lead concentrations are approximately normally distributed, the standard normal distribution can be used to calculate the desired probability.

4.3.2 Lognormal distribution

Many exposure measurements are strictly positive and right skewed (i.e., asymmetric). Examples include the size distribution of suspended particulate matter, personal exposures to various air pollutants and human time-activity patterns. The lognormal distribution is one possible model for describing data with these characteristics. The natural log (\ln) transform of a lognormally distributed random variable has the properties of a normally distributed random variable. In other words, the distribution defined by the mean ($\mu_{\ln x}$) and standard deviation ($\rho_{\ln x}$) of the \ln -transformed values is bell-shaped and symmetric and can be standardized according to the procedure outlined in the previous section. Exponentiation of $\mu_{\ln x}$ and $\rho_{\ln x}$ gives values termed the geometric mean (GM) and geometric standard deviation (GSD), respectively. The GM and GSD can also be used to define a lognormally distributed exposure measure.

A histogram of the blood faeces data from the Maltese sample population is presented in Fig. 16a. The data depart from normality as they are clearly right skewed. The histogram in Fig. 16b shows that the \ln -transformed values are approximately symmetric and indicates that the data approximate a lognormal distribution rather than a normal distribution. In this data set, $\mu_{\ln x} = 2.5$ and $\rho_{\ln x} = 0.7$ with corresponding $\text{GM} = e^{2.5} = 11.8 \mu\text{g/litre}$ and $\text{GSD} = e^{0.7} = 2.0$. The degree to which the lognormal distribution accurately describes the data can be evaluated by plotting the raw data on lognormal probability paper. This procedure is identical to that described in relation in to Fig. 13, except that the y axis is expressed on a

logarithmic scale. The Maltese faecal lead data are plotted on lognormal probability paper in Fig. 17. The nearly straight line formed by the faecal lead measurements displayed on a logarithmic scale versus Z indicates that the data are approximately lognormally distributed.

4.3.3 Binomial distribution

In some situation, the analyst may be interested in characterizing the frequency of a binary exposure outcome (e.g., yes/no; true/false). The binomial distribution is useful for modelling

Table 10. Density functions for selected probability distributions and related formulas

Normal distribution	
	$f(x, \mu, \sigma^2) = \frac{1}{\sqrt{2\pi\sigma^2}} \exp\left\{-\frac{1}{2}\left(\frac{x-\mu}{\sigma}\right)^2\right\}$
	Equation (4.6)
Transformation to the standard normal random variable	
	$Z = \frac{X - \mu}{\sigma}$
	Equation (4.7)
Binomial probability distribution	
	$P_k = \binom{n}{k} p^k (1-p)^{n-k}$
	Equation (4.8)
with mean	
	$E(k) = np$
	Equation (4.9)
and variance	
	$\text{Var}(k) = np(1-p)$
	Equation (4.10)
Poisson probability distribution	
	$P_\lambda = \frac{e^{-\lambda} \lambda^x}{x!}$
	Equation (4.11)

□FIGURE 16a;V214EH21.BMP

□FIGURE 16b;V214EH22.BMP

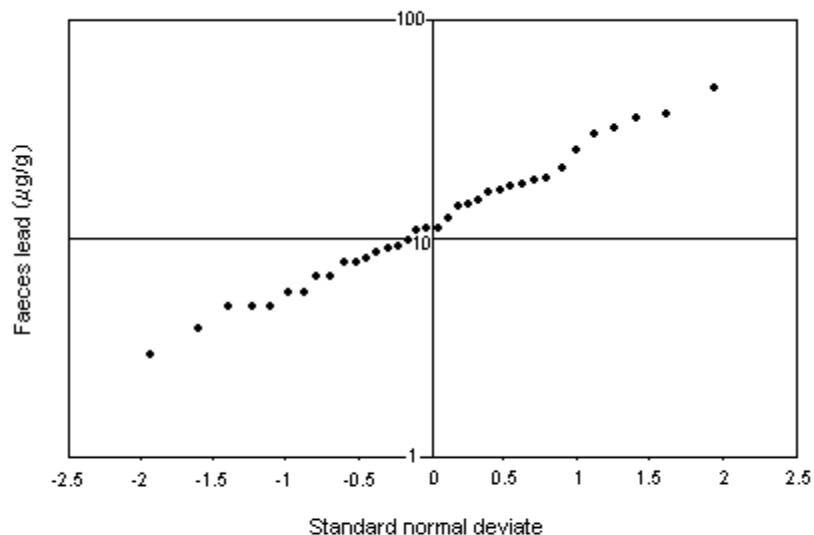


Fig. 17. Faecal lead data from the Maltese sample population plotted on lognormal probability paper (WHO, 1985b)

binary responses. The possible responses can be generally labelled as success or failure. Often we are not interested in a single outcome, but rather in the number of successes (k) and failures ($n - k$) for a specific number (n) of repeated independent trials for the outcome. The probability of exactly k successes in n independent trials, given a probability of success (p) in a single trial, is given by the binomial probability distribution (P_k) in Table 10.

For example, assume daily exceedances of an ozone air quality standard are independent events in a study of 1-year and 3-year time periods. Let k be a random variable describing the total number of exceedances encountered in a 1-year period ($n = 365$ days). Further assume from historical data that the expected number of exceedance days each year is 1, thus $p = 1/365 = 0.00274$. The calculated probabilities of k days of exceedance per year are shown in Table 12. Examination of the resulting probabilities in this example reveals a right-skewed distribution with the greatest probability occurring between $k = 0$ and $k = 4$ days.

4.3.4 Poisson distribution

Some exposure-related measurements are expressed as a rate of discrete events, i.e., the number of times an event occurs per unit time, such as the frequency (times per week) that a person consumes an ocean fish containing a methylmercury concentration greater than 5.0 ppm. The Poisson distribution is used for describing potentially unlimited counts or events that take place during a fixed period of time (i.e., a rate), where the individual events are independent of

one and other. The Greek letter lambda is typically used to denote the average or expected number of counts per unit time. In a Poisson distribution, the parameter lambda also describes the variance of the random variable. We can think about this intuitively by noting that as the expected number of counts or events increases (i.e., the rate of

events increases), the amount of variability should increase as well. For example, if we expect a count of 1 then it is not too difficult to imagine observing 0 or 2. Likewise, if we expect a count of 20 000 then it is not difficult to imagine 20 100 or 19 900 as reasonable observations. However, the variance is definitely larger in the second case. The formula used to compute the probability of a specific number of counts being observed over a fixed time interval is listed in Eq. 4.11 of Table 10.

For example, the Poisson distribution can be used in an exposure model to characterize the frequency with which a person comes in contact with a contaminant; say, the number of times per day a person encounters benzo [a]pyrene associated with environmental tobacco smoke. Assume that based on existing data, the expected number of encounters is anticipated to be 2 per day. Using Eq. 4.11, with $\lambda = 2$, there is a 9% chance that an individual will have 4 (i.e., $n = 4$) encounters with benzo [a]pyrene on a given day. Subject to limitations associated with the independence assumption noted above, the Poisson distribution can be a useful exposure modelling tool.

4.4 Parametric inferential statistics

Inferential statistics is the process of using the observed data and assumptions about the distribution and variation of the data to draw conclusions. The two complementary components of inference are *parameter estimation* (either point or interval estimation) and *hypothesis testing*. Only frequentist, or classical, inference will be discussed here. However, Bayesian statistical inference, as well as decision theory, can be valuable for incorporating other aspects such as prior belief and loss into a statistical analysis, and they are worth consideration. Further information on Bayesian statistics may be found in Carlin & Louis (1996).

4.4.1 Estimation

Exposure measurement data can be used to estimate the parameters of a model (e.g., a probability distribution), especially those that describe the mean and variance of the variable. The two types of common reported estimates are *point estimates* and *interval estimates*.

Point estimation for quantities is commonly performed using maximum likelihood, ordinary least squares or weighted least squares methods. All estimates are chosen because they optimize (i.e., find the maximum or minimum of) some objective function such as the likelihood function or squared error function. One example is the sample mean for the population mean when the data are normal, using maximum likelihood, or for any data, using least squares.

Two different forms of interval estimation are used to characterize variability in point estimates. The first is based on error propagation and is the result of simulating data to see what distribution of results might be expected under the model; the second is the usual statistical notion of confidence intervals. This approach focuses more on the variability of a modelled outcome due to variability of the input, and is useful in designing studies and determining which factors will have the greatest effect on the variability of the exposures. These procedures are described more fully in Chapter 6.

The second form of interval estimate, the statistical (1-alpha)% confidence interval, gives a range of estimates, for a parameter, which is generated in a manner such that it contains the true parameter value (1-alpha)% of the time. For a normally distributed random variable, a one-sided confidence interval for the estimate of the mean is derived from the standard error and $Z_{1-\alpha}$, while

$Z_{1-\alpha/2}$ is used for a two-sided confidence interval. The standard error (ρ_{hox}) is an expression of uncertainty about the mean and is calculated as the standard deviation divided by the square root of the number of observations (n) (Table 9). Continuing with the example from the Maltese study, the standard error of the blood lead sample data is 11.8 $\mu\text{g}/\text{litre}$ (Table 8). For $\alpha = 0.05$, the two-sided 95% confidence interval about the estimated mean is computed as 243 $\mu\text{g}/\text{litre} \pm 23.1 \mu\text{g}/\text{litre}$, where the latter is equal to $Z_{1-(\alpha/2)} \times \rho_{\text{hox}}$ or 1.96×11.8 (Table 11). Details of this procedure and related considerations may be found in most introductory statistics textbooks, for example Kleinbaum et al. (1988).

4.4.2 Measurement error and reliability

The term measurement error refers to the accuracy and precision of a given sample collection and analysis methodology. *Accuracy* describes the degree to which a measurement is free of bias. *Bias* is systematic deviation in a measurement from the true value of the process being measured. *Precision* refers to the reproducibility of a particular measurement system. Measurement reliability is a closely related concept in that a measurement with a high degree of accuracy and precision can be considered to be more reliable than one with a low degree of accuracy and precision. Additional information on measurement error and reliability is contained in Chapter 11, where the topic is discussed in the context of QA in exposure studies. Methods for assessing the accuracy of an exposure measure are also discussed in Chapter 11. Here, an approach for quantitatively estimating the precision of an exposure measurement system is presented.

Statistical analysis of environmental samples collected simultaneously in space and time can be used to estimate the precision of a measurement method. Such samples are often referred to as *duplicates* and are often collected in pairs. The difference in the measurement parameter (e.g., concentration) between a duplicate pair

Table 11. Standard normal cumulative probabilities

z	p(Z < z)	z	p(Z < z)
-4.265	0.00001	0	0.50
-3.891	0.00005	0.126	0.55
-3.719	0.0001	0.253	0.60
-3.291	0.0005		
-3.090	0.001	0.385	0.65
-2.576	0.005	0.524	0.70
-2.326	0.01	0.674	0.75
		0.842	0.80
-2.054	0.02	1.036	0.85
-1.960	0.025		
-1.881	0.03	1.282	0.90

-1.751	0.04	1.341	0.91
-1.645	0.05	1.405	0.92
		1.476	0.93
-1.555	0.06	1.555	0.94
-1.476	0.07		
-1.405	0.08	1.645	0.95
-1.341	0.09	1.751	0.96
-1.282	0.10	1.881	0.97
		1.960	0.975
-1.036	0.15	2.054	0.98
-0.842	0.20		
-0.674	0.25	2.326	0.99
-0.524	0.30	2.576	0.995
-0.385	0.35	3.090	0.999
		3.291	0.9995
-0.253	0.40	3.719	0.9999
-0.126	0.45	3.891	0.99995
0	0.50	4.265	0.99999

is indicative of the precision of the collection and analysis methodology. Descriptive statistics generated from a set of differences between duplicate samples can be used to characterize the average degree of precision as well as variability in precision.

Consider a hypothetical study of respirable particulate matter (RSP) in outdoor air where 20 duplicate pairs of 24-h average measurements were made. Assume the average 24-h average concentration among the 40 measurements was $50 \mu\text{g}/\text{m}^3$. Further assume that the distribution of differences between the 20 pairs of duplicate samples was normally distributed with a mean and standard deviation of 5 and $1 \mu\text{g}/\text{m}^3$, respectively. On average, then, a single measurement can be expected to be within $5 \mu\text{g}/\text{m}^3$ of the actual concentration. Utilizing

Table 12. Probability distribution for the number of exceedances, using the with expected number of exceedances of 1.0

Number of exceedances k	1-Year period		3-Year period	
	Probability Pk {k}	Cumulative probability Fk{k}	Probability PM{k}	Cumulative probability FM
0	0.36737	0.36737	0.04958	0.
1	0.36838	0.73576	0.14916	0.
2	0.18419	0.91995	0.22414	0.
3	0.06123	0.98118	0.22435	0.
4	0.01522	0.99640	0.16826	0.
5	0.00302	0.99942	0.10086	0.
6	0.000498	0.999920	0.05034	0.

7	0.000070	0.9999904	0.02152	0.
8	0.0000086	0.9999989	0.00804	0.
9	0.0000009	0.9999999	0.00267	0.
10	0.00000009	0.9999999	0.00080	0.
11	0.000000008	0.9999999	0.00022	0.
12	0.000000001	0.9999999	0.00005	0.

concepts presented in Chapter 4.4.1, a single measurement can be expected to be within approximately 3-7 $\mu\text{g}/\text{m}^3$ of the true concentration 95% of the time, i.e., within ± 2 standard deviations of the average difference.

For a probability distribution, the coefficient of variation is defined as the ratio of the standard deviation to the point estimate of the mean. In this way, the coefficient of variation error describes the degree of dispersion of a data set relative to a measure of its central tendency. The coefficient of variation provides a quantitative estimate of the relative degree of variability among the observations

in a data set. Using data from the hypothetical example described above, the coefficient of variation among the pairs of duplicate samples is 0.2. Thus, on average, a single measurement can be expected to be within 20% of the actual concentration.

4.4.3 Hypothesis testing and two-sample problems

Exposure assessments are often performed to determine whether the level of exposure to a pollutant is different between two or more groups of people or locations or periods of time. Additional attributes typically considered to be determinants of exposure include any number of demographic factors (e.g., age, gender, ethnicity) and behaviour patterns. This section describes the statistical procedure used to address this type of study objective.

Statistical hypothesis testing is a procedure where a choice is made between two hypotheses that are not weighed equally; the null and the alternative. The *null hypothesis* typically reflects what can be stated with confidence about a particular phenomenon on the basis of existing information. In practice, concluding that the null hypothesis is false indicates that the data provide strong evidence for a departure from conventional wisdom or practice. Thus, hypothesis tests are generally constructed such that the conclusion will lie with the null unless the evidence strongly suggests otherwise.

Two types of errors can arise from hypothesis testing:

- * concluding that the alternative hypothesis is true when it is in fact false (false negative)
- * concluding that the null hypothesis is true when in fact it is false (false positive).

The first type of error is known as a *type I error* and the second

one is a *type II error*. The probability of a type I error is denoted by alpha and the probability of a type II error by β . Only alpha is considered in the construction of the hypothesis test. However, as described later, both type I and type II errors are considered in sample size determinations.

The general procedure for common tests that try to determine if some factor has an effect on the exposure outcome is as follows: a test statistic is constructed whose value is known if the null hypothesis is true. For example, if the null hypothesis is that the population mean is 1 ($H_0: \mu=1$), then under the null hypothesis, $\bar{x} = 0$, where \bar{x} is the sample mean. Next, adjustments are made so that the distribution of this test statistic is known. For example, with s denoting the sample standard deviation and n the sample size, the test statistic T defined by Eq. 4.12 in Table 13, where T has a distribution which follows a t -distribution with $n-1$ degrees of freedom. Now, using the known distribution of the test statistic, we construct ranges of values for which we reject (rejection region) and fail to reject (acceptance region) the null hypothesis. The rejection region is any area which has probability alpha, usually chosen to correspond to likelihoods between 0.025 and 0.05.

Table 13. Formulas used for hypothesis testing

T-statistic

$$T = \frac{\bar{x} - \bar{\mu}}{s/\sqrt{n}} \quad (\text{Equation 4.12})$$

Two-sample *t*-statistic

$$t = \frac{\bar{x}_1 - \bar{x}_2 - \Delta_0}{\sqrt{(s_1^2/n_1) + (s_2^2/n_2)}} \quad (\text{Equation 4.13})$$

A large number of problems in exposure assessment involve the comparison of two groups, for example, control and treatment; old method and new method; or normal and abnormal. If we focus on the location problem, where the means or the medians are compared, then depending on the assumptions we make with regard to the data, different tests can be performed. Assumptions typically made include:

- * The data consist of a random sample from population 1 ($X_{1,i}$, $i = 1, \dots, n$), and a random sample from population 2 ($X_{2,i} = 1, \dots, n_2$)
- * The two samples are independent of each other.

- * Observed variables are on a continuous scale.
- * Measurement scale is at least ordinal.
- * Population 1 (X_1) has approximately the same distribution as X_2 .

If we assume that the data follows a normal distribution and that the data are independent, with the first group distributed $N(\mu, \rho^2_1)$ and the second group distributed $N(\mu, \rho^2_2)$ so that the variances are possibly different, a test can be constructed to see if the difference (Δ) between the means for the groups is equal to a hypothesized value (Δ_0), typically set to zero. This scenario would result in a two-sample t -test, and the test statistic is presented in Eq. 4.13 in Table 13, where t is compared with a

t -distribution with $df = \min(n_1 - 1, n_2 - 1)$ degrees of freedom, and s_i^2 is computed as described in section 4.2.1. The possible alternatives are that $\Delta > \Delta_0$, $\Delta < \Delta_0$, or the general alternative that Δ not equal Δ_0 . If we are looking for differences, we reject the null hypothesis that the groups are the same for the respective alternative if $t > T_{df, \alpha}$, $t < -T_{df, \alpha}$, or $|t| > T_{df, \alpha/2}$, where α is the prespecified type I error for the decision to be made.

Referring once again to the blood lead example presented earlier, the following null hypothesis may be tested: mean blood lead concentrations in the Maltese sample population are equal to those in the Mexican sample population. The corresponding alternative hypothesis is: mean blood lead concentrations are not equal in the two sample populations. As indicated in Fig. 13, the point estimates of the respective sample means are different. Completion of the two-sample t -test will allow for determination of whether the difference is statistically significant with $1 - \alpha\%$ confidence. Using Eq. 4.13, the t -statistic is computed to be 3.30. Setting $\alpha = 0.05$, the critical t -value is 1.96. Thus, the Maltese and Mexican sample mean blood concentrations are significantly different at the 0.05 level.

4.4.4 Statistical models

Statistical models make explicit the potential sources of variability to be measured. The response, exposure, is dependent upon a combination of measured factors and background variation from unmeasured influences. For example, in examining pesticide exposures, one might consider methods and amounts of applications, climate conditions and duration of potential exposure. Unmeasured factors might include exact knowledge of individual behaviours and locations, which may cause different levels of exposure between two individuals who are equal with respect to other exposure characteristics. One must consider as many of the potential relationships between the responses as possible, as well as how the possible factors will affect each other, before finalizing a study design.

Since no simple model will perfectly describe all relationships, the goal is to construct a parsimonious model that describes the major factors of the process resulting in exposure. For example, in studying the exposure of children to lead, the presence of lead in paint, in

house dust or in water could be important factors, whereas gender and age might have an indirect effect on exposure by influencing the location and patterns of play. However, both types of data will be important in determining response, even though one is only an indirect cause. The average outcome described above could be the annual average exposure to lead or perhaps the maximum daily exposure, depending upon whether a cumulative or a threshold effect is the focus.

As noted in Chapter 3, by considering the statistical model before finalizing the study design one can help ensure that most influential factors would be accounted for, and more importantly, that the true effects of factors can be estimated from the study data. It is possible to design a study where some influential factors were not accounted for. Suppose there is interest in the effects of location and time of day on outdoor ultraviolet radiation exposures. If measures are only taken at one site at one time of day, and then at another site at a different time of day, then the effects of location and time of day are not distinguishable from the collected data.

The mean, or average, outcome is the most common summary used for modelling and testing of situations of different conditions, but other parameters, such as the variance, the percentiles or the median, can be used for estimation and testing. Common models and statistical analyses, such as the multiple linear regression model, the *t*-test and analysis of variance (ANOVA) use the mean for modelling and testing. The models can be as simple as taking the sample, dividing it into groups and comparing the means in the different groups. The models can also be as complex as trying to construct a physical model for the means with the addition of terms which incorporate randomness due to unmeasured factors or other sources of variation.

4.4.4.1 Analysis of variance and linear regression

ANOVA is a technique for assessing how several nominal independent variables affect a continuous dependent variable, and is usually concerned with comparisons involving several group means. Regression and ANOVA models are closely related and can be analysed within the same framework. The major difference is that for ANOVA, all the independent variables are treated as being nominal; whereas for regression analysis, any mixture of measurement scales (nominal, ordinal, or interval) is allowable for the independent variables. Examples of ANOVA used in exposure assessment can be found in Liu et al. (1994a), who used ANOVA models to examine the effects of wind speed, ozone concentrations, human subject and interaction between wind speed and concentration on the performance of an ozone passive personal sampler.

Estimation for both ANOVA and linear regression models consists of obtaining point estimates for the parameters that describe the mean exposure under a certain set of conditions. Part of the estimation procedure is to determine how well the model fits. The first diagnostic is to examine the residual error (residual). A residual is simply the difference between the exposure estimated by the model and the actual exposure. By examining the residuals, one can determine for what ranges of actual exposures or conditions the model does not fit well, and use this to decide how to adjust the model.

The simplest design (and corresponding model) occurs when measurements are taken while varying only one possible factor over a finite, *k*, number of levels. Consider PM_{2.5} exposure; let the factor

be the time of day when the levels are measured. For simplicity, divide time into three categories -- morning, afternoon, or evening -- so $k = 3$. If there is no known or hypothesized functional form for the relationship, the resulting abstract model for exposure, Y , during a particular time period, i , should be the sum of the mean (average) during the time period i , denoted by γ_i , and an error, ϵ , which will represent the natural variation of the measurement. It is common to assume that the variation of the outcome is the same among all levels of the factor; this assumption is known as *homoscedasticity*.

This model is referred to as the one-way ANOVA. The resulting model for the observed data, with Y_{ij} denoting the j th $PM_{2.5}$ measurement collected during the i th time period with i ranging from 1 to 3, is $Y_{ij} = \gamma_i + \epsilon_{ij}$ where γ_i represents the average outcome due to the i th factor level (in this example i ranges from 1 to 3), and ϵ_{ij} (the error term) represents independent random variation. One common assumption is that the error terms follow a normal distribution with variance ρ^2 . The parameters which need to be estimated in this model from the data are the means of the subsamples, γ_i , and the variance of the outcome, ρ^2 . This type of model, which compares the means of distinct groups, is the basis for ANOVA.

Increasing the level of complexity leads to multiway or multifactor ANOVA as well as the multiple linear regression model, which is a more specific model for the effects of independent variables on the dependent variable. Let Y denote the exposure level for a particular person or location; this is the dependent variable. Let X_1, \dots, X_n denote n independent variables (known as covariates) which potentially influence the exposure level Y . If the assumption of the existence of a linear relationship between the independent and dependent variables is reasonable, then a model for the outcome, Y , based on the covariates X_i , can be written as

$$Y = \theta_0 + \theta_1 X_1 + \dots + \theta_n X_n + \epsilon$$

where the information not conveyed by the covariates results in the error (ϵ), which is assumed to be normally distributed. θ_0 denotes the average exposure when all the X values are zero, and θ_i denotes the change in exposure for a unit change in the i th variable. An example would be 24-h personal exposures to nitrogen dioxide. In this case, the factors may be distinct times and locations (or microenvironments) where nitrogen dioxide exposure may occur; for example, outdoors, indoors while home cooking on a gas range, and in an automobile.

A regression model is used to evaluate the relationship of one or more independent variables X_1, X_2, \dots, X_k to a single, continuous dependent variable Y . It is often used in exposure assessment to characterize the relationship between the dependent and independent variables (continuous and discrete) by determining the extent, direction and strength of the association. For example, in the particle total exposure assessment methodology (PTEAM) study, indoor

PM_{2.5} concentration (Y) was regressed against outdoor air concentrations (X_1), smoking rates (X_2), cooking durations (X_3), air exchange rates (X_4) and house volumes (X_5) to determine the major factors affecting indoor PM_{2.5} concentrations (Ozkaynak et al., 1996).

Further information on ANOVA and linear regression may be found in Ott (1995), Kleinbaum et al. (1988) and most introductory statistics textbooks.

4.4.4.2 Logistic regression

An approach which is different from the linear or additive relationship described above is to consider a categorical outcome for exposures, e.g., exposure measurements grouped into ordinal levels such as low, medium and high. When the response is binary, that is, if an exposure is either present or absent (i.e., a *threshold effect*), then a linear relationship is not appropriate. In this case, we must use an alternative model, for example:

$$\text{logit } P(Y = 1) = \alpha + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_k X_k$$

where the logit function is $\text{logit}(x) = \ln(x/(1-x))$, the function $P(Y = 1)$ denotes the probability that the response variable Y will take on the value 1 (denoting "success"), and the role of epsilon from the previous model is taken by modelling the parameter representing the probability that $Y = 1$, as opposed to Y itself. This model is known as logistic regression. In this model, alpha denotes the baseline odds for exposure given that the associated factors, $X \dots, X_k$, are zero, and β_i denotes the change in the log-odds that the response is $Y = 1$ given a 1-unit increase in X_i . This approach can be adjusted to allow for the analysis of other types of categorical outcomes (McCullagh & Nelder, 1990). One common parameter which describes logistic regression results is the *odds ratio*. For a particular set of covariates, X_i , the odds of the event occurring ($Y = 1$), is $\exp(\beta X_i)$. To compare the odds ratio for two situations, compute the first set of odds and take its ratio over the second odds. Usually, the situations will be identical, except that the covariate of interest will be zero for one of the sets. For example, if the model for the linear combination of covariates is $1.3 + 2.5 X$, then the odds ratio for $Y = 1$, comparing $X = 1$ versus $X = 0$, is $e^{(1.3+2.5)}/e^{1.3}$. A similar computation can be done when X is a continuous random variable, for two different values of X . In exposure assessment, a logistic regression model

could be used to evaluate the importance of demographic or temporal factors on the likelihood that an individual will engage in an activity such as applying pesticides.

4.4.5 Sample size determination

Hypothesis testing attempts to determine if the data reject or fail to reject a particular (null) hypothesis. The test is based upon statistical considerations, and hence just reports how likely or unlikely the null hypothesis is. If there is minimal information, it will be difficult to statistically reject the null hypothesis; hence, sample size calculations are done in order to ensure that there is sufficient information from which to make a decision. The decision is

between two unequally weighted hypotheses; the first is the null hypothesis, H_0 , which is the safe hypothesis, and the second is H_1 , the alternative or sceptical hypothesis, which requires sufficiently large evidence to believe in. The specifications of the test, based upon sceptical scientific belief or common usage, are the type I error and the type II error (defined in section 4.4.3). Introductory information on sample size determination is presented here; the reader is referred to Lemeshow et al. (1990) for details.

To determine the minimum sample size required to observe the desired outcome, one needs to determine the smallest effect that is scientifically worth detecting (i.e., based on measurement limit or scientific principles), and use that to collect a sample with enough information to detect such a difference. The effect is the minimum significant difference in exposure between two groups. The smaller the effect, the more information is required to distinguish it. This effect is related to the type I error of a hypothesis test. There are two components, the type II error and the sample size, which are unspecified. When the type II error is specified, the resulting sample size can be determined. Once the sample size is determined, the power (1-type II error) of a study can be computed. The smaller the difference to be detected, the larger the sample size needed for fixed type I and type II error probabilities.

The following describes the formula for a two-group comparison. To compare the means of two groups with equal sample size, let Delta represent a scientifically significant difference that we would like to detect, if it exists. Suppose that the first group can be modelled by $Y_1 = \mu_1 + \text{epsilon}_1$, where μ_1 is the mean and $\text{epsilon}_1 \sim N(0, \rho^2)$ is the error term, and the second group can be modelled by $Y_2 = \mu_2 + \text{epsilon}_2$ with the error term $\text{epsilon}_2 \sim N(0, \rho^2)$. The only difference between the two groups is the mean response. The groups will be considered statistically different only if $|\mu_2 - \mu_1| \geq \text{Delta}$. The minimum number of observations in each group is given by Eq. 4.14 in Table 14 where z_{gamma} is defined as the value satisfying $P(Z > z) = \text{gamma}$, where Z follows the distribution of a standard normal random variable, α is the type I error, and β is the type II error. This formula can also be used to approximate the sample size needed for a difference of proportions (e.g., for dose-response models comparing two groups), by letting Delta represent the difference in proportions (instead of a difference in means).

Table 14. Formula used for sample size determination

Two-sample comparison

$$n \geq \frac{2(z_{1-\alpha} + z_{1-\beta})^2 \sigma^2}{\Delta^2} \quad (\text{Equation 4.14})$$

4.5 Non-parametric inferential statistics

Each of the statistical analysis methods described previously assumes that the data can be adequately described by a probability distribution with known parameters, and that distribution can be transformed, if necessary, to meet the assumptions of the statistical model (e.g., normally distributed, independence, etc.). Many exposure-related data sets do not fit this description, however. One reason for this is that the data may not be normally distributed or cannot be transformed so that they are approximately normal. A more common reason is that although the underlying distribution of the population from which the sample is drawn may be reasonably assumed to be approximately normal or lognormal, there are too few samples to allow the nature of the underlying distribution to become apparent. In exposure studies sample sizes are often small (e.g., 10 or less) because of logistic difficulties in collecting samples and the expense of collecting and analysing the samples. In this case, the point estimates of the standard deviation and standard error are considered to be highly unstable. Consequently, confidence intervals generated using the estimation methods described above are considered to be unreliable. Non-parametric statistical analysis methods can be used to analyse data with these characteristics.

Non-parametric statistical methods rely on rank statistics, i.e., the order of observations in a data set. Glantz (1987) provides a concise introduction to non-parametric statistical methods with regard to health statistics. The sign test and Mann-Whitney rank sum test are two non-parametric methods for evaluating the equivalence of the median from two sample populations. These methods are analogous to the two-sample *t*-test described in Section 4.4.3. The Kruskal-Wallis test is analogous to the *k*-sample ANOVA method described in Section 4.4.4 and is used to test whether the medians of more than two sample populations are equal. For further information on this topic, the reader is referred to Mosteller & Rourke (1973), a classic text on non-parametric methods, and also to Gilbert (1987) and Ott (1995) for a discussion of statistics based on rank order in an environmental context.

4.6 Other topics

Many new developments in statistical theory can be applied to the analysis of exposure assessment data. These include the topics of measurement error, missing data, spatial statistics, non-linear models, mixed effects, generalized mixed effects models, simulation models (e.g., Monte Carlo analysis), as well as others. Modern computing methods such as re-sampling and the bootstrap have made possible estimation, evaluation, and testing of complex models. In addition, other inferential philosophies, such as Bayesian and decision-theoretic approaches, can be useful. Recommended references for further reading on these and related subjects are Sachs (1986), WHO (1986), Gilbert (1987), Glantz (1987), Kleinbaum et al. (1988) and Ott (1995).

4.7 Summary

Statistical methods are a critical tool in applied and research-oriented exposure assessment studies. It is recommended that a statistician be involved in all aspects of an exposure

investigation, especially during the design and data analysis stages. Sample size determination is an important use of statistics during the planning of an exposure assessment study. Numerical and graphical descriptive statistics can be used to summarize exposure data and perform preliminary analyses of relationships between and among exposure variables. In many cases, exposure data are approximately normally or lognormally distributed and can thus be readily incorporated into standard parametric statistical inference methods such as estimation and hypothesis testing. In addition, other parametric statistical models such as ANOVA, linear regression and logistic regression can be used to quantify associations among exposure measures. In situations where the number of observations is small or the data cannot be transformed to an approximately normal distribution, non-parametric methods such as the sign, Mann-Whitney and Kruskal-Wallis tests can be used to test hypotheses.

5. HUMAN TIME-USE PATTERNS AND EXPOSURE ASSESSMENT

5.1 Introduction

Methods for the collection and application of time-use data in exposure studies are critically reviewed in this chapter. All methods have their limitations. With appropriate quality assurance, however, information on time use and activity patterns collected by questionnaire, diary, interview, observation or technical means can be very valuable for interpreting and modelling exposures. Although the methodologies of time-activity data collection are universal, they need to be applied and their vocabularies selected keeping in mind the population and culture of concern and objectives of the study. Accurately and reliably documenting the time-activity patterns of the general and target populations are important components of understanding and mitigating human exposure (see Table 15).

People's activity patterns, eating and drinking habits, and lifestyle characteristics must be superimposed over concentrations in environmental media before it is possible to derive realistic estimates of actual human exposure. Too often in the past, pollutant concentrations in a particular medium have been assumed to represent exposure, only for it to be found later that they did not provide an accurate picture owing to modifying factors such as the time people spend indoors rather than outdoors, food preparation and cooking, and use of bottled water instead of tap water. Experience has shown that exclusive reliance on central monitoring sites (e.g., urban air pollution monitoring sites, samples from drinking-water reservoirs) and bulk sampling procedures (e.g., spot checks for pesticides in food) for determining human exposures may be insufficient in many cases.

In an exposure context, data about human time use and activity patterns (often referred to as time-activity data) have four related purposes.

1. Knowledge of the activities performed while a study participant carried a personal monitor can aid in identifying the determinants of exposure, i.e., "What did this person do that led her/him to have such a high exposure?" and "To what extent can exposure be explained the amount of time spent in specific activities or locations?" For instance, several studies in which activity pattern data were collected in conjunction with monitoring data have shown that indicators such as commuter status, work status, cooking fuel type,

season, residential location and day of week are important in differentiating exposure to carbon monoxide and nitrogen dioxide (Akland et al., 1985; Ryan et al., 1990; Schwab et al., 1990; Berglund et al., 1994a). Investigations of VOC exposure have found that people who reported engaging in auto-related activities (e.g., exposure to vehicle exhausts, pumping gasoline and visiting a service station) were associated with statistically significant increases in breath and personal exposure levels of several aromatic and aliphatic compounds;

Table 15. Features of time-activity studies aimed at exposure assessment

Location	Pollutant	Participant characteristics	Survey characterist
Cincinnati, Ohio, USA	No pollutant	487 people under age 70; representative; includes children; oversample asthmatics; data on age, gender, race, income, work status, health status	March and August 19 diary; minute resol 3-day sample; time year; day of week; of day
California, USA	No pollutant	1780 people over age 11; representative of English-speaking households; stratified by region; data on demographics and socio-economic status	October 1987-July 1 recall and question time of year; day o time of day
California, USA	No pollutant	1200 children under age 12; representative of English-speaking households; stratified by region; data on demographic and socio-economic status	April 1989-March 19 recall and question time of year; day o time of day
Kanawha Valley, West Virginia, USA	No pollutant	90 children aged 9-11; longitudinal (4 weeks); stratified by gender, respiratory health; data on demographic, socio-economic status and health variables	July and September diaries; 30-min res except travel (15 m time of year; day o time of day

Table 15. (continued)

Location	Pollutant	Participant characteristics	Survey characterist
New York, New Jersey; Pennsylvania, Oregon; Washington; California, USA	No pollutant	1000 children aged 5-12; stratified by state, weekday/weekend and season; data on demographic, socio-economic status and community type	Mid-1990 to mid-199 24-h recall of chil activities by adult caregiver; 30-min r questionnaire; time year; day of week; of day

Berkeley, California, USA	Ozone	168 college freshmen (aged 17-21) raised in California; convenience sample; long-term ozone exposure	Test-retest reliability study to recall life residential history
Athens; Basel; Grenoble; Helsinki; Milano; Praha	PM _{2.5} , CO, VOC, NO ₂	450 adults (aged 25-55) personal air sampling; approximately 1200 adults with time-activity diary; random population sample; demographic and socio-economic status	Mostly 1997; 48-h period indoor, outdoor and monitoring; time-activity diary (Fig. 19); special tasks
Washington, USA	CO	700 adults aged 18-65; representative; oversample long commutes and gas ranges; excluded smokers; data on age, gender, work status	1982-1983 (winter); and questionnaire; resolution; 1-day survey time of year; day of week and day

Table 15. (continued)

Location	Pollutant	Participant characteristics	Survey characteristics
Denver, Colorado, USA	CO	452 adults aged 18-65; representative; oversample gas ranges and long commutes; excluded smokers; data on age, gender, work status	1982-1983 (winter); questionnaire; minute resolution; 2-day survey time of year; day of week time of day
Elizabeth/ Bayonne, New Jersey, USA	VOCs	355 people; representative; oversampled high-exposure occupations; data on age, gender, race, socio-economic status, and proximity to VOC sources	Fall 1981; follow-up in summer 1982; follow-up 49 in early 1983; 2 recall diary; active questionnaire
Portage, Wisconsin	NO ₂ , RSP	120 children; selected from larger (600) cohort; stratified by cooking fuel; data on gender, age, parental education	1987; retrospective and prospective diary 10-15-minute resolution of year; day of week of day
Steubenville, Ohio	NO ₂ , RSP	150 winter, 250 summer; selected from cohort of 600 children; stratified by cooking fuel; data on gender, age, parental education	1987; retrospective and prospective diary 10-15-minute resolution of year; day of week time of day.
Topeka, Kansas, USA	NO ₂ , RSP	300 winter, 300 summer; selected from cohort of 600 children; stratified by	1988; retrospective and prospective questionnaires; 10-

cooking fuel; data on gender, resolution; time of
age, parental education day of week; time o

Table 15. (continued)

Location	Pollutant	Participant characteristics	Survey characterist
California, USA	VOCs	188 people; representative; oversampled high-exposure occupation; data on age, gender, race, socio-economic status and proximity to VOC sources	February-March 1984 follow-up: 52 in Ma 1984 and 51 in Feb March 1987; 24-h re diary; activity questionnaire
Boston, Massachusetts, USA	NO ₂	325 (winter), 298 (summer) ages 8 and above; representative; stratified by range type; no personal data	1986; diary and questionnaire; 15-30-min resolutio sample; time of yea of week; time of da
Los Angeles and Orange Counties;	NO ₂	620 people ages 8 and above sampled two 24-h periods; 65 sampled eight cycles; representative; data on age, gender, work status	May 1987-May 1988; () questionnaire; 15-m resolution; two-day time of year; day o time of day
Albuquerque, New Mexico, USA	NO ₂	1000+ infants; stratified by range type; data on child's health and parents' socio-economic and demographic characteristics	January 1988-Decemb every 2 months for first 18 months of 60 min; time of yea day of week; time o

reporting a smoker present in the home was associated with increased indoor concentrations and personal exposures of aromatic compounds; visiting dry cleaners, self-reports of proximity to smokers, pesticide use, exposure to solvent, degreasing compounds, and odorous chemicals, and employment status in certain occupations (e.g., paint, chemical or plastics plants) were associated with increased personal exposure to several VOCs (Wallace et al., 1985, 1986, 1988). Occupational exposure may be an important component of total exposure for some individuals or sub-populations.

2. Time-activity data allow modelling of human exposure to pollutants for which personal monitors are not yet available or are very expensive, or for which exposure is a function of multiple pathways. Total exposure can be simulated from information on the time spent doing various activities and/or in specific locations, coupled with knowledge about the likely range of pollutant concentrations in each situation. For example, the models SHAPE (Ott et al., 1988), NEM (Johnson et al., 1990), SIMSYS (Sexton & Ryan, 1988), and REHEX (Hall et al., 1992) are currently being used to estimate exposure to carbon monoxide, ozone, particulates, sulfur dioxide and nitrogen dioxide.

Techniques are also being developed to allow prediction of dermal and ingestion exposures based on assumptions about human activity patterns (e.g., Fenske, 1993). The usefulness of all of these models is dependent upon the accurate characterization of pollutant-relevant time-activity patterns.

3. From an epidemiological perspective, activity patterns can be used to assess the relationship between exposure and health status (e.g., Armstrong, 1985). For instance, "Do those who engage in potentially high-exposure activities experience more frequent or severe illnesses?" or "Do sensitive individuals avoid potentially high-exposure activities or limit them to certain times of day or locations?" In epidemiology, time-activity data may serve four purposes:

- * They may be a surrogate of the exposure of interest. For example, people may be asked about the hours they spend indoors with smokers to assess health effects of environmental tobacco smoke (Leuenberger et al., 1994).
- * They may be used to improve another imperfect measure of exposure. For example, estimates of long-term exposure to ozone may be derived from fixed site monitor data, weighted, however, for duration of time spent in outdoor activities (Künzli et al., 1997a,b).
- * They may be used as a surrogate for a cofactor which might confound the association between health and some other exposure. For example, the effect of ambient air pollution on lung function may be thought to be confounded by environmental tobacco smoke exposure (ETS). Time spent with smokers could thus be used to control this potential confounding.
- * The association of an exposure with some health outcome might not be the same in subgroups of different time-activity patterns (modified effect). In this case, time-activity data will allow the investigator to address such interactions.

4. Another purpose of time-activity data is to describe patterns of population behaviour. The proportion of time spent by the population in various microenvironments or frequency of use of various facilities (e.g., swimming pools) may provide an indication for the contribution of each of the microenvironments or activities on total population exposure. In such studies, the emphasis is on characteristics of groups, and not on individual data. Therefore the precision of the estimates may be improved by the increased sample size although the survey tools may remain relatively simple and inexpensive.

An understanding of the frequency and duration of the activities in which the target population engages can be used to set priorities for public health strategies designed to reduce exposure by limiting contact with contaminated media. Comprehensive exposure factor data for the US population may be found in AIHC (1994) and US EPA (1996a). Although this information is focused on the USA it may serve as a useful model to follow in other countries.

5.2 Methods

5.2.1 Activity pattern concepts

Activity pattern data that may be useful in assessing exposure can be divided into three categories:

- * the distribution of time among activities, referred to in this document as *time allocation parameters*
- * the factors that influence the degree of media contamination in the activities or locations of interest, referred to in this document as *microenvironmental parameters*
- * the *intensity of contact* while engaging in each activity.

5.2.1.1 Time allocation parameters

Time allocation parameters include the amount of time spent in a given activity, the time of day, week and year of contact, and the expected frequency with which the person or population engages in the activity. The relevant spatial resolution for describing time-use patterns, thus grouping activities for exposure assessment, depends upon the characteristics of the pollutant, the media, the location and the emission source(s).

The concept of microenvironment has been used to define an area across which the concentration of an air pollutant is assumed to be homogeneous (Duan, 1982). The most basic division of microenvironments is whether a person is indoors or outdoors, although more refinement is necessary for many exposure assessments. Time spent indoors is especially important with regard to pollutants which depend on indoor sources. Other typical microenvironments of interest in studying air pollution are home, work or school, and modes of transportation.

Depending on the characteristics of the media and the pollutant, a description of the actual activity may also be required to understand exposure. General activity categories such as "socializing" and "recreation" are less important than knowing whether the participant is involved in specific activities that lead to contact with environmental media in addition to or other than air. For instance, swimming leads to water contact, and farming and gardening lead to soil contact.

5.2.1.2 Microenvironment parameters

The distinction between people's activities and the pollutant concentration in a microenvironment is not always clear. The use of household appliances and consumer products that emit environmental contaminants and/or influence pollutant fate and transport affect microenvironmental concentrations. Thus, information on the microenvironmental parameters, i.e., the factors affecting the concentration in a given location, have also been included under the rubric of time-activity data. Important microenvironmental parameters for air pollution exposure assessment include building structure and household characteristics (e.g., the type of heating and cooking fuel used, the presence of parking garages and air conditioning units), information on proximity to specific sources (e.g., heavy traffic, cigarette smoking, cooking, solvent, pesticides), timing of emissions for each source, indoor/outdoor air exchange rates and meteorological and topographic factors.

5.2.1.3 Intensity of contact

In addition to time allocation measures and microenvironmental parameters, information on the intensity of contact is needed to assess exposure. Here the focus is on micro-level activities that affect the rate of contact with the contaminated media while the person is in a certain microenvironment (e.g., outdoors at home) and performing a specific activity (e.g., cleaning). The potential for dermal contact depends upon the surface area of exposed skin, thus clothing type and fabric consistency as well as the size of the person, whether the individual is sitting, crawling, kneeling or using their hands on the contaminated surface, or otherwise handling the contaminant. In addition, exposure for the given event depends upon the duration and frequency of each contact between the exposed skin and the contaminated media; e.g., 50 1-min contacts between the person's hand and the floor while cleaning. As described in Chapter 7, dietary factors, including the type of foods that are consumed and the

amount consumed per time period of interest, are the most obvious. Concern also has been raised about the potential for contamination of foods from contact with surfaces during storage, preparation and consumption (Berry, 1992, Freeman et al., 1997). Hand-mouth and object-mouth contact, although difficult to measure, may be one of the most important routes of exposure to contaminants such as pesticides and lead that reside in house dust, especially in children (Charney et al., 1980; Rabinowitz & Bellinger, 1988; Davies et al., 1990). For pollutants for which inhalation is the primary route of exposure, the intensity of contact is influenced by one's level of exertion (often referred to as "activity level"). Breathing rate or heart rate is needed to predict dose (the amount of contaminant that enters the body), thereby producing a more accurate estimate of the resulting health effects.

Finally, depending on the purpose of the exposure assessment, the required temporal resolution of the time-activity data may vary substantially. Whereas short-term time-activity patterns may be important for acute exposures, long-term average time-activity patterns may be more relevant in other circumstances. If long-term exposure is of major interest, e.g., over years or lifetime, residential history is an important information to assign respective ambient monitor data for the entire period of interest (Künzli et al., 1996).

5.2.2 Surrogates of time-activity patterns

For many exposures surrogates of time-activity patterns may be developed on the basis of generalizations about the activities of people at a particular time, who live in a specific geographic location or who share a specific set of living conditions. Usually the most important time-activity surrogate is age group. Some activities that are useful for predicting exposure to air pollutants, such as distance and timing of travel or duration of work and its locations, also show systematic differences in their frequency and duration by demographic characteristics. For instance, Schwab et al. (1990) documents how time in the kitchen, which influences exposure to combustion products, is greater among women in the USA than among men, even after adjusting for whether the woman works outside the home; likewise, men spend more time in transit, regardless of their age or employment status. It is likely that the frequency of contact with a wide variety of toxins differs across groups defined by gender and age, owing to traditional divisions of labour in many cultures.

Similarly, information about an individual's health condition may be important in characterizing their time-activity pattern. For instance, the limited data available on asthmatics suggests they may spend more time indoors than the general population (Goldstein et al., 1986, 1988; Lichtenstein et al., 1989; Schwab et al., 1991). As asthmatics are particularly sensitive to air pollutants, this activity information is important.

Socioeconomic status may influence time-activity patterns related to, for instance, time spent travelling to work or outdoors. Currently, however, the gap existing in time-activity databases with respect to the activity patterns of sensitive (e.g., elderly) and potentially high-risk (e.g., low socioeconomic status) subgroups, is a limitation for extension of exposure models to these groups. Further study is needed to determine the extent to which income, education and occupation are reliable surrogates for exposure-related factors (e.g., housing unit size and condition).

5.2.3 Data collection methods

Sociologists pioneered studies of activity patterns (Szalai, 1972; Chapin, 1974; Robinson, 1977). These "time budget" investigations, which have been conducted in several nations, emphasize the purpose of activities (cooking, eating, TV watching). Ott (1989) summarizes such studies in relation to their usefulness to exposure assessment; a basic drawback for exposure assessment applications is the lack of information on location, particularly distinguishing whether the participant was indoors or outdoors. In the 1960s and 1970s, a series of time-activity studies was conducted by geographers interested in the influence of the economic and physical structure of cities on travel patterns, e.g., journey to work (Hanson & Hanson, 1981), access to facilities (Fox, 1983) or shopping behaviour (Douglas, 1973). As such, the emphasis was on collecting information on the geographic location of trip origins and destinations as well as timing and mode use. Finally, the US Department of Transportation, in conjunction with the Census Bureau, has been collecting information on the travel activities (durations and mode use) of a representative national sample approximately every 7 years since 1969 (US Federal Highway Administration, 1986, 1992).

A variety of methods are available for collecting data about time-activity patterns, including interviewer-administered recall questionnaires, self-administered real-time diaries, direct observation and video recording. The diary techniques used in the social sciences for eliciting time-activity data have been applied to studies of total human exposure to air pollutants (see methodological reviews by Robinson (1988), Ott (1989), Quackenboss & Lebowitz (1989)). Specifically, participants are asked to complete a diary or questionnaire regarding their activities during the designated period (usually 12-48 h). The survey instruments used in these exposure studies, however, depart from any single type used previously. Rather than focusing on activity purposes or transportation exclusively, the instruments used in exposure studies probe for changes in location or activity that might lead to changes in the level of pollution to which the person came into contact.

Time allocation measures for assessing exposure to air pollutants frequently have been collected using self-completed real-time diaries. Because this approach requests that participants record all activities over one or more 12-h or 24-h periods, it has the potential to provide

the most comprehensive information on time allocation, sequencing, and frequency. Real-time diaries are particularly useful when it is important to know the time of day during which each activity was performed (e.g., the amount and location of exercise in the morning versus the afternoon when ozone levels tend to be higher).

Two diary formats are common for collecting time-activity data: the open-ended style requires participants to describe their exact activity (see, for example, the instruments described in Akland et al. (1985), Johnson (1989), and Jenkins et al. (1992)), whereas the close-ended format (Fig. 18) involves simply checking the appropriate microenvironment for the given time of day (see, for example, the instruments used in EXPOLIS (Fig. 18) (Jantunen et al., 1998) or those described by Schwab et al. (1990) and Samet et al. (1992). Several researchers are developing electronic monitors to supplement diaries by detecting whether a participant is indoors or outdoors, a key parameter for assessing exposure to air pollutants (e.g., Hinton, 1990; Moschandreas & Relwani, 1991; Waldman et al., 1991b).

Date: ___/___/___		LOCATION										ACTIVITIES				
Time	Briefly Describe Activity	IN TRANSFER					NOT IN TRANSFER					COOKING		SMOKING		
		look at the meter by test	on bus	on train	on street	on other	home in	work in	other in	other out	other out	other out	other out	other out	other out	other out
8	0	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	15	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	30	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	45	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
9	0	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	15	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	30	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	45	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
10	0	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	15	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	30	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	45	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
11	0	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	15	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	30	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	45	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
12	0	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	15	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	30	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
	45	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Fig. 18. The time-microenvironment-activity diary (TMAD) marks each in 15 min of the day the appropriate microenvironment-activity category/ies. Multiple entries are accepted for each 15 min (EXPOLIS Study; Jantunen et al., 1998)

Interviewer-administered questionnaires that ask participants to recall frequency and duration of time spent in specific activities during either the previous or typical day, month, year or age-period (i.e., usual activity patterns) also have been used to collect time allocation measures, microenvironmental parameters and exposure surrogates. Juster et al. (1985a) points out that data collected in this fashion are most accurate when the survey focuses on activities that are done frequently or on a routine basis (e.g., the daily commute to work). Questionnaires that take the form of checklists are also particularly useful when the researcher is only interested in certain well-defined activities. Questions to recall activity patterns over a long period may refer to defined age groups and/or to each residential location lived in (see Fig. 19). In environmental exposure studies, information on the proximity of the study participant to

local contaminant sources is typically collected via questionnaires that ask whether or not the participant engaged in a certain activity. For instance, studies of VOC exposure have asked about use of household cleaners, visits to petrol stations and storage of gasoline products indoors (Wallace et al., 1987a,b). Questionnaires are also used to solicit information on housing unit characteristics (e.g., type of cooking equipment or house volume) that influence concentrations indoors (Lebowitz et al., 1989). Surveys may request information on a variety of parameters that affect the concentration of combustion products to which an individual is exposed during travel, including traffic speed, time of day, mode of transportation, age of vehicle, trip timing and roadway used.

Researchers have experimented with a variety of methods for collecting information on the intensity of contact. As described in Chapter 7, a number of approaches are used for quantifying food consumption rates. An inexpensive technique that has been used to link breathing and activity patterns is to have participants record the level of activity (e.g., high, medium, low) associated with each activity entry in the diary. This method has been used in several population-based studies (Johnson, 1989; Lichtenstein et al., 1989; Schwab et al., 1990; Wiley et al., 1991). Others have used questionnaires that request information about specific high-exertion activities such as exercising and working outdoors (Goldstein et al., 1986; Lebowitz et al., 1989). Categorical exertion-level data is not useful for calibrating activity pattern data, however, without an increased understanding of (1) the range of reported activities associated with each exertion level and (2) the range of breathing rates associated with each exertion level. A compendium on energy expenditure, which closely relates to ventilation rate, has been published for a variety of physical activities (Ainsworth et al., 1993). These data may be used to categorize activity data depending on levels of exertion (Künzli et al., 1997a,b). Data are becoming available through the application of electronic methods of tracking exertion levels; heart-rate and breathing-rate monitors have been used in the field studies by Raizenne & Spengler (1989), Shamoo et al. (1991) and Terblanche et al. (1991).

The Activity Table Approach, ATAB

To be completed for outdoor activities at the 'last residence' only:

Activity	Month of the year that you perform this activity							Average times per month done May-Oct.	Average amount of time per session h min	No. of years done in relation to this residence (nearest 6 months)	Where activity performed in relationship to residence <3 miles >3 miles At school of home from home (1 = usually, 2 = sometimes, 3 = never, 4 = don't remember) (circle choice in each column)		
											1-2-3-4	1-2-3-4	1-2-3-4
1.								h min		1-2-3-4	1-2-3-4	1-2-3-4	
2.								h min		1-2-3-4	1-2-3-4	1-2-3-4	
3.								h min		1-2-3-4	1-2-3-4	1-2-3-4	
4.								h min		1-2-3-4	1-2-3-4	1-2-3-4	
5.								h min		1-2-3-4	1-2-3-4	1-2-3-4	
6.								h min		1-2-3-4	1-2-3-4	1-2-3-4	
7.								h min		1-2-3-4	1-2-3-4	1-2-3-4	
8.								h min		1-2-3-4	1-2-3-4	1-2-3-4	

Fig. 19. Example of a retrospective long-term time-activity questionnaire (Künzli et al., 1997b)

Standardized methods are not available for collecting information on hand-mouth contact. Several researchers (Charney et al., 1980; Brunekreef et al., 1983; Bellinger et al., 1986) have administered questionnaires to parents of toddler-age participants in order to qualitatively characterize the frequency with which children suck their fingers (i.e., usually, sometimes, never). Direct observation may be better suited to capturing micro-level activities, but such approaches have rarely been used in large-scale field studies owing to the expense of following more than a few participants and because of concerns that the observation process will lead to bias or alterations in typical patterns. Video techniques have now made it possible to record participant activities with less interference. Davies et al. (1990), for instance, used video methods to obtain data on the number of times 2 year olds put their hands and objects in their mouth while in standardized play situations. Zartarian et al. (1995) used videotape data to collect micro-level data on four young farm children at play inside their homes to quantify dermal and ingestion exposure to pesticides. As Zartarian et al. point out, however, researcher presence may still have influenced the participants' behaviour. Observation of children's hand-mouth contact also has been performed in clinical settings (e.g., Madden et al., 1980). All of these methods, however, share the limitation that they cannot quantify the full variability in factors that influence hand-mouth contact. Indeed, capturing this variability may not even be possible, as is discussed in a subsequent section of this chapter. In the absence of information on hand-mouth contact, several researchers have measured mineral levels in children's faeces to estimate typical soil ingestion rates (Binder et al., 1986; Calabrese et al., 1989, 1990). Such estimated ingestion rates can then be used to model exposure in areas with measured soil contamination levels.

For dermal exposure, questionnaires are most appropriate for collecting categorical-type information, such as whether a person performed a certain activity during a designated activity. The US

Environmental Protection Agency 1992 report entitled *Dermal Exposure: Applications and Principles*, reviews the literature regarding methods for estimating soil and water contact (US EPA, 1992b). Hawley (1985) has used data from previous studies and professional judgement to develop assumptions for use in estimating outdoor soil contact time, but these estimates do not account for indoor exposure such as soil tracked into the house or for exposure to contaminants that reside primarily in indoor dust (e.g., pesticides) (US EPA, 1992b). The US EPA report cites Tarshis (1981) and James & Knuiman (1987) as sources of data on the frequency with which people shower and bathe. Few data are available on swimming (US EPA, 1992b) which could be important because of elevated chloroform concentrations found within air just above the pool-water surface, or other contaminants which can be swallowed or dermally absorbed from lakes or river waters.

Linking activities with measurements of dermal exposure, researchers are testing innovative approaches to assessing skin contact with contaminated surfaces. For instance, Fenske et al. (1986a,b) applied non-toxic fluorescent tracers to lawns in lieu of insecticides; after participants engaged in a standard set of play activities, video imaging was used to ascertain the amount of tracer on the exposed skin. The degree of soil adherence to skin is a closely related issue and has been examined by several researchers (Driver et al., 1989; Finley et al., 1994a; Kissel et al., 1996).

5.3 Potential limitations

Time-activity data can enhance an understanding of sources and behaviours important in assessing exposures. Inferences can be drawn from simulations, case studies or even studies using large randomized designs. However, all users of time-activity data should be aware of its limitations for assessing human exposure to environmental contaminants.

The feasibility of collecting time-activity data is often limited by the burden which such studies impose on participating individuals. The data collection requires constant, or regular, attention to the fact that the subjects are participating in the study, that they have to remember about all activities and to fill in the diaries. This is often inconvenient and takes respondent's time. Collection of the data by an observer, which often is a method of choice in studies involving children, may be of limited feasibility owing to the restricted access of the observer to the subject under study and because typical activities may possibly be modified by the fact of being under observation.

5.3.1 Activity representativeness

One of the uses of time-activity data is to allow characterization of the distribution of exposure for a given geographic, demographic or socioeconomic segment of the population. However, the study protocol may call for certain types of days or individuals to be excluded (e.g., travel that takes the participant away from the home for more than the 24-h or 48-h sampling period may lead to disqualification). Although standard techniques such as weighting and imputation can be used to treat non-response, these methods assume that refusal to participate is random and there is information about the non-respondents (Kalton & Kasprzyk, 1986). In the case of time-activity studies, however, once contacted, people may

participate or not because of the variables that the study is designed to predict. As shown in the European multi-city study EXPOLIS, the subjects in Basel ready to participate had lower traffic density around their homes than non-participants (Oglesby, 1998). The potential for misrepresenting the exposure distribution must, therefore, be considered because there is no method for quantifying the direction and/or extent of the bias with respect to high-exposure behaviours.

The representativeness of the activity data collected may also be influenced by the increased burden imposed upon participants by exposure assessment studies. Epidemiologists and social scientists have found that participation rates and compliance with instructions may decline with increasing study periods, longer questionnaires, more complicated questions and more complex tasks. Whitmore (1988) speculated that the higher than average refusal rates experienced in air pollution exposure studies are related to the burden associated with carrying monitors and completing activity diaries. This has been shown in the European multi-city EXPOLIS study in Grenoble where participants had different time activity patterns in days with personal exposure monitors compared to days when only time-activity data was collected (Boudet et al., 1997).

5.3.2 Validity and reliability

Survey researchers in a number of fields have raised questions about the validity of data collected via self-administered surveys: i.e., is the instrument measuring what is intended (Laporte et al., 1985). Data validity is of particular importance when trying to link measured exposure with a given day's activity diary. The error introduced by an inaccurate diary affects both efforts to explain the contribution of certain activities to personal exposure and efforts to estimate the distribution of personal exposure from time-weighted microenvironmental measurements. The relationship between the degree of error in the diary and the degree of error in the predictive model depends upon the concentration in the microenvironment and the total time spent there. Neglecting to report even short-duration activities in high-concentration microenvironments will have more effect than underestimating a similar amount of time in a low-concentration microenvironment in which a large portion of the day is spent.

Scientists who use activity pattern data have raised a variety of concerns about the effects of inadvertent and/or deliberate errors in reporting. For instance, activity diary data may be compromised by participants' misunderstanding of the definitions of various locations (microenvironments). Discussions with participants have revealed the potential for confusion about: How far is "far from home?" Is a "parking garage" inside or outside? Is "walking" a light- or medium-exertion activity? (Schwab et al., 1991, 1992).

To a certain extent, the quality of the data can be controlled during data collection. Detailed instructions can improve participant compliance. Field and laboratory pretesting of the survey instrument and instructions, important components of the survey design process, can yield improvements in protocol and clearer definitions of survey terminology such as distinctions between microenvironmental categories (Bercini, 1992). Extensive training of participants in keeping the diary can be expensive, but detailed reference sheets and one-on-one sessions can greatly improve data quality. One of the more time-consuming but necessary steps is reviewing the returned diaries

for temporal completeness and clarity of responses. Ideally, this should be done in the presence of the participant, and within 24 h of

completion of the monitoring period. Another quality assurance step involves the use of a uniform system to code information on individual activities into microenvironmental categories.

The validity and reliability of the diary data may be increased by the use of study forms that are simple and easy to understand. The language of the questions and instructions must be simple and the method of selection of answers, or of filling in data, obvious to minimize coding errors. The number of items on the questionnaire should be kept to a necessary minimum. Only the information for which there is clear use in analysis and data interpretation and which serves directly the study objectives should be included in the diary form.

Verifying the validity of time-activity data is extremely difficult, if not impossible, because an absolute standard does not exist. Several researchers have sought to assess the reliability of self-reported data through test-retest procedures and by comparing different methods of collecting the same type of information (Laporte et al., 1985). The University of California at Berkeley ozone study required college students to recall time spent in physical activities outdoors, over years. The information was used as a surrogate to improve long-term ozone exposure assignment in an epidemiological study (Künzli et al., 1997b). The test-retest study revealed rather high correlations for time spent in heavy ($r = 0.81$) or moderate ($r = 0.61$) activity (Künzli et al., 1997b). This level of concordance is similar to that observed in dietary intake validation studies where food-frequency questionnaires and diet records correlated in the order of $r = 0.6$ for the intake of a variety of nutrients (Rimm et al., 1992). Robinson (1985) found that a variety of methods for collecting time-activity data, including 24-h recall surveys, same-day diaries, records of the activities during 40 randomly selected moments throughout the day (signalled using a beeper), and recall of the activities during a randomly chosen hour yielded essentially similar sample distributions of time the sample spent in a variety of activities. Quackenboss et al. (1986) also found consistency between diaries and the responses to self-administered recall questionnaires. Juster (1985b) found reasonably strong agreement in the reports of spouses regarding whether their partner was present at any given time throughout the day. Other comparisons of methods show that when asked about the usual time spent in selected activities, respondents tend to over-report time in unscheduled activities (relative to that recorded on their diaries), but reports are consistent for habitual activities such as commuting to work (Robinson, 1985). Waldman et al. (1991b) showed similar results when comparing activities recorded in electronic diaries with next-day recall; concordance between the methods was highest for routine, long-duration activities. Additional research, however, is necessary to determine the extent and direction of bias for the activities and the time frames of most concern in an exposure context (e.g., the frequency with which a person uses household cleaning products rather than the total time spent cleaning).

5.3.3 Inter- and intra-person variability

To be of use in exposure assessment, time-activity data must describe the aspects of human behaviour that influence the variability

in pollutant concentrations contacted. There is both between- and within-individual variability in people's activities, which has implications for the use of time-activity data in exposure assessment.

At one end of the spectrum are aspects of human activity patterns that tend to be highly regular. For instance, many people tend to follow daily routines with respect to how long they sleep and the time they depart for work. In addition, because basic routines are fairly uniform across individuals, diary data from several studies has shown that the distribution of time reported in the microenvironments that comprise the majority of the day (i.e., inside at home and inside at work/school) exhibit relatively little variation from year to year within a given study population or from place to place within the USA (Robinson, 1985; Schwab et al., 1990).

The only large time-activity study done in conjunction with a continuous monitoring device was the Denver/Washington, DC study of CO exposures (Akland et al., 1985); this study yielded time-weighted concentrations in specified microenvironments. Analyses of these results suggest that variations in activities or locational attributes (e.g., variations in source strength) that are finer than those captured by these simple microenvironments explain much of the variability in exposure. Although less variability in the concentrations of some other air pollutants may be expected, these results confirm the concerns raised above regarding the ability to predict variations in exposure from the time allocation measures typically collected in diary-type studies.

At the other end of the spectrum with respect to consistency in activity patterns are aspects of human behaviour that influence the intensity of contact with contaminated media. By their nature, these activities are highly variable both across individuals and across time for a given person. First, physical and demographic characteristics influence the frequency and duration of activities. For instance, in the case of dermal exposure it may be hypothesized that contamination from lying on a surface (e.g., a lawn to which a weedkiller has recently been applied) will be greater for a heavy person than a lighter person. Similarly, a child's standing and sitting height, in addition to crawling activities, mean that its breathing zone is much closer to the floor than that of an adult, raising the possibility of dust inhalation. Children also choose play locations that typical monitoring studies might ignore, such as stairwells and corners.

5.4 Summary

Information on people's activity patterns can be used to identify the determinants of measured exposures, predict unmeasured or unmeasurable exposures, assess relationships between exposure and health status, and identify high risk exposure situations that may be

amenable to public health actions. Some of the main activity patterns important for assessing exposures by various media that were discussed in this chapter are summarized in Table 16.

The relative cost of field sampling and laboratory analysis for environmental and biological measurements highlights the potential value of time-activity data. Assessments of long-term activity patterns (e.g., lifetime) may only be feasible using time-activity questionnaires. Various methods are used to collect information about human activities, including diaries and questionnaires, mechanical

devices, and observation. Methods have only recently begun to be developed for assessing the role of time-activity patterns on dietary and non-dietary ingestion and dermal exposure pathways. Concerns about the ability of data collection methods to ensure activity representativeness and data validity and about the implications of inter- and intra-person variability in behaviour place limits on the application of time-activity data for human exposure assessment. However, with appropriate quality assurance programmes, information on time use and activity patterns can be very valuable for interpreting and modelling exposures.

Table 16. Type of information obtained from time-activity data relevant to specific exposure pathways

Personal air	<ul style="list-style-type: none"> time and location spent outdoors type of indoor location use of sources In the presence of sources: <ul style="list-style-type: none"> ventilation and filtration of indoor location
Water	<ul style="list-style-type: none"> quantity of water consumed direct and indirectly accidental ingestion from swimming (pools, rivers, etc.) dermal contact, time in showering/bathing hand/body washing frequency
Food	<ul style="list-style-type: none"> amount and type of food products consumed preparation methods including cleaning preparation location (e.g., street vendors) storage practices
Soil	<ul style="list-style-type: none"> amount of contact time and type of soil (e.g., farm, garden/possible pesticide application) skin surface contact frequency and duration of washing since contact

6. HUMAN EXPOSURE AND DOSE MODELLING

6.1 Introduction

An exposure model is a logical or empirical construct which allows estimation of individual or population exposure parameters from available input data. Such data may be measured or collected for this purpose, or obtained from other sources. Technological, logistic and financial constraints can make it difficult to monitor the exposure of humans to the various environmental agents. It is, therefore, prudent in many situations to use models to assess contaminant exposures. Models provide an analytic structure for combining data of different types collected from disparate studies in a manner that may make more complete use of the existing information on a particular contaminant than is possible from direct study methods (EC, 1997b). Exposure models, if supported by adequate observations, can be used to estimate

group exposures (e.g., a population mean) or individual exposures (e.g., the distribution of exposures among members of a population). Model results also can be used to evaluate exposures at various points of population distributions which cannot be measured directly because of limitations of methods or resources (e.g., the upper 5% of exposures for a population). This chapter introduces the principal aspects of exposure modelling, including those for single and multiple environmental media. In addition, the concepts of variability, uncertainty and model validation are discussed.

6.2 General types of exposure model

Exposure models can be divided into three broad categories; statistical, deterministic and practical or combinations of statistical and deterministic models (Fig. 20). Statistical (often regression) models are in their simplest form numerical best fits between collected exposure measurements and potentially related factors (e.g., demographics). In statistical models, the magnitude and direction of association between the variables are inferred from the observations themselves. Such models cannot be considered reliable for predicting exposures outside the original study population and environmental setting without first validating them for that specific purpose. Deterministic (or physical) models are based on a logical expression of the physical environment and human behaviour in it. Such models need to be validated by actual exposure data, and can in principle be used for exposure prediction of new populations and settings. Although deterministic models can be useful for estimating mean population exposure, input data to estimate the distribution of exposure within a population are often not available. Probabilistic exposure models (section 6.6.3) are normally based on deterministic models, but because they incorporate the measured or estimated distributions of the input variables, they produce more realistic population exposure distributions than deterministic models. Practical models can combine features from these different types, e.g., a statistical model may include parts of a logical construct. Several important types of statistical models are discussed in Chapter 4, and deterministic and practical models are discussed here.

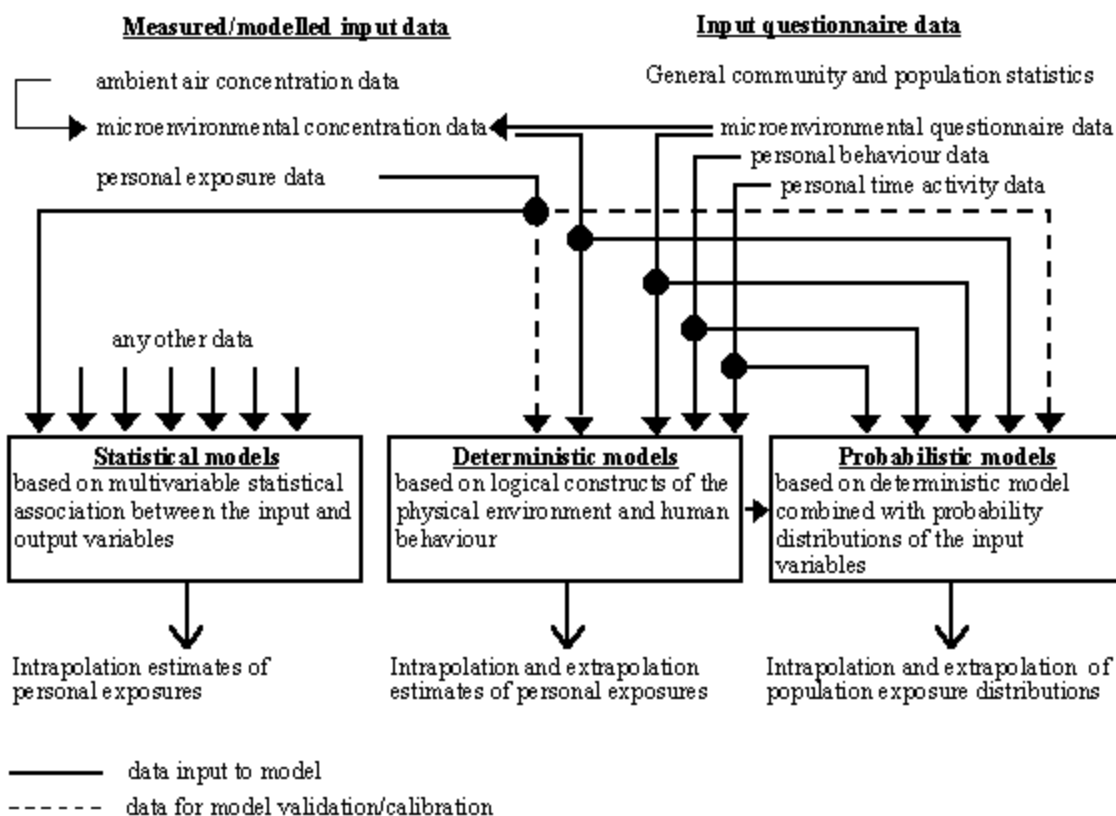


Fig. 20. Broad categories of exposure models

Using a deterministic model for a given contaminant, exposure concentration is estimated as a concentration averaged over a given period of time (see Eq. 3.1, p. 46).

For the inhalation and dermal exposure routes, concentrations in the different microenvironments occupied by a person are integrated over time. The integrated time period is usually 24 h, 1 year or a lifetime of 70 years, although any time period may be used. The concept of microenvironment is often unnecessary for the ingestion route. In this case, the concentration of contaminants in the food consumed and the amount of food and beverages consumed during a given period of time are sufficient to determine exposure.

6.3 Environmental media and exposure media

In exposure analysis, we use human exposure assessments to translate contaminant levels in environmental media into quantitative estimates of the amount of contaminant that comes in contact with the human-environment boundaries, that is, the lungs, the gastrointestinal tract and the skin surface of individuals within a specified population. Environmental media of principal relevance to human exposure include air, ground-surface soil, root-zone soil, plants, groundwater and surface water in the contaminated landscape. As described in Chapter 2, exposure pathways define a link between an environmental medium and an exposure medium. Important exposure media include outdoor air, indoor air, food (commercial and homegrown), exterior soil, interior soil or household dust, and drinking and cooking water. Exposure then occurs by contact with contaminants in

these exposure media via inhalation, ingestion and dermal uptake. Fig. 21 illustrates the types of exposure pathways we use to carry out a multiple-media, multiple-route, multiple-pathway exposure assessment.

Exposure assessments often rely implicitly on the assumption that exposure can be linked by simple parameters to ambient concentrations in air, water and soil. However, total exposure assessments that include time-activity patterns and microenvironmental data reveal that an exposure assessment is most valuable when it provides a comprehensive view of exposure routes and pathways and identifies major sources of uncertainty. Listed in Table 17 are potential interactions among environmental media, exposure media and exposure pathways that are addressed in this chapter.

An assessment of intake requires that we determine how much crosses these boundaries. Thus, we see the need to address many types of "multiples" in the quantification of human exposure, such as multiple media (air, water, soil); multiple exposure pathways (or scenarios); multiple routes (inhalation, ingestion, dermal); multiple chemicals; multiple population subgroups; and multiple health end-points. The matter is further complicated by the fact that pollutants may have both systemic and route specific health effects. For the compounds that have mainly systemic effects the total exposure -- sum of all routes -- is most relevant; for other agents such as pneumococci aerosols in the lung, dermal vs. ingestion absorption of

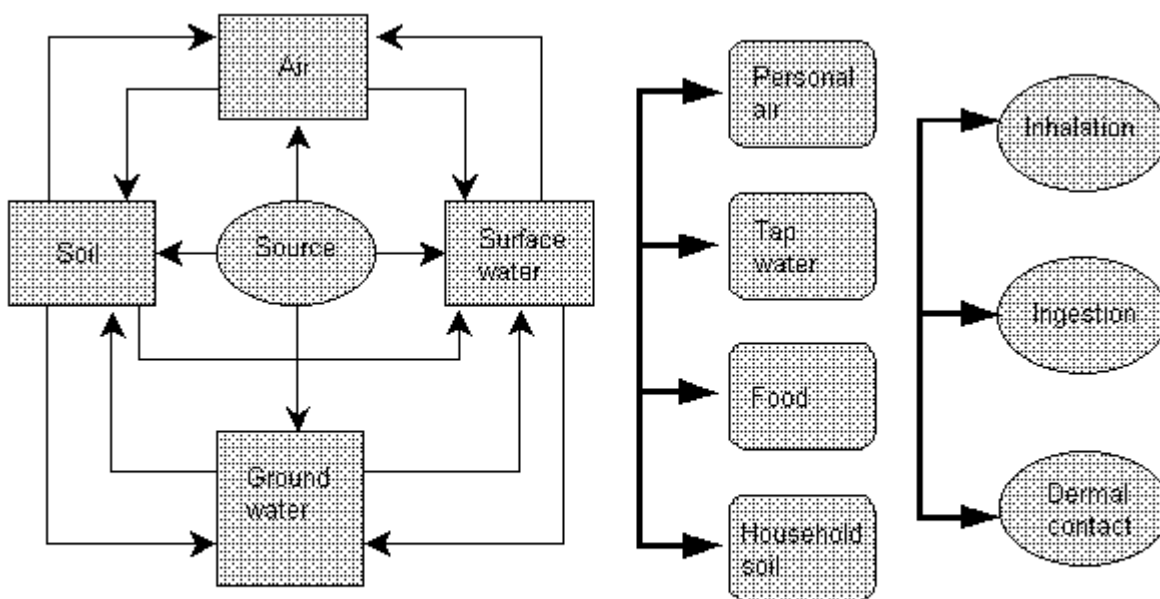


Fig. 21. Multiple-media, multiple-route, multiple-pathway exposure/dose assessment (adapted from Eisenberg & McKone, 1998)

Table 17. Interactions among environmental media, exposure media and exposure routes

Exposure routes

Media

Air

Soil

	(gases and particles)	(ground-surface soil, root-zone soil)
Inhalation	gases and particles in outdoor air	soil vapours that migrate indoor air
	gases and particles transferred from outdoor air to indoor air	soil particles transferred indoor air
Ingestion	fruits, vegetables, and grains contaminated by transfer of atmospheric chemicals to plant tissues	soil fruits, vegetables, and gr contaminated by transfer f
	meat, milk, and eggs contaminated by transfer of contaminants from air to plants to animals	meat, milk, and eggs conta by transfer from soil to p to animals
	meat, milk and eggs contaminated through inhalation by animals	meat, milk, and eggs conta through soil ingestion by
	mother's milk	mother's milk
Dermal contact	(not included)	soil

solvents which are rapidly metabolized in the liver, or fine particulate matter in the ambient air, the route of exposure is crucial, and total exposure as a sum of all exposure routes may be meaningless. Multiple media exposure models are discussed in section 6.5.

6.4 Single-medium models

Most of the transport models that have been developed for describing the behaviour of contaminants in the environment have dealt with specific environmental media, such as indoor and outdoor air, surface water and sediments, groundwater and soils. These single-medium models operate at various levels of spatial and temporal detail, depending on the particular conditions being assessed. The following discussion will highlight some of the more commonly used methods for characterizing contaminant transport in environmental media. Additional information on transport modelling for use in exposure assessments can be found in Masters (1991).

6.4.1 Outdoor and indoor air

Substances in outdoor air are transported from sources to receptors by atmospheric advection and dispersion. In general, pollutant concentrations in outdoor air are directly proportional to emission strength and inversely proportional to dispersion. The physical relationship, e.g., lateral and vertical distance, between sources and receptors is also an important factor. Meteorological parameters have an overwhelming influence on the dispersion of contaminants in the lower atmosphere. Among them, wind parameters

(direction, velocity, and turbulence) and thermal properties (stability) are the most important. A number of models are available for estimation of ambient concentrations of pollutants. Most of them are founded on the Gaussian air dispersion model, an introduction to which may be found in Wilson & Spengler (1996). Two of the seminal works in this field are Pasquill (1961) and Gifford & Hanna (1973).

Another area of air quality models focuses on determining the sources of pollutants in outdoor air. As discussed in Chapter 2, information on sources of exposure is important for evaluating alternative strategies for managing risk. These models are commonly used for apportioning concentrations of airborne particulate matter among its various sources (e.g., coal-fired power plants, gasoline-powered vehicles and diesel-powered vehicles). In such source apportionment models, profiles of element concentrations in particulate matter emitted from different sources are combined with sophisticated statistical methods (e.g., principal component or factor analysis) to estimate the relative abundance of particles from each source type. Glover et al. (1991) and Daisey et al. (1986) provide a good introduction to source apportionment models for particulate matter, while Edgerton & Shah (1991) describe a source apportionment model for VOCs.

Several approaches have been used to estimate expected indoor air pollution concentrations (for reviews see Cooke, 1991; WHO, 1997b). These include deterministic models based on a pollutant mass balance around a particular indoor air volume; a variety of empirical approaches based on statistical evaluation of test data and (usually) a least squares regression analysis; or a combination of both approaches, empirically fitting the parameters of a deterministic model with values statistically derived from experimental measurements (see Chapter 4). All three approaches have advantages and weaknesses. The deterministic model provides more generality in its application, but the results lack accuracy and precision. Deterministic models include single- and multiple-compartment models. The empirical models, when applied within the range of measured conditions for which they were fitted, provide more accurate information. An example of an empirical model for indoor concentrations of respirable particulate matter may be found in Chapter 12. Often the compartment of the indoor air mass balance models that is most difficult to represent is the role of indoor surfaces as sources or sinks for contaminants. This is an important field of inquiry with respect to inhalation exposures to ozone and VOCs (Reiss et al., 1995).

6.4.2 Potable water

Exposure to contaminants in water may occur via the ingestion, dermal absorption and inhalation routes. Ingestion of water primarily occurs via two pathways: direct ingestion via drinking or cooking and intrinsic water intake (i.e., the water intrinsic in foods prior to preparation). It is important to consider both routes. Drinking-water ingestion rates have also been shown to vary according to cultural differences and can be an important source of uncertainty about chemical exposure when extrapolating results of epidemiological studies from one culture to another (e.g., Mushak & Crocetti, 1995). Lognormal distributions of drinking-water ingestion rates for individuals comprising various age groups in the USA (Table 18) are available in the literature (Roseberry & Burmaster, 1992). Additional information on drinking and cooking water as exposure media may be found in Chapter 7.

Dermal absorption of contaminants in residential water sources may occur during bathing and other forms of washing or cleaning. There are three principal mechanisms by which molecules can transverse the skin and enter the body: passive transfer or diffusion, facilitated diffusion and active transport. Passive diffusion is the mechanism most commonly expressed in dermal exposure models. The rate of passive diffusion is a function of the concentration gradient of the contaminant on the surface of the skin and in the tissue immediately below the skin and the ease with which a molecule of the contaminant can move through the lipophilic interior of the skin membrane. Ease of passage is a function of the partition coefficient of the contaminant (e.g., the octanol-water partition coefficient, K_{ow}), molecular size, the degree of ionization and the porosity of the skin. Porosity of the skin to VOCs present in drinking-water treated with chlorine has been shown to be temperature dependent (Gordon et al., 1998).

Table 18. Lognormal distributions of water intake by age group in the USA. Source: Roseberry & Burmaster (1992)

Age group	Geometric mean (ml/day)	Geometric standard deviation
Drinking and cooking water intake		
≤ 1 year	267	1.85
2-11	620	1.65
12-20	786	1.72
21-65	1122	1.63
> 65	1198	1.62
Total water intake (direct + intrinsic)		
≤ 1 year	1074	1.34
2-11	1316	1.40
12-20	1790	1.41
21-65	1926	1.49
> 65	1965	1.50

Inhalation exposures to VOCs transferred from water to air could be as great as, or even greater than, exposures from ingestion. Inhalation pathways include contaminants transferred to the air from showers, baths, toilets, dishwashers, washing machines and cooking. Several models have been proposed to explain the mass-transfer process; in particular, a time-dependent, three-compartment model for residential exposure (McKone et al., 1987). The three compartments used in such a model are the shower/bath stall, the bathroom and the remaining residential volume. Factors that affect the projected exposure are chemical mass-transfer rates from water to air, compartment volumes, air-exchange rates and human occupancy factors.

6.4.3 Surface waters

The transport of contaminants in surface waters is determined by two factors: the rate of physical transport in the water system and the chemical reactivity. Physical transport processes are dependent to a large extent on the type of water body under consideration (e.g., oceans, seas, estuaries, lakes, rivers or wetlands). Schnoor (1981) and Schnoor & MacAvoy (1981) have summarized important issues related to surface water transport. At low concentrations, contaminants in

natural waters exist in both dissolved and sorbed phases. In rapidly moving water systems, advection controls mass transport and dissolved substances move at essentially the same velocity as the bulk of the water in the water system. Contaminants that are sorbed to colloidal materials and fine suspended solids can also be entrained in the current, but they may undergo additional transport processes that increase their effective residence time in surface waters. Such processes include sedimentation, deposition, scour and resuspension. Thus, determining the transport of contaminants in surface waters requires that we follow both water movement and sediment movement.

A water balance is the first step in assessing surface water transport. A water balance is established by equating gains and losses in a water system with storage. Water can be stored within estuaries, lakes, rivers and wetlands by change in elevation or stage. Water gains include inflows (both runoff and stream input) and direct precipitation. Water losses include outflows and evaporation.

6.4.4 Groundwater

In groundwater, the dilution of contaminants occurs much more slowly than it does in surface water. After precipitation, water infiltrates the ground surface where it travels vertically down through the unsaturated zone until it contacts the water table, and then flows approximately horizontally. This horizontal movement is driven by the hydraulic gradient, which is the difference in hydraulic head at two points divided by the distance (along the flow path) between the points. Bear & Verruijt (1987) and Freeze & Cherry (1979) have compiled extensive reviews on the theory and modelling of groundwater flow and on transport of contaminants in groundwater. The movement of contaminants in groundwater is described by two principal mechanisms: gross fluid movement (advective flow), and dispersion. Dispersion depends on both fluid mixing and molecular diffusion. The transport of many chemical species in groundwater is often slowed or "retarded" relative to the flow of the bulk fluid by sorption of the contaminant material to soil particles or rock. As is pointed out by Bear & Verruijt (1987), many groundwater models are available for assessing the transport of contaminants in the subsurface environment, ranging from simple one-dimensional hand calculations to large three-dimensional computer programmes. The choice of an appropriate model for any situation depends to a large extent on the information available, the type of information needed to carry out an exposure assessment and the tolerance of the analyst for large, complex computer programmes.

6.4.5 Soil

Soil, the thin outer zone of the earth's crust that supports rooted plants, is the product of climate and living organisms acting on rock. A true soil is a mixture of air, water, mineral and organic components (Horne, 1978). The relative mix of these components determines to a large extent how a chemical will be transported and/or transformed within the soil. The movement of water and contaminants in soil is typically vertical as compared to horizontal transport in the groundwater (i.e., saturated) zone. A chemical contaminant in soil is partitioned between soil water, soil solids, and soil air. For example, the rate of volatilization of an organic compound from the soil solids or from soil water depends on the partitioning of the compound into the soil air and on the porosity and permeability of the soil.

Models developed for assessing the behaviour of contaminants in soil can be categorized in terms of the transport/transformation processes being modelled. Partition models such as the fugacity models of Mackay (1979) and Mackay & Paterson (1981, 1982) describe the distribution of a contaminant among the liquid, solid and water phases of soils. Jury et al. (1983) have developed an analytical screening model that can be used to calculate the extent to which contaminants buried in soil evaporate to the atmosphere. The multiple-media model GEOTOX (McKone & Layton, 1986) has been used to determine the inventory of chemical elements and organic compounds in soil layers following various contamination events. This model addresses volatilization to atmosphere, runoff to surface water, and leaching to groundwater and first-order chemical transformation processes.

6.5 Multiple-media modelling

Human beings come directly into contact with certain media via certain routes and are exposed to the chemicals therein as depicted in Table 19. Efforts to assess human exposure from multiple media date back to the 1950s when the need to assess human exposure to global fallout led rapidly to a framework that included transport both through and among air, soil, surface, water, vegetation and food chains (Whicker & Kirchner, 1987). Efforts to apply such a framework to non-radioactive organic and inorganic toxic chemicals have been more recent and have not as yet achieved such a high level of sophistication. In response to the need for multiple-media models in exposure assessment, a number of transport and transformation models have recently appeared. In an early book on multiple-media transport, Thibodeaux (1996) proposed the term "chemodynamics" to describe a set of integrated methods for assessing the cross-media transfers of organic chemicals. The first widely used multiple-media compartment models for organic chemicals were the fugacity models proposed by Mackay (1979, 1991) and Mackay & Paterson (1981, 1982). Cohen and his co-workers introduced the concept of the multiple-media compartment model and more recently the spatial multiple-media compartment model, which allows for non-uniformity in some compartments (Cohen & Ryan, 1985, Cohen et al., 1990). Another multiple-media screening model, called GEOTOX (McKone & Layton, 1986; McKone et al., 1987), was one of the earliest to explicitly address human exposure.

The preceding models deal with inter-media transfer of contaminants on a relatively large scale, but other models are scaled to the residence and exposures that may occur therein. Exposure to chemicals in consumer products such as cleaning agents and paint are the focus of a model called CONSEXPO (van Veen, 1996).

All multiple-media exposure models have at least two features in common, regardless of the objective for which they were designed. First, movement of contaminants from one medium to another is characterized. Second, the rate and/or frequency of human contact with environmental media is modelled. The former may be referred to as *inter-media transfer factors* and the latter as *exposure factors*.

Table 19. Potential human exposure media and routes

Environmental medium	Exposure routes
----------------------	-----------------

Air	dermal contact inhalation
Tap water	dermal contact ingestion
Food and beverages	ingestion
Surface soil	dermal contact ingestion
Surface water	dermal contact ingestion

6.5.1 Inter-media transfer factors

Transfer of contaminants between media is commonly modelled as partitioning of a chemical between two or more media. Thus, multiple-pathway models require the measurement or estimation of partition coefficients of contaminants between several pairs of environmental media. There are two general classes of partitioning coefficients. The first class relies on basic physicochemical properties of the compounds of interest such as aqueous solubility, vapour pressure and dipole moment; they describe partitioning due to diffusive processes. Coefficients in the second class describe partitioning resulting from what may be considered advective processes, but also implicitly include diffusive partitioning.

6.5.1.1 Diffusive partition coefficients

The class of diffusive partition coefficients includes those between soil and water in soil (e.g., groundwater), air and plants, soil and plants, animal intake and food, surface water and fish, mother's uptake and breast milk, residential water and indoor air, soil-gas and indoor air, human skin and soil, and human skin and water. In many cases, partition coefficients developed from laboratory-scale experiments are the basis for modelling partitioning of a compound between environmental media (Lyman et al., 1990). For example, the octanol-water partition coefficient is often used as a proxy for partitioning non-polar organic compounds (e.g., organochlorine substances) between water and fish lipids. In this case, *n*-octanol is considered a good model for fish lipids. Similarly, the organic carbon-water partition coefficient is used to characterize partitioning of non-polar substances between organic matter in soil and water. Finally, Henry's constant describes partitioning of volatile and non-volatile compounds between air and water. Connell et al. (1997) provide a comprehensive introduction to the use of this type of partition coefficient in environmental science and exposure assessment.

6.5.1.2 Advective partition coefficients

The second class of partitioning coefficients jointly describe bulk transfer of compounds from one medium to another and diffusive partitioning. They are often used to model active uptake of contaminants by animals, principally livestock and game such as fish or fowl. Factors of this type are used to model transfer of semi-volatile compounds (SVOCs) such as dioxins from air to soil, soil to beef and soil to cow's milk (e.g., Nessel et al., 1991; Fries, 1995). Bioaccumulation of lipophilic compounds and some forms of heavy metals (e.g., methylmercury) in fish from ingestion of contaminated prey and diffusive uptake through respiration is also modelled using

partition coefficients such as these (e.g., MacIntosh et al., 1994).

6.5.2 Exposure factors

In constructing exposure models one needs to define the characteristics of individuals in various age and sex categories and the characteristics of the microenvironments in which they live or from which they obtain water and food. The types of data needed to carry out the exposure assessment include exposure duration and averaging time, time-activity patterns of individuals, food consumption patterns, household parameters, human factors such as body weight, surface area, soil ingestion and breast milk intake, and parameters associated with food crops and food-producing animals.

Time-activity patterns provide information on how individuals distribute their time among a number of potential exposure media. Time-activity pattern data describe such things as the average number of hours spent indoors at home and in what rooms and the nature of activity. Time-activity data also includes information on time spent outdoors at home or spent in microenvironments, such as bathrooms (including shower and bathing time). Exposure times are activity data that involve the number of days per year and hours per day spent in contact with soil during recreation and home gardening and in contact with surface water during swimming or other water recreation. Household factors relate to drinking-water supply and use, room-ventilation rates, and soil and dust concentrations within homes. Soil ingestion rates and soil contact on skin are also needed. Methods for measuring time-activity patterns and related considerations are discussed in detail in Chapter 5.

Input data of these types may be measured in the population under investigation, i.e., site specific, or may be drawn from standard references such as AIHC (1994), Finley et al. (1994b) and US EPA (1996a). Site-specific data are preferred, in case the population of interest may exhibit unique characteristics expected to influence exposure. If site-specific data are not available, values observed in other populations or estimates may be applied. Some model applications may rely solely on estimated inputs. For example, screening models are often used to assess exposure and health risks associated with new products such as pesticides designed for agricultural and residential use. In this case, model inputs may be determined in a manner such

that the model result is unlikely to underestimate the true level of exposure experienced by the population of interest. Models such as these are often referred to as "worst-case" models. An exposure modelling system recently developed by the European Union contains a suite of screening models (EC, 1996).

6.5.3 Multiple-media/multiple-pathway models

Multiple-media or so-called "total" exposure models provide methods for integrating multiple exposure pathways from multiple environmental media into a model system that relates concentrations of toxic chemicals to potential total human dose at toxic substances release sites. This type of simulation matrix is used to generate the hypothetical histogram shown in Fig. 22. The scenarios used to develop this particular histogram are for a representative VOC incorporated in the top several metres of soil. Here we can see that, based on a multiple-media and multiple-pathway assessment, we get indications of where it is most valuable to focus our resources to more fully

characterize distributions of population exposure. In this way, we characterize total potential dose using comprehensive, simple and possibly stochastic models to focus efforts on those exposure pathways, media and scenarios that require more realistic assessment of the distribution of dose within the population. This matrix allows us to make both pathway-to-pathway and medium-specific comparisons of total potential doses from multiple environmental media.

6.6 Probabilistic exposure models

Variability and *uncertainty* are two important and related concepts in exposure modelling, but it is important to distinguish between them. *Variability* arises from true heterogeneity across people, places or time; *uncertainty* represents a lack of knowledge about factors affecting exposure (or risk). Thus, *variability* can affect the precision of model estimates and the degree to which they can be generalized, whereas *uncertainty* can lead to inaccurate or biased estimates (Hoffman & Hammonds, 1994). It should be noted that *variability* and *uncertainty* can complement or confound one another. They may also have fundamentally different manifestations. For example, *uncertainty* may force decision-makers to judge how practicable it is that exposures have been over- or underestimated for every member of the exposed population, whereas *variability* forces them to cope with the certainty that different individuals are subject to exposures both above and below any of the exposure levels chosen as reference points (US NRC, 1994).

Failing to distinguish between *variability* and *uncertainty* makes it difficult to accurately characterize the population distribution of exposure and to make informed decisions about priorities for future research objectives. Exposure models can allow for consideration of both *variability* and *uncertainty*.

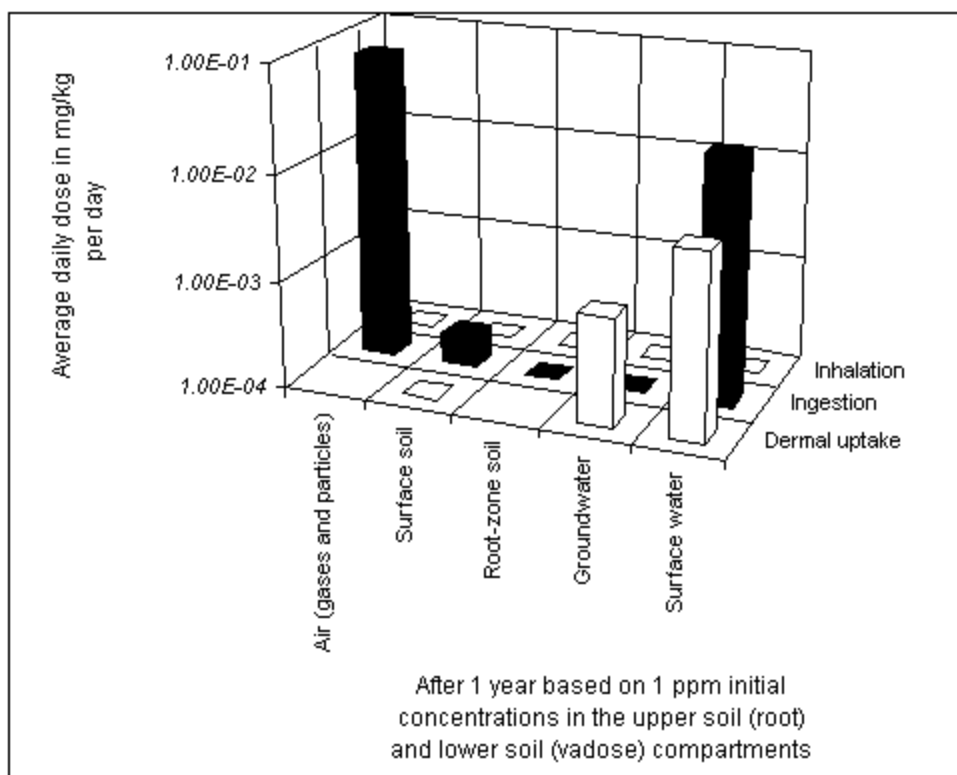


Fig. 22. Exposure matrix for dioxin (TCDD)

6.6.1 Variability

Diverse sources of environmental contaminants lead to various contaminated media (e.g., soil, dust, water, air, food), which in turn result in a multitude of routes and pathways of human exposure. For a given contaminant, the magnitude and relative contribution of each exposure route and pathway may vary among geographic regions and over time. In addition, differences in activities among individuals lead to disparate rates of contact with contaminated media. In aggregate, these factors result in varying levels of personal exposure to a particular contaminant among the members of a population, i.e., a *distribution* of exposures.

Exposure model inputs expressed as distributions can be used to model inter-individual variability of exposures. Examples of probabilistic human exposure models that explicitly consider variability of exposure among individuals may be found in Finley et al. (1994a) and MacIntosh et al. (1995, 1996). Variable parameters are those that are stochastic with respect to the reference unit of the assessment question (IAEA, 1989) and are described by probability distributions that reflect their intrinsic randomness. Exposure concentrations may vary between individuals owing to the influence of personal activities (e.g., cigarette smoking contributions to indoor respirable particulate levels). Such differences represent true variability of factors that affect exposure among individuals and can determine the relative position of an individual or type of individual within the distribution of exposures for the population.

6.6.2 Uncertainty

Several publications have stressed the importance of distinguishing among different types of uncertainty (IAEA, 1989; US EPA, 1992c). Explicit consideration of uncertainty in exposure and risk assessments is important for understanding the range and likelihood of potential outcomes and the relative influence of different assumptions, decisions, knowledge gaps and stochastic variability in inputs on these outcomes (Bogen & Spear, 1987; Iman & Helton, 1988; IAEA, 1989; Morgan & Henrion, 1990; US EPA, 1992c). This understanding can help the analyst advise the decision-maker on an appropriate course of remedial action, decide whether it is worthwhile to collect additional information regarding model parameters, choose the appropriate model to use and evaluate which of these actions could be most effective in reducing uncertainty about the outcomes (IAEA, 1989; Morgan & Henrion, 1990).

Three types of uncertainty are commonly considered: *scenario uncertainty*, arising from a lack of knowledge required to fully specify the problem; *model uncertainty*, arising from a lack of knowledge required to formulate the appropriate conceptual or computational models; and *parameter uncertainty*, arising from a lack of knowledge about the true value or distribution of a model parameter (US EPA, 1992c). In practice, scenario and model uncertainty are commonly considered to be negligible relative to parameter

uncertainty, although in many cases they may be the largest sources of true uncertainty.

Uncertain parameters are those for which the true value is not known or cannot be measured. For example, the true annual mean concentration of respirable particles in Mexico City during 1996 is uncertain because it can only be estimated from existing data which do not cover every day of the year nor every location of the city. Another example, is the mean and variance of soil ingestion by children aged 6-10 years in Taipei. Presumably, a single distribution can be used to describe this behaviour; however, its parameters can only be estimated.

The uncertainty about various parameters of an assessment can be formally incorporated into exposure models to estimate uncertainty about the prediction end-point, identify the components that influence prediction uncertainty and prioritize future research needs (Bogen & Spear, 1987; IAEA, 1989). Uncertainty about the true population distributions is characterized by propagating the estimated uncertainty about model inputs through to the distributions of the prediction end-points.

6.6.3 Implementing probabilistic exposure models

Although probabilistic exposure models are computationally more challenging to implement than deterministic (i.e., point estimate) models, the advantages of being able consider population distributions and sources and magnitude of uncertainty are often worth the additional effort. Several tools are available for propagating input parameter variability and uncertainty through to the assessment end-point. Classical error propagation techniques may be convenient for models with relatively few inputs and small coefficients of variation (Bevington, 1969; Seiler, 1987). For more complex models, computer-based simulation techniques are likely to be the method of choice.

Probabilistic exposure models may be run in one or two dimensions. *One-dimensional models* estimate either variability among exposures to individuals or uncertainty about a single exposure metric; for example, the mean 8-h average carbon monoxide exposure for individuals in a specific area. *Two-dimensional simulation models* may be used to estimate both population distributions (i.e., inter-individual variability) and uncertainty about the population distribution. The IAEA (1989) has suggested a Monte Carlo simulation approach for conducting two-dimensional simulations. In the first phase, a single realization is obtained from the distribution of each uncertain parameter. In the second phase, repeated realizations are obtained from the variable parameters. The entire process of a single sampling from the uncertain parameters, followed by repeated sampling from the variable parameters, is referred to as a *simulation*. A single model run consists of generating k simulations each composed of i iterations, which produces a family of k predicted distributions of population exposures. Prediction uncertainty is

represented by the distribution of individual estimates for a specific percentile or summary statistic among the family of population distributions. In this way, the type of plot shown in Fig. 23 contains probabilistic information on estimates of both inter-individual variability in the prediction end-point, and uncertainty about any specific percentile of the population distribution.

6.7 A generalized dose model

The magnitude of exposure (dose) is the amount of agent available at human exchange boundaries (skin, lungs, gastrointestinal tract) where absorption takes place over a specified period of time. Depending upon boundary assumptions, a number of dose questions may be derived. The *average daily dose* (ADD) is one of the most useful approaches, and is applied for exposure to non-carcinogenic compounds (for carcinogens, *lifetime average daily dose*, LADD, is often employed). The ADD is calculated by averaging the potential dose (D_{pot}) over body weight and the appropriate averaging exposure time:

$$\text{ADD} = \text{total potential dose/body weight} \times \text{averaging time},$$

where the potential dose is a product of contaminant concentration (C) in the exposure medium contacting the body, intake rate (IR) and exposure duration (ED):

$$\text{total potential dose} = C \times IR \times ED.$$

The intake rate refers the rates of inhalation, ingestion or dermal contact depending on the route of exposure.

The concentrations in air, water and soil used for an exposure assessment are those measured or estimated to be available in these environmental media at the nearest receptor point to the source (e.g., soil or groundwater at a hazardous waste site). When an environmental concentration is assumed constant over a long time period, the population-averaged potential dose (for ingestion or inhalation pathways) or absorbed dose (for dermal contact) is expressed as an average daily dose (ADD) in $\text{mg kg}^{-1} \text{day}^{-1}$:

$$ADD = \left[\frac{C_i}{C_k} \right] \times \left[\frac{IU_i}{BW} \right] \times \frac{EF \times ED}{AT} \times C_k$$

where $[C_i / C_k]$ is the intermedia-transfer factor, which expresses the ratio of contaminant concentration in the exposure medium i (i.e., personal air, tap water, milk, soil, etc.) to the concentration in an environmental medium k (ambient air gases or particles, surface soil, root-zone soil, surface water and groundwater); $[IU_i / BW]$ is the intake or uptake factor per unit body weight associated with the exposure medium i . For exposure through the

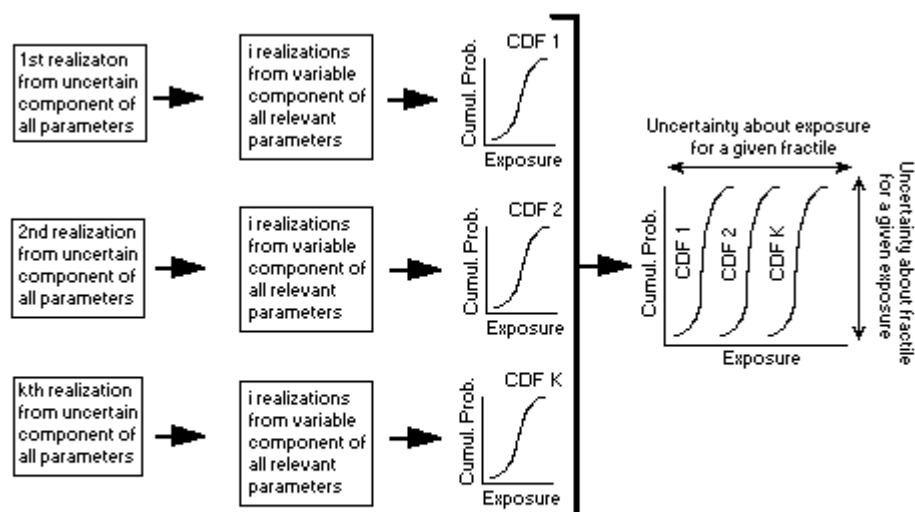


Fig. 23. Schematic of procedure for two-dimensional simulations (from MacIntosh et al., 1995) (CDF, cumulative distribution function)

inhalation or ingestion pathway $[IU_i / BW]$ is the intake rate per unit body weight of the exposure medium such as $m^3(\text{air}) \text{kg}^{-1} \text{day}^{-1}$, litres(milk) $\text{kg}^{-1} \text{day}^{-1}$, or $\text{kg}(\text{soil}) \text{kg}^{-1} \text{day}^{-1}$. For exposure through the dermal pathway, $[IU_i / BW]$ is replaced by UF_i , the uptake factor per unit body weight as a fraction of the initial concentration in the applied medium with nominal units [litres(water) $\text{kg}^{-1} \text{day}^{-1}$ or $\text{kg}(\text{soil}) \text{kg}^{-1} \text{day}^{-1}$]; EF is the exposure frequency for the exposed population in days per year; ED is the exposure duration for the exposed population in years; AT is the averaging time for the exposed population in days; and C_k is the contaminant concentration in environmental medium k .

The potential dose factor, $PDF(k \rightarrow i)$, is defined as the ratio of dose to concentration, as expressed in the following equation:

$$PDF(k \rightarrow i) = \frac{ADD}{C_k} = \left[\frac{C_i}{C_k} \right] \times \left[\frac{IU_i}{BW} \right] \times \frac{EF \times ED}{AT}$$

The ADD is used to make route and route-to-route comparisons and allows one to consider the relative significance of several exposure routes. With the ADD, we compare inhalation, ingestion or dermal exposures to the same medium such as tap water and compare exposures through indirect pathways (e.g., food-chain transfers) to those from direct pathways (e.g., inhalation or ingestion). As an example, the ADD for the ingestion route for chloroform for a 70-kg individual ingesting 2 litres/day of tap water containing 1 µg/litre chloroform, 365 days/year for a lifetime is 2 µg/day divided by 70 kg or 0.029 µg/kg⁻¹ day⁻¹. This ADD can be used as the basis for determining the relative significance of dermal, inhalation, and other ingestion exposures attributable to tap water.

6.8 Physiologically based pharmacokinetic models

Human exposure to contaminants results in dose to the critical organs. A mass balance on the contaminants that enter the body accounts for the distribution in the various organs, transformation into by-products, and excretion via specific mechanisms. The three major exposure routes by which contaminants enter the human body are inhalation, dermal absorption and ingestion. The vehicle that moves contaminants between organs is blood. Transformations include the metabolism of specific contaminants in specific organs. Mechanisms of excretion include exhaled air, sweat, urine and faeces.

The above processes that occur in the human body can be modelled by using physiologically based pharmacokinetic (PBPK) principles (Masters, 1991). These principles can be applied at differing levels of complexity. Simple models assume steady states and total absorption

and estimate dose to critical organs in a gross manner. They can be solved by using linear algebraic relationships. Complex models include time dependency, assume the human body to consist of multiple homogeneous boxes, each representing an organ or a portion thereof, and determine the distribution of contaminants in the different boxes as a function of time. The relationships usually end up as non-linear ordinary differential equations that are solved by using numerical integration techniques. Examples of PBPK models may be found in Cox (1996) for inhalation of benzene, Bookout et al. (1997) for dermal absorption of chemicals and Rao & Ginsberg (1997) for multiple-route exposure to methyl *tert*-butyl ether. A wide array of PBPK models have been developed for other chemicals and chemical classes and may be found in the relevant literature.

Whatever the complexity of the model representing the human body, the difficulty is interpreting the dose results to characterize risk. Usually, these human models are extrapolated to parallel animal models for which toxicological data are available.

6.9 Validation and generalization

The modelling approaches described above are mathematical abstractions of physical reality that may or may not provide adequate estimates of exposure. The preferred way to be sure that a model is capable of providing useful and accurate information is by validation, i.e., comparing model predictions with measurements independent of these used to develop the model. Models can be validated in terms of prediction accuracy and precision by comparing predicted values to those measured in the field. Although measurements are preferable as the "gold standard" in validation of models, comparison of results from different assessment methods or modelling approaches can also be used to evaluate validity, or at least agreement. This may be the only option when measurements are not feasible; for example, in retrospective assessment of exposure. Model validation is a necessary precondition for the generalization of model results to a different or larger population (Ott et al., 1988).

In the statistical modelling approach, data collection is an integral part of model construction. If the data are known to be from a statistically representative sample of the population, then there is no need for further validation. However, validation is necessary if the results are to be extrapolated beyond the range for which the existing database provides a statistical description. The physical and physical-stochastic modelling approaches must be validated with actual data from separately conducted field studies. Care must be taken that the data used to validate a model are not biased with respect to crucial model parameters. The validation step is useful only to the degree that the sample population is representative of the group to which results will be extrapolated.

Finally, when modelling environmental-response-health processes, and when validating such models, it is important to realize that in principle perfect modelling is possible only for closed systems, and

the systems described in this report are very open-ended. The practical implication of this fact is that even the best models need to be validated for each new population and environmental setting before application.

6.10 Summary

An exposure model is a logical or empirical construct which allows estimation of individual or population exposure parameters from available input data. Exposure models, if supported by adequate observations, can be used to estimate group exposures (e.g., a population mean) or individual exposures (e.g., the distribution of exposures among members of a population). Models may be used to estimate exposure via single or multiple media. The latter is particularly useful for comparing the magnitude of exposures likely to occur from different media and thus for priority-setting. Exposure models may be statistical or deterministic in nature or a combination of both. Probabilistic methods may be applied to all three types as a means to estimate population distributions of exposure, i.e., variability of exposure among individuals. In addition, probabilistic methods may be used to characterize uncertainty in model input parameters and propagate that uncertainty through to the prediction end-point. Evaluation of the accuracy of model results is critical before relying on model output for decision-making.

7. MEASURING HUMAN EXPOSURES TO CHEMICALS IN AIR, WATER AND FOOD

7.1 Introduction

This chapter describes sampling methods used in environmental exposure assessment to analyse chemical concentrations in air, water and food. The information presented provides a general description of available sampling methods and guidance for their selection. It is not intended to be comprehensive and the reader should refer to the research literature for specific details.

Assessment of human exposures to contaminants in environmental media requires establishing measurement strategies and selecting appropriate sampling instruments and analytical methods. Taken together, these three elements define a monitoring programme. Monitoring methods can be used to determine the magnitude, duration and frequency of exposure to an environmental contaminant. Magnitude of exposure is defined as the concentration of a specific pollutant averaged over a predetermined time interval, such as 1 h, 24 h or a lifetime. Different measurement methods have specific characteristics that determine the locations in which they are feasible for use. In the case of air, the method's sensitivity to pollutants determines the averaging times over which it will provide reliable responses. Therefore, a clear understanding of the concentration range anticipated, averaging time of interest, and expected frequency of exposure events is needed to identify appropriate field and laboratory methods. In the absence of any prior information, pilot studies may be performed to obtain the information needed to finalize the design of the monitoring programme.

Selection of instruments will depend on the target population (e.g., children or adults) and study objectives. In some situations, understanding the distribution or the average population exposure to a contaminant may be sufficient. In fact, most environmental monitoring of contaminants in outdoor air, water at the point of distribution and "market basket" surveys implicitly assumes that indicators of population exposure are more relevant than information at the individual level. Studies assessing individual exposures using such surrogate measures should select sampling instruments and analysis methods based on sensitivity, selectivity, response rate, portability, durability and cost, among other factors. Table 20 summarizes these concepts.

7.2 Air monitoring

Air sampling methodologies should conform to the exposure assessment approach selected, either direct or indirect, as described in Chapter 3.

Direct monitoring methods for exposure measurements include the use of personal air monitors and/or analysis of human tissue and/or biological fluids. Aspects of biomonitoring are described in Chapter 10. Indirect air monitoring methods can include

Table 20. Selection factors for instruments and methods

Factor	Comment
Sensitivity	The magnitude and duration of contaminant exposure define th

	guide, one order of magnitude below and above the concentration. Reproducibility (precision) as measured by percentage relative error is usually inversely proportional to integration time or amount.
Selectivity	Response to a specific compound or analyte without interference. Instruments may be appropriate if exposure situation (e.g., specific or selective response may require more expensive equipment and analytical procedures).
Response rate	There are two aspects of response rate: (i) time required for a step change in concentration; (ii) time required between sampling. Appropriate instrument response rate depends, in part, on the magnitude and the health effect of interest. Acute effects may require frequent exposures over intervals of minutes. If health effects from chronic exposures or the metabolic half-life is long, then rapid response is not necessary.
Portability	Instruments and sampling procedures should not modify behavior. Size, weight, noise, power, and safety considerations. Portability usually involves a tradeoff with sensitivity and response rate (continuous).
Durability	Instruments used for air sampling are subjected to a broad range of conditions and humidity are potentially interferences and are not easily repaired. Instruments/methods must be fully evaluated.
Cost	Instrument cost and analytical expenses will influence study design. Tradeoff sample cost for accuracy, precision, and response rate. Subject and/or the number of subjects, or relaxing resolution may allow use of less expensive methods.

microenvironmental sampling in combination with questionnaires and time-activity logs. Ambient air monitors can also be used to estimate exposures when combined with information such as building characteristics, indoor/outdoor contaminant ratios and time-activity patterns.

The direct approach depends largely on the availability of sensitive, small, quiet, lightweight and portable personal monitors. Personal air monitors can be used for microenvironmental monitoring as well. In addition, microenvironmental monitors with larger sampling flows are used for indoor/outdoor sampling. Ambient monitors are generally high-volume samplers and are not suitable for indoor use. Suitable air monitors must also fulfill several requirements, such as detection limits, interferences, time resolution, easy operation and of course, cost. There are several good references on air monitoring and analysis. The reader is referred to *Air Sampling Instruments for Evaluation of Atmospheric Contamination* (ACGIH, 1995). Additional general publications include US EPA (1994, 1996b), and Lodge (1988). It is important, however, to refer to the published scientific literature for the most appropriate and recent air monitoring methods.

The following sections describe methods available for air sampling of gases and vapours, airborne particulate matter, SVOCs and reactive gases. The methods are classified into active and passive or continuous monitors. A detailed list of sampling methods, air pollutants for which they are used, sources and other pertinent information is presented in Table 21-24. An indicator of their

suitability for personal, indoor or ambient monitoring is also included.

7.2.1 Gases and vapours

7.2.1.1 Passive samplers

Commercial passive samplers are available for a variety of air pollutants, including inorganic gases such as carbon monoxide, nitrogen dioxide, sulfur dioxide and ozone, and VOCs (e.g., benzene, toluene, xylene, etc.). Passive air samplers are probably the most convenient tool for conducting large-scale personal exposure assessments because they are small, inexpensive and easy to use. However, sampling rates are of the order of 10-50 ml/min and absorbing capacity is limited. Passive samplers operate on the principle of molecular diffusion. The rate of diffusion is related to the diffusion coefficient of the compound, the cross-sectional area of the absorbing surface and the length of diffusion path. Specific information on the calculation of sampling rates can be obtained from the manufacturers. The collection mechanism relies either on physico-chemical absorption or adsorption or chemical reactions. The samplers for inorganic gases rely on reaction of the contaminant with a chemical coating on the collection surface. The samplers for VOCs typically rely on absorption by a liquid or adsorption by a solid collection medium. Selection and use of passive samplers should take into consideration potential

sources of error such as wind effects, temperature, humidity and interfering gases.

In practical applications, personal monitoring is performed by mounting the passive sampler on a participant's collar to estimate air pollution concentrations in the breathing zone. After collection, the adsorbent is removed from the sampler and extracted with the recommended solvent. The extract is then analysed by a suitable method (e.g., spectrophotometry, gas chromatography with specific or unspecific detectors, HPLC, etc.). As with any monitoring procedure, measures should be taken to evaluate sample preservation and integrity. These procedures should be described as part of the quality assurance (QA) protocol and the standard operation procedures (SOPs) (see Chapter 11).

7.2.1.2 Active samplers

There are many commercially available liquid-media samplers for reactive and soluble gases, such as liquid-containing bottles, and solid-sorbent tubes for insoluble and non-reactive gases and vapours, such as activated charcoal, silica gel, porous polymers or other materials. Pollutants are transported with the carrier gas (air), and are captured by collecting media. The most frequently applied mechanisms in the collection of air pollutants in these media are chemical reactions (e.g., acid-base and colour-forming), and absorption/adsorption of the pollutant molecules on collecting media. Solid sorbent collection efficiency depends on contacting surface area, air flow rate, temperature, humidity and presence of interfering compounds.

The sampling rate, breakthrough volume and method limit of detection are important parameters which need to be considered for an accurate exposure assessment by active samplers. The identification and quantification of collected air pollutants are usually performed

by analytical instruments, such as spectrophotometry, gas chromatography with specific or non-specific detectors, HPLC, etc. Although not yet used extensively, small, evacuated canister samplers have been developed for personal monitoring (Pleil & Lindstrom, 1995). These have the advantage of not using sorbents. Analysis is typically done by gas chromatography following thermal desorption.

7.2.1.3 Direct-reading instruments

The concentration of gases and vapours (e.g., carbon monoxide, sulfur dioxide) in an individual's breathing zone can also be determined with the use of portable direct-reading instruments. Commercially available direct-reading instruments have data logging capabilities to store measurements at a rate of 1 s⁻¹. Depending on the frequency of measurements, these instruments can operate up to 2 weeks continuously. Instrument software allows for direct calculation of concentrations with different averaging times and statistical analysis of the data.

Table 21. Air sampling methods for inorganic gases

Carbon monoxide	Manufacturer	Comments
<u>Continuous</u>		
Electrochemical	Energetic Sciences	0-50, 0-100 ppm; portable and LOD ~ 2 ppm
	Interscan	Various ranges; LOD ~ 1 ppm
	Bacharach	Based on the measurement of Hg from a pellet oxidized by CO. 0-20 dl: 1 ppm Sample flowrate litre/min
Photometers	Beckman Instruments	Based on dual-isotope fluoresc LOD = 0.1 ppm
<u>Passive</u>		
Diffusion detectors	Lab Safety Supply Co.	Changes colour; LOD ~ 50 ppm f
	Quantum Group Inc.	Simple colour change detector
	3M Corporation	Indicates presence of CO by co change
	Wilson Safety Products	Dosimeter badge. Colour change proportional to CO concentrati
<u>Active</u>		
	MSA	Air is pumped through activate tubes that change colour when
	Sensidyne	

Table 21. (continued)

Carbon monoxide	Manufacturer	Comments
<u>Continuous</u> Infrared	GasTech	300-5000 ppm
	Rosemount Analytical	Measures CO, CO ₂ , NO and hydro
	SKC West	Sampling frequency: 8 s to 30
Electrochemical	Devco Engineering	Based on conductivity in water ionization of gas
Nitrogen oxides <u>Continuous</u> Electrochemical	Trasducer Research	LOD > 2 ppb
	Interscan	Various ranges; LOD > 20 ppm
Chemiluminescence	Beckman Instruments	Range: 0.1-1 ppm. Operates con for 7 days. Analyses NO, NO ₂ , I on the excitation of molecules
	Columbia Scientific	Uses the chemiluminescence rea with NO. Sampling rate: 1.2 li
	Rosemount Analytical	Designed to monitor continuous
Colorimetric	Phillips Electronics Instruments	Set for a variety of chemicals on the electrolyte. Measures c based on a specific chemical r

Table 21. (continued)

Carbon monoxide	Manufacturer	Comments
<u>Passive</u> Diffusion tubes/badges	Env Sciences and Physiology	LOD ~ 500 ppb for a 1-h exposu
	MDA Scientific	Palmer sampler is an acrylic t stainless steel grids coated w triethanolamine placed at the
	RS Landauer Jr. & Co	Pen-shaped badge for the colle N ₂ O on a molecular sieve. Anal; IR
<u>Active</u> Electrochemical	MDA Scientific	2-3 ppm; measurement on a 15-m
Ozone <u>Continuous</u> Chemiluminescence	Beckman Instruments	Operates continuously for 7 da the reaction of ozone with eth

		produce light DL: 0.01 ppm
	Philips Electronics Instruments	Operates continuously for 7 da on the reaction of ozone with to produce light
	Columbia Scientific	Based on the reaction of ozone ethylene. Ranges: 0-0.1, 0-0.2 0-1.0 ppm
UV Vis photometer	Dasibi Environmental	Concentration is determined by the absorption level of UV wit of air

Table 21. (continued)

Carbon monoxide	Manufacturer	Comments
	Mast Development	Portable. Sampling rate 2 liter measurement cycle 20 s
<u>Passive</u> Diffusion monitors	Ogawa	Uses 2 multitube diffusion bar with collection on glass fibre coated with nitrite

LOD: Level of Detection

Table 22. Air sampling methods for organic vapours

	Manufacturer	Comment
<u>Continuous</u> Photo-ionization detector	Thermo Environmental Instruments	Based o detecto variety
Flame ionization detectors	Columbia Scientific	
	Foxboro	Measure equival 20 ml/m
		Mainly equipme ionizat flowrat
Thermal ionization detector	Photovac International	Semiqua
Infrared photometers	Foxboro	Miran p to its detect

		Samplin
	Infrared Industries	2 model
Portable gas chromatographs	Photovac International	Portabl Benzene to ppb
	H-Nu Systems	Portabl differe PID, EC

Table 22. (continued)

	Manufacturer	Comment
	Microsensor Systems	Portabl chromat concent analyse
<u>Passive</u> Charcoal badges	3M	Single Samplin
	SKC	of wind
	Gilian Instrument	Minimum 0.2 ppm
	Perkin Elmer	Require
	Pro-Tek	
	3M	Two cha breakth amount. the num
	SKC	35-70 c
	Gilian Instrument	sample:
	Perkin Elmer	Desorpt the amo
	Pro-Tek	Require

Table 22. (continued)

	Manufacturer	Comment
<u>Active</u> Charcoal tubes	Perkin Elmer	The mos is acti
	National Draeger	2 sizes 100/50

	SKC	
Formaldehyde		
<u>Passive</u>	GMD Systems	LOD > 0
	InterScan	Various
	Air Quality Research	LOD ~ 0
	DuPont	1.6-54
	3M	LOD ~ 0 Require
	SKC	
	AirScan Environmental Technologies	Based o nucleat proport
	Environmental Science and Physiology	LOD ~ 5
	Envirometrics Products	Based o with a

Table 22. (continued)

	Manufacturer	Comment
Gases and Vapours		
<u>Active</u>		
Solid adsorbents	Barneby Cheney	Large n collect
	Columbia Scientific Instruments	conditi The cho
	Draeger	designe efficie
	Fischer Scientific	selecti
	Perkin Elmer	Approxi are ava
	3M	treated collect
	SKC	Most tu section
	Supelco	used to
	Westvaco	Require
Polyurethane foam	Supelco	Collect
<u>Passive</u>		
Diffusion monitors	3M	In gene

Gilian Instrument	activat screen.
SKC	Some mo used to
Supelco	Each co diffusi

Table 22. (continued)

Manufacturer	Comment
	Require
	Desorpt with th the cha and typ

Table 23. Air sampling methods for particulate matter/aerosols

	Manufacturer	Comments
<u>Continuous</u> Light-scattering photometers	PPM	LDL ~ 10 µm/m ³ Handheld
	Air Technique	Portable. Sample rate 2 Suction: vacuum pump. P collected downstream of
	Virtis	Near-forward sampling, litre/min. Suction: vac Particles can be collec of the filter
	Hund	Measures respirable aer concentration by IR sca detection. Average of 8
		Measures fine dust (0.2 concentration by IR sca detection. Average of 8
	MIE	Detects respirable dust Sample rate 2 litre/min Averages measurement ov
		Miniram dust monitor. P instantaneous or 8 h av
	Negretti	Portable dust monitor, 0.01-20/0.1-200 mg/m ³ . 1 be collected on a filte

Table 23. (continued)

	Manufacturer	Comments
	Casella	Handheld, Range 0.01-20 size >0.1 µm. Particles on a filter
	TSI	Integrating nephelometer 30-s periods. Has difference depending on the aerosol Laser photometer for particles µm diameter. Measures a concentration in mg/m ³
	Belfort Instruments	Integrating nephelometer 10 litre/min
<u>Instantaneous</u>	MIE	0.01-10 mg/m ³ or 0.1-10 µg/m ³
Condensation nucleus counters	Met One	2 models. Sample flow rate 1 litre/min. Ultrafine particles in alcohol vapour condensation
Optical particle counters	Climet Instruments	6 models. Flow rate 0.3-1.0 litre/min. Size range: 0.3-20 µm, 6 channels. Light source: laser
	Hiac/Royco	6 models. Flow rate 0.01-1.0 litre/min. Range: 0.3-10 µm, 6 size channels. Light source: white light

Table 23. (continued)

	Manufacturer	Comments
	Met One	3 models. Flow rate 0.1-1.0 litre/min. Range: 0.1-1 µm, 6 size channels. Light source: white light
	Particle Measuring Systems	Flow rate 0.1-1.0 litre/min. Range: 0.05-5 µm, 4-16 size channels. Illumination source: laser
	Faley International	4 models. Flow rate 0.01-1.0 litre/min. Range 0.3-5 µm, 2-5 size channels. Light source: white light

	TSI	Flowrate: 0.1-1.0 litre 0.05-5 µm; 4-16 size ch
Piezobalance	TSI	Less reliable for conce <10 µg/m ³ . Difficult to
Beta gauge	Wedding & Assoc	The particulate collect continuously measured b gamma-radiation
<u>Active</u> (Total) Open cassette	SKC	Air is pulled through a size selection device
IOM inlet	SKC	Samples inhalable dust filter cassettes. Sampl Cut point 100 µm
<u>Active</u> (size selective) PM ₁₀ impactors	BGI	Sampling rate 28.3 litre Suction: pump aerosol s

Table 23. (continued)

	Manufacturer	Comments
	MSP	Sampling rate 4 or 10 l Suction: pump 10-2.5 µm virtual impac Sampling rate 1130 liter
	TSI	Sampling rate 1 litre/m Suction: pump
	MIE	Sampling rate 2 litre/m Suction: pump
	Air Diagnostics	Sampling rate 4 litre/m Suction: pump environmental
	Graseby Andersen	Virtual dichotomous. Cu and 2.5 µm; sampling ra High-volume sampler. Sa 1100 litre/min
	SKC	Personal impactor. Sing personal pump. Sampling litre/min
PM _{2.5} impactors	URG	Sampling rate 4 litre/mi collected in filters an

polyurethane foam

MSP

Sampling rate 4 or 10 l
Suction: pump

Table 23. (continued)

	Manufacturer	Comments
	SKC	Personal impactor. Sing Suction: personal pump. Sampling rate 2, 4 or 1
Cascade impactors	BGI	7 stages. Sampling rate Cut points: 32, 16, 8,
	Graseby Andersen	13 stages; sampling rat Cut points: 13-0.08 µm
		9 stages; sampling rate Cut points: 18, 11, 4.4 0.53, 0.32, 0.16 µm
		8 stages; sampling rate Cut points 10-0.4 µm
		7 stages; sampling rate Cut points 6, 4.6, 3.3,
		6 stages; sampling rate Cut points 0.5-20 µm
		5 stages; sampling rate Cut points 7.2, 3, 1.5,
		4, 6 or 8 stages; flowr Cut points 20-0.6 with µm with 6, and 20-3.5 w
		Radial slot impactor. 6 an optional cyclone

Table 23. (continued)

	Manufacturer	Comments
	Hauke KG	Sampling rate 30 litre/ Cut points below 0.1 µm
	in-Tox Products	4 models of 7 stages ea Cut points 3.1-0.33 µm 4.5-0.32 µm @ 1 litre/m

		2 litre/min; 5-0.0.5 µm
	MSP	8 stages, Sampling rate Cut points: 10, 5.62, 3 0.56, 0.316, 0.178, 0.1
Virtual impactors	BGI	3 virtual stages, flowr Cut points 1.2, 4 and 1
	Graseby Andersen	The dichotomous sampler particles in 2 sizes: 1 Sampling rate 17.6 liter
	MSP	Sampling rate 30 litre/ Cut points below 0.1 µm
		High-volume operates at Cut point 2.5 µm
Cyclones	Mine Safety Appliances	Measures respirable par diameter of 3.5 µm @ 2
	Sensidyne	Measures respirable par air @ 240 litre/min

Table 23. (continued)

	Manufacturer	Comments
		Measures respirable par air @ 9 litre/min
		Measures respirable par 1.7 litre/min
	SKC	Measures respirable par point of 3.5 µm @ 1.9 l
Elutriators	Casella	Horizontal elutriator t with a cut point of 3.5 of 50 litre/min
		Horizontal elutriator t with a cut point of 3.5 2.5 litre/min

LOD: Level of detection

Table 24. Air sampling methods for reactive gases

	Manufacturer	Comments
		Hydrogen sulfide/sulfur dioxide/ammonia/chloride

Continuous Electrochemical	Devco Engineering	
	CEA Instruments	
	Sensidyne	All based on conductivity c water due to ionization of
	Teledyne	
Colorimetric	Bacharah	
	Phillips Electronics Instruments	Based on the reaction of th the reagent to produce a co product Each compound has a specifi for its detection
Potentiometric	CEA Instruments	
	AIM	Conductivity of the reagent proportion to the concentra gas being sampled and is me by an electrode
	Calibrated Instruments Eitel Manufacturing	
UV and visible light photometers	Barringer Research	Based on the correlation wi absorption spectra of SO ₂ i Sensitivity 2 ppm
UV and visible light photometers	Beckman Instruments	Based on the fluorescence o under UV light

Table 24. (continued)

	Manufacturer	Comments
Passive Solid adsorbents	Rosemount Analytical	For SO ₂ uses a non-dispersi "transflectance" analysis
	Columbia Scientific	Uses a continuous UV source intensity to detect SO ₂
	Barneby Cheney	Large number of chemicals a efficiently collected under variety of conditions
	Columbia Scientific Instruments	Choice of adsorbent is desi maximize collection efficie retaining low selectivity
	Draeger	Approximately 50 sorbent ty available; some are chemica to facilitate their collect properties
	Fischer Scientific	Most tubes contain a primar section and a backup bed th used to indicate breakthrou
	Perkin Elmer	

3M	Require laboratory analysis
SKC	
Supelco	
Westvaco	

Table 24. (continued)

	Manufacturer	Comments
Active		
Annular denuders	URG	Different models can be use only gases or gases and par Especially used for acid ae H_2SO_4 , HNO_3 , $(NH_4)_2SO_4$, NH_4HS

7.2.2 Aerosols

At present, active sampling is the only feasible way to perform exposure assessments on particulates directly. Active particle samplers operate by drawing aerosols into a sensor or on to a collection surface (e.g., a filter) by means of a pump (Hinds, 1982; Lehtimäki & Willeke 1993). Large stationary samplers that operate with a standard flow rate of approximately 1000 litre/min are available commercially and are useful for collecting large sample volumes. Small stationary samplers that operate with flow rates in the range of 1-10 litre/min are also commercially available. Both sizes are available in configurations that allow for sampling of total suspended particulate matter (i.e., not size separated) or specific size fractions (e.g., $PM_{2.5}$ or PM_{10}). Personal aerosol samplers that allow collection of total inhalable particulate matter of specific size fractions are also available.

The cyclone and, particularly, the impactor are the two most commonly used size preselectors. Cyclones can collect suspended particulate matter of various sizes depending on the geometry of the cyclone and the flow rate. It operates on the principle of centrifugal forces that drive particles in the direction of the outer wall of the cyclone (Hinds, 1982). Particles with aerodynamic diameter greater than the cut-point of the cyclone impact upon the wall and/or the bottom of the cyclone. Particles with aerodynamic diameter less than the cut-point remain in the air stream and are collected on a filter downstream.

Impactors rely on inertial forces to separate particles based on aerodynamic diameter. Air is accelerated through a nozzle or jet and then forced to make a 90° turn around an impaction plate before passing through a filter and exiting the sampler. Depending on their size, particles suspended in the air stream pass through the acceleration nozzle and then either remain entrained in the flow or collide and are retained on the impaction plate. The cut-point of an

impactor is determined by the flow rate, jet size and shape (e.g., the distance between the jet and the impaction surface) (Pastuska, 1988; Lehtimäki & Willeke, 1993). The air flow rate must be calibrated carefully because correct size selection depends largely on precise flow rates.

Filters are made either from fibre mats of glass, cellulose or quartz or from synthetic membranes (e.g., Teflon). The selection of appropriate filters depends on the pump, filter static pressure, collection efficiency, extraction and analytical requirements, and the potential for sampling artefacts. Filter mass is determined by weighing the filter under controlled temperature and humidity conditions before and after use following a conditioning period of at least 24 h at those same conditions. The collected mass can be extracted and analysed for chemical composition. The extraction and analysis procedures used depend on the analytes of interest. A recent summary of methods for extraction and analysis of components of particulate matter may be found in Koutrakis & Sioutas (1996).

7.2.3 Semivolatile compounds

For airborne contaminants that are present in both the particle and the vapour phase at typical environmental conditions, it is necessary to use a combination of sampling methods. The most common approach consists of an aerosol sampling inlet (with or without size preselector) followed by a sorbent cartridge or tube. Examples of such contaminants include airborne PAHs, pesticides, polychlorinated biphenyls (PCBs), dioxins and furans. Semivolatile sampling systems are commercially available for personal air monitoring. Extraction and analysis of these samples are done separately for the particle and vapour phase and then the results are combined to provide a total concentration. An introduction to sampling and analysis methods for VOCs in air may be found in Binkova et al. (1995), Wallace & Hites (1996), Wallace et al. (1996) and Simonich & Hites (1997).

7.2.4 Reactive gas monitoring

Certain gases present in air may react with chemicals present in particles. For example, sulfuric acid particles collected on filters can be neutralized by the ammonia gas present in the sample or air stream. The preferred sampling approach to avoid this is to use a denuder to remove the reactive gas before it reaches the downstream filter. In the case of sulfuric acid monitoring, a citric-acid-coated denuder is used to remove the ammonia gas. Small denuder systems are commercially available for personal monitors. Denuder technologies are described in Lodge (1988) and Koutrakis & Sioutas (1996).

7.3 Water

The sampling and analysis of drinking-water characterizes the extent to which this carrier medium represents a source of specific chemical exposure. Contaminated drinking-water supplies contribute to the human intake of numerous chemical contaminants, including heavy metals, fertilizers, pesticides, aromatic hydrocarbons and organohalogens, among others. In some cases, drinking-water may be the primary source of human exposure. Chemical pollutants in water may originate from one or more of a myriad of sources, as summarized in Table 25. In the selection of measurement and sampling methods, it is important to consider raw water sources, water treatment processes, and distribution and service systems, all of which can either reduce

or increase the contaminant concentrations in drinking-water.

Samples collected at the end of the distribution system provide a better measure of potential exposure to individuals than samples collected at the source prior to any removal or treatment that might take place. Numerous texts detail sampling and analytical techniques specific to drinking-water, and these methods can be used to develop comprehensive exposure assessment protocols (UNEP/WHO, 1986; WHO, 1992,1993).

Table 25. Origins of chemicals commonly occurring in drinking-water (Hickman

<u>Substances affecting the source (raw water)</u>	
"Naturally occurring"	Leached from geological formati Derived from soil and sediments
Pollutants derived from point sources	Domestic sewage treatment (e.g. Industrial effluents (e.g., syn Landfill waste disposal (e.g.,
Pollutants derived from non-point sources	Agricultural run-off (e.g., fer Urban run-off (e.g., salt, PAHs Atmospheric fall-out (e.g., PAH
<u>Substances resulting from treatment</u>	
Substances formed during disinfection	Trihalomethanes, chlorophenols
Treatment chemicals	Chloramines, fluorides
Treatment chemical impurities	Acrylamide monomer, carbon tetr
<u>Substances arising from the distribution and service systems</u>	
Contaminants arising from contact with construction material and protective coatings	Lead, vinyl chloride monomer an cadmium from fittings, PAHs fro
Substances arising from point-of-use devices	Sodium, silver

In developing countries it is quite common for individuals not to have access to treated water from distribution systems, so analysing water quality solely from distribution systems may not provide a true reflection of exposure. Even if drinking-water is obtained from piped supplies, it may not provide an adequate indication of exposure as many individuals are forced to store water after collection, when gross contamination may occur. In some areas of the world, run-off water is routinely collected from roofs for drinking and cooking needs. Dustfall attributable to traffic, industry, or construction may contribute to variable (potentially high) pollutant concentrations in this source.

Exposure to contaminants in water is not limited to oral routes. For instance, disinfection by-products and radon gas dissolved in groundwater may be released into an indoor atmosphere providing an inhalation route. Heating water also releases dissolved VOCs. Exposure to contaminants may also occur through inhalation of aerosols from

irrigation sprays. During other water-based activities (e.g., swimming, showering and bathing), other contaminants may be absorbed via a dermal (percutaneous) route. Although the contribution of non-oral routes is usually much less than that of oral routes, these pathways should not be overlooked in the selection of measurement methods to assess exposure. Methods for modelling exposure through these pathways are discussed in Chapter 6.

7.3.1 Factors influencing water quality

In order to select appropriate measurement and monitoring methods, it is important to understand the following factors that influence the quality of the water being sampled, and the resultant exposure:

- * treatment systems
- * distribution networks
- * storage practices
- * spatial and temporal variations
- * climatic and seasonal changes.

Water treatment encompasses a variety of processes, ranging from simple screening and filtration to multi-step purification. The latter includes methods for coagulation, aeration, de-aeration, colour removal, softening, disinfection, fluoridation, stabilization and demineralization. Some of these steps constitute "removal", and others involve the "addition" of treatment chemicals to mitigate the hazards of contaminants in water. A list of chemical additives typically used in water treatment systems is shown in Table 26. The reaction of treatment chemicals with other substances present in raw (untreated) water often results in the generation of intermediate reaction products with adverse health significance. For instance, chlorine,

accepted worldwide for disinfection and oxidation, results in the formation of disinfection by-products such as trihalomethanes (e.g., chloroform).

Table 26. Water treatment chemicals

Activated alumina	Sodium bicarbonate
Aluminum sulfate	Sodium calcium magnesium polyphosphate
Ammonia	(glassy)
Ammonium hydroxide	Sodium carbonate
Bentonite clay	Sodium chlorite
Calcium hydroxide	Sodium fluoride
Calcium hypochlorite	Sodium hydroxide
Calcium oxide	Sodium metabisulfite
Carbon (activated, granular, and powder)	Sodium polyphosphate (glassy)
Carbon dioxide	Sodium silicate
Chlorine	Sodium siliconfluoride
Ferric chloride	Sodium tripolyphosphate
Ferric sulfate	Sodium zinc polyphosphate (glassy)
Ferrous sulfate	Sodium zinc potassium polyphosphate (glassy)

Fluosilicic acid	Sulfur dioxide
Potassium permanganate	Sulfuric acid
Sodium aluminate	Tetrasodium pyrophosphate

Distribution networks constitute another potential source of chemical contaminants in drinking-water. The materials used in distribution networks may serve as a pollutant source by leaching into the water over time. Some examples include lead from lead-containing solders and pipes, asbestos fibres from the surface of asbestos-cement pipes and cadmium from metallic fittings. Other contaminants include PAHs from coal-tar-based sealants, plasticizers, stabilizers and solvents used in the manufacture of plastic pipes.

Water sources experience considerable variations in quality over time and geographic location. The quality of river water may change rapidly during heavy storms, melting snows and droughts. The quality of water in lakes may be affected by climate, season, location or some combination thereof. Groundwater historically has enjoyed the most consistent quality, with relatively constant composition. However, the vulnerability of groundwater to contamination is gaining widespread attention, with particular emphasis on synthetic organic substances, surface impoundments, landfills, agriculture, leaks and spills, land disposal of wastewater, septic tanks and the petroleum/mining production industries.

7.3.2 Water quality monitoring strategies

There are numerous considerations in the design of a monitoring and measurement strategy for water quality assessment. The International Organization for Standardization (ISO) has provided guidance on a number of issues related to sampling strategies for water quality assessment (Table 27). A sound monitoring methodology must be followed by the appropriate sample storage and transportation, to minimize changes in sample composition. Losses can occur due to several physical, chemical and biological changes, such as ion exchange, adsorption with the container material, oxidation to precipitated forms, loss of volatiles to the vapour space and biochemical conversions. For contaminants at low source concentrations, these changes can introduce significant errors in the analytical results.

Table 27. ISO standards of water quality giving guidance on sampling

ISO standard number	Title (water quality)
5667-1: 1980	Sampling - Part 1: Guidance on the design of sampling programmes
5667-2: 1982	Sampling - Part 2: Guidance on sampling techniques
5667-3: 1985	Sampling - Part 3: Guidance on the preservation and handling of samples
5667-4: 1987	Sampling - Part 4: Guidance on sampling from lakes, natural and man-made
5667-5: 1985	Sampling - Part 5: Guidance on sampling of drinking-water and water used for food and beverage

processing
5667-6: 1985 Sampling - Part 6: Guidance on sampling of rivers and streams

The design of a water monitoring programme would be incomplete without consideration of the demographic and socioeconomic characteristics, and also an understanding of the historical development, of the potentially exposed community. The evolution of materials used in distribution systems changes the profiles of pollutants requiring measurement. Cultural and socio-economic factors affect usage patterns, which in turn influence the extent of exposure to contaminants in drinking-water.

In order to ensure the representativeness and validity of water samples, sampling techniques must be carefully selected (WHO, 1992, 1993). The first step in the design of a sampling programme is to develop concise objectives, accounting for

- * the nature of the substance to be measured
- * point of exposure
- * the duration of time over which measurements will be taken.

The type and magnitude of spatial and temporal variations in the concentration of water constituents will depend upon both their sources and their behaviour in the distribution and service systems.

Substances can be classified into two main types:

- * *Type 1.* Substances whose concentration is unlikely to vary during distribution. The concentration of these substances in the distribution system is largely governed by the concentration in the water going into the supply, and the substances do not undergo any reaction in the distribution system. Examples of such substances are arsenic, chloride, fluoride, hardness, pesticides, sodium and total dissolved solids.
- * *Type 2.* Substances whose concentrations may vary during distribution. These include
 - substances whose concentration during distribution is dependent mainly on the concentration in the water going into the supply, but which may participate in reactions (which change the concentration) within the distribution system. Examples are aluminium, chloroform, iron, manganese and hydrogen ion (pH).
 - substances for which the distribution system provides the main source, such as benzo [a]pyrene, copper, lead and zinc.

This classification applies only to piped water supplies. In all other types of supply, water constituents should be regarded as type 1 substances. The same substance may belong to different classes in different distribution systems.

7.3.3 Sample collection

The location, frequency and time of sampling is strongly

dependent on the spatial and temporal variations for the particular pollutant of interest. There are many different methods to collect water samples and measure contaminant concentrations. The choice of a particular technique can have a profound effect on the analytical results. Some conventional measurement methods are briefly described below:

- * *Grab samples* represent a "snapshot" of a situation at a particular time and place. Using samples taken at intervals and analysed individually, this method can characterize variations in source composition.
- * *First-draw (static) samples* are collections immediately following a stagnation period (e.g., overnight). This reflects the influence of domestic plumbing on the inorganic content of water quality.
- * *Flushed samples* are taken after taps have been run for a sufficient length of time to eliminate stagnant water.
- * *Composite samples* involve regular sampling, usually over a 24-h period, followed by pooling of samples and analysis of the composite. This integrated method overcomes the disadvantages inherent in first-draw sampling. Time-composite samples approximate the potential exposure to drinking-water contaminants.

7.4 Assessing exposures through food

Exposure to chemical compounds in food can be measured directly by analysing duplicate diets or indirectly by analysing foods or total diets, matching food consumption data with information of chemical concentration in the foods or, for certain chemicals, estimating the total amount of the chemical available divided by the population of concern (called *per capita* estimates). The consumption of water and the resulting exposure should also be determined if appropriate (FAO/WHO, 1997). The estimation of exposure to food chemicals is a complex activity and no single approach is suited to all circumstances. The method chosen depends on the information available, the population group of concern, whether acute or chronic effects of the chemical are being assessed, and the intended use of the result (Rees & Tennant, 1993). The Intake Assessment Group which has been added to the Joint FAO/WHO Expert Committee on Food Additives is also examining other means of evaluating dietary exposure assessments for food additives and contaminants.

Direct approaches tend to consider samples of food as actually consumed because the method by which food is prepared for consumption (e.g., washing, peeling, cooking and commercial processing) can influence contaminant residue levels. For example, malathion concentrations were found to decrease by 99% when raw tomatoes were processed into canned tomatoes (Elkins, 1989). In contrast, concentrations of ethylenethiourea, a carcinogenic degradation product of maneb (manganese ethylene bisdithiocarbamate), rose 94% when turnip greens were washed, blanched, frozen and subsequently sautéed (Elkins, 1989; Houeto et al., 1995). Although cooking may lead to a reduction in the lead content of vegetables, in areas where the lead concentrations in drinking-water are higher than average (e.g., due to lead pipes), cooking water can be a significant source of lead intake (UK MAFF, 1989). Therefore, preparation and processing can alter contaminant levels present in foods, or introduce new contaminants. For these reasons, the concentration of the target analyte in

ready-to-eat foods is the most useful measure for purposes of dietary exposure assessment.

7.4.1 Duplicate diet surveys

Duplicate diet surveys are particularly useful because they reflect the range of preparation habits of the study population. These studies require that respondents save a serving of each meal or components of each meal and store them until collection by the research team. Following collection, the food is composited over predetermined time intervals (e.g., by meal or by day) and analysed for the target analytes. In duplicate diet studies, logistic and cost constraints typically require that foods be composited. The principal disadvantage of composite samples is that they do not allow for identification of the contribution of individual foods to total dietary exposure. A high degree of respondent burden is associated with duplicate diet studies, so they are not conducive to assessing chronic dietary exposures and may underestimate intake. Such approaches are only suitable for chemicals that can be analysed accurately, so direct diet methods are not traditionally used for assessing food additives exposure, for example. A summary of dietary exposure assessments for chemical contaminants in food using the duplicate diet performed worldwide may be found in Thomas et al. (1997).

There are many indirect methods for estimating exposure to food chemicals because there are a variety of ways to collect consumption data, to express residue levels in the foods concerned (for example, legislative levels, manufacturer or industry use levels, predicted, proposed or analysed levels or any combination of these) and there are several approaches which can be used to combine the information to assess exposure (Rees & Tennant, 1994). Some methods are better than others, depending on the chemical; for example several countries have found it useful to assess food additive exposure by using *per capita* methods (Ito, 1993). More information on these indirect methods is given below, but the reader is strongly advised to refer to more comprehensive documents on dietary survey methodology and dietary exposure assessment approaches (WHO, 1985a, 1997c; FAO/WHO, 1995a,b, 1996, 1997).

7.4.2 Market basket or total diet surveys

Market basket or total diet surveys utilize food chemical concentrations measured in ready-to-eat foods prepared in the laboratory linked to model diets derived from food consumption data and standard recipe preparation for large populations, households or individuals. Food products or food groups selected for sampling and analysis are generally intended to be representative of those most commonly consumed by the population of interest. Total diet studies have been carried out since the 1960s in many countries. Market basket surveys are often employed by regulatory agencies charged with ensuring and monitoring the safety of a national food supply (FAO/WHO, 1995b). Initially this purpose was to estimate background exposures of the population to pesticides residues and radioactive contaminants. The emphasis has shifted from pesticides to toxic metals and more

recently has included a variety of trace elements and organic contaminants.

For example, the US FDA Total Diet Study (US TDS) is a market

basket survey based on heavy metal and pesticide data measured in samples of 234 different ready-to-eat food products selected to be representative of over 4000 foods common in the diet of residents in the USA, and the results of national food consumption surveys (Pennington, 1992). However, more commonly total diet (market basket) studies consider smaller food groups rather than individual foods (UK MAFF, 1985). The main advantage of the total diet (market basket) approach for estimating exposure is the ability to monitor trends without burdening study participants. The total diet approach allows data from separate studies of food consumption and contaminant residues to be combined (e.g., Tomerlin et al., 1996). Moreover, this approach allows analytical chemistry resources to be directed to the foods that are most likely to yield the greatest exposure (e.g., the foods consumed in greatest amounts and foods that are likely to contain the highest residue concentrations). Such foods may be indicated by information available from existing data such as the GEMS/Food (WHO, 1978, 1997c) and the US TDS (Pennington & Gunderson, 1987).

However, this method cannot be used for all contaminants. This is because the analysis of food groups may be too expensive for some contaminants and may not be feasible for others. Analytical methods may not be sufficiently reliable, the limit of detection may be too high or the grouping of the foods (compositing) may decrease the likelihood of finding the source of the contaminant. Analysis of individual food products affords a detailed examination of contaminant levels in specific commodities -- either raw, processed or prepared. Sampling may be designed to characterize geographic and temporal variability of contaminant levels that may be a result of varying application rates of pesticides, natural levels of elements (e.g., heavy metals), climate and other factors. In addition, samples can be collected at all steps in the process from field to consumer thereby providing insight into the sources and fate of contaminants in food.

Further information on the strengths and limitations of each of the approaches described above have been published in the comprehensive *Guidelines for the Study of Dietary Intake of Chemical Contaminants* (WHO, 1985a).

7.4.3 Food consumption

The FAO/WHO Consultation on Food Consumption and Exposure Assessment of Chemicals (called Exposure Consultation) reviewed current methodology for food additives, contaminants, pesticides, veterinary drugs and nutrients. The Exposure Consultation agreed to expand and revise the regional diets presently used by the GEMS/Food for pesticides and recommended that this consumption data can be used for estimate dietary exposure to certain other chemicals. The regional diets will be based on 1990-1994 FAO Food Balance Sheets which reflect

a country's amount of raw commodities for consumption, and may not necessarily refer to foods in the forms people consume them. Waste at the household or individual level is not usually considered.

Major methods for determining food consumption at the national levels were identified as population-based, household-based and individual-based. The report from a FAO/WHO consultation on the preparation and use of food-based guidelines (FAO/WHO, 1996) gives more information on food consumption study designs. The Exposure Consultation supported the concept that an improvement in dietary

exposure assessments can be achieved by refining any combination of the contributing elements: food consumption data, food chemical concentration data or the method used to combine the two. This allows the risk assessor a greater flexibility in selecting cost-effective approaches to refine dietary exposure assessments using the resources available (WHO, 1997c).

The five basic approaches discussed by the Exposure consultation for describing the diet of individual people are:

- * food record/diary survey
- * 24-h recall
- * food frequency questionnaire
- * meal-based diet history
- * food habit questionnaire (WHO, 1997c).

The 24-h recall is a widely used dietary assessment method and is utilized in many exposure-related studies including the National Health and Nutrition Examination Survey conducted by the US Centers for Disease Control and Prevention (Witschi, 1990).

7.4.3.1 Food diaries

Food diaries are detailed descriptions of types and amounts of foods and beverages consumed, meal by meal, over a prescribed period, usually 3-7 days. Food diaries and recalls may be presented in numerous formats or combined with food models and weighing procedures to characterize serving size more accurately; however, regardless of the specific details, dietary recording places a substantial burden on the subject (Witschi, 1990).

7.4.3.2 24-h recall

The short-term nature of the 24-h recall and the facility to consider meal occasions or daily consumption from diary surveys make this method ideal for assessing exposure to substances that can give rise to acute health effects, such as the cholinesterase-inhibiting organophosphate and carbamate pesticides. Diary methods may be used for assessment of long-term exposure but the underlying assumption is

that the food consumption is representative of usual habits. Probabilistic approaches can be useful to predict consumption and resulting exposure over longer periods of time.

7.4.3.3 Food frequency questionnaires

Food frequency questionnaires (FFQs) are a standard tool for characterizing food intake over extended periods of time. A food frequency questionnaire consists of two basic components: a list of foods and a frequency response section for respondents to indicate how often a specific serving size of each food is consumed (Table 28). The underlying principle of the food frequency approach is that average long-term diet, for example, intake over weeks, months or years, is important rather than intake on a few specific days. This may not be true for all contaminant-health effect combinations (e.g., acute and reversible effects such as cholinesterase inhibition); however, it is

reasonable in the context of assessing health effects that may be caused by cumulative exposure, such as cancer, or reproductive and developmental effects that may follow a threshold dose-response curve. Some FFQs include questions on usual food preparation methods, trimming of meats, use of dietary supplements and identification of the most common type or brand consumed. FFQs can be used to rank individuals by exposure to selected chemicals. Although FFQs are not designed to measure absolute exposure, the method may be more accurate than other methods for estimating average exposure to chemicals having large day-to-day variability and for which there are relatively few food sources. FFQs have several disadvantages too: specifically, they are less reliable in estimating consumption of rarely consumed foods and the food lists are often designed to assess nutrients and may require substantial revision to assess chemical exposures.

7.4.3.4 Meal-based diet history

Meal-based diet history methods are designed to assess usual individual food consumption. It consists of a detailed listing of the types of foods and beverages commonly consumed at each meal over a defined time period which is often a "typical week".

7.4.3.5 Food habit questionnaires

Food habit questionnaires are designed to collect either general or specific types of information, such as food perception and belief, food likes and dislikes, methods of preparing foods, use of dietary supplements and social setting surrounding eating occasions. This type of information is frequently considered with other methods but may be used on its own.

Although the last two methods are seldom used in dietary exposure assessments they can contribute very useful background information and may be the only information for specific population group issues (e.g., organic food consumption by vegetarians). They can be targeted to answer specific questions or prioritize issues of concern and provide a cost-effective tool for the risk assessor.

Table 28. An example of food listing and frequency response options of an F

For each food listed, fill in the circle indicating how often, on average, you have used the amount specified, during the past 3 months		Average use of the last 3 months			
		Per month			Per wee
		Never or less than once	1-3	1	2-4
DAIRY FOODS	Skim or low-fat milk (8 oz glass)	0	0	0	0
	Whole milk (8 oz glass)	0	0	0	0
	Sherbet or ice milk (1/2 cup)	0	0	0	0
	Ice cream (1/2 cup)	0	0	0	0

Food consumption data is often collected for nutritional or economic purposes, and foods may not be described in the detail required for exposure assessment (e.g., fish consumption may be recorded but the contaminant of interest may be found primarily in fatty fish or fish caught in a particular location). There are number of difficulties using the different types of consumption data. A report from the European Commission provides a good summary of the practical problems in using consumption data to estimate dietary exposure (EC, 1997a).

7.4.4 Contaminants in food

The vast majority of food that is actually consumed has undergone some form of processing, ranging from simple washing to complete reconstitution, as it progresses from the producer to ultimately being ingested by a consumer (FAO/WHO, 1995b). Several factors can influence contaminant concentrations in foods that are ready to eat. These factors include those that may vary by season and/or geographic region, such as food source (e.g., homegrown, locally grown by a small producer, domestically grown by a mass producer and imported), and former or current application of pesticides (US NRC, 1993). The form in which food is consumed (e.g., raw apple, apple sauce, apple juice) can be very different in different subpopulations (e.g., adults, elderly or young children).

Residue levels measured in raw agricultural commodities collected at the producer, processor or distribution level are unlikely to be an accurate reflection of contaminant concentration in food as actually consumed. With the exception of the GEMS/Food, which collects contaminant and pesticide residue data from member countries, there are no centrally coordinated reference databases for other food chemicals in foods. Potential data sources at the national level may include supervised trial data, government monitoring and surveillance data (Pennington & Gunderson, 1987), national food composition databases (nutrients) and industry funded surveys. A number of analytical methods for contaminants in food have been published by the US FDA, EOAC and US EPA (e.g., US FDA 1997a,b). Different approaches have been used for calculating exposure when the contaminant concentrations fall below the detection limit (e.g., assuming the concentration is zero or some percent of the detection limit).

7.5 Summary

This chapter has introduced available sampling methodology for chemicals in air, water, and food. Common to the selection of these methods are considerations of detection limits, interferences, ease of operation and cost. Personal, microenvironmental and ambient air sampling methods are available for monitoring gases and vapours, both passively and actively, aerosols, SVOCs and reactive gases.

Sampling considerations for assessing water quality are numerous. An important consideration is that exposure to contaminants is not limited to oral routes and that not all individuals have access to treated water from distribution systems. Guidance for sampling and monitoring programmes is provided.

There are a number of methods for measuring estimating food consumption and contamination. The method chosen will depend on the information available, the population group of concern, whether acute or chronic effects of the chemical are being expressed, the intended use of the results and available resources. The reader is strongly advised to refer to more comprehensive documents on dietary survey methodology and dietary exposure assessment approaches.

8. MEASURING HUMAN EXPOSURE TO CHEMICAL CONTAMINANTS IN SOIL AND SETTLED DUST

8.1 Introduction

This chapter is intended to provide the reader with important concepts and a basic understanding of soil and settled dust sampling so that effective sampling strategies can be designed to meet specific research needs. Choices in sampling methods, sampling locations, sampling areas and the sampling time of the sample collection may be particularly important when the results are used for exposure assessment purposes. For these methods to be used successfully, it is important that the investigators understand the basic concepts behind collecting soil and settled dust and the limitations of different methods and strategies. Because this field of research is currently evolving rapidly, it is recommended that researchers consult the literature for new and complete information before designing a study to measure toxic metals, pesticides, PAHs, other products of incomplete combustion, fibres and biological matter. The most appropriate method for sampling soil and settled dust depends on the living conditions of the study population and the target contaminants. The information in this chapter is therefore intended to provide general guidance on approaches that might be taken.

Soil is a mixture of air, water, mineral and organic components (Horne, 1978). The relative mix of these components determines to a large extent the capacity of a soil for containing chemical contaminants and the potential for it to be an important source of exposure. Settled dust, which may be found outdoors or indoors, is often a complex mixture of material from several sources. Outdoor settled dust is material deposited on roadways, streets and other paved surfaces. Indoor settled dust (house dust) is material deposited on indoor surfaces such as floors, carpets and furniture. Chemical contaminants present in indoor dust can originate from activities in the home or can be tracked into the home from road dust, soil or work sites (US EPA, 1991). Material present in soil, outdoor dust and indoor dust may include clay, sand, bacteria, viruses, allergens, products of incomplete combustion, environmental tobacco smoke, heavy metals, pesticides, asbestos fibres, paint fragments, solvents, flame retardants, cleaners, and residues from synthetic fibres, building products and many other materials and pollutants (Robert & Dickey, 1995).

Unintentional ingestion of house dust, particularly for children, may be a significant contributor to the total human exposure to many potentially toxic substances, depending on personal living conditions and frequency of contact with this media. Because children spend more time in contact with soil and indoor surfaces than adults and have a greater dose given the same exposure, these exposure pathways are particularly relevant to children. For example, it is likely that children's lead exposure from settled dust is an important contribution to total lead exposure because of the past and present

use of gasoline, lead-based paint on housing and steel structures, and airborne emissions from industrial point sources that settle in residential environments. In the USA, house dust is considered a major source of lead to most children (CDC, 1991; Lanphear & Roghmann, 1997). Older homes are especially susceptible to lead dust exposure if paint is peeling or renovations are being done (Roberts et al., 1992).

Soil and settled dust can be a significant source of exposure to numerous other toxicants in addition to lead, including pesticides and PAHs. Pesticides, although designed to degrade to different extents through natural environmental processes such as sun, rain and soil microbial activity, may accumulate in soil and dust and persist for long periods of time. Because of the lack of these external degradation processes, pesticides may be particularly persistent in indoor settled dust (Simcox et al., 1995). Studies have shown that in the general population in the USA the highest concentrations and largest number of pesticides are found in house dust as compared to soil, air and food (Whitmore et al., 1993; Lewis et al., 1994). Although many pesticides in house dust come from outdoor sources, many households use pesticides indoors. Because little or no training is provided for users of household pesticides, unnecessary exposures often occur. Pesticides often found in house dust include those used for control of insects; e.g., chlordane and heptachlor in homes treated for termites, pentachlorophenol and lindane in homes where wood preservatives had been used, and other harmful pesticides contained in flea and garden treatment (Roberts et al., 1992).

Hazardous substances that originate at the worksite may also find their way (e.g., via clothes) into the homes of workers. The US National Institute for Occupational Safety and Health compiled a bibliography of more than 350 published and unpublished accounts of take-home, or "para-occupational" contamination worldwide (NIOSH, 1994). The reports identified by NIOSH document the spread from workplace to home of toxic metals (lead, beryllium, cadmium and mercury), asbestos, and various other potentially hazardous substances. Settled dust was a major source of familial exposure in most of these studies.

8.2 Selected sampling methods

8.2.1 Soil

Soil constitutes a potential exposure pathway through direct contact and ingestion or inhalation of resuspended soil particles. Children's activities make them more likely to be affected by such exposures. In addition, contaminated soil can be tracked inside homes, or may infiltrate indoors when resuspended. In either case, soil may become a component of settled indoor dust. There are no standard collection methods for soil sampling, as discussed later for settled dust (section 8.2.2). This limitation affects the ability to make comparisons of results from soil sampling across studies. However, information on soil contamination can provide insights into the relative importance of multimedia contaminants as they may affect exposure.

8.2.1.1 Surface soil collection

The most commonly used approaches make use of an auger or similar sampler such that a sample is defined by cross-sectional area and

predesigned depth of the auger. Alternatively, a predetermined amount of surface soil may be scooped with a small trowel, with less precise definition of sampler depth. In either case, the sample is stored in a clean, inert container and transferred to the laboratory for analysis.

8.2.1.2 Soil contact and intake measurements

Skin contact has been measured by methods similar to those used for settled dust (e.g., self-adhesive labels, hand wipes), and controlled application followed by recovery of the fraction of deposited soil on the skin (Lepow et al., 1975; Roels et al., 1980; Que Hee et al., 1985). The amount of soil that adheres to the skin depends on a number of variables including soil properties (e.g., water content, particle size, carbon content), region of the body and activity (Kissel et al., 1996). A number of studies have attempted to estimate soil ingestion based on hand adherence estimates and scenarios of activities, as well as analyses of soil tracers (e.g., concentrations of aluminium, silicon or titanium) (e.g., Calabrese et al., 1989, 1990).

8.2.2 Settled dust

Although indoor dust is becoming recognized as a reservoir for many toxic substances and a potentially significant source of human exposure, there is no uniform standard for sampling settled dust. More than 15 methods have been described in the literature to date. Scientists do not yet agree either on the definition of settled dust or on the methods to measure it. This issue is further complicated by the fact that results from one settled dust sampling method may not be directly comparable to results from others. Even with these limitations, settled dust sampling methods have been used effectively and provided valuable insights into the total human exposure paradigm.

Selected sampling methods are described below to give the reader an indication of the diversity of techniques available. The list is by no means exhaustive. Several of the methods described are simple to use and readily available to researchers worldwide. Brief descriptions of how to use the simpler methods are provided. Other methods require specialized equipment that is relatively expensive and may be difficult to obtain in some regions of the world. The methods are distinct from one another, but most fall into three categories: wipe, vacuum sampling and sedimentation methods. These methods are widely used for sampling settled dust indoors; however, in principle they may be applicable for outdoor settled dust as well. Bulk sample collection methods, such as sweeping, are not covered here. Key features of the various methods for collecting settled dust samples described in this chapter are summarized in Table 29.

Table 29. Comparison of features of different methods for collected settled

Feature	Common wipe	HUD wipe	Preweighed sample	Commercial vacuum	DVM vacuum	Rota vacu
Widely available	Yes	Yes	Yes	Yes	No	No

Cost	Low	Low	Low	Medium	High	High
Simple method	Yes	Yes	Yes	Yes	Yes	Yes
Loading	Yes	Yes	Yes	No	Yes	Yes
Concentration	No	No	Yes	Yes	Yes	Yes
Sieving possible	No	No	No	Yes	No	No
Portable	Yes	Yes	Yes	No	Yes	Yes
Samples small areas	Yes	Yes	Yes	Yes	Yes	Yes
AC powered	No	No	No	Yes	Yes	Yes
Size selective	No	No	No	No	Yes	No

8.2.2.1 Wipe sampling methods

A common wipe sampling method uses *premoistened towelettes* to wipe a measured area defined inside a template placed on the sampling surface (Vostal et al., 1974; US HUD, 1995). Typical sampling areas are in the range of 0.1 m² and masking tape is commonly used as a template. The actual surface area inside the template is not critical as long as it is measured and recorded. However, sampling areas greater than 0.2 m² are not recommended because larger areas cannot be wiped effectively with one towelette. This method has been used extensively in the USA to measure lead amounts in settled dust, but has also been used to ascertain levels of cadmium, chromium and arsenic, as well as many other metals and organic compounds.

With the *HUD method*, the person collecting the sample should wear a clean disposable glove on the hand that will come in contact with the towelette. To collect a sample, the surface inside the template is wiped with a towelette back and forth in vertical S-strokes. The exposed side of the towelette is then folded inward, exposing a clean portion, and the same area is wiped with horizontal S-strokes. The towelette is folded once more, again exposing a clean portion, and the area is wiped a final time with additional vertical S-strokes. The towelette is then folded, exposed side in, placed into a clean sealable plastic bag or container, and sent to a laboratory for analysis.

Several researchers have used *preweighed wipe material*, such as cotton gauze or filter paper, in order to determine the quantity of settled dust collected (Lepow et al., 1974; Stark et al., 1982; Rabinowitz et al., 1985; Levallois et al., 1991). The sampling material is then reweighed in a laboratory after sample collection. Theoretically, the weight of total dust collected can be calculated by subtraction, and toxicant concentration could be determined after analysis on a mass basis.

An important issue that needs to be addressed when using the preweighed wipe methods is the potential loss of sampling material or dust during handling in the field or laboratory. Furthermore, Chavalitnitikul & Levin (1984) noted that filter paper tends to fall apart when rough surfaces are wiped. Loss of sampling material in the

field would underestimate the amount of total dust collected when final weights are obtained, which would in turn overestimate the calculated mass concentration results. Because of water loss or gain, changes in humidity may also significantly affect the before and after weights of the samples. These potential sources of error must be carefully controlled to make the results from preweighed wipe methods reliable.

A specially designed preweighed wipe sampling method has been developed to minimize the potential sources of error mentioned above. This method, known as the *Lioy-Weisel-Wainman* (LWW) method, was developed to quantitatively measure the toxicant concentration (mg/g)

and surface loading (mg/m²) of dust on flat surfaces (Lioy et al., 1993). The sampling device is not made from common materials and is at this time only available from the research group that developed it.

8.2.2.2 Vacuum methods

Many researchers have collected samples from commercial household vacuum cleaners, which are often referred to in the refereed literature as research dust samplers. Some researchers state that they sampled only the fine dust that settled to the bottom of the bag. (Kaye et al., 1987; Moffat, 1989; Davies et al., 1990; Thornton et al., 1990; Jensen, 1992). Other researchers modified their vacuum cleaners to hold filters (Diemel et al., 1981; Watt et al., 1983).

A settled *dust vacuum method*, commonly called the DVM, is constructed from conventional industrial hygiene sampling materials that are likely to be available to researchers worldwide (Que Hee et al., 1985). The sampler consists of a common personal air-monitoring pump, usually operated at 2.5-3.0 litres/min. Sampling areas with this method are typically 25 cm x 25 cm, and often take more than 5 min to sample completely. A three-sided template is sometimes used on bare floors to vacuum dust that has migrated to the walls. Sampling areas are covered three times with overlapping passes in the horizontal and vertical directions. Que Hee et al. (1985) state that the sampler was designed to collect only small dust particles that would most likely stick to a child's hands, not total lead on a surface. Therefore, the amount of dust collected by this method from a given surface is usually less than collected by other methods. This sampler has been used in numerous studies in the USA and elsewhere, and its use has provided considerable information linking lead in settled dust to lead in children (e.g., Bornschein et al., 1985).

Researchers have also used laboratory *rotary vane vacuum pumps* connected to the same three-piece filter cassettes as used with the DVM described above, but with a much higher flow rate. The filter cassette is often used openface or with a wide diameter nozzle so sampling areas can be covered in fewer passes than required for the DVM, thus reducing the time spent collecting samples (Solomon & Hartford, 1976).

Prpic-Majic et al. (1992) described another vacuum pump sampling method that used a prescreen at its nozzle entrance to prevent coarse particles and small objects from being collected on the membrane filter that served as the sampling surface. Total dust measurement was obtained from the dust particles that reached the membrane filter. There was no mention of potential loss of fine dust trapped in the prescreen, especially after it was loaded with fibres and debris.

A sophisticated vacuum sampling device, called the *HVS3*, was designed to make dust collection efficiency from different surface types as consistent as possible (ASTM, 1993). The *HVS3* is a high-powered vacuum cleaner equipped with a nozzle that can be adjusted to a specific static pressure and air flow rate to allow for consistent dust collection. The sampler uses a cyclone to separate particles greater than about 5 mm from the air stream and collects them in a 250 ml sample bottle screwed into the bottom of the cyclone. Smaller particles are not collected. The *HVS3* can collect large, representative samples of settled dust from indoor surfaces, such as rugs and bare floors, and dust from outdoor surfaces, such as streets, sidewalks, lawns and bare, packed dirt. However, it cannot be used to sample from small or uneven areas because of the large size of the device. The *HVS3* has been used in numerous exposure assessment studies to measure toxic metals and pesticides in settled dust. The sampler is not made from standard materials and is therefore relatively expensive to buy. Interested readers should consult the ASTM standard method (D5438-93) for more information on the specifications and availability of the *HVS3* sampling device (ASTM, 1993).

Farfel et al. (1994) modified the *HVS3* by using the same cyclone as in the *HVS3* but with a commercially available handheld vacuum to make the device smaller and more portable. These authors also used flexible tubing as the pickup nozzle to allow small surfaces, such as windowsills, to be sampled. This modification, called the *BRM method*, does not allow control of either the sampling flow rate or the static pressure at the pickup nozzle. The ASTM standard method for the *HVS3* does not apply to the *BRM*, except for its description of the cyclone.

Another settled dust vacuum sampling method that has been used in several research studies, the *Sirchee-Spittler method*, is a hand-held, battery-powered vacuum unit (Rinehart & Yanagisawa, 1993; Weitzman et al., 1993; Aschengrau et al., 1994). The sampler is simple to use, highly portable and can cover large areas in a short period of time. Unfortunately, there are not many *Sirchee-Spittler* sampling devices in service and its availability to researchers worldwide is therefore limited.

8.2.2.3 Sedimentation methods

Sedimentation methods involve measuring the amount of dust which settles on a clean, preweighed surface over a given period of time. Such procedures can make use of a simple collecting cup (Aurand et al., 1983) or a flat plate (Pellizzari et al., 1995). After a specified period of time, the sample is collected and measured, and the dust is then analysed in a laboratory. Data from the German Environmental Survey (Schulz et al., 1995) on domestic dust precipitation is given in Table 30. Sedimentation methods are useful for collecting samples over a specific period of interest (e.g., a day, week or month). In contrast, the integration times of settled dust samples collected using the wipe or vacuum methods described above are not well characterized.

Table 30. Sedimentation of elements in indoor dust, Germany 1990-1992 (Schu

Element	No. of	No. of	Percentiles	Maxim
---------	--------	--------	-------------	-------

	samples	values >LOQ				value (GM)
			10	50	95	
Dustfalla	3282	-	1.4	21.0	579	4.52
Arsenicb	3279	965	< 4	33	1313	5.4
Boron	2896	511	< 0.06	0.64	47.1	0.13
Cadmiumb	3282	0	5	44	833	11.7
Calcium	3277	25	17	273	2679	51.2
Chromium	3282	14	0.02	0.28	3.92	0.07
Copper	3277	1167	< 0.3	1.5	48.8	0.33
Iron	3277	74	2	41	765	7.7
Lead	3282	0	0.11	1.17	86.6	0.29
Magnesium	3277	26	2	25	342	5.2
Phosphorus	3277	1063	< 1.8	17	542	2.8
Zinc	3277	15	0.9	8.6	108	2.2

Units are $\mu\text{g m}^{-2}\text{d}^{-1}$ unless otherwise indicated.

^a $\text{mg m}^{-2}\text{d}^{-1}$.

^b $\text{ng m}^{-2}\text{d}^{-1}$.

8.3 Sampling design considerations

Section 8.2.2 describes numerous innovative methods that have been developed and used by researchers to collect settled dust from surfaces. Many more examples can be found in the literature. However, there has been little standardization among the methods. Differences in vacuum pump flow rates, nozzle shapes and sizes, and sampling technique will affect dust-pickup characteristics of vacuum sampling methods and will, therefore, affect the results. Differences in wipe sampling material and technique will also affect the results from wipe samples. Different recovery rates of dust from alternative sedimentation methods can also have a large effect on analytical results. These differences among methods, which are not well documented in the literature, can make interpretations and comparisons between studies difficult. It is important that sampling methods are well described when results from settled dust sampling are reported.

Sampling design considerations for soil should follow the objectives of the study and consider the particular conditions of the site being monitored. For example, multiple soil samples can be obtained around the perimeter of a house at a sufficient distance so that the soil is representative of material that might be tracked into the home. In this case, the samples might be composited. Backyard soil might vary in the number and amounts of contaminants present, as well as usage and specific activities by residents. The number and location

of samples to be obtained should be based on these considerations.

8.3.1 Concentration and loading

Almost all settled dust contains measurable levels of common environmental contaminants such as heavy metals and pesticides, and most residential surfaces, such as floors and windowsills, contain settled dust (CDC, 1991). The actual concentration of a target analyte in a sample of settled dust depends on the amount of dust collected that does not contain the analyte and the amount of dust collected that does contain the analyte.

The analyte concentration, sometimes called a *mass concentration*, is usually expressed as micrograms of analyte per gram of dust ($\mu\text{g/g}$). The amount of dust on a surface can be expressed as grams of dust per unit area, such as per square metre, and is usually called *dust loading* (g/m^2). The analyte concentration, multiplied by the dust loading on a surface, gives a *analyte loading* value and is commonly expressed as micrograms of analyte per unit area ($\mu\text{g/m}^2$). The dust loading and analyte loading measurements are both *area concentrations*, that is, the concentration of dust or contaminant per unit area. In this report, "concentration" refers to mass concentration and "loading" refers to area concentration.

The example of residential sampling for lead is used to simplify the discussion. Common wipe sampling methods, such as the HUD method, measure lead loading directly, without measuring lead concentration

and dust loading. Fig. 24 illustrates what common wipe samples can measure, using realistic results collected from floors in a hypothetical residence. Assume that each diagonal line in the figure represents the lead loading results from one wipe sample. The diagonal lead loading lines show the infinite number of lead concentration (y axis) and dust loading (x axis) combinations that might result in the measured lead loading. As mentioned earlier, the product of the two parameters is the lead loading ($\mu\text{g/g} \times \text{g/m}^2 = \mu\text{g/m}^2$). Using a log scale on the x and y axes ensures that the infinite number of combinations that result in the same lead loading value fall on a straight line. As noted in Chapter 4, the distribution of many measures of environmental exposure is skewed right and may often be approximated by a lognormal distribution. For lognormal distributions, geometric relationships (e.g., factorial) exist among quantiles of the distribution, in contrast to the linear relationships present in measures that follow a normal distribution. As described in Chapter 4, lognormal distributions can be "normalized" in a numerical sense by expressing the data as the log-transformed values or in a graphical sense by plotting data on log scales. This example assumes that lead concentration and dust loading are lognormally distributed and perfectly correlated with each other, i.e., lead loading in $\mu\text{g lead/m}^2$ is assumed to be constant. A scatter plot of two perfectly correlated and lognormally distributed measures depicted on a normal scale would exhibit a curved relationship, but appears as a straight line when depicted on a log scale.

Because common wipe sampling measures lead loading directly, but does not measure lead concentration and dust loading, the results from wipe sampling cannot be used to determine which combination of lead concentration and dust loading is present. Similarly, Davies et al. (1990) states that for a given contaminant loading value, the contaminant concentration can range from high where there is little

dust to, conversely, low where there is a large volume of dust. The only way to measure both lead concentration and dust loading is to collect a house dust sample with one of the vacuum sampling methods, or with one of the preweighed wipe sampling methods. Common wipe sampling methods do not measure lead concentration.

Although research studies have shown that estimates of both lead concentration and lead loading (area concentration) correlate significantly with children's blood lead levels, it is unclear which measure is better at predicting the true, long-term, lead dust exposures to children. Results from Davies et al. (1990) suggest that the average lead loading (lead area concentration) measured in a child's environment expressed more realistically the exposure of children to lead than did lead concentration (lead mass concentration) measurements. Results from the Lanphear et al. (1995) study also suggest that lead loading measurements correlate better with children's blood lead levels than does lead concentration. However, Bornschein et al. (1985) showed that, for their conditions, lead concentration and lead loading have very similar correlations with

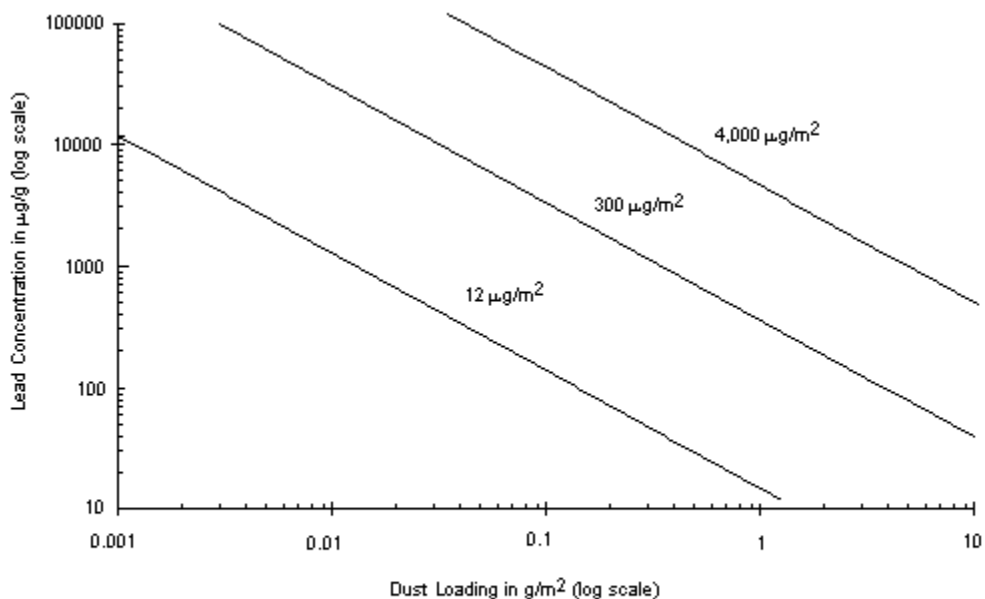


Fig. 24. Three wipe sampling results from a hypothetical residence. Theoretical relationship among lead loading, lead concentration, and dust loading (Diagonal lines represent constant lead loading values)

children's blood lead levels. Laxen et al. (1987) found that blood lead levels did not correlate better with lead dust loading than with concentration.

8.3.2 Collection efficiency

Another important concept to understand is that the type of surface from which the dust is sampled directly affects the efficiency of dust collection from the surface. Furthermore, different sampling methods recover different amounts of total dust from the same sampled surface. These differences are due to different collection efficiencies of the methods. Differences in collection efficiency on different surface types and among sampling devices may influence

measurements of toxicant levels in settled dust.

Roberts et al. (1991) documented total dust recoveries that ranged from greater than 90% by weight on a smooth painted surface to about 30% on a carpet. Chavalitnitikul & Levin (1984) compared several types of wipe sampling methods. They conducted a laboratory wipe sampling experiment with wipe materials on a smooth surface (Formica) and a rough surface (plywood). The study examined different wipe materials, such as Whatman filters, paper towels and adhesives -- paper labels, adhesive cloth and dermal adhesive. The researchers determined that, on smooth surfaces, all techniques were comparable, with about 85-90% recovery with carefully prescribed protocols. On plywood, however, recoveries dropped to less than 43%. They also noted that the Whatman filters fell apart on the rough surface. Other sampling method characterization studies document similar differences (US EPA, 1995a,b).

Three commonly cited methods used to sample lead in settled dust (the DVM, BRM, and HUD methods) may collect very different amounts of total dust from the same surface (Lanphear et al., 1995). Assuming that a smooth hard surface is sampled, the difference in collection efficiency between the DVM and the other two methods may be greater than a factor of 10, with the DVM consistently collecting less dust than the BRM and HUD methods. The latter two methods would probably collect similar amounts of dust on a smooth hard surface.

Since contaminant loading is directly related to total dust collected from the sampled surface, the DVM sampler will consistently measure lower contaminant loading values on hard surfaces than the BRM or HUD methods. This does not imply that a high collection efficiency is better than a low efficiency. An argument in favour of the DVM's low collection efficiency is that it measures the more biologically active fraction of leaded dust available to a child (Que Hee et al., 1985). However, results from the only study to use all three methods side by side in children's homes suggest that the BRM and HUD methods correlate slightly better with children's blood lead levels than the DVM method (Lanphear et al., 1995). The same study showed that the BRM collects much more dust from carpeted surfaces than the DVM or HUD methods. The point to note is that lead loading measurements on the same surface differ among sampling methods. Further research is needed

to determine the importance of collection efficiency for exposure assessment studies.

As with contaminant loading, differences in collection efficiency on different surface types and among sampling methods may affect measurements of contaminant concentration. Differences in the relative recovery of contaminant-containing dust and non-contaminant-containing dust can result in different contaminant concentration measurements. Theoretically, however, concentration measurements are likely to vary less among methods than are loading measurements. Results from the Lanphear study, which collected hundreds of side-by-side lead dust samples with the DVM and BRM methods, are consistent with this theory. Geometric mean lead levels and the corresponding standard deviations suggest that, on average, side-by-side lead loading measurements differ more between the two sampling methods than do the lead concentration measurements (Lanphear et al., 1995).

8.4 Sampling strategies

Choosing an appropriate sampling method is an important part of designing a study to measure toxicants in house dust. However, it is only part of designing a sampling strategy. The sampling method specifies how to collect settled dust, whereas the sampling strategy specifies the process of sampling. Several of the questions that need to be answered when developing a sampling strategy are:

- * What age group is targeted by the study?
- * Which surfaces and substrates should be sampled?
- * When and how should sampling take place?
- * Should a composite sample be created?
- * How will the samples be analysed?

As noted in the first section of this chapter, young children who play on floors are likely to have higher exposure to settled dust than adults. Children may be also routinely exposed to dust in areas of a residence that adults do not contact. Different sampling strategies may be appropriate for different age groups.

The potential effect of the surface type and substrate on dust collection should be factored into the strategy because dust collection efficiencies from different surface types can vary greatly. For example, toxicant loading or concentration measurements may correlate relatively well with biological measurements when dust is collected on hard floors or on carpets. However, if the person's relative exposure to dust from floors versus carpets differs from the sampling method's relative collection efficiency on these surfaces, the relationship between biological and settled dust measurements will be different for each surface. Similar differences between a human's exposure and a sampling method's collection efficiency may be found

between components within a room, such as between a windowsill and a floor.

Another issue to note is that the sources of dust, its temporal and spatial variability, and accessibility to humans, especially to young children, may vary greatly from person to person, room to room and house to house. However, little research has been done to examine this variability across space and time. Interpretations of house dust sample results may, therefore, be affected by this variation in addition to the variation introduced by the choice of sampling method. Short-term changes in a person's environment before sampling, possibly influenced by sporadic house cleaning practices or by a person who has just returned home from vacation, may offset the dust/biological relationships owing to the timing of sample collection.

The toxicant levels in settled dust to which a person is exposed may be thought of as a weighted average across the areas where the person has dust contact, with weights roughly proportional to the time a person spends in different areas. From a sampling perspective, the average toxicant level to which a person is potentially exposed may be estimated by collecting many individual samples of settled dust for separate analysis and combining the results by calculating a weighted average after analysis. Or, field composite samples can be collected before laboratory analysis by collecting and physically combining two or more settled dust samples from each of several areas in a dwelling.

Researchers have used both strategies for collecting dust samples (Farfel & Rhode, 1995).

A common criticism of composite sampling is that toxicant variation across a floor or throughout a residence cannot be determined; toxicant "hot spots" may be missed. It must be acknowledged, however, that any settled dust sampling strategy may miss hot spots. The important issue is how much these hot spots contribute to the total exposure of the average person. This question has not been answered by scientific studies. In any case, the statistical relationship between biological toxicant levels and average toxicant levels in settled dust levels across large areas in which a person may be exposed are likely to be better than the relationship between biological levels and a potential high-dose source of toxicant exposure for a short period of time. Davies et al. (1990) used this assumption to design a sampling strategy that collected settled dust "taken over all the exposed floor surface in the rooms concerned" (thus, the average level was measured in a room) rather than from small areas in the room, and found a relatively high statistical relationship with children's blood lead levels ($r = 0.46$).

Possibly the best measures of toxicants in settled dust for exposure assessment purposes are averages of dust measurements taken repeatedly over time. If one were to repeat sampling over time, averages across space and time could be obtained. However, most sampling strategies used in previous studies collected settled dust at only one point in time. An obvious advantage to cross-sectional (one time) studies is that they are less expensive than longitudinal (repeated measures) studies, which require repeated visits to a dwelling, greater occupant burden, and higher laboratory analysis costs.

One possible, but untested, approach to strengthening estimates of time-weighted average dust levels in cross-sectional studies may be to measure exposure-weighted average levels based on the activity of the person. This may be done by listing indoor locations where the person spends time, then roughly estimating the percent of time spent actively in each location, rounded to a convenient percentage. Samples can then be composited from the specific areas by adjusting the subsample areas to be proportional to the percent of time spent in each area. An exposure-weighted average toxicant dust level could then be estimated from the result.

Finally, laboratories performing the chemical analysis should be consulted before settled dust samples are collected. This is particularly true when collecting composite wipe samples. An excess of towelette material may present problems during the laboratory digestion phase of analysis, requiring more reagents and larger beakers than normally used, and potentially reducing the toxicant recoveries owing to matrix effects. Similarly, vacuum sampling may collect more dust than is required for analysis. If this is the case, techniques need to be employed by the laboratory to ensure that the fraction of dust analysed represents the whole. Another potential source of error in the results lies in how the dust is handled after sampling and prior to analysis. If measurements of lead concentration in dust are important for the objectives of the study, sampling methods that present the dust to the laboratory in an easy-to-handle form should be considered over alternate methods. These issues and

others should be well thought out before the commencement of a settled dust sampling effort.

8.5 Summary

Human contact with soil and settled dust can be an important source of exposure to chemical contaminants, especially for children. Although many sampling methods have been developed, no single approach has been demonstrated to be superior to the others. As a consequence, it is difficult to compare results from studies that utilize different sampling methods. Important factors to consider when selecting a sampling method include collection efficiency, differences in human activity patterns, physical variability of soil and dust levels over space and time, surface and substrate sampled, timing of sample collection and analytical methods used to measure toxicants in the laboratory.

9. MEASURING BIOLOGICAL HUMAN EXPOSURE AGENTS IN AIR AND DUST

9.1 Introduction

Microbiological organisms have long played an important role in human ecology. Fungi are critical to the production of cheese and the fermentation of beer, and in some cases are a direct source of nourishment. In the first half of the 20th century, *Penicillium chrysogenum* colonies were discovered to inhibit growth of other organisms. Today pharmaceutical companies, among others, are exploring fungal enzymes for a variety of reasons including new drugs, non-chemical pesticides, biodegradation of waste and possible catalysis of chemical reactions.

However, natural does not mean benign. Human exposures to microorganisms have resulted in allergic, toxic and infectious disease. As humans have modified the environment through cultivation, landscaping and building structures, ecological balances have been disturbed. The distribution of moisture and nutrients has been altered to a point where it is quite common to encounter reservoirs of fungi, bacteria and algae, and infestations of mites and cockroaches.

Through airborne dispersion, ingestion or direct contact, humans confront components of microorganisms continuously. We may be affected through an immune reaction requiring sensitization. Predisposed individuals may not experience a reaction for some time after they have been exposed. Once an individual is sensitized, a reaction such as an asthmatic attack might be delayed hours following the exposure event. However, there are many infectious diseases induced by fungi and bacteria that require no period of sensitization before illness develops. There is yet another route whereby microorganisms can evoke irritation and health effects: some metabolites from moulds are carcinogenic (e.g., aflatoxin B) or immunosuppressors; some cause dermatotoxic effects; others cause annoyance and irritation by the VOCs they release.

Table 31 provides basic categories for the microorganisms of primary interest and some possible sources. Assessing exposures to microorganisms is very different in some aspects from assessing exposures to physical or chemical agents. For virtually all microorganisms, exposure-response or dose-response information is currently limited. Nevertheless, exposures to allergens, fungal spores, *Legionella*, and tuberculosis, among many others, are being

inferred from sampling. And, particularly for assayable antigens and endotoxin, dose-response data are accumulating rapidly. Observed increases in tuberculosis and asthma as well as atopy have brought a resurgence of epidemiology and expanded interest in exposure assessment.

Table 31. Common bioaerosols, related diseases and typical sources

Bioaerosol	Examples of diseases	Common sources
Pollens Spores Plant parts	hay fever allergic rhinoconjunctivitis asthma upper airway irritation	plants, trees, grass shiploading
Fungi	asthma, allergic diseases infection toxicosis tumours	plant material, soil animal droppings; glues, wool
Bacteria	endotoxigenesis tuberculosis pneumonia, respiratory and wound infections, legionellosis, Q and pneumonia	humans, birds and dental secretions water sprays and pools, drinking water
Other allergen sources Arthropods Vertebrates	asthma dermatitis hypersensitivity pneumonitic	mite excreta, insect moths, midges dander and saliva mice and rats, birds
Viruses ^a	respiratory infections, colds, measles, mumps, hepatitis A, influenza, chicken pox, Hanta virus	infected humans, animals insect vectors, plants

^a Viruses are included in table for completeness but are not covered in this chapter.

^b Protozoa in the form of free-living amoebae can be direct acting pathogens or interact with bacteria (e.g., *Legionella* growth within amoebae).
Source: developed from Burge (1995).

This chapter discusses the strategy and methodology for exposure assessment of five major categories of biological particles:

- * house dust mites and their faeces
- * allergens from pets and cockroaches
- * allergens and/or toxins derived from
 - fungi
 - bacteria
 - pollen

For each category information will be presented regarding

sampling methods, methods of analysis, and advantages and drawbacks of the different methods. Seasonal variations in mite allergen and fungi are illustrated by showing the summary results of an extensive survey conducted in Australia. Mite and pollen antigen as well as fungal organisms can vary substantially within homes and buildings, as illustrated in the figures in this chapter. The reader is referred to texts such as ACGIH (1989) and Burge (1995) for details on instrumentations, specific information relevant to the allergenic, infectious and toxigenic properties of many microorganisms and their constituents and metabolic by-products.

There are three different basic approaches for the exposure assessment of biological particles: observational sampling, reservoir sampling (dust, surfaces, water) and air sampling.

- * *Observational sampling* means that one uses sensory perception to collect data about potential sources of exposure to biological particles (e.g., visible fungal growth).
- * *Reservoir sampling* refers to the collection of bulk material (e.g., surface contact, bulk material, water sample or dust sample) to estimate the potential exposure.
- * *Air sampling* is the most likely to be representative of human exposure.

This chapter will emphasize reservoir (primarily indoor dust) and air sampling of bioaerosols and not gaseous metabolic products.

Designing a specific sampling programme requires consideration of the aim of the sampling, the nature of the biological particles (including size and expected concentrations) and parameters that influence the actual exposure to these particles. These parameters determine the choice of the sampling and quantification method, the sampling strategy (e.g., location, season, duration and frequency), and approaches for statistical analysis and interpretation of the data. For most situations, the exposure route of interest is inhalation. Therefore, ideally, the exposure should be assessed by

personal air monitoring. As will become clear from the remainder of this chapter, however, no single sampler fulfils the characteristics of the ideal sampler to measure the total exposure to biological particles. Many of the methods used for estimating environmental concentrations of biological particles are not truly representative of an individual's exposure to these particles. As stated earlier, this is, in part, because the exposure measure of biological importance is not well understood. In addition, the field of environmental aeromicrobiology developed from a laboratory biology base that borrowed sampling techniques and equipment from other fields. Until recently there had been little convention or need for uniformity of methods. It is not surprising, therefore, to find a general lack of data regarding the validity of the methods used to estimate the exposure to biological particles. This situation has certainly changed as those investigating exposure assessment aspects of aerobiology have cooperated with environmental epidemiologists.

Useful reference texts with regard to sampling and analysis of biological particles include those by the American Conference of Governmental Industrial Hygienists (ACGIH, 1995), the European Commission (EC, 1993), Hamilton et al. (1992), Pope et al. (1993),

Burge (1990, 1995), and Burge & Solomon (1987), Reponen (1994), and Verhoeff (1994a,b).

9.2 House dust mites

House dust mites are members of the arachnid family having eight legs and an exoskeleton. They can be up to 300 μm in length and live off organic debris found in house dust (e.g., skin flakes, hair follicles and fungi) (Colloff, 1991). Because mites absorb water vapour they are critically dependent on the absolute humidity. Survival in the adult stage requires environmental moisture conditions be sustained not lower than 7-8 g/m^3 (Korsgaard & Iversen, 1991; Fernandes-Caldas et al., 1994). This is equivalent to a relative humidity of about 50% at 20°C.

Mite antigen is mainly found in the faecal pellets which may be 10-20 μm in diameter and will not remain suspended for very long. Feather et al. (1993) identified enzymes derived from the mite gut as the source of allergens. These enzymes might remain as potent allergenic material in bedding, mattresses, carpets and furnishings long after the mite population has diminished, further complicating exposure determination.

Two different approaches, the sampling of air and of settled dust, are available to measure the presence of house dust mites and their allergens as indicators of environmental exposure. The latter is the most commonly used approach.

9.2.1 Air sampling for house dust mites

Several techniques exist for volumetric sampling of airborne mite allergens, using cascade impactors or high- and low-volume samplers in combination with membrane filters (Swanson et al., 1985; Price et al., 1990; Sakaguchi et al., 1993; Oliver et al., 1995). These techniques have the advantage that they sample airborne allergens and might therefore be more representative of the true exposure than assays of settled dust. The literature is limited, however, on the validity of air sampling as measure of exposure to house dust mite allergens (Swanson et al., 1985; Price et al., 1990; Sakaguchi et al., 1993), and further research is needed.

Mites themselves are not seen in air samples. Furthermore, in undisturbed rooms amounts of airborne mite allergens are small and difficult to detect, even after prolonged sampling. Most of the mite allergens bind to faecal pellets, which become airborne only as a result of disturbance, and little allergen is associated with particles that remain airborne for more than a few minutes. Therefore, practical disadvantages of airborne sampling of mite allergen are the requirements for long sampling periods (2-24 h) and very sensitive assays (Thien et al., 1994). Price et al. (1990) used a low-volume air sampler (2 litre/min) for 3 h to sample suspended dust mite allergen in homes. They reported that the airborne allergen levels correlated better with sensitization to mites among children than the levels in dust. Further, the air and dust antigen levels were not correlated. Although this is the only study linking atopy to airborne mite allergens, it does suggest potential limitations of using dust sampling as a surrogate exposure measure. In a small number of studies, air sampling and dust sampling were carried out in parallel (Price et al., 1990; Sakaguchi et al., 1993; Oliver et al., 1995). In only one study were significant correlations found between the levels

of house dust mite allergens in air and dust (Oliver et al., 1995). Allergenic responses to dust mite allergens may be induced by short-duration high-concentration exposure events. Therefore, the clinical importance of integrated air samples may be more relevant in predicting prevalence of atopy to mites rather than predictive of acute health effects.

At present no reliable information is available that will support adoption of a standardized method for air sampling of house dust mite allergens. According to an international workshop held in 1987 (Platts-Mills & De Weck, 1989) airborne sampling has not been shown to be better than dust sampling to measure the level of mite infestation in homes or schools. This was confirmed by a second international workshop in 1990 (Platts-Mills et al., 1992). It was also stated that there are few or no data showing a relationship between airborne measurements and sensitization to house dust mites or symptoms. In contrast, a relationship is apparent between the concentrations of mite allergens in settled house dust and sensitization or symptoms. Therefore, air sampling was not recommended (Platts-Mills et al., 1992).

9.2.2 Dust sampling for house dust mites

Dust sampling for measurement of the level of mite infestation is accepted and recommended as the best-validated "index of exposure" to house dust mite allergens. The approach assumes that the quantity of allergens released into the air is a function of what is present in settled dust, or, conversely, that the measurement of allergen in settled dust is related to both the long-term dose a person receives and to the short-term airborne levels experienced during events that raise dust.

Standardized sampling procedures to measure house dust mites and their allergens in house dust have been proposed (Platts-Mills & De Weck, 1989; Platts-Mills et al., 1992; EC, 1993; Dreborg et al., 1995). Sampling sites should be consistent throughout the study and preferably include the upper mattress surface and the floors of the living room and bedroom. Sampling can be conducted with vacuum cleaners equipped with a special attachment to collect dust on a paper filter. Vacuuming 1 m² of surface in 2 min is a commonly used sampling method. Depending on experiences with the amount of dust recovered in specific situations, investigators may have to modify the sampling procedures. Samples can also be obtained from upholstered furniture, soft toys and clothing. Alternative techniques for collecting dust samples include shaking blankets in a plastic bag and scraping flat surfaces higher than floor level with a piece of firm card. However, these techniques are less effective than collection by vacuum cleaner and not standardized. The dust samples may be sieved before analysis to obtain a sample of fine dust that can be weighed accurately. Unfortunately, dust samples may still vary in density after sieving. An alternate method for sampling airborne mite allergens is to collect settling dust on large Petri dishes over a period of 14 days (Tovey et al., 1992; Oliver et al., 1995). Brown (1994) developed a variation on the integrated settling method. A 100-cm² piece of sticky tape is placed in contact with the surface for 24 h. Under low-power magnification (36×), the trapped mites are counted. Using an empirically derived collection efficiency of 30%, the number of live mites per area is estimated. However, this does not reflect the true extent of exposure to mite allergens (see section 9.2.3.1).

9.2.3 Available methods of analysis for house dust mites

There are three types of method for estimating the concentrations of house dust mites or their allergens in (airborne) dust samples: mite counts, immunochemical assays of mite allergen and guanine determinations. The choice of a particular method depends on the specific purpose of a study.

9.2.3.1 Mite counts

The prevalence of mites in settled house dust can be determined by counting under a microscope after separation from the dust sample by flotation or suspension. This technique permits the identification

of the predominant species and the recognition of live, dead, larval or adult types. The disadvantages of this method include:

- * the need for training and development of skill in determining different mite species
- * the failure to quantify faecal pellets and disintegrated mite bodies and therefore to reflect the true extent of exposure to mite allergen levels
- * the unsuitability for large-scale (epidemiological) studies owing to the time-consuming nature of the work (Platts-Mills & De Weck, 1989; EC, 1993).

A further limitation of this method is variation among the actual extraction techniques. Bischoff et al. (1992) estimates that less than 10% of the mites are removed from the carpet by typical vacuuming techniques, but this number varies with the type of surface, the type of vacuum used and the vacuuming technique.

9.2.3.2 Immunochemical assays of dust mite allergens

Immunochemical assays are widely used to measure the concentrations of house dust-mite allergens. The dust mite germ is *Dermatophogoides* and allergens have been identified for three species. The conventional labelling of these allergens are denoted by the prefix "Der" followed by a letter indicating the species. These assays are possible because the major allergens produced by house dust mites, i.e., the group 1 allergens (Der p I, Der f I, Der m I) and the group 2 allergens (Der p II, Der f II, Der m II) are well characterized and purified. For immunochemical analysis, the dust sample is extracted (e.g., in a buffered saline solution), and then stored frozen until analysis.

Total mite allergen content can be assessed by radioallergosorbent tests (RAST). This method provides a good estimate of the relative potency of different allergen extracts, but cannot be used for absolute quantification of mite allergen levels. An advantage of the method is that it measures "relevant" antigenic determinants that have elicited a response in allergic subjects, since human IgE is used. Results vary with the composition of the extract used on the solid phase and with the composition of the serum pool used for detecting bound allergen. However, RAST inhibition results are difficult to reproduce over an extended period of time.

Individual mite allergens can be measured with enzyme-linked immunosorbent assays (ELISA) or radioimmunoassays (RIA). Sandwich radio- or enzyme immunoassays employ either rabbit polyclonal or mouse monoclonal antibody for capture, and a second monoclonal antibody for detection (see Fig. 25). These assays are more sensitive than RAST. Those using monoclonal antibodies in particular have also the great potential advantage of long-term reproducibility. Furthermore, ELISA assays have been shown to be highly reproducible (e.g., Munir et al.,

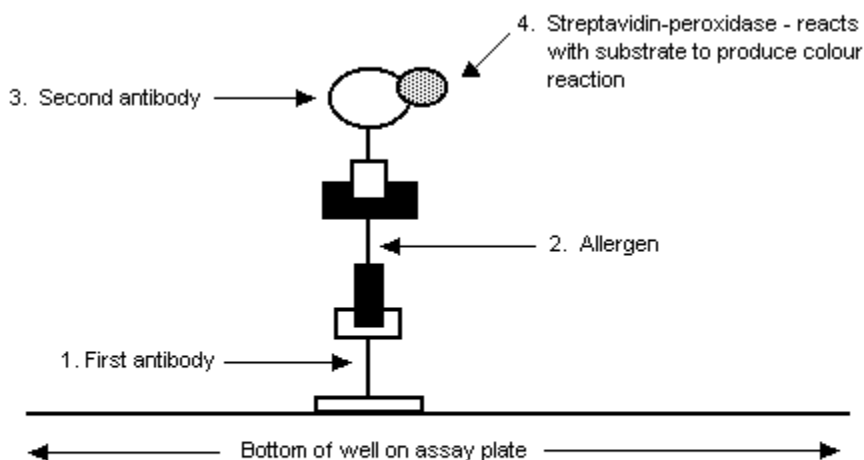


Fig. 25. General diagram of ELISA method for detecting dust mite antigens. This assay uses "designer" antibodies that bind specifically to the allergen of interest

1993; Van Strien et al., 1994) and can quantify antigen levels to less than 1 ng/mg dust.

Immunochemical assays are highly specific and the results obtained with these assays can be expressed in absolute units of a defined protein by unit weight of dust or by unit area sampled. They are suitable for large-scale surveys because they can be automated. However, a sophisticated laboratory is required.

9.2.3.3 Guanine determination

The third possibility is the measurement of guanine, which is a nitrogenous excretory product of arachnids, found in house dust. Since mites are predominant among arachnids in house dust, determination of guanine content in the dust is an indirect method for assessing mite allergen levels. Analysis of guanine content is based on a colour reaction between guanine and an azo compound (Le Mao et al., 1989; Hoyet et al., 1991). The amounts of guanine can be measured quantitatively on a weight/weight basis using a spectrophotometer, or semiquantitatively using a commercially available test kit (Pauli et al., 1995). The quantitative assay has been reported to demonstrate a good correlation with the assay of Group 1 allergens (Platts-Mills et al., 1992), whereas the semiquantitative test was found to be less sensitive (Lau et al., 1990).

9.2.4 Mite allergens

Sampling strategies may vary depending on objectives but most

studies collect vacuum samples using a protocol that, at least internally, standardizes equipment, area, duration and location. Mites are typically found in higher concentration in bedding. Typical areas

would include mattresses, pillows, blankets and bedroom floors. Because of spatial variability, mixed floor samples can be used. Other areas of high use include living room, upholstered chairs and couches, and covered floors. Bischoff et al. (1992) describes an approach used to avoid depletion of the dust reservoir during routine and repeated sampling.

Mite-antigen levels have been shown to vary with season, reflecting the moisture and temperature dependency controlling mite development stages. Garrett (1996) conducted a yearlong study in 80 homes in eastern Australia. Fig. 26 reveals the temporal variation in Der p I, the prominent allergen. The allergen levels in dust collected from the bedroom and living room are higher during the warmer and more humid months of the year. Garrett (1996) has shown that the allergen level for Der p I is consistently higher in dust collected directly from the bedding. The between-home variation is quite apparent, ranging over almost two orders of magnitude. Examining Fig. 27 offers an explanation for the higher levels of greater variability in the allergen levels recovered from the bedding dust. Mites survive better in mattresses with spring cones than in foam rubber. Presumably, less moisture is retained in the hydrophobic foam material. Also, wool sheets and blankets favour the growth and retention of mite antigens more than alternative bedding material. Other studies on mites in wool rugs suggest that the thermal properties of wool help mites to survive fluctuations in temperature and moisture and, perhaps, inhibit their removal.

9.3 Allergens from pets and cockroaches

For estimating the exposure to allergens derived from pets (e.g., cats and dogs), and cockroaches, the same approaches are available as for house dust mites and their allergens (i.e., the sampling of air and dust). The major allergens of the cat (Fel d I), dog (Can f I), and the German cockroach (Bla g I, Bla g II), and the American cockroach (Per a I), have been characterized and purified (Chapman et al., 1988; Pollart et al., 1991a; Schou et al., 1991, 1992). Research is still in progress to further unravel the structure of the allergens derived from pets and roaches (and house dust mites) using techniques for allergen cloning and sequencing.

9.3.1 Air sampling for allergens from pets and cockroaches

Cockroaches are year-round inhabitants of homes. They need access to both food and water, so they are often found in kitchens and bathrooms. Unlike mites, where the antigen source is in faecal matter, cockroaches are thought to secrete their allergen on to their bodies and on to surfaces (Vailes et al., 1990). This means that body parts, egg shells, faecal particles and saliva might contain allergens (Lehrer et al., 1991).

Similarly, a wide range of materials derived from mammals contain potentially allergenic material, including hair, dander, serum, saliva, urine and faecal matter. Direct contact as well as inhalation

and ingestion can cause allergic reactions (Burge, 1995). Because of the popularity of cats and dogs as domestic pets, they have been the

subject of much of the work on mammalian allergenic reactions. Cat allergens from saliva and sebaceous gland secretions reside on particles less than 2.5 μm in size. Much of the dog allergen is believed to be associated with dander and hair, but saliva and serum are also important sources.

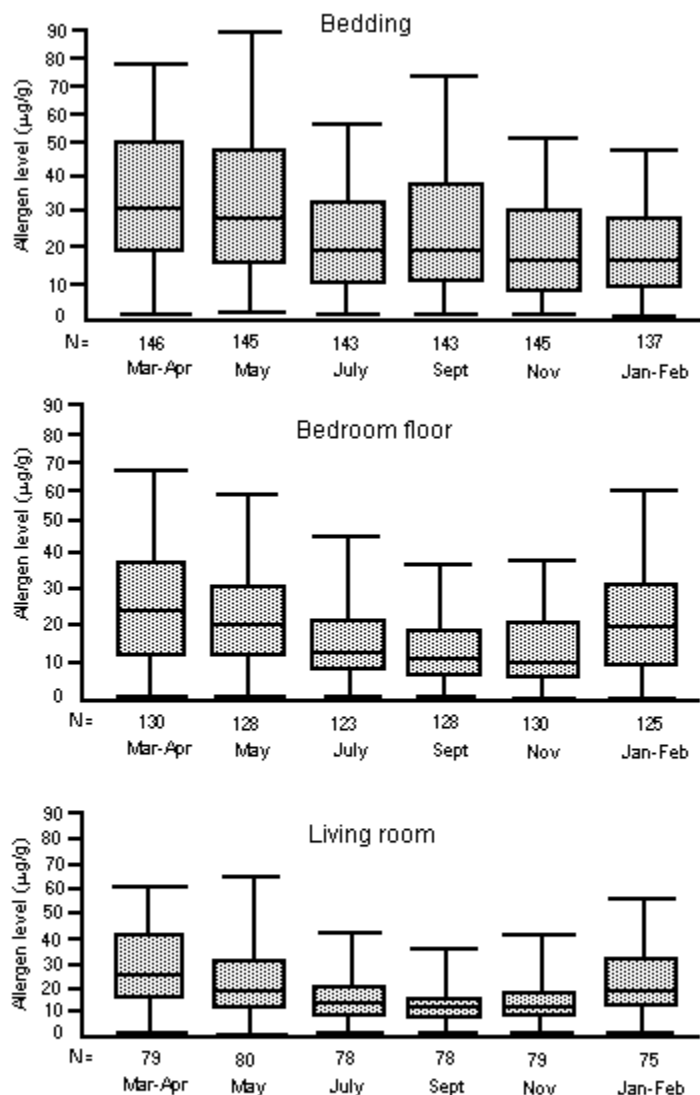


Fig. 26. Seasonal and between home variations in house dust mite allergen levels in bedding, bedrooms, bedroom floors and living rooms, by sampling period in eastern Australia (from Garrett, 1996)

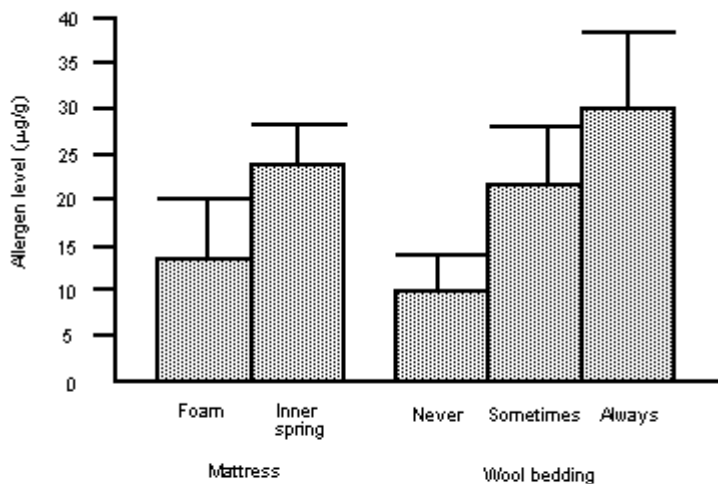


Fig. 27. Allergens (Der p I) levels in beds by mattress type, and use of wool bedding; geometric means with a 95% confidence interval (Garrett, 1996)

There are only limited data on the size ranges for airborne allergen particles from dogs, rabbits, rats and other animals. In general, however, saliva sources tend to be small (<2 µm) whereas dander and urine particles are larger (10 µm).

For the sampling of airborne allergens derived from cats, dogs and cockroaches, the same methods can be used as for the sampling of airborne mite allergens (see section 9.2.1). These allergens have been sampled using cascade impactors (Luczynska et al., 1990; De Blay et al., 1991), high-volume samplers in combination with fibreglass filters (Swanson et al., 1985; Sakaguchi et al., 1993) and liquid impingers (Luczynska et al., 1990).

As is the case for house dust mite allergens, only limited data have been published on the validity of air sampling as a measure of exposure to allergens derived from pets and cockroaches. At present there is no reliable information to support adoption of a standard method for air sampling of these allergens. Airborne sampling has not yet been shown to be a better estimation of the exposure to these allergens than dust sampling. Therefore, further research to compare the usefulness of air and dust sampling is needed.

9.3.2 Dust sampling for allergens from pets and cockroaches

The sampling of house dust to investigate the presence of allergens derived from pets and cockroaches can be conducted exactly as for house dust mites and their allergens (see section 9.2.2).

9.3.3 Available methods of analysis

Immunochemical assays (ELISA) are available for detection of the allergens derived from cats (Chapman et al., 1988), dogs (Schou et al., 1992) and cockroaches (Pollart et al., 1991b; Schou et al., 1991) in (airborne) dust samples. The allergens of the American and German cockroach (i.e., Per a I and Bla g I) were demonstrated to be immunologically cross-reactive proteins and can be measured in the

same assay (Schou et al., 1991). For immunochemical analysis, the dust sample is extracted (e.g., in a buffered saline solution), and then stored frozen until analysis.

The ELISA assays for Fel d I and Can f I were found to be highly reproducible (Chapman et al., 1988; Schou et al., 1992). For the Bla g I and Bla g II ELISA assays the intra- and interassay variability were also found to be small (Pollart et al., 1991b).

9.3.4 Typical allergen concentrations

Cat and dog allergens have been reported more often than allergens from other mammals. Homes with cats have dust levels of Fel d I exceeding 10 µg/g, whereas homes without cats have typically less than 1 µg/g. A provisional value of 8 µg/g of dust has been proposed as indicating significant exposure. Cat antigen has been found in dust samples collected in theatres, offices, aeroplanes, schools and homes without a cat. Because of its small particle size, cat antigen can stick to clothing and be transported to other locations. Dog allergens have not been as extensively examined for non-residential sites. Dybendal et al. (1989) has reported that dog allergen was present in homes and schools where dogs were not kept.

9.4 Fungi

Fungi are a large and diverse class of microorganisms. They live on organic nutrients and have no chlorophyll or internal organs. The cells that make up fungal colonies contain complex carbohydrate macromolecules. Fungi must produce spores or conidia for their reproduction. Spores are usually 2-20 µm in size and oblong in shape. In the appropriate setting, spores reproduce new organisms.

The two different approaches to assess the exposure to fungal particles are air sampling and dust sampling. For completeness, other approaches to "dust" sampling include lifting spores from a surface with sticky tape or direct contact with culture agar. The most commonly used approach is air sampling of culturable (viable) fungal particles.

9.4.1 Air sampling for fungi

Several techniques have been described for volumetric sampling of fungi in outdoor and indoor environments. Table 32 presents an overview of the techniques most commonly used for the sampling of fungal particles. Detailed information on the different sampling

devices can be found in ACGIH (1995). Some of the techniques give total counts of all airborne particles, viable and non-viable, whereas others only give counts of viable fungal particles (e.g., propagules or colony forming units (CFU)). A few methods are discussed that provide not only total counts, but also viable counts (e.g., filter samplers). The sampling efficacy of a bioaerosol sampler is both a physical and a biological problem. For air sampling of fungal particles the following physical sampling principles may be distinguished: impaction on to a solid or semi-solid surface (e.g., a culture medium or an adhesive), centrifugal impaction, filtration and liquid impingement.

Impaction on to a culture medium (e.g., for culturable fungi) is the most widely used technique, particularly in non-industrial indoor

environments. This process depends on the inertial properties of the particles, such as size, density and velocity, and on the physical parameters of the impactor, such as inlet-nozzle dimensions and airflow paths. Because of differences in characteristics, samplers differ in cut-off size (d_{50}) (e.g., the particle size above which 50% or more of the particles are collected). As most impactors have very sharp cut-off characteristics, almost all particles larger than the d_{50} are collected and d_{50} is therefore assumed to be the size above which all particles larger than that size are collected (Nevalainen et al., 1992). No sampler collects all particles with equal efficiency, and it is therefore not surprising that different quantitative and qualitative results are obtained using different sampling devices for culturable fungi (Verhoeff et al., 1990). The choice of the collection (culture) medium also affects the kinds and levels of fungi recovered (Verhoeff et al., 1990). No single collection medium will enable the entire range of viable fungi in the air to be isolated. Media which are generally accepted for aerobiological studies include malt extract agar (MEA), V8 juice agar and dichloran 18% glycerol agar (DG18) (EC, 1993; ACGIH, 1995). MEA and V8 agar are broad spectrum media, whereas DG18 is intended to be a selective medium for xerophilic fungi, but many of the common fungal species in air can also be isolated (Verhoeff et al., 1990).

Few published data are available on the validity (accuracy and precision) of the measurement of fungi in air as estimate of exposure. All commonly used cultural air samplers use short sampling periods, typically 30 seconds to several minutes (Table 32). The reproducibility of parallel duplicate samples and sequential duplicate samples is only moderate, both in terms of CFU/m³ and in terms of species isolated (Verhoeff et al., 1990). More importantly, repeated sampling within weeks has demonstrated that variation in time within homes is much higher than the variation between homes (Verhoeff et al., 1992). This means that a single air sample has only a low predictive value for exposure over time. Furthermore, the use of cultures for quantifying fungal particle concentrations in air samples will give an underestimate of the actual particle concentrations, and may cause significant fungal contamination to be missed altogether. The culturable fungal particles may comprise only a few percent of the

Table 32. Overview of sampling techniques for airborne fungal particles^a

Method with examples	Sampling rate and time	Rem
<u>Non-viable, non-volumetric</u>		
- settling surface, adhesive-coated	undefined, minutes to days	sem lar
<u>Non-viable, volumetric</u>		
- rotating tape/slide impactors Burkard trap	10 litre/min, 7 days	cut
- rotating arm impactors Rotorod sampler	47 litre/min, intermittent	cut
- filter methods cassette filters	1-4 litre/min, hours	via

high-volume filters	150-2000 litre/min, hours	fro
<u>Viabile, non-volumetric</u>		
- settlement plates	undefined, hours	sem lar
<u>Viabile, volumetric</u>		
- multiple hole impactors		
Andersen 6-stage sampler	28.3 litre/min, 1-30 min	cut
Andersen 2-stage sampler	28.3 litre/min, 1-30 min	cut
Andersen 1-stage (N6)	28.3 litre/min, 1-30 min	cut
Surface Air System sampler	90/180 litre/min, 20 sec-6 min	cut
Eight-stage personal impactor	2 litre/min, 5-30 min	cut
Burkard portable sampler	10/20 litre/min, 1-9 min	cut
- centrifugal impactors		
Reuter Centrifugal sampler (RCS)	ca. 40 litre/min, 20 sec-8 min	cut
Reuter Centrifugal Plus (RCS-Plus)	ca. 50 litre/min, 30 sec-8 min	cut

Table 32. (continued)

Method with examples	Sampling rate and time	Rem
- rotating slit-to-agar impactors		
Mattson-Garvin air sampler	28 litre/min, 5-60 min	cut
- liquid impingers		
single-stage all glass impingers	12.5 litre/min	cut
three-stage impingers	20 litre/min	cut

^a For detailed information see ACGIH (1995).

total number of fungal particles (Horner et al., 1994). Thus, in order to optimize the information available from air sampling, both types of particle should be sampled. However, even using the best available method, a large number of airborne spores will not grow in culture and cannot be visually identified with available methods.

At present, there is no standardized method for the sampling of airborne fungi, although the American Conference of Governmental Industrial Hygienists (ACGIH, 1989) and the European Commission (EC, 1993) have given recommendations. An outline for selecting a bioaerosol sampler is presented by the American Conference of Governmental Industrial Hygienists (ACGIH, 1995). Selection criteria include sampling location, form of recovered particles (intact or dispersed), the need for size separation and the expected concentrations of the particles.

9.4.2 Settled dust for fungi

Settled house dust can be sampled for viable fungi in exactly the same way as for house dust mites and their allergens (see section 9.2.2). The dust samples can be stored at room temperature but the analysis should be performed within a few days.

Few published data are available on the validity of the measurement of culturable fungi in settled dust as estimate of exposure. The results, both quantitatively and qualitatively, depend on the method of inoculation of the dust and on the culture medium used (Verhoeff et al., 1994a). The reproducibility of duplicate analyses in terms of CFU/g dust is acceptable, but in terms of species isolated only moderate. However, as is the case for air sampling, a single dust sample is a poor estimate of exposure to fungi over time (Verhoeff et al., 1994a).

9.4.3 Available methods of analysis for fungi in air

Air samples obtained with sampling devices collecting total fungal particles can be analysed by direct examination to obtain total counts of fungal particles. Samples collected on culture media have to be incubated to obtain counts of viable fungal particles. Dust can be plated either directly on to a culture medium or suspended and diluted prior to plating. Total counts of fungal particles in dust can also be obtained by partitioning into an aqueous two-phase system followed by epifluorescence microscopy (Strom et al., 1987).

Samples are incubated for at least 4 days; up to 7 days is the typical time needed for spores to generate identifiable colonies. The temperature at which samples are incubated affects the recovery of culturable fungi. Since most environmental fungi grow well between 20°C and 30°C, the incubation temperature is generally 25°C (EC, 1993).

Sporulating colonies are identified by colour and texture, by the naked eye or microscopically. Non-sporulating spores might be transferred to different agar and exposed to different lighting in an attempt to colonize them. Fungal genera are sometimes reported and provide important insight into sources and possible health effects. Common outdoor fungi are *Cladosporium*, *Alternaria*, *Botrytis* and *Epicoccum*. *Penicillium*, *Aspergillus* and *Stachybotrys* can be found in higher concentrations indoors. It is difficult to generalize and there is considerable variability over time so it is important to simultaneously collect outdoor samples. Fig. 28 shows the distribution of viable mould spores collected inside and outside homes in Australia (Garrett, 1996). Outdoor viable spore counts decrease in the winter and so do the indoor levels for homes without substantial sources of sporulating fungi.

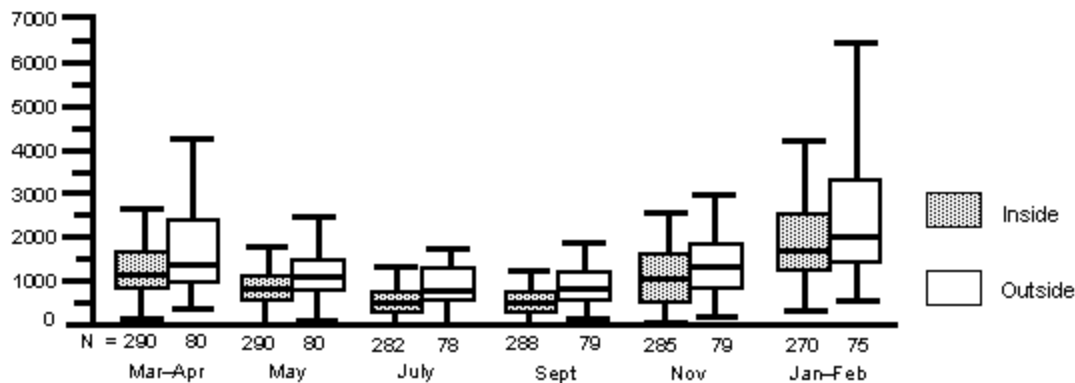


Fig. 28. Viable mould spore concentration (CFU/m³) by location and sampling period (southern hemisphere). Outliers are not shown (Garrett, 1996)

Immunochemical assays for fungal allergens are available for only a few fungi, primarily because fungal allergens are poorly characterized and purified. Alternative indicators of exposure to fungi, to be measured in (airborne) dust, may also be considered. For example, one can assess the levels of cell wall components such as β -1,3-glucan (Rylander et al., 1992), or ergosterol, a membrane steroid (Horner et al., 1994), or extracellular polysaccharides (EPS) (Kamphuis et al., 1991). Immunochemical assays (ELISA) are presently being developed to measure these components in (airborne) dust. However, in one study by Miller et al. (1988), ergosterol in house dust correlated with CFU/m³ in the air and Saraf et al. (1997) have shown ergosterol in house dust correlated with fungal CFU/g in the dust samples. In addition, Abramson et al. (1996) showed an association between ergosterol and atopy in adults.

9.4.3.1 Total counts of viable and non-viable fungal particles

Total counts of fungal particles can be obtained by counting with a light microscope. If more detail is required, the samples can also be viewed with a scanning electron microscope (SEM) or a direct epifluorescence microscope. These techniques cannot be recommended as giving a good assessment of the composition of air spora because only fungi with distinctive spores can be identified. It is often difficult to identify the fungal spores to species or even genus. As indicated above, filter methods may be used not only to give total counts (e.g., by direct epifluorescence microscopy), but also to obtain counts of viable fungal particles by plating washings from the filter. Furthermore, filter samples may be analysed for mycotoxins, EPS and glucans or tested for toxicity. The same applies for samples of settled dust.

9.4.4 General considerations for fungi

Since fungi vary so widely it is difficult to generalize about the presence of fungi in outdoor and indoor air. In temperate climates, outdoor spore counts are highest during and just following the growing season. Tropical climates show less variation by season. Garrett's (1996) doctoral thesis provides a useful comparison of viable mould spores from studies conducted in different climates.

Spore counts can vary greatly indoors for several reasons including the presence of colonizing fungi. Fig. 29 illustrates this point. The figure shows the mean values of CFU per culture plate for four fungal taxa and all others collected during the summer in nine Portage, Wisconsin (USA) homes. Living room and bedroom samples reflect the taxa found outdoors. The basement samples show *Penicillium* and *Aspergillus* fungi which grow favourably in damp areas (Burge, 1990).

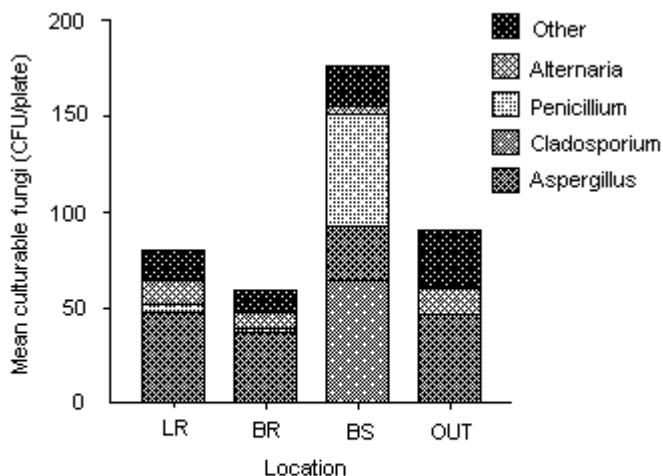


Fig. 29. Taxon prevalence in air of living rooms (LR), bedrooms (BR), basements (BS), and outside (OUT) of nine homes in Portage, Wisconsin (USA), summer 1987 (from Burge, 1990)

In addition physical activity, such as vacuuming, starting an air-conditioning fan, children playing on a carpet or changing a filter, might raise spore concentrations by a factor of 10 or more. Even without mechanical disruption, periodic shedding or ejection of spores from growing fungi might similarly elevate concentrations.

9.5 Bacteria (including actinomycetes)

Bacteria are prokaryotic cells. Certain bacteria are infectious and can be transmitted by air and contact, including ingestion. Common contagious airborne diseases include tuberculosis and some forms of pneumonia. Other diseases, such as legionellosis from water, respiratory infections from *Pseudomonas* in humidifiers and several others from handling animals are not transmitted from person to person.

Sampling and identifying specific bacteria is very important in many settings, especially in hospitals with immune-compromised and immune-suppressed patients. There are numerous other situations where infectious diseases have been transmitted by airborne bacteria. These include tuberculosis transmission in aircraft, and *Legionella* transmission in hospitals, in hotels, in supermarkets and on cruise ships or even in buildings in locations affected by cooling tower mist. The two approaches available to measure the presence of bacteria as indicators of exposure are sampling of air and sampling of soil, dust or water.

9.5.1 Air sampling for bacteria

Most of the air sampling devices listed in Table 32 can also be used for bacteria. The most widely used devices for bacteria include multiple-hole impactors, centrifugal impactors and slit-to-agar impactors, provided with collection media suitable for viable bacteria. For sampling airborne viable bacteria, the same limitations apply as for viable fungal particles. Thus, the results, both quantitatively and qualitatively, will depend on the sampling device and collection medium used. A single air sample has only a low predictive value for exposure over time (EC, 1993). Media that collect viable bacteria include tryptone soya agar, tryptone yeast glucose agar, soybean casein digest agar, and nutrient agar (EC, 1993; ACGIH, 1995). To prevent fungal growth, a suitable antimycotic may be used (e.g., cycloheximide). For specific groups of bacteria, selective media could be employed, such as half-strength nutrient agar for thermophilic actinomycetes.

9.5.2 Dust sampling for bacteria

The sampling of settled house dust for bacteria can be conducted in exactly the same way as for house dust mites and their allergens (see section 9.2.2).

9.5.3 Available methods of analysis for bacteria

Air samples obtained with sampling devices collecting total bacteria can be analysed by direct examination. Samples collected on culture media have to be inoculated to obtain counts of viable bacteria. Dust can be plated either directly on to a culture medium or suspended and diluted prior to plating. Dust can also be analysed for total bacteria counts. Furthermore, an assay is available to measure endotoxin content of (airborne) dust. Gram-negative bacteria contain endotoxins as integral components of their outer membrane. Endotoxins are potent biological agents.

9.5.3.1 Total count of viable and non-viable bacteria

Total counts of bacteria, with some information on shape, can be obtained from some samples, for example, water and air, using epifluorescence microscopy (most commonly, with acridine orange). This method becomes less reliable as the amount of debris in the sample, both organic and inorganic, increases. More detail on bacterial shape is obtained using a scanning electron microscope but quantitative results are less reliable. Filter samples can also be used to obtain counts of viable bacteria, with subsequent taxonomic differentiation if desirable (using Gram staining and other biochemical tests). Filter samples can be analysed for endotoxin as well (see below).

9.5.3.2 Viable bacteria

Environmental samples are usually incubated for 2-7 days at 25°C or 37°C. For bacteria, as with fungi, the incubation temperature affects the recovery. Most environmental bacteria grow well between 20°C and 30°C, and more species were recovered with incubation at 20°C than at 37°C (Hyvarinen et al., 1991). Therefore, it is recommended that plates be incubated at room temperature (20-25°C) and examined daily for several days (EC, 1993). For isolation of human pathogenic organisms, plates can be incubated at 37°C, and for thermophilic

actinomycetes at 55°C. After incubation the number of colonies is counted and expressed as CFU/m³.

9.5.3.3 Endotoxins

Endotoxins are a group of lipopolysaccharide (LPS) molecules making up the outer membrane of Gram-negative bacteria. Specific LPS macromolecules that exist in the cells or as fragments of cell structures are known to cause fever, malaise, respiratory distress and a variety of biochemical changes in humans. Endotoxins are ubiquitous in nature but occur in high concentrations in particular industrial and agricultural settings. Cotton mills and industrial processes using recirculating water, waste-water collectors, humidifiers and swine barns are some locations where endotoxin contamination has been associated with respiratory disease (Milton, 1995).

Airborne and settled dust samples can be examined for the presence of endotoxins. The *Limulus* amoebocyte lysate (LAL) assay is commonly used to quantify environmental endotoxin (Walters et al., 1994; Douwes et al., 1995). The assessment of endotoxin exposure depends strongly on sampling, extraction and storage procedures (Douwes et al., 1995) and further validation studies are needed to adopt standard methods for sampling and analysis. Variation in the LAL reagent from lot to lot and between manufacturers may be a major cause of variation in results within and between laboratories (Saraf et al., 1997).

In airborne endotoxin, filter material and type of aerosol (e.g., cotton dust, machine oil or saline mist) will affect the binding of endotoxin to the filter. Walters et al. (1994) showed that polycarbonate capillary pore membrane filters were optimal. Any conventional air sampler can be used with filter cassettes. Glass impingers have been used as alternatives to filters. Fluids and bulk samples can be collected directly if care is taken to ensure the use of endotoxin-free glass or plastic ware with low binding affinity. Samples should be analysed promptly and preferably not frozen. Endotoxin (LPS) is removed by solubilizing in a buffer solution (after Milton, 1992). Sonication might be necessary to dislodge particles. Concentrations, as measured by the *Limulus* assay, are expressed as standard endotoxin units (EUs) which are defined as the potency of 0.10 ng of a reference standard endotoxin (EC6, US Pharmacopoeia).

9.6 Pollen

Most people associate pollen with the common experience of hay fever and seasonal allergic rhinitis. Although only 10% of flowering plants shed wind-borne pollen, there are locations and times when the ambient concentrations exceed 1000 pollen grains/m³. Pollen grains generally are spheroidal or somewhat elongated and have a very durable outer wall. Most airborne pollen is between 10 and 70 µm in diameter. Larger pollen grains (>200 µm) are more likely to be transported by insects. Weather conditions such as higher temperature and lower relative humidity and wind promote pollen emissions (Ogden et al., 1969; Hart et al., 1994; Burge, 1995). Plant lifecycle stage, daylight and moisture affect the time and rate of shedding. Flowering of most plants, trees and grasses is seasonal and therefore cyclic.

Although hay fever in association with plant pollen has been known for 175 years, the association of natural pollen with airway reactions and asthma has not been adequately studied. Most pollen

measurements have been conducted by independent observers using a variety of samplers.

9.6.1 Air sampling for pollen

Several techniques exist for volumetric sampling of pollen grains in indoor or outdoor air. Table 33 provides an overview of the devices most commonly used for the sampling of pollen. Detailed information on

the different sampling devices has been published by the American Conference of Governmental Industrial Hygienists (ACGIH, 1995). In all cases, the pollen impacts a semi-solid surface (tape strip or glass slide mounted with an adhesive). The main difference between the devices is that the moving tape/slide impactors provide the possibility of obtaining time-discriminated data, as opposed to the stationary and rotating rod impactors. The sampling devices listed in Table 33 may also be used to sample large fungal spores. Published data on the validity of air sampling to estimate the exposure to pollen are lacking.

9.6.2 Dust sampling for pollen

The sampling of settled dust to investigate the presence of pollen grains or allergens derived from pollen can be conducted exactly as for house dust mites and their allergens (see section 9.2.2) Dybendal et al. (1989) and Yli-Panula & Rantio-Lehtimäki (1995) describe dust sampling techniques for pollens.

9.6.3 Available methods of analysis for pollen in air

Analysing air samples for pollen is commonly done by light microscopy, but scanning electron microscopy is also used. Immunochemical assays are not routinely used to assess the presence of pollen allergens in air or dust samples. It should be recognized that optically counted pollen grains may not relate to the pollen antigenic activity because empty grains do not contain allergenic protein material.

For light microscopic counting and identification of pollen, staining of the sample is recommended. Staining can be done with basic fuchsin and phenosafranin, which stain the exine of the pollen (i.e., the outermost portion of a pollen grain) red and dark pink respectively. The choice of the dye depends on the type of sample to be analysed. Pollen identification rests on the microscopic appearance, using published keys for identification. (Faegri & Iversen, 1989; Nilsson & Praglowski, 1992).

Immunochemical assays have been used to analyse samples of settled house dust for the content of grass-pollen allergens (ryegrass, Lol p I) by direct RAST (Platts-Mills et al., 1987). Birch (Bet v I) and alder (Aln i I) pollen allergens have been analysed by means of RAST-inhibition (Dybendal et al., 1989). Jensen et al. (1989) have analysed outdoor air samples taken with a high volume sampler for timothy and birch pollen allergens by means of a RAST-inhibition assay. They found a strong correlation between the amounts of allergens and pollen counts obtained with a Burkard trap. As indicated above, immunochemical assays are not routinely used to measure pollen allergens.

Table 33. Overview of sampling techniques for airborne pollen grains^a

Method	Examples	Sampling rate and ti
Rotating tape/slide impactors	Burkard trap	10 litre/min, 7 days
Moving slide impactors	Lanzoni sampler	10 litre/min, 7 days
	Allergenco air sampler	15 litre/min, interm
Stationary slide impactors	Burkard portable sampler	10 litre/min, 1-9 mi
Rotating arm impactors	Rotorod sampler	47 litre/min, interm

^a for detailed information see ACGIH (1995).

9.6.4 General considerations for pollen sampling

The source of indoor pollens can be considered as entirely outdoors. Bringing flowers indoors might be a transient source, but only about 10% of flowering plants and trees spread their pollen through the air. Ventilation, footwear and clothing bring outdoor pollens indoors. Yli-Panula & Rantio-Lehtimäki (1995) demonstrated that antigenic activity indoors was lower, and peaked 3 weeks later than outdoors. They inferred that transport by occupants and pets is a more important vector for indoor pollen levels in the Finnish homes they sampled. O'Rourke & Lebowitz (1984) sampled pollen in dust from homes in the dry southwest of the USA (Tucson, Arizona). Higher loadings were found in the dust samples closer to entrances. Both of these studies, as well as others, indicate that indoor pollen allergens may be a major cause of asthma, especially since significant antigenicity can persist more than 2 months after pollen searches at peak outdoors. Once indoors, if not physically removed, pollen grains are protected from "weathering" which will denature the antigenic proteins.

9.7 Summary

Bioaerosols includes a variety of microorganisms or their components that can become airborne and inhaled. These include viruses, bacteria, pollens, fungi, protozoa and algae as viable organisms that can cause illness. Fragments or metabolic components of bacteria and fungi along with protein structures contained in these organisms as well as in the excreta and parts of insects, animals and arachnids can cause allergenic reactions. This chapter focused on the most ubiquitous bioaerosols commonly found indoors and contributing to allergenic reactions: mites, fungi, bacteria and pollen. Methods and strategies for sampling and analysing these agents in air and settled dust are presented. Examples of how some of these parameters vary indoors and outdoors across time and location are offered.

Exposure assessment for microbiologicals is as advanced, at this time, as it is for many air contaminants. Personal samplers have not been developed. In fact, many of the techniques for sampling aerobiological agents have been adapted from instruments designed for other purposes. The field is maturing as professional organizations attempt to improve and standardize measurement methods, culturing and analysis protocols and data reporting. These aspects are of critical importance in comparing results reported by different investigators.

By their very nature, bioaerosols have compositions and concentrations that are highly variable. The conditions favourable for growth, reproduction and dispersion vary within a wide range of temperature, moisture and nutrient conditions. These same factors influence by interactions with human and animal activities. Mechanical systems and machines can cause amplification and distribution of biological aerosols. As a result personal exposures are quite variable; this, in turn, has led many investigators to rely on area air sampling and/or bulk sampling of materials. For example, it is

recommended that a surrogate measure of mite allergen exposure is derived from bedding and floor dust samples. Home samples, whether air or dust is sampled, are often the "exposure" value used in epidemiological investigations.

Finally, the advancement of aerobiological exposure assessment to eventual use in quantitative risk assessment will require better understanding of relevant dose to cause sensitization and reactivity for many different organisms and/or agents.

10. ASSESSING EXPOSURES WITH BIOLOGICAL MARKERS

10.1 Introduction

This chapter presents a summary of the major concepts, definitions, advantages, limitations, sampling, media and uses of biological markers as applied for exposure assessment to environmental contaminants. These exposures are frequently characterized by low contaminant concentrations, multiple sources and multiple types of chemicals. Use of biological markers has been extensively reviewed from both epidemiological and occupational monitoring perspectives as well as their use in risk assessment (Bernard & Lauwerys, 1986; Harris et al., 1987; US NRC, 1987; Hulka & Wilcosky, 1988; Cullen, 1989; Griffith et al., 1989; Henderson et al., 1989; Monster & Zielhuis, 1991a,b; Schulte, 1991; Hulka & Margolin, 1992; IPCS, 1993; Aitio, 1994; Grandjean et al., 1994; Silbergeld & Davis, 1994). The reader should refer to the research literature for a comprehensive and detailed understanding of the complex issues relevant to the development, validation, and application of biomarkers in studies of human exposure. The specific issue of using biological markers in occupational settings is beyond the scope of this chapter.

It is important to indicate that, to date, very few biomarkers can be effectively used for quantitative estimation of prior environmental exposure to contaminants (e.g., carbon monoxide or lead). In most cases, there are qualitative or semi-quantitative indicators for monitoring such exposures. However, as the field evolves, and knowledge of the pharmacokinetics and pharmacodynamics of xenobiotics develops, the number of quantitatively validated biomarkers of exposure will also increase.

Biological markers present unique advantages as tools for multimedia exposure assessment. They are highly sensitive indices of an individual's exposure to chemicals, since they provide a measure of the internal dose, account for all routes of exposure and integrate over a variety of sources of exposure (Friberg, 1985; Baselt, 1988; Sim & McNeil, 1992). Therefore, they can represent past exposure (e.g., the presence of lead in shed teeth), recent exposure to an external source (e.g., VOCs in exhaled breath) and even future

internal exposure sources (e.g., pesticides in adipose tissue). Furthermore, their use may result in improved monitoring of total population exposure, characterization of individual and population exposures and evaluation of internal sources of exposure. These markers are also useful surveillance tools for monitoring chemical exposure in both individuals and populations over time.

Use of biological markers of exposure can improve the risk assessment process by providing a critical link between chemical exposure, internal dose and health impairment (IPCS, 1993). Biological markers of exposure can improve clinical diagnoses where there is a well-established relationship between biological marker and outcome.

10.2 General characteristics

Biological markers represent events or changes in human biological systems as a result of exposure or disease (US NRC, 1991b). They are classified as markers of exposure, effect, and susceptibility and are considered to represent events along a theoretical continuum from causal exposure to resulting health outcome (US NRC, 1987; Schulte, 1989). A biological marker of exposure is defined as a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule(s) or cell(s) that is measured within a compartment of an organism (US NRC, 1989; IPCS, 1993). Biological markers of effect are measurable biochemical, physiological, behavioural or other alterations within an organism that, depending upon the magnitude, can be recognized as associated with an established or possible health impairment or disease (IPCS, 1993). Biological markers of susceptibility are indicators of inherent or acquired abilities of an organism to respond to the challenge of exposure to a specific xenobiotic substance (IPCS, 1993). Although the distinction between some biological markers of exposure and effect may be overlapping, this chapter will focus on those biological markers which can be applied to environmental exposure assessment.

10.3 Considerations for use in environmental exposure assessment

The use of biological markers for exposure assessment represents a different perspective for evaluation of human exposure to a contaminant than traditional exposure assessment. Biological markers of exposure are considered measures of internal dose, whereas exposure is frequently defined as the concentration of an agent at the boundary between an individual and the environment multiplied by time (US NRC, 1991b; IPCS, 1993). Owing to long-term storage of specific contaminants in biological tissues (e.g., bone and fat), some biological markers are markers of both cumulative dose and future internal exposure.

Biological markers of exposure have been used most frequently in industrial hygiene and occupational medicine (Elkins, 1954, 1967; Lauwerys, 1983; Schulte, 1991). Before widespread application of biological markers for exposure assessment of the general population can occur, it is important to consider the situations which are best suited for biological monitoring. Ideally, a biological marker of exposure should be chemical-specific, detectable in trace quantities, available by non-invasive techniques and inexpensive to assay. Also, it must relate consistently and quantitatively to the extent of exposure and ideally also integrate the exposure over time (Bond et al., 1992). Currently there are very few biological markers that

possess all these characteristics. However, the use of biological markers for exposure assessment is increasing.

Biological markers represent one type of monitoring approach available for environmental exposure assessment. Validation of biomarkers is a complex process that should include determination of:

specificity of the available biological marker, exposure-related toxicokinetics and toxicodynamics, dose-response relationship, biological variation associated with the marker, route of exposure and type of health effect associated with exposure. In addition, validation should consider behavioural factors that influence exposure, participant acceptance, feasibility and cost-effectiveness (Verberk, 1995), as well as biological variability and specificity within a human population of interest, and generation of baseline or normative data for the biological marker. These issues are addressed later in the chapter.

Collection of samples from humans involves important ethical issues. Ethical concerns may limit the extent of investigations of chemically exposed individuals and populations (IPCS, 1993). Ensuring confidentiality both for subjects and for the obtained individual results is imperative (Schulte, 1992). Subjects have the right to know the implications of their participation, the analyses to be performed, the nature of the sampling procedure, the use of the data collected and the possible ramifications of positive findings. Knowledge of previous exposure or genetic predisposition may have adverse implications for an individual; for example, individuals may be denied health insurance on the basis of presumed future risk. Since biological markers are a relatively new tool, interpretation of results and subsequent health implications is difficult. For many biological markers, little information is available to interpret the result for the subject; this may lead to concern on the part of the individual. For example, knowledge of the presence of pesticides in breast milk may lead an individual to avoid breast-feeding without consideration of its advantages (Vandenberg, 1991; Sim & McNeil, 1992).

10.3.1 Toxicokinetics and toxicodynamics

Toxicokinetics describes the absorption, distribution, metabolism and excretion of a contaminant. Understanding the toxicokinetics and toxicodynamics of the agent is critical for development and use of a biological marker of exposure (Sampson et al., 1994). This information predicts the location and form of the chemical or its metabolite and identifies sources of biological variability in the population (Droz & Wu, 1991; Droz, 1992, 1993). Toxicokinetic modelling may be used to estimate the optimal time for sampling (Saltzman, 1988; Droz & Wu, 1991; Droz, 1993). Differing kinetics determine whether the biological marker reflects recent exposure, historic exposure, or an integrated measure of exposure over time (Bernard, 1995).

The utility of biological markers for assessing exposure can be evaluated on the basis of timing of sampling relative to the exposure and the biological half-life of the chemical. The parameter which best describes the toxicokinetic behaviour of a chemical in biological systems is the *elimination half-life*, which reflects both the affinity of the chemical for the biological medium and the efficiency of the processes of elimination (Bernard, 1995). For samples taken

immediately following exposure (e.g., solvents in exhaled air, blood and urine), the half-life reflects elimination from the central compartment of blood and vessel-rich tissues. For samples taken days, weeks or even years after exposure, the half-life corresponds to the elimination from those compartments from which chemical clearance is much slower; for example, lead from bone or lipophilic organic chemicals from adipose tissue (Bernard, 1995).

Toxicokinetic data from animals and humans can aid in the determination of the utility of biological markers in assessing individual or population exposures. Fig. 30 illustrates how toxicokinetic data could be utilized to select biological markers of exposure based on the timing and concentration of exposure (IPCS, 1993). In order to interpret the extent of exposure, it is critical to collect the biological sample after the exposure has reached an equilibrium state. This can be especially important for chemicals with short half-lives, such as benzene in exhaled air with a half-life of 22 h (Bernard, 1995). For example, in occupational settings, biological monitoring has no advantages over environmental monitoring for airborne chemicals with biological half-lives less than 10 h, since the integration time for the marker is too short to allow accurate representation of exposure (Droz, 1993).

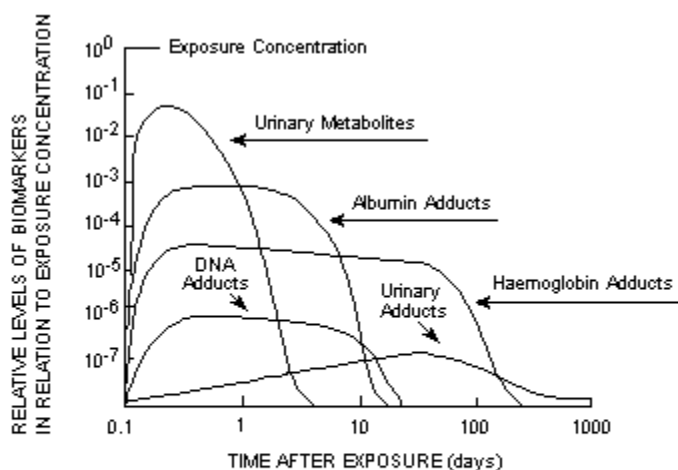


Fig. 30. Hypothetical relationships among different biomarkers of exposure with respect to their relative levels and time of appearance after a single dose (Henderson et al., 1989)

10.3.2 Biological variability

The use of biological markers can also be affected by biological parameters. Variation can depict true differences in individual exposures, as represented for example by differing microenvironments or differing behaviour. It may also represent inherent inter-individual differences which affect the biological response to exposure (Droz, 1992). Sources of biological variability include demographic factors (e.g., age and sex), anthropometric characteristics (e.g., body size and fat distribution), behaviour (e.g., activity level or contaminant avoidance behaviours), biological/circadian rhythms and toxicokinetic differences due to genotype (Kompaore & Tsuruta, 1993), previous exposure, lifestyle

factors (e.g., smoking) or dietary habits (Perera & Weinstein, 1982; Droz, 1992). Biological variability can complicate assessment of an individual's exposure using biological markers. However, the factors contributing to biological variability influence the internal dose and may ultimately be informative about potential health effects relating to exposure. For chemicals with large inter-individual variability in biological response to exposure, biological monitoring techniques are more useful for groups than for individuals.

10.3.3 Validation of biological markers

Validation of biological markers of exposure occurs at three levels.

- * The first validation level involves sample collection and determination of sample stability following collection and during transport and storage. Sample collection and handling can influence external contamination both during the sample collection and from the sample collection material. Stability of the sample prior to analysis can be affected by chemical degradation, evaporation, biological activity and interaction between the sample and its container or with other compounds (Bernard, 1995).
- * The next level pertains to the analytical method itself and the ability to measure the marker accurately and reproducibly at levels relevant to environmental exposure. Low limits of detection and high analytical sensitivity (i.e., instrument response) are critical for evaluation of environmental exposures.
- * The third validation level stems from the sensitivity and specificity of the biological marker itself. The biological marker must demonstrate that an exposure is occurring or has occurred, and separate individuals on the basis of their level of exposure (Hulka, 1991). Components of this level of validation include understanding the temporal relevance of the marker, identifying background variability and determining potential confounding factors (Perera, 1987; Sato, 1993). Temporal relevance is critical since it relates the timing of exposure to the appearance of a measurable biological marker and to the duration of time that the

biological marker is measurable following the cessation of exposure. This includes both toxicokinetic and toxicodynamic considerations.

Validation occurs in the laboratory, in pilot studies and in populations (Schulte & Talaska, 1995).

For environmental exposure assessment, chemical-specific markers of exposure such as blood lead concentrations are preferred. However, for some chemicals, compound-class specific markers (e.g., PAH-DNA adducts) or non-specific markers (e.g., acetylcholinesterase inhibition) may be available. Non-specific markers of contaminants (i.e., some metabolites or non-chemical specific biological changes) as indicators of exposure may be more sensitive than external measures of exposure to predict an individual's total dose (van Welie et al., 1991; Smith & Suk, 1994). However, since non-specific markers are neither source- nor chemical-specific, characterization of the variability in these markers is an important validation component prior to use in exposure assessment. To date, few biomarkers of environmental exposure can be utilized to estimate such exposure

quantitatively. In most cases, biomarkers of exposure provide a semi-quantitative or qualitative indication of exposure.

10.3.4 Normative data

Currently many biological markers are being developed for research purposes (Schulte, 1987; Kelsey, 1990; Bond et al., 1992; Fowle & Sexton, 1992). However, collecting population baseline data on these markers is necessary before they can be useful for monitoring and surveillance purposes. Longitudinal and cross-sectional information on normal ranges and correlation with environmental exposures and demographic characteristics are required. Reference ranges are available for some biological markers. For example, blood concentration data for a number of pesticides and metals were collected in a representative sample of the US population in the National Health and Nutrition Evaluation Survey (NHANES IV) and the German Environmental Survey (Krause et al., 1992). The ranges may vary in different exposed populations owing to differing residual levels in the environment (Grandjean, 1986; Alessio, 1993). Data from specimen banks are beginning to provide some exposure information on geographic and demographic parameters (Kemper, 1993).

10.4 Advantages of biological markers for exposure assessment

Biological markers integrate over all sources of exposure, which allows for efficient characterization of exposure to multiple sources and evaluation of past exposures (US NRC, 1991a; Sim & McNeil, 1992). When contaminants are found in many environmental media, biological monitoring can be the most effective way to determine an individual's total exposure. Biological markers may also indicate the presence of additional exposures; for example, biological markers used in occupational settings have been applied to determine if non-occupational exposures to similar agents are occurring (Lauwerys, 1983). Some biological markers (e.g., PCB concentrations in breast milk) represent cumulative exposure to environmental contaminants. Markers which integrate over long periods of time can be used to evaluate past exposure in a much more accurate manner than historical record review and exposure reconstruction (DeRosa et al., 1993; Sampson et al., 1994). Biological markers can also be the best way to measure recent exposures, especially those where dermal contact is the primary route of entry. Table 34 summarizes the advantages and limitations of using biological markers in exposure assessment.

Table 34. Advantages and limitations of biological markers for environmental exposure assessment

Advantages	Limitations
Demonstrate exposure has occurred	source and route identification
Integration over all exposure routes	kinetics and timing of exposure
Characterization of individual exposure-doses	biological variability and confounding
Inclusion of internal sources	altered response as a result of multiple exposure

Improved health effects investigations	invasive sampling
Improved population risk assessment/risk management	availability of human samples specificity/sensitivity
Validation of exposure models	lack of normative values for comparison

10.4.1 Characterizing inter-individual variability

A fundamental issue in the quantitative aspect of exposure assessment is the characterization of inter-individual variability in exposure. The pattern of exposure may differ within individuals, groups or populations. For example, workers in the same factory may have different exposures as a result of differing work habits (Rappaport et al., 1993); families living in very airtight houses may have greater exposure to indoor contaminants than families living in draughty homes. Biological markers represent one strategy to assess inter-individual variation in exposures, when measured environmental concentrations do not differ between individuals. Genotype, dietary habits, body size, state of health, lifestyle habits (e.g., smoking) and behaviour may all play a role in determining an individual's

exposure (Bernard & Lauwerys, 1986). Biological markers of susceptibility may also be used to explore biological variation in response to exposure. For example, phenotypic differences in Delta-aminolaevulinic acid dehydratase (ALAD) may influence both blood lead levels and the health effects of lead (Wetmur, 1994; Milkovic-Kraus et al., 1997). Incorporation of biological markers of both exposure and susceptibility into biological monitoring studies may result in further insight into inter-individual variability.

10.4.2 Efficacy of use

In some situations, biological markers can be more efficacious tools than external exposure measurements for monitoring human exposure in population studies. For example, participant burden may be lower than in traditional monitoring schemes for some activities (e.g., motor vehicle repair) and for some subjects (e.g., children and the elderly) wearing a personal monitor may not be a practical strategy to monitor a subject's exposure. For some exposure routes such as dermal exposure, there is no adequate way to determine the extent of exposure using non-biological methods (Ward et al., 1986; Fiserova-Bergerova, 1987; Hemminki, 1992; Levesque et al., 1994). For example, chloroform in exhaled breath has been used as a biological marker to evaluate dermal exposure while swimming and showering (Levesque et al., 1994). Under certain conditions, wearing a sampling device alters behaviours that may, in turn, affect exposures as measured by a sampling device. Wearing a sampling device may be unduly burdensome in certain populations. Finally, monitoring devices may not exist to evaluate these exposures. In these cases, biological markers could be a preferred method to evaluate exposure.

Biological markers can improve the evaluation of human health effects associated with environmental exposure to contaminants (Schulte, 1987; US NRC, 1987; Hulka, 1991; Hulka & Margolin, 1992). These markers have been advocated as a means to reduce measurement

error in environmental epidemiology (Schulte, 1987; Hulka & Wilcosky, 1988; Hatch & Thomas, 1993). Since they represent internal dose, they are anticipated to be more predictive of health effects than external measures of exposure (US NRC, 1987; Hulka, 1991) and they can be used to validate population exposure models (Georgopoulos & Liroy, 1994). For risk assessment purposes, biological markers can be useful tools in evaluation of intermediate end-points and improving the transition from environmental exposure assessment and animal dose-response models to actual human health outcomes (Hattis, 1986; IPCS, 1993; Mercier & Robinson, 1993).

10.4.3 Internal exposure sources

Contaminants can be stored long-term in the body and may be produced endogenously. These sources of exposure cannot be characterized without biological markers. Breast milk, bone mineral and adipose tissue as well as blood represent biological media available to assess body burden of contaminants, especially those that concentrate in biological tissue. Mobilization of contaminants from

internal storage can be assessed using biological markers; for example, pesticide mobilization from adipose tissue can be measured in blood following fasting.

10.5 Limitations of biological markers for exposure assessment

Although the use of biological markers may result in improved exposure assessment, their use is not without limitations, since few validated markers are currently available. Challenges associated with the use of biological markers include source identification, pharmacokinetics, timing of exposure, biological variability, altered response as a result of exposure, potentially invasive sampling procedures and ethical concerns.

10.5.1 Source identification

Although the ability to integrate over all exposure sources is an advantage for total human exposure assessment, it limits the ability to identify the sources that contribute to exposure. Considerations for source identification include multiple exposure sources, multiple exposure regimes, non-specific biological response to exposure and endogenous production. Multiple sources of exposure can result in multimodal excretion rates because some exposures may be constant whereas additional exposures may be intermittent. Therefore, performing cross-sectional studies may miss multiple exposures (Que Hee, 1993) or changes in exposure patterns and/or concentrations. Some organic chemicals can be produced endogenously; this may result in an overestimate of the impact of external sources of exposure.

10.5.2 Biological variability and altered exposure response

Variability of biological response is an inherent characteristic of biological markers. Although variability may be associated with exposure levels, genetic differences in toxicokinetics and lifestyle factors such as diet, smoking and alcohol consumption may also result in biological variability. The impact of the inherent biological variability can be reduced by stratified sampling and the use of large sample sizes. Quantification of biological variability is difficult, and without adequate information on sources of variation the interpretation of results for exposure assessment purposes may be

limited. Of particular concern is uncharacterized biological variability which may influence uptake, distribution, metabolism or excretion of the contaminant of interest and, therefore, the internal dose. Some authors consider that the influence of genetic variation is limited in comparison to the impact of other susceptibility factors (Perera & Weinstein, 1982). During validation studies, it is necessary to gather information on potential confounding factors. Baseline data on pre-exposure biological marker concentrations and demographic variables should be obtained to assess inter-individual biological variability more accurately.

Previous exposure and pathophysiological states can change the biological response to current exposure. This is of particular concern in cross-sectional investigations or in studies of individuals with previous or long-term exposure. Previous or concurrent exposure to agents that elicit similar responses to the contaminant of interest may alter metabolic activity in response to exposure. These alterations may lead to an increase or decrease in the rate of metabolism or excretion, or a change in the type or amount of metabolites formed, which thereby alters the internal dose and potentially, the biologically effective dose. Interactions between the exposure of interest and other environmental exposures, diet, medication use, cigarette smoking and alcohol consumption may affect the outcome of the exposure and the interpretation of the biological monitoring results.

In some cases, exposure to chemicals can cause maladaptive changes and the biological markers of exposure may represent subclinical disease. For example, long-term exposure to metals at high concentrations can result in kidney damage and thereby alter the processing of metals in the kidney. This results in potentially low excretion of metals in urine and subsequent underestimation of exposure (Lauwerys, 1983). In some situations, clinical tests can be conducted at the same time to address issues such as reduced kidney function. Conversely, individuals with long-term exposure may represent those individuals who are least susceptible to the agent's effects; this may be problematic when using workers to validate biological markers at high levels of exposure (Hauser et al., 1995).

10.5.3 Participant burden

Collection of biological media presents challenges different from collection of environmental samples. At the minimum, it requires active participation on the part of the study subject. In designing studies, it is critical to recognize that collection of biological samples can be invasive. Some routine medical procedures, such as collection of a small vial of blood, may be more acceptable to participants than more involved, yet non-invasive, sampling methods such as collection of a 24-h urine specimen or wearing an air sampling pump for a day. Other sampling strategies, such as fat biopsies or collection of large volumes of blood, may be impractical for environmental exposure assessments because of excessive participant burden. Ethical considerations also include how participants should be informed about their results.

10.5.4 Biosafety

Biological media can serve as vectors of infectious disease, such as AIDS and hepatitis. Because of this hazard, special procedures must be used when collecting, transporting, storing, analysing and

disposing of any human biological samples. All personnel must be trained for the proper handling of biological samples and protocols must include instructions for this.

10.6 Media available for use

Numerous biological media are available for use in environmental exposure assessment. Selection of sampling media depends on the contaminant of interest, the pattern of exposure, the timing of exposure, the population studied, ease of collection and storage and participant burden. Biological monitoring is frequently considered invasive; however, several media are available for exposure assessment that can be collected in a non-invasive manner. For occupationally used chemicals, biological exposure indices and monitoring protocols are available (Lauwerys, 1983; ACGIH, 1991; Que Hee, 1993); these may be regarded as starting points for biological sampling in environmental studies.

Historically, blood and urine have been the primary media for biological exposure markers. Blood and urine, as well as exhaled breath and saliva, can be used to document recent exposures; past exposure can be evaluated using blood and urine as well as keratinized tissues (hair and nails), ossified tissue (teeth and bone), adipose tissue and breast milk. Adipose tissue and bone can also represent future sources of internal exposure. Other media available for biomarker studies include faeces, nasal lavage, tears, sputum, semen, cord blood and buccal cells, which can be feasible means for population exposure monitoring. Other media from cadaver or biopsy specimens (e.g., liver and kidney samples) have been collected in select populations but these cannot be used for exposure assessment of healthy individuals. Table 35 summarizes the media available for use in biological monitoring in environmental settings.

10.6.1 Blood

Blood has been frequently used for biological monitoring, especially in clinical settings such as occupational medicine. Blood can integrate all sources of exposure, including internal sources, and provide an indication of current internal dose. Since blood transports all agents throughout the organism, it represents an opportunity to sample all types of contaminants, such as gases, solvents, metals and fat-soluble compounds. Both specific (e.g., blood lead) and non-specific (e.g., sister chromatid exchange) analyses can be performed. Components of blood available for sampling are whole blood, red blood cells, white blood cells, plasma, serum and blood proteins, primarily haemoglobin and albumin.

- * *Whole blood* consists of all the blood components and is preferable when the distribution of the analyte between plasma and cellular elements is unknown (Que Hee, 1993).
- * *Red blood cells* make up a large portion of blood and their primary role is to transport oxygen via haemoglobin throughout the body. Mature red blood cells contain no nucleus and therefore no DNA, and have a 120-day lifetime. Chemicals that interact with haemoglobin, such as carbon monoxide, are found in red blood cells.

Table 35. Biological media available for sampling

Media	Chemicals (examples)	Type of samples	Collection	Storage
Adipose tissue	lipophilic chemicals, pesticides, PCBs	surgical specimens, fat biopsies	invasive, minor surgical procedure	fat sample archived
Blood	gases, metals, pesticides, semivolatile organics, VOCs	whole blood, red blood cells, white blood cells, plasma, protein	invasive, quick, requires trained phlebotomist	for use sample frozen sample
Bone	metals (lead)	cortical bone, trabecular bone (X-ray fluorescent spectra)	non-invasive, 30-60 min collection time	not applicable
Breast milk	lipophilic compounds	fat and aqueous phases	non-invasive	sample stored refrigerated
Breath	gases, semivolatile organics, volatile organics	mixed air, alveolar air	non-invasive, quick, requires air sampling apparatus	sample analyzed collected easily

Table 35. (continued)

Media	Chemicals (examples)	Type of samples	Collection	Storage
Faeces	high molecular weight organic compounds, lipophilic substances, metals	faeces	non-invasive, poor compliance by subjects	
Hair	cotinine, metals, PCBs	scalp, pubic hair	non-invasive, important to standardize collection location	sample and analyzed
Saliva	metals, pesticides, semivolatile organics	mixed saliva	non-invasive, easy for participant	sample stored refrigerated
Teeth	metals	shed deciduous teeth	non-invasive	sample and analyzed

Toenails	metals	single toenail or composites	non-invasive, requires participant to collect sample	sample and ar
Urine	low molecular weight metabolites, metals, mutagens, pesticides, semivolatile organics	spot or grab samples, first morning void, 24-h urine samples	non-invasive, 24-h urine sample requires motivated participant for accurate sample collection	sample

* Numerous types of *white blood cells* are present in blood. These cells have a half-life ranging from 18-20 days to decades (Carrano & Natarajan, 1988). Since these circulating cells have DNA which can itself be altered or the expression of which can be changed as a result of exposure to a genotoxic agent, they may be used for biomarkers of exposure to genotoxic agents (Carrano & Natarajan, 1988; Kelsey, 1990). Interpretation of genotoxic response is complicated because DNA damage can result in either cell death or removal of the marker by DNA repair, or may alter cell functions (Perera, 1987). Regardless of this, correlations have been seen between environmental exposures and DNA adducts and other cytogenetic responses (Perera et al., 1988; Heddle et al., 1991; Santella et al., 1993; Yager et al., 1993).

* *Plasma* and *serum* represent the non-cellular component of blood. Plasma is a straw-coloured aqueous solution of electrolytes, non-electrolytes and macromolecules (including clotting factors); serum is plasma without the clotting factors (Que Hee, 1993). Plasma represents a component of whole blood (approximately 60%), and it may contain the most biologically active fraction of blood borne contaminants, since plasma is in more immediate contact with tissues (Silbergeld, 1993). Plasma can be used for analysis of lipophilic chemicals, thereby avoiding the need for fat sampling.

* *Blood proteins* can be sensitive monitoring tools for chemicals that bind to macromolecules including DNA (Osterman-Golkar et al., 1976; Bond et al., 1992). Protein adducts, unlike DNA adducts, are not repaired and may prove to be a useful dosimeter of mutagen exposure (Grassman & Haas, 1993; Que Hee, 1993). Haemoglobin and albumin are two proteins available for use in exposure assessment. Haemoglobin is located in red blood cells in high concentration and has the half-life of red blood cells (120 days); albumin is present in serum and has a half-life of 21 days. Because of their differing biological half-lives, these proteins can be used to investigate the timing of exposure.

Collection, storage, and shipping of blood samples can be resource-intensive. Blood sampling is invasive to the subject and requires a trained phlebotomist. Two primary methods of blood collection are venipuncture and finger stick. Blood from finger sticks is more subject to surficial contamination, has a higher percentage of red blood cells and is a smaller volume than that collected using venipuncture (Graziano, 1994). However in some populations, such as small children who have veins that are hard to find or who have fears

of venipuncture, finger sticks can be the collection method of choice.

The analytes of interest influence the sample collection regimen. Concerns about external contamination, interaction between the analyte and the sample collection vessel, and degradation, bacterial contamination and time until processing should be considered when designing the sampling protocol (Aitio & Järvisalo, 1984). Test tubes, additive agents such as EDTA and sample stoppers all represent

potential contamination sources. Processing of serum samples should occur in a timely fashion to prevent degradation of the analytes of interest. For example, collection of serum samples for organochlorine pesticide analysis requires that:

- * all equipment be solvent-rinsed before collection and processing
- * care be taken to avoid contact between the blood and the stopper of the test tube
- * the sample be centrifuged within 24 h of collection
- * the serum be kept frozen prior to analysis.

Shipment of frozen samples requires special precautions to prevent thawing during transport. For results to be valid, the biological sample should be analysed within holding time, as required by the specific medium and analyte.

10.6.2 Urine

Urine is another frequently collected biological medium. The concentrations of compounds found in urine usually reflect time-weighted averages in plasma during collection and storage in the bladder (Que Hee, 1993). The presence of a contaminant or its metabolite in urine generally represents recent exposure, though in some cases it may represent release from storage within the body (Lauwerys, 1983). Urine can be analysed for metabolites of organic chemicals (e.g., benzene and styrene), metals (e.g., arsenic and mercury) and pesticides as well as for mutagenic potential (Lauwerys, 1983; Baselt, 1988; Que Hee, 1993). Since collection of urine samples is non-invasive, some investigators feel that, when validated, urine may be a better sampling medium than blood for monitoring (Smith & Suk, 1994).

Three types of urine samples are used for biological monitoring: spot urine specimens, first morning voids and 24-h urine specimens (Baselt, 1988).

- * *Spot urine samples* are relatively easy to collect but there may be significant variability with respect to exposure prediction as a result of metabolism, liquid consumption and kidney function.
- * *First morning void samples* have less variability since they are more concentrated than spot samples, but require motivated subjects to collect the samples.
- * *Twenty-four hour urine samples* control much of the intraindividual variability but require highly motivated subjects in order to collect useful samples (Baselt, 1988).

The choice of sampling type is dependent upon the analyte of interest, the pattern of exposure, the anticipated concentration and the population. Urine samples should be refrigerated before analysis to reduce biological degradation and bacterial growth. Sample processing and storage should occur as soon as possible after collection in the manner required for the analyte of interest.

To make the results of urine monitoring comparable between individuals, analytical results are frequently standardized to creatinine concentration or specific weight. Standardization reduces some of the variability of body size and urinary output (Lauwerys, 1983; Sato, 1993). However, kidney damage can alter the creatinine excretion and therefore standardization may not be appropriate in all cases. Clinical data can be used to evaluate kidney function.

10.6.3 Exhaled breath

Exhaled breath analysis has been used in both occupational and environmental settings. Breath analysis is useful for assessing recent exposure to gases (e.g., carbon monoxide) and organic vapours and solvents (e.g., acetone and toluene). Limited studies have been made on the use of breath analysis for airborne particles and associated PAHs (Sugita et al., 1997). To be useful, breath measurements must relate both to exposure and to blood concentration (Bond et al., 1992). Breath sample concentrations of contaminants can vary as a function of body build, metabolism, sex, physical activity and ventilation rate as well as the exposure route (Que Hee, 1993). Two types of samples are available for collection: mixed exhaled breath and alveolar air, or end-expired air (Wallace, 1987; Wallace et al., 1991a,b; Que Hee, 1993).

- * *Exhaled breath* can be a mixture of inhaled and exhaled air. If the exhaled biological marker is not present in inhaled air, then exhaled breath analysis is an effective means to measure internal exposure. For example, when alcohol has an internal source only (i.e., ingestion) a mixed breath sample is appropriate.
- * *Alveolar air* provides a measure of the air that is in equilibrium with the blood in the deep lung (Bond et al., 1992). For analytes present in inhaled air, it is necessary to collect an alveolar air sample.

Breath samples can be used to assess microenvironmental exposure as well as exposure to chemicals with short biological half-lives that enter the body through non-inhalation routes (Wallace, 1987; Levesque et al., 1994). A number of methods are available to collect exhaled breath samples for organic and other gaseous contaminants (Wallace, 1987a; Pellizzari et al., 1988; Periago et al., 1992). Exhaled breath collection is quick and easy for the participant, but the actual sample collection can involve complex air collection apparatus to gather a sufficient sample. The sampling tools are similar to those currently employed for sampling of air contaminants. Methods for airborne particles and components thereof have been used to a limited extent (Goto et al., 1997, Sugita et al., 1997). Potential sample collection error concerns in sample collection include loss of sample volume, sample storage prior to analysis and cross-reaction among analytes.

10.6.4 Saliva

Glands at four locations in the mouth produce saliva; the secretion rate varies at each location. Chemicals enter saliva via passive diffusion from plasma. Therefore, saliva may become a useful tool to non-invasively characterize plasma levels of contaminants (Silbergeld, 1993). Social science research has used saliva sampling because of its ease of collection and storage (Dabbs, 1991, 1993). Contaminants found in saliva include cotinine, drugs, metals, organic solvents, pesticides and steroid hormones (Tomita & Nishimura, 1982; Nigg & Wade, 1992; Silbergeld, 1993).

Collection of saliva is relatively easy. One approach consists of having the subject rinse the mouth and chew on a stimulant, typically a piece of clingfilm or sugar-free gum. The subject then spits into the sampling container. Another method uses pumps to sample from the salivary glands. In either case, care should be taken to minimize contamination from the mouth. Because the concentrations of chemicals in saliva can fluctuate with circadian rhythm, the collection of saliva samples should occur at the same time each day (Dabbs, 1991). Saliva samples are quite stable and can be stored at room temperature for several days (Dabbs, 1991, 1993). However, in order to reduce viscosity from proteins, saliva samples are typically frozen prior to chemical analysis.

10.6.5 Keratinized tissue (hair and nails)

Keratinized tissues, primarily hair and toenails, are practical sampling media for evaluation of past exposure to metals (Bencko et al., 1986; Bencko, 1991; Subramanian, 1991; Kemper, 1993; Bencko, 1995). Toenails are usually the medium of choice: see below. These media integrate exposures over a period of months, contain relatively larger concentrations of trace elements than blood or urine and are easy to collect, store and transport (Garland et al., 1993; Kemper, 1993). Therefore, archiving specimens for future analyses is a viable option. Since hair and toenails are no longer in contact with the blood supply, they can provide a picture of past exposure. Because of the ease of collection, hair and toenails have been collected in numerous environmental studies, especially of children (DiVincenzo et al., 1985; Bencko et al., 1986; Wilhelm et al., 1989, 1991; Sukumar & Subramanian, 1992; Bustueva et al., 1994; Santos et al., 1994). Hair and toenails have been collected for elemental analyses in both environmental exposure assessment and nutritional evaluation studies (Garland et al., 1993; MacIntosh et al., 1997).

Hair might be a useful medium to study exposure to environmental tobacco smoke (ETS). For example, in the framework of the German Environmental Survey (Krause et al., 1992) it was concluded that in large population studies nicotine and cotinine in urine as well as nicotine in hair are useful indicators of exposure for different levels of active and passive smoking. Cotinine and nicotine concentrations in hair have also been used to study fetal exposure by maternal smoking (Klein et al., 1993). Hair has also successfully been used in studies evaluating exposure to organic mercury (Suzuki et al., 1989) or PCB (Que Hee, 1993).

One of the major concerns in the use of hair as a sampling medium is the potential for surficial contamination, in part due to the large surface area and the oily nature of hair. Sources of contamination include sweat, cosmetics, dirt and clothes (Doi et al., 1988; Raghupathy et al., 1988). Other potential disadvantages of sampling

hair include sample preparation, differing growth rates at different locations on the body, unknown correlation with biological effects and biological variability (Wilhelm et al., 1990; Kemper, 1993). Hair grows approximately 1 cm/30 days (Que Hee, 1993) and can be evaluated along the shaft to provide a profile of exposure over time. Since growth rates of hair differ based on body location, standardization of sampling location is crucial.

Because of concerns about contamination, exposure assessors usually prefer toenails to hair; however, some authors prefer hair for exposure assessment based on correlations with concentrations measured in environmental media and ease of collection (Wilhelm et al., 1991). When sampling nails, toenails are usually the medium of choice, since they are thicker and less subject to contamination than fingernails. Toenails can be collected by participants, shipped to distant research sites and stored in paper envelopes prior to analysis. To reduce problems associated with surficial contamination, the outer layer of the toenail can be removed. Each toenail grows at a different rate and therefore each nail may represent a different time period of exposure; long-term average exposure can be evaluated using a composite of all toenails (Garland et al., 1993).

10.6.6 Ossified tissue

10.6.6.1 Teeth

Teeth constitute a unique medium for assessment of past exposure. Depending on the tooth type and part of the tooth, one can reconstruct early childhood exposures to bone-seeking elements, such as lead (Rabinowitz et al., 1989). However, sample collection opportunities are limited to shed deciduous teeth in young children. Sample collection and storage are easy; removing the outer layer of the tooth minimizes external contamination.

10.6.6.2 Bone

Bone represents both past exposure to bone-seeking elements and is a source for future internal exposure to these elements. The concentrations of elements in bone represent long-term exposure and storage of contaminants. For example, the half-life of lead in bone is approximately 10-40 years (Rabinowitz, 1991). Although numerous elements can be detected in bone tissue using destructive analyses such as atomic absorption spectroscopy (AAS), *in vivo* measurement of environmental contaminants in bone has been limited to lead (e.g., Somerville et al., 1988; Hoppin et al., 1995). Lead concentration in bone can be analysed non-invasively using a technique known as X-ray fluorescence (XRF) (Hu et al., 1995). Bone lead concentrations in adults correlate well with integrated measurements of blood lead concentrations (Somerville et al., 1988; Hu et al., 1995). Sources of variation in bone lead measurement include the degree of bone mineralization, the concentration of lead in bone, the overlying skin thickness and subject movement during the measurement. Lead and other elements can be mobilized from bone during physiological events such as pregnancy, lactation and osteoporosis (Silbergeld, 1991).

10.6.7 Breast milk

Environmental studies have used breast milk to evaluate past exposure to lipophilic chemicals (e.g., pesticides and PCBs) and metals (WHO, 1996b) and to examine potential exposures for

breast-feeding infants (Niessen et al., 1984; Davies & Mes, 1987; Sikorski et al., 1990; Sim & McNeil, 1992). Organic chemicals found in breast milk have high lipid solubility, resistance to physical degradation or biological metabolism and slow or absent excretion rates (Rogan et al., 1980). Breast milk represents a major route of excretion of lipophilic chemicals for lactating women (Rogan et al., 1980; Sim & McNeil, 1992). Concentrations of chemicals in breast milk are a function of parity, age, body mass, time of sampling, nutritional status, lactation period and fat content of milk (Rogan et al., 1986; Sim & McNeil, 1992). Breast milk results are generally standardized to milk fat levels.

Breast milk sampling represents a non-invasive method to estimate body burden of contaminants in adipose tissue. The correlation between contaminant concentrations in the lipid phase of milk and adipose tissue is good (Sim & McNeil, 1992). External contamination is a concern for breast milk samples; all sampling equipment should be cleaned in a manner that will prevent contamination. Although breast milk sampling is an applicable way to estimate population exposure to chemicals that bioconcentrate, sampling is limited to lactating women, who may or may not be representative of the population as a whole.

10.6.8 Adipose tissue

Exposure assessment studies using adipose tissue have been limited primarily to ecological studies comparing fat from cadavers or surgical specimens to general pollution levels. Adipose tissue represents a long-term reservoir of lipophilic compounds that the body slowly metabolizes and may release into the bloodstream. Unfortunately there is no non-invasive manner to sample fat stores directly, and many subjects see fat sampling as exceedingly invasive. The analytical method and detection limit requirements determine the quantity of adipose tissue necessary. In studies measuring body burden of dioxins in fat, a minor surgical procedure was necessary to collect a 20 g sample from healthy potentially exposed subjects (Patterson et al., 1986). When a smaller sample size is sufficient (200 mg or less), needle biopsies of fat stores in the buttocks can be used (Que Hee, 1993; Kohlmeier & Kohlmeier, 1995).

10.6.9 Faeces

Faeces are a highly fat-soluble medium that provides information on compounds of high-molecular weight that exit the body via biliary excretion and on unabsorbed chemicals that enter the body via ingestion. Metals may also be monitored in faeces; however, it is unclear whether the metals found in faeces represent absorbed or unabsorbed elements (DiVincenzo et al., 1985; Vahter et al., 1991). Although collection of faeces is regarded as non-invasive, very few subjects are sufficiently motivated or interested in their collection (Bihl et al., 1993).

10.6.10 Other media

Several additional biological media have been used for determination of biomarkers of exposure including tears (e.g., Ellegard, 1997), nasal lavage and nasal plugs (Steerenberg et al., 1997), sputum (e.g., Pizzichini et al., 1997) and semen (e.g., Sram et al., 1996). In most cases, these studies have focused on biomarkers of inflammation as indicators of exposure to airborne oxidants.

10.7 Summary

Biological markers represent a means to monitor environmental exposure by characterizing an individual's total dose of a contaminant from all sources of exposure. The main advantage of this strategy is in evaluation of an individual's total exposure using a measure which integrates over all exposure sources and is influenced by human behaviour. Biological markers are also believed to be more predictive of health effects than external measures of exposure. They address several exposure assessment needs:

- * characterizing an individual's or a population's exposure
- * generating population distributions of dose
- * identifying the environmental and demographic determinants of exposure.

The main disadvantage of biological markers is the difficulty in characterizing the individual sources which contribute to the subject's total exposure. When developing and utilizing biological markers, understanding the toxicokinetics of the contaminant in the system is crucial to characterize the biological variability and to determine whether the biological marker is valid for exposure assessment purposes at the concentration of interest. Biological markers have been crucial in improving our understanding of human exposure to certain contaminants, such as lead. Numerous non-invasive methods are available for biological monitoring, and exposure assessors should try to include these when developing environmental monitoring protocols.

11. QUALITY ASSURANCE IN EXPOSURE STUDIES

11.1 Introduction

Human exposure studies are complex and often utilize specialized instrumentation and management of large amounts of data. Consequently, quality assurance (QA) should be applied to all aspects of an exposure study, including its design, implementation and reporting, to ensure the reliability and reproducibility of the results. A successful QA programme will monitor occurrence of potential errors in various components of the study and establish protocols for remedying such errors. In this chapter, important types of potential error in exposure results are described, and tools for identifying them are introduced.

Exposure studies involve evaluations and comparison of exposures over time, geographical locations and populations. It is important that the results of the study accurately represent the exposures, rather than reflecting bias or error introduced by the study design or method. The reader is referred to the previous chapters on strategies and designs for exposure studies (Chapter 3) and related statistical concepts (Chapter 4) with respect to the principles of designing a high quality exposure study.

The reader is also referred to *Environmental Health Criteria 141: Quality Management for Chemical Safety Testing* (IPCS, 1992) a monograph which deals explicitly with the organization of a QA programme. A prerequisite for producing data of good quality in exposure studies is the availability of adequate facilities,

equipment, and personnel who are both well educated and trained. Studies need to be adequately designed and planned. Field and laboratory procedures need to be well defined, so that they can be carried out in the most appropriate way and in a consistent and reproducible manner. Other key elements in performing and reporting exposure studies include the final report and, lastly, the archiving and retention of data (IPCS, 1992)

11.2 Quality assurance and quality control

It is important to distinguish between the related concepts of QA and quality control (QC). QA refers to the overall management and organizational systems instituted to assess and maintain the integrity of the study. It includes independent monitoring that assures end users of the data that facilities, equipment, personnel, methods, practices, records and controls conform to accepted quality management principles. An effective QA programme provides confidence that the overall study meets the pre-established quality standards of accuracy, precision, completeness and clarity. QA should be integrated within the entire study so that the results are valid and that the final report accurately reflects these results (IPCS, 1992). Assessing data periodically is an essential aspect of QA.

QC is a valuable QA tool that is applied to individual components of the study. Examples of such components are selection of study participants, collection of environmental samples, chemical analysis and analysis of data. The quality of an analytical measurement may be evaluated, for example, by comparing analytical results against a known standard, determining the sensitivity, accuracy, and precision of the analysis and ensuring that the analytical equipment has been properly maintained. These measurements would be part of a QC system (IPCS, 1992).

Auditing procedures, on the other hand, are used to assess the quality of other aspects of a monitoring operation such as sampling procedure and transport of samples, as well as recording and reporting data. These procedures, although not necessarily quantitative, will generally promote vigilance by the operator against possible errors (WHO, 1986).

11.3 Elements of a quality assurance programme

All exposure studies must have a QA programme with a corresponding quality assurance plan that describes the implementation of the programme. The US EPA, for example, requires the development of detailed QA project plans that contain a complete description of all elements of the QA programme associated with the collection, measurement, validation and reporting of data. Common elements in QA plans are given in Table 36.

Table 36. Common elements in quality assurance plans

Organization and personnel
Record keeping and data report
Standard operating procedures

Equipment maintenance and calibration

Internal audit and corrective action

Sample handle management

A fundamental step in the QA process is the delineation of the study objective and a description of the study design which describes the study population, the data to be collected and the statistical analysis to be performed to meet the objectives. The programme management must be described (which identifies individuals in the programme and defines their responsibility from management, field monitoring, sample handling, sample analysis, data reduction and reporting). All programmes must have a QA officer who is independent of the programme and organization and who has oversight of all QA

activities. The QA plans must define data quality objectives (accuracy, precision, detection limit, representativeness and completeness) and demonstrate that they are adequate to meet the study objectives. Specific procedures for generating and validating study data are given. An important component of any exposure study is demonstrating the feasibility of all study procedures through a pilot study which should be included in the QA plan. For complex field studies where methods of procedures may require modification in the field, it is important to clearly delineate corrective action procedures. Standard operating procedure (SOPs), detailed protocols for all components of the study, are appended to the QA plan. A description of these are given in section 11.4.3.

11.4 Quality assurance programme

Important elements in assuring that the outcome and data generated from the laboratory is accurate and reliable depends on the QA programme implemented by the laboratory. Key elements are given in the following.

11.4.1 Organization and personnel

It is important for the competent laboratory to establish an organization that can function to best serve the need of the testing facilities, regardless of the specific organization structure, personnel include management, study directors, QA coordinator and support staff. Properly trained personnel are crucial to the conduct of a quality study. The training requirements and procedures should cover professional, technical and support staff, to assure that they have adequate knowledge and skills to carry out their duties.

11.4.2 Record-keeping and data recording

Detailed records, with dates, should be kept on the introduction of new batches of so-called useable supplies (e.g., filters, reagents, sample containers, plasticware, pipettes, etc). Likewise, any changes in instrumentation or personnel have to be recorded. Afterwards, when identifying the reasons for changed analytical performance, this kind of thorough record-keeping is of utmost importance.

The risk of introducing errors while transcribing data into record books or entering them into computer files is quite large. These are so-called clerical or human errors which may involve not

only numerical errors but also formatting errors, identification errors, etc., which can lead to a serious bias in the analysis of data. There are several procedures for spotting such errors, from simply reviewing the data visually to computerized procedures which flag questionable data.

Finally, data sets should be validated, that is approved for analysis. Data validation should form part of QA, and its procedures should be clearly defined. Data validation usually consists of two parts: data entry procedures to identify formatting errors at the time of entry, and acceptance procedures which are designed to compare the reported data against specified criteria in order to judge the reasonableness of reported values. Acceptance procedures identify various types of anomalies in the data including impossible values, individual and multiple outliers and entire subsets of incorrect data.

11.4.3 Study plan and standard operating procedures

QA involves the development and use of study plans and SOPs. The study plan (which should be very explicit and detailed) is the most important document for providing information to all participants on all aspects of the study, including information on responsible personnel, sample collection, sample storage and pre-analytical treatment, analytical procedures and data analysis. Deviations from the study plan in, for example, sampling frequency, sampling media or sampled population, necessitate a detailed amendment to the study plan. This is very important since in many monitoring studies sampling occurs on a regular basis, and the data obtained may be worthless if the present sampling scheme is not followed.

SOPs are written instructions which describe how to perform all field and laboratory activities. These should be available to all personnel involved in the field and laboratory work and be a component of their training programme. SOPs ensure that all personnel associated with study operations will be familiar with and use the same procedures. If different individuals perform important study functions, such as storing samples, preparing solutions, running analytical equipment, or archiving documents, these operations should be performed in the same manner. By standardizing procedures for the conduct of studies, SOPs have a valuable QA function. They prevent the introduction of many potential errors in the generation, collection and reporting of data.

The development of SOPs includes the following aspects: who should prepare, review and authorize SOPs; which field and laboratory operations require SOPs; and what information the SOPs should contain. The nature of the laboratory work being done and the training and experience of the laboratory personnel at a particular facility should determine exactly how extensive the content needs to be (IPCS, 1992).

11.4.4 Collection of samples

The potential for contamination is a major issue in environmental sampling. The highly sensitive analytical instrumentation currently available permits analysis of very small analyte quantities where the amounts of pollutants or chemicals present in environmental media are often quite low (e.g., parts per billion). The risk of significant contamination is particularly great when monitoring low concentrations of substances ubiquitous in the environment or present in the

materials and tools coming into contact with the samples.

Samples must be handled and stored in such a way that the level of the substance to be analysed remains stable. Processes that are most likely to decrease sample stability include precipitation, chemical deterioration (e.g., photolysis), surface absorption and evaporation of the analyte. Another factor that could be important is changes in the matrix, which may affect recovery of the analyte.

11.4.5 Equipment maintenance and calibration

Adequate equipment should be available for the receipt, handling, storage and analysis of samples. Its maintenance and calibration is essential to QA practise. Equipment used for analysis must be tested, calibrated and standardized.

11.4.6 Internal audit and corrective action

Internal audit and corrective action are critical activities in QA management. Audit procedures are to verify that the procedures are conducted the way they were planned and described in the study plan. Non-conformance must to be corrected to attain the study objectives.

11.5 Quality control/quality assurance for sample measurement

11.5.1 Method selection and validation

A chemical compound can usually be analysed by a variety of different methods. Some methods emphasize quality of analysis, i.e., accuracy and precision, whereas others are directed mainly towards practicality and low cost. However, even the best method may give incorrect results if improperly used. Methods are customarily classified according to their main use in the analytical field into definitive, reference and field routine methods. The best approximation of the true value obtained by analysis is the *definitive value*, i.e., the result obtained by the definitive method. The definitive method is, however, generally not considered practicable for daily laboratory use. Therefore, the purpose of a *reference method* is often to serve as a basis for the determination of the accuracy of the field methods. *Field methods* (or *routine methods*) are those in everyday use in the laboratory. They are not necessarily as precise and accurate as reference and definitive methods. Their use is justified, however, because the definitive and reference methods are often too cumbersome and expensive and may not be available. The precision and bias relating to the method should be known for every routine method used.

The following data quality specifications have to be validated in method selection to meet the requirements and objectives of the exposure assessment project.

11.5.1.1 Accuracy

Accuracy is defined as the closeness of agreement between a test result and the accepted true value. Accuracy or validity of an analysis is primarily determined by the specificity of the method and the analytical recovery.

Fig. 31A illustrates the ideal case where the reported values correspond exactly to the expected values. However, all analytical

procedures are subject to a variety of analytical inaccuracies or biases. Fig. 31B shows the effects of a *proportional bias* in which the reported values are higher than the expected values. This bias is called proportional because the amount of bias increases in direct proportion to the concentration of analyte in the specimen. Fig. 31C illustrates the effect of a *constant bias*, in which the reported values are higher than the expected values by a constant amount, at all concentrations of analyte. The biases shown in Figs. 31B and 31C are positive biases, because the reported values are greater than the expected values. Of course, negative biases may also occur; furthermore, the reported values may fall along a curve rather than a straight line. Fig. 31D illustrates combined positive and negative proportion biases. When combined biases are present, there is frequently one concentration at which the reported value corresponds to the expected value. This phenomenon -- that the reported value at some analyte concentration is the same as the expected value whereas there is disagreement at all other concentrations -- is commonly observed and must be considered when interpreting quality control data. Because of this, it is recommended that reference samples should cover the range of expected measurement values.

11.5.1.2 Precision

Precision or reliability of an analysis refers to the uniformity of the results of replicate analyses irrespective of the true concentration of the analyte. The precision of an analysis may vary depending on many factors, such as the skill and experience of the analyst, the purity of the chemicals, the quality of measuring devices and the time interval between replicate analyses. The precision is determined by calculating the percentage relative standard deviation among replicate analyses. In this manner precision can be defined as the closeness of agreement between independent test results obtained under prescribed conditions.

The effects of random variation on analyses are illustrated in Figs. 32A and 32B, which show how laboratory's results may, on the average, fall along some operational line even though the individual results are distributed about the line, within certain limits of variability. Fig. 32A illustrates limits of variability that increases in proportion to the mean analyte concentration.

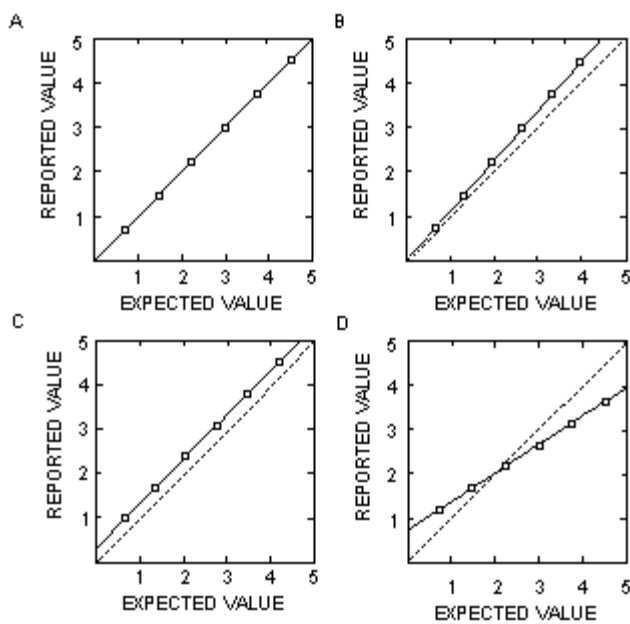


Fig. 31. Illustration of various types of bias (A, no bias; B, proportional positive bias; C, constant positive bias; D, combined positive and negative proportional bias) (from UNEP/WHO, 1986)

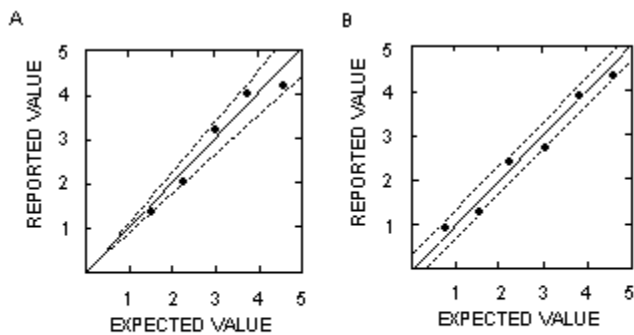


Fig. 32. Illustration of random analytical variability (A, variance proportional to concentration; B, variance independent of concentration)

11.5.1.3 Sensitivity

Sensitivity of a test method can be defined and measured as the *limit of detection* (LOD) and the *limit of quantification* (LOQ).

11.5.1.4 Detection limits

Appropriate determinations of detection limits is crucial to exposure data analysis and interpretations. Since there are several types of detection limits, each with its specific applicability, it is important that the methods and procedures to determine such limits be

clearly presented as part of the QA/QC procedures. The term "lower limit of detection" (LLD) may refer to very different concepts. For example, the instrumental detection limit is defined as a multiple of the noise level of the analytical instrument, usually a factor of 3. However, when sampling and analysing environmental media, the instrumental detection limit constitutes only a fraction of the true limit of detection. The LOD takes into consideration the response of the analytical instrument to the specific analyte in standards of known concentration or, preferably, a matrix similar to that of the sample. Since the response of the instrument to repeated analysis of the same analyte concentration varies, the LOD is estimated as a function of the standard deviation (SD) of the repeated analysis, typically as $t_{n-0.01} \times SD$, where t is the value of the Student t distribution with $n-1$ degrees of freedom, $\alpha = 0.01$ is the type I error and n the number of repeated analyses, usually 7.

However, sampling methods can have a background of one or more of the target analytes. For example, when using solid sorbent for air sampling, the sorbent may contain varying levels of background contamination across samples (e.g., varying benzene concentrations in Tenax). The *method detection limit* (MDL) includes the background contamination in the sampler. It is determined using a similar statistical approach as the LOD, but using field and/or laboratory blanks instead of the known analyte concentrations. The MDL can be defined as the analyte concentration at which we have a given certainty (e.g., $1-\alpha = 0.99$) that the sample concentration differ from background. Finally, the lower quantification limit (LOQ) is defined as 10 SD, where SD is derived from the LOD determination. LOD, MDL and LOQ differ across laboratories using the same methods. More importantly, they vary over time for the same laboratory.

The treatment of values below the MDL in statistical analysis of the data can have a strong impact on estimates of exposure distribution parameters. The reader may refer to Gilbert (1987), for more specific information. There also are upper limits of detection, defined by the range of linear response of the analytical method. In that case the detector may be overloaded with the result that it is not working in its linear detection range.

11.5.2 Internal quality control

The purpose of internal QC is to document that the method is in statistical control and without systematic errors so that the observed sampling results consistently fall within established control limits. Internal QC procedures are used primarily for the control of analytical precision (Taylor, 1988).

11.5.2.1 Control charts

Sometimes changes in the analytical performance are not abrupt but take place gradually ("drift"). Such gradual changes are difficult to perceive from a single central result, but many become evident with time if the results of control samples are graphically displayed with respect to time or sequence of measurements.

Control limits are used as criteria for signalling the need for action, or for judging whether a set of data does or does not indicate a state of statistical control. Control limits can be based entirely on the data from the samples, in which case the chart illustrates whether the method or procedure is repeatable. If the control chart

contains limits that are based on analytical standards, then the chart is useful for discovering whether the observed measures for a sample value differ from the adopted standard values by an amount greater than should be expected by chance alone. Generally, control charts consist of warning limits and action limits. Warning limits often correspond to ± 2 SD from the mean, whereas action limits are set at ± 3 SD from the mean. Such thresholds mean that as long as the process is in control at the centre value there is a 5% chance that a result will exceed the warning limits and a 0.3% chance that a result will exceed the action limit, thus erroneously signalling an "out of control" message (WHO, 1986; ISO, 1993).

To set up a Shewhard control chart (Fig. 33), measurements of, for instance, standard solutions, duplicates or spiked samples must be gathered while the analytical procedure is in control. The control parameters most frequently evaluated in Shewhard control charts include the average or median of control measures (average or median charts) and the range (difference) between duplicate analyses on the same test sample (range charts) (UNEP/WHO, 1986; AOAC, 1991; ISO, 1991; Christensen et al., 1994). In a cumulative sum (cusum) chart (Fig. 34) a reference value, usually the intended or expected value, is subtracted from each observation. The cumulative sums of the deviations from the reference value are formed, and these cusums are plotted against the serial numbers of observations. The cusum chart is usually more sensitive to small shifts in level than the Shewhard chart and highlights persistent and recurring differences (Christensen et al., 1994; ISO, 1997).

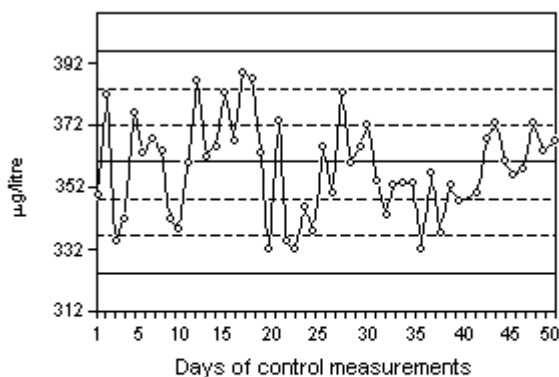


Fig. 33. The Shewhard chart. The mean of two control measurements are plotted in order of appearance (run number or days of control measurements) (from Christensen et al., 1994)

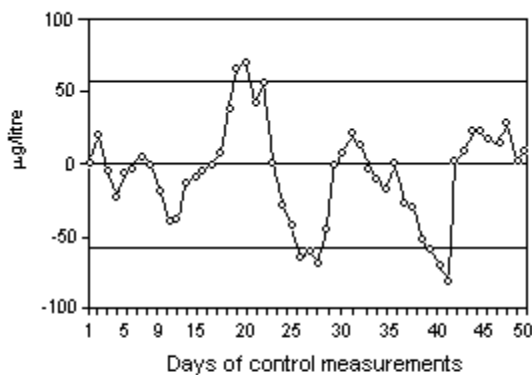


Fig. 34. Cusum control chart calculated on the basis of the previously shown QC plotted in the Shewhard chart (Fig. 33) (Christensen et al., 1994)

The Shewhard chart has six control limit lines corresponding to $\pm\rho_p$, $\pm 2\rho_p$, and $\pm 3\rho_p$ ($\rho_p = \rho_y / n^{1/2}$) (ρ_p , appointed standard deviation in the control chart; ρ_y , estimated standard deviation of the distribution of results; n , number of control results) (Christensen et al., 1994).

11.5.3 External quality control

The aim of external QC is to demonstrate that analytical results obtained are accurate and comparable with the results ascertained by other laboratories. Usually, external QC measurements form part of external QA schemes or proficiency testing programmes. In such a scheme or programme, the coordinating laboratory prepares a homogeneous reference sample and distributes portions to the participating laboratories for analysis. Participating laboratories are required to examine the reference samples within a specified time, preferably together with collected samples, and submit the results of the reference samples to the coordinating laboratory which collates the data, performs a statistical analysis and sends an evaluation report back to the participating laboratories. In cases of poor performance, the laboratories may be contacted, and suggestions may be made for improving performance.

External QC schemes offer participating laboratories many advantages. They demonstrate the reliability of laboratory results and provide independent evidence of the quality of laboratory performance and individual analyst proficiency. In addition, external quality schemes allow participating laboratories to compare their own performance with that of other laboratories. Participation in an external QC scheme can encourage self-appraisal and minimization of laboratory errors. It can also be used to reduce the frequency of internal QC efforts when consistently favourable results are achieved on external QC test samples. Furthermore, it can assist in identifying needs for training and changes in laboratory procedures (AOAC, 1991).

Examples of existing external QC schemes are given in Table 37 (see also Christensen et al. (1994)).

A specific example for an approach used in external QC is the UNEP/WHO regression method. The regression method is based on the QC programmes developed in the UNEP/WHO pilot project on assessment of human exposure to pollutants through biological monitoring for the determination of lead in blood and cadmium in kidney cortex (Vahter, 1982). This external QC method was also applied in the UNEP/WHO Human Exposure Assessment Location (HEAL) study. For the studies on lead and cadmium, reference external QC samples of blood, air filter material, dust and diet were sent to participating laboratories (Vahter & Slorach, 1990). The same procedure was also adopted for the HEAL nitrogen dioxide study, using standard sodium nitrite solutions and nitrogen dioxide-exposed sample badges as QC samples (Matsushita & Tanabe, 1991).

Table 37. External QC schemes

Scheme	Country	Reference
Centre de Toxicologie du Quebec (CTQ)	Canada	Weber, 1988
Danish External Quality Assessment Scheme (DEQAS)	Denmark	Anglov et al., 1993
External quality control in the toxicological analyses of biological materials, German Society of Occupational Medicine	Germany	Schaller, 1991
Japanese External Quality Assessment Scheme	Japan	Sugita et al., 1990
NIOSH Proficiency Analytical Testing Programme	USA	NIOSH, 1979
United Kingdom National External Quality Assessment Schemes (UKQAS)	United Kingdom	UKNEQAS, 1993; Bullock, 1986

The accuracy and precision of the analytical results were evaluated by using a statistical technique known as the maximum allowable deviations (MAD) method (Vahter, 1982; WHO, 1986; UNEP/WHO, 1991). This method is based on the linear regression line of reported versus "true" values and established acceptance criterion on how much the line may deviate from the ideal line where the measured equals the expected value. Acceptance criteria or the MADs have to be decided on separately for each pollutant or for each medium. The stringency of the MAD is primarily based on the required quality of the actual monitoring data and the sensitivity, accuracy and precision of the analytical methods. As in the use of control charts, decision concerning acceptance and rejection of results is based on statistical criteria, i.e., on the probability of making right or wrong decisions. A laboratory may be erroneously rejected when in fact its methodology is satisfactory, or it may be erroneously accepted when its methodology is not satisfactory. Power analysis is done to determine the probability of including an unsatisfactory laboratory. The concept

of statistical power is described more fully in Chapter 4.

On the basis of the power analysis, acceptance intervals (AI) can be calculated for a laboratory. The AI will be narrower than the interval between the MAD lines and the AI lines will be closer to the MAD lines with increasing number of QC samples. Also, methods with inherently smaller errors will decrease the difference between the MAD

lines and the AI. Fig. 35 shows the regression line for the reported results of analysis of six QC samples versus the reference values. The MAD interval is indicated by solid lines and the acceptance interval by broken lines (Vahter, 1982). Fig. 36 shows the results of lead in blood from one laboratory during the training phase in the global UNEP/WHO Project on Assessment of Exposure to Lead and Cadmium through Biological Monitoring. The results of QC 2 and QC 3 were rejected, i.e., the regression lines fall outside the acceptance lines when evaluated between the reference values 100 and 400 µg/litre (Lind et al., 1987).

The experience from the QA programme of the WHO/UNEP HEAL Programme shows that detailed protocols, instructions, and control activities covering the whole process, from sampling to analysis and data reporting, are essential if reliable data are to be obtained. The results clearly demonstrated that good analytical performance for a pollutant in one medium (e.g. lead in blood) is no guarantee of good performance for the same pollutant in another medium (e.g., lead in air filters). Similarly, good analytical performance at one concentration is no guarantee of good performance at higher or lower concentrations. It is, therefore, important that the QC samples have a matrix similar to that of the monitoring samples and that the concentrations of the QC samples cover the expected range of concentrations. One, or a few, reference samples are not sufficient for the evaluation of the evaluation of analytical performance using rigorous MAD criteria (Vahter & Slorach, 1990).

11.5.4 Reference materials

Reference materials are important means of ensuring comparability of analytical results across laboratories, over time, among populations and among studies. Reference samples for internal as well as external QA have been used in the analysis of environmental media, such as air, water and food, as well as for biological tissues and body fluids, such as internal organs, blood and urine. It is important that reference materials have a matrix which is the same or very similar to the matrix the "real" monitoring samples are comprised of. Matrix effects may seriously invalidate analytical results. The concentrations of a substance to be measured should also cover the same range as is expected in the monitoring samples. For several substances, the chemical forms in which they may exist must be taken into consideration. For example, arsenic, mercury, tin and several other metals occur in a number of different valence states and in organic and inorganic forms which vary in stability.

Various types of reference samples are commercially available. The International Atomic Energy Agency (IAEA) conducted a survey on analytical reference materials of biological and environmental origin. The IAEA database presently contains over 10 000 analyte values for 455 substances in 650 reference materials produced by 30 different suppliers (IAEA, 1995, 1996). It is expected that this survey will help analysts to select reference materials for QA purposes that match

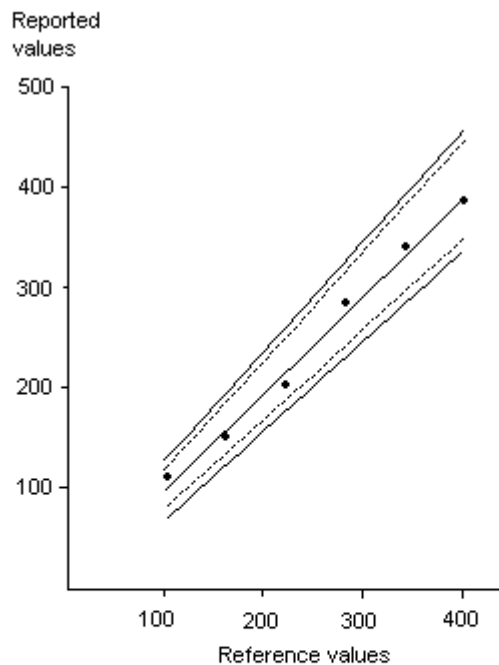


Fig. 35. Regression for the reported results of analysis of six QC samples versus the reference values. The MAD interval is indicated by solid lines and the AI by broken lines. MAD lines which are not including the operating error of the methods or AIs which include the operational error represent a power of 90%, which means that the probability of accepting an unsatisfactory performance is 10% (Vahter, 1982).

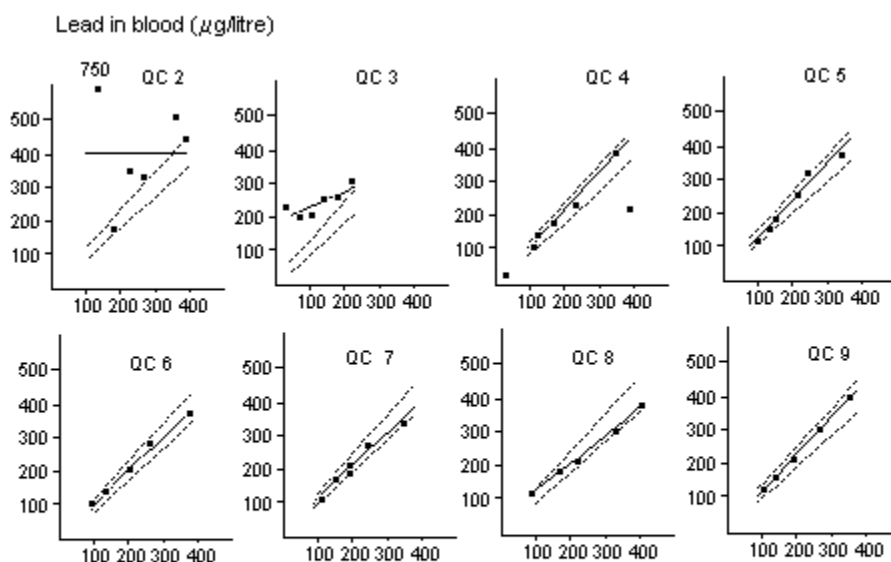


Fig. 36. An example of lead results from QC runs in the UNEP/WHO assessment of Human exposure to lead and cadmium through biological monitoring study. QC runs 2 and 3 (QC 2 and QC 3) were rejected. x-axis, reference values (µg/litre); y-axis, reported values (µg/litre).

as closely as possible, with respect to matrix type and concentrations of the samples and analytes of interest.

The availability of certified reference materials is still limited, however. In addition, owing to their relatively high cost, these materials can only occasionally be used for QC. Alternatively, a laboratory may prepare control materials calibrated against and, therefore, traceable to certified reference materials, or a conventional true value may be established by one or more reference laboratories, preferably using a validated definitive method (ISO, 1994).

11.6 Quality assurance and control issues in population-based studies

Population-based studies present specific challenges to QA/QC programmes that are not common to more conventional exposure investigations. A description of the potential problems and alternative approaches to address them, avoid them and estimate the biases that they may introduce in the results should therefore be part of the study plan. Study design, including QA/QC procedures, should consider methodologies that address configurations as they occur in the field, and provide for modifications that will not compromise the stated objectives.

Among the most important considerations in human population studies are the potential differences in cultural, geographical or social class framework between the exposure assessment study team and the target population. The investigators should be cognizant of local culture and conditions and include those considerations in the study design. For example, perceptions and customs with regard to the importance of time in daily life varies across cultures and even among subpopulations within the same country. As a result, appointments for

household visits and interviews may not be kept as the field personnel expect.

A good approach for identifying problems and alternatives is the use of pilot studies before full implementations of the field component of a study. In pilot studies, trained staff perform the complete set of SOPs established for the full investigation on a small subset of the sample population. Thus, pilot studies also have the purpose of effectively providing final training of all field personnel. The information collected during these studies is very useful for adjusting the study plan and SOPs for local conditions. It is important that all personnel participating in a field study, i.e., study design personnel, principal and co-investigators, laboratory staff and field personnel require practical experience with the local field conditions. Pilot studies provide the means to obtain such experience.

Another potential confounder in population studies is the *Hawthorne effect*; that is, the alteration of behaviour patterns that might affect exposures as a result of participation in the study. For example, many population-based field studies provide compensation to individuals who agree to participate. Monetary compensation could alter behaviour patterns that may affect exposure: for example, the participant may decide not to go to work (a typical activity) the day he receives the payment and instead spend the time performing an activity that is not customary. This problem can be resolved by offering the payment a short time after the participants have completed the monitoring period. The presence of an environmental monitor (e.g., an air sampling inlet and pump) may cause participants to avoid situations in which they may feel conspicuous, such as their place of employment. An innovative approach for assessing the influence of this effect is to expand the study to include a subsample of participants who engage in only a portion of the study (e.g., a time-activity questionnaire) and to compare the results for this group to those for the remainder of the population that completed the full monitoring programme.

11.7 Summary

QA includes independent study monitoring that assures laboratory management and users of data that facilities, equipment, personnel, methods, practices, records and controls confirm to accepted quality management principles. Errors in exposure data may be due to analytical variation as well as changes that may take place during sample collection and handling, preparation and storage of samples, and data keeping and data recording. Analytical variation can be divided into two major categories: accuracy, which refers to the agreement between the amount of analyte measured and the amount actually present, and precision, which refers to the random variability or reproducibility of the method.

The study plan is the most important document for providing information on the critical components of an investigation, e.g., responsible personnel, sample collection, sample storage and pre-analytical treatment, analytical procedures and data analysis. SOPs are appended to the study plan and contain written detailed instructions on how to perform certain routine field and laboratory activities. The study plan and SOPs can be seen as management directives designed to ensure that all personnel associated with study

operations will be familiar with and use the same procedures.

QC refers specifically to the quality of the laboratory results. It has two components. Internal QC is a set of procedures used by staff of a laboratory for continuously assessing results as they are produced. External QC is a system for objective checking of laboratory performance by an independent agency. Internal QC includes displaying results of control samples in control charts (e.g., Shewhard and cusum charts), and use of control limits as criteria for signalling the need for action, or for judging whether a set of data does or does not include a state of statistical control. External QC, on the other hand, provides independent evidence of the quality of laboratory performance and individual analyst proficiency. Usually, a

coordinating laboratory distributes samples of known concentration to the participating laboratories. Participating laboratories examine the reference samples and submit the results to the coordinating laboratory for performance evaluation.

Reference samples used in internal and external QC should have a matrix and pollutant concentration which is similar to the real sample. In addition, for several substances it is necessary to take into consideration the chemical form in which they may exist.

Finally, interactions with human populations present a unique set of study design and QA considerations that should be carefully evaluated together with the conventional issues of sampling analysis and procedures.

12. EXAMPLES AND CASE STUDIES OF EXPOSURE STUDIES

12.1 Introduction

Exposure studies have helped to establish a subdiscipline of environmental science. Exposure analysis is now essential to environmental epidemiology and quantitative risk assessment. Exposure studies have called attention to practices, locations and populations subjected to higher risk owing to environmental contamination. However, the full promise of exposure analysis has not been realized. Exposure information can influence public opinion and policy and offer cost-effective innovative strategies for those looking for alternatives to current regulatory approaches. Our current practice is to partition problems into specific media (air, water, soil and food) and structure our management as restrictive commands limiting discharge. Exposure analysis is an integrated and more comprehensive approach for dealing with risk management.

Kirk Smith discusses the potential of human exposure assessment for air pollution regulation (in WHO, 1995a). He argues that for developing countries, without the investment in monitoring, regulation and control infrastructures, exposure reduction strategies "may provide a much more efficient pathway of control over time than the path followed by the currently developed countries". Structuring a regulatory control programme that bases performance on the reduction of human exposure while also considering cost should appeal to market economies in both developed and developing countries. In order to implement such strategies effectively one must have the ability to quantitatively assess the relative contribution of various sources to human exposure and risk by measurement or modelling. With the development of exposure science, trading exposures among sources and

pathways results in the possibility of integrating the concept of *product stewardship*, which would include extraction, manufacturing, consumer use and disposal. If society sets the performance goal of exposure minimization both for humans and for the ecosystem, the commercial and governmental institutions can devise more cost-effective responses. For example, a company might receive credit for reformulating a product that reduces exposures to VOCs in the home. The cost to the company might be far less in terms of exposure reduction *per capita* than equipping the manufacturing site with emissions control equipment that reduces local concentrations.

Before exposure trading across media, across pollutants or between employees and the general public can seriously be considered, the science of exposure assessment must mature. A great deal more must be learned about risk-producing behaviours and activities, about variation in individual susceptibility, and about the chronic as well as acute implications of mixtures of pollutants. Progress has been made in these areas, and studies are continuing. Perhaps the contribution of exposure assessment to environmental epidemiology best exemplifies its advancements in recent years. As environmental epidemiology is practised today, quantification of exposure measures play a significant role vital to study design and to interpretation.

Linet et al.'s article (1997) on residential exposures to magnetic fields and acute lymphoblastic leukemia in children is an excellent case in point. They measured magnetic field strength in the current and former housing in over 1200 cases and controls. No associations were reported for direct measures of magnetic field strength exposures in this study, although some previous studies had found association between childhood leukemia and surrogate indicators of exposures to magnetic fields (power line classification schemes).

Exposure information has influenced risk management and public policy. A well-known example involves materials containing asbestos. In the USA, as a result of US EPA's response to actions regarding the handling of asbestos-containing material in schools as well as numerous legal suits on behalf of asbestos industry workers, there was a costly and widespread effort to remove all asbestos from buildings. Eventually the review and public dissemination of studies showing insignificant exposures to asbestos to building occupants in the vast majority of situations resulted in a clarification of US EPA's policy and an end to the indiscriminate removal of all asbestos-containing material regardless of its condition (HEI, 1991; Camus et al., 1998).

We now see the concern for protecting the public from environmental risk requiring more information about exposures. Recently, the US Congress passed the Food Quality and Protection Act. For the first time legislation has explicitly recognized the problem of multiple source exposure. The Act requires that EPA and other agencies account for aggregate or multiple sources of exposure when setting maximum allowable levels (i.e., tolerances) for pesticides in food. In this case, regulations are ahead of the science as current knowledge on the numerous pathways of pesticide exposure is not sufficient to establish a standardized methodology.

So in recent years, we have seen exposure analysis gain status. In 1998 the International Society of Exposure Analysis (ISEA) held its 8th annual conference in conjunction with the International Society for Environmental Epidemiology. ISEA has a journal with more than 500 subscribers worldwide. The European Commission in 1995 published

reports on *Exposure Assessment* (EUR 14356EN) and *Time-activity Patterns in Exposure Assessment* (EUR 15892EN) along with a report on *Study Design* (EUR 15095EN) for air pollution epidemiology in which exposure assessment was featured.

The US EPA (1996a) updated its 1989 *Exposure Factors Handbook* (EPA/600/8-89/043) with a comprehensive three-volume compilation of statistical data on various factors used in assessing exposure. The updated document incorporates new information available from the late 1980s through the first half of the 1990s. Used by risk assessors in conjunction with the revised *Guidelines for Exposure Assessment* (US EPA, 1992a), the new *Exposure Factors Handbook* gives point estimates for many parameters along with distributional information. The median as well as the high end of individual and population risk can be calculated using these inputs and appropriate concentration data.

As described earlier in the book, the WHO has been promoting exposure assessment methodology and investigations for almost 20 years. The HEAL project has provided training, documents and assistance to investigators worldwide. Notable successes of HEAL have been the establishment of high-quality measurements for metals such as lead and cadmium (see Foreword and Chapter 11).

A number of professional organizations have contributed to the promotion of exposure sciences through conferences, workshops and publications. Although a comprehensive description of all these efforts is beyond the scope of this chapter, readers may find some of the publications listed in Table 38 useful.

12.2 Exposure studies

Exposure studies described in this chapter serve as examples of the variety of approaches and purposes such investigations have taken. Exposure studies are conducted for different reasons. Some were designed for the simple purpose of demonstrating methodology for generating hypotheses. Other studies were components of epidemiological studies. Still others were designed for regulatory purposes to determine possible exposure routes and dose rates for specific products or applications. Such studies may have participants adhere to a certain regime. There are also examples of large and expensive studies recruiting representative populations to provide generalizable exposure and risk estimates. Brief descriptions of different types of studies are presented in this chapter. Those included illustrate a variety of design strategies. The following discussion is not intended as a comprehensive review but may give the reader the sense of how exposure assessment can serve a variety of purposes.

12.3 Air pollution exposure studies

Perhaps the most numerous examples of exposure studies are in the field of air pollution. This section briefly presents examples of air pollution studies performed for a variety of purposes.

12.3.1 Particle studies

Particle exposures have taken a new importance in light of a substantial and growing literature on morbidity and mortality effects of ambient particulate matter (Wilson & Spengler, 1996). In 1986, the US Congress mandated that the US EPA Office of Research and

Development "carry out a TEAM study of human exposure to particles." The EPA Atmospheric Research and Exposure Assessment Laboratory joined with California's Air Resources Board to sponsor a Particle Total Exposure Assessment Methodology (PTEAM) study in the Los Angeles Basin. The study was carried out primarily by the Research Triangle Institute and the Harvard University School of Public Health. The main goal of the study was to estimate the frequency distribution of exposures to particles for residents of Riverside, California, a city of approximately 250 000 inhabitants located 75 km east of downtown

Table 38. Guide to documents on exposure assessment

The Potential of Human Exposure Assessment for Air Pollution Regulation (WHO, 1995a)
Human Exposure Assessment for Airborne Pollutants: Advances and Opportunities (US NRC, 1991b)
Methods for Assessing Exposure of Human and Non-human Biota (Tardiff & Goldstein, 1991)
Biological Monitoring of Metals (IPCS, 1992)
Guidelines for Exposure Assessment (US EPA, 1992a)
Dermal Exposure Assessment: Principles and Applications (US EPA, 1992b)
Methodology for Assessing Health Risks Associated with Indirect Exposure to Combustion Emissions (US EPA, 1990)
Estimating Exposures to Dioxin-Like Compounds (US EPA, 1994)
Superfund Exposure Assessment Manual (US EPA, 1988a)
Selection Criteria for Models Used in Exposure Assessments (US EPA, 1987, 1988b)
Standard Scenarios for Estimating Exposure to Chemical Substances During Use of Consumer Products (US EPA, 1986a)
Pesticide Assessment Guidelines, Subdivisions U and K (US EPA, 1984, 1986b)
Methods for Assessing Exposure to Chemical Substances, Volumes 1-13 (US EPA, 1983-1989)
Assessment of Human Exposure to Lead: Comparison between Belgium, Malta, Mexico and Sweden (Bruaux & Svartengren, 1985)
Guidance on Survey Design for Human Exposure Assessment Locations (HEAL) Studies (Kollander, 1993)
Air pollution in African villages and cities (Koning de, 1988)
Exposure Monitoring of Nitrogen Dioxide. An international pilot study within the WHO/UNEP Human Exposure Assessment Location (HEAL) Programme (Matsushita & Tanabe, 1991)
Assessment of Human Exposure to Selected Organochlorine Compounds Through Biological Monitoring (Slorach & Vaz, 1983)
Assessment of Human Exposure to Lead and Cadmium Through Biological Monitoring (Vahter, 1982)
Global WHO/UNEP: Environment Monitoring System. Exposure Monitoring of Lead and Cadmium (Vahter & Slorach, 1990)
Human Exposure to Carbon Monoxide and Suspended Particulate Matter in Zagreb, Yugoslavia (WHO, 1982a)
Human Exposure to SO₂, NO₂ and Suspended Particulate Matter in Toronto (WHO, 1982b)
Human Exposure to Suspended Particulate Matter and Sulphate in Bombay (WHO, 1984)
Human Exposure to Carbon Monoxide and Suspended Particulate Matter in Beijing, People's Republic of China (WHO, 1985c).
Guidelines for integrated air, water, food and biological exposure monitoring (WHO/UNEP, 1986)
Indoor Air Quality Study Maragua Area, Kenya (WHO/UNEP, 1987)

Indoor Air Quality in the Basse Area, The Gambia (WHO/UNEP, 1988)

Table 38. (continued)

An introductory guide to human exposure field studies: survey methods and statistical sampling (WHO/UNEP, 1992a)

Endemic fluorosis: a global health issue (WHO/UNEP, 1992b)

Human Exposure to Pollutants. Report on the pilot phase of the Human Exposure Assessment Locations Programme (UNEP/WHO, 1991)

Los Angeles. Another goal was to determine particle concentrations in the participants' homes and immediately outside the homes.

The study had a three-stage probability sampling procedure (Ozkaynak et al., 1996). Ultimately 178 residents of Riverside, took part in the study in the fall of 1990. Respondents represented 139 000 \pm 16 000 (SE) non-smoking Riverside residents aged 10 and above. Their homes represented about 60 000 Riverside homes.

Each participant wore a personal exposure monitor (PEM) for two consecutive 12-h periods. Concurrent PM₁₀ and PM_{2.5} samples were collected by a stationary indoor monitor (SIM) and stationary outdoor monitor (SAM) at each home. The SIM and SAM were essentially identical to the PEM. A total of 10 particle samples were collected for each household (day and night samples from the PEM₁₀, SIM_{2.5}, SIM₁₀, SAM_{2.5}, SAM₁₀). Air exchange rates were also determined for each 12-h period.

Up to 4 participants per day could be monitored, requiring 48 days to conduct the study. A central outdoor site was maintained over the entire period (22 September-9 November 1990). The site had 2 high-volume samplers with 10 μ m inlets (actual cut-point about 9.0 μ m), 2 dichotomous PM₁₀ and PM_{2.5} samplers (actual cut-point about 9.5 μ m), 1 PEM₁₀, 1 SAM₁₀ and 1 SAM_{2.5}.

More than 2750 particle samples were collected, about 96% of those attempted. All filters were analysed by XRF for a suite of 40 metals. More than 1000 12-h average air exchange rate measurements were made. A complete discussion of the quality of the data is found in Thomas et al. (1993a). LODs, based on 3 times the standard deviation of the blanks, were of the order of 7-10 μ g/m³. All field samples exceeded the LOD. Duplicate samples ($n = 363$) showed excellent precision for all types of particle samplers at all locations, with median relative standard deviations ranging from 2 to 4%.

Daytime mean personal PM₁₀ concentrations (150 μ g/m³) were more than 50% higher than either indoor or outdoor levels (95 μ g/m³). Overnight mean personal PM₁₀ concentrations (77 μ g/m³) were similar

to the indoor (63 μ g/m³) and outdoor (86 μ g/m³) levels. The higher personal concentrations do not appear to be due to skin flakes or clothing fibres; many skin flakes were found on filters (up to an

estimated 150 000 per filter) in subsequent scanning electron microscope (SEM) analyses, but their mass does not appear to account for more than 10% of the excess personal exposure (Mamane, 1992).

Mean $PM_{2.5}$ daytime concentrations were similar indoors ($48 \mu\text{g}/\text{m}^3$) and outdoors ($49 \mu\text{g}/\text{m}^3$), but indoor concentrations fell off during the sleeping period ($36 \mu\text{g}/\text{m}^3$) compared to $50 \mu\text{g}/\text{m}^3$ outdoors. Thus the fine particle contribution of PM_{10} concentrations averaged about 51% during the day and 58% at night both indoors and outdoors. Unweighted distributions are displayed in Fig. 37 for 24-h average PM_{10} personal, indoor and outdoor concentrations. About 25% of the population of Riverside was estimated to have 24-h personal PM_{10} exposures exceeding the $150 \mu\text{g}/\text{m}^3$ 24-h US National Ambient Air Quality Standard (NAAQS) for ambient air. Central-site $PM_{2.5}$ and PM_{10} concentrations agreed well with backyard concentrations. Overall, the data strongly suggest that a single central-site monitor can represent well the $PM_{2.5}$ and PM_{10} concentrations throughout a wider area such as a town or small city, at least in the Los Angeles basin.

Stepwise regressions resulted in smoking, cooking, and either air exchange rates or house volumes being added to outdoor concentrations as significant predictors of personal exposure. Smoking added about $30 \mu\text{g}/\text{m}^3$ to the total $PM_{2.5}$ concentrations. Cooking added $13 \mu\text{g}/\text{m}^3$ to the daytime $PM_{2.5}$ concentration, but was not significant during the overnight period. At night, an increase in air exchange of one air change per hour resulted in a small increase of about $4.5 \mu\text{g}/\text{m}^3$ to the $PM_{2.5}$ concentration, but was not significant during the day. The house volume was not significant at night, but was significant during the day, with larger homes resulting in smaller $PM_{2.5}$ concentrations. Since air exchange and house volume were weakly correlated (negatively), they were not included together in the same regression.

Following Koutrakis et al. (1992), a non-linear least squares regression equation was used to estimate penetration factors, decay rates and source strengths for particles and elements from both size fractions (Ozkaynak et al. 1996). Penetration factors were very close to unity for nearly all particles and elements. The calculated decay rate for fine particles ($< PM_{2.5}$) was $0.39 \pm 0.16 \text{ h}^{-1}$, and for PM_{10} was $0.65 \pm 0.28 \text{ h}^{-1}$. Since PM_{10} contains the $PM_{2.5}$ fraction, a separate calculation was made for the coarse particles ($PM_{10} - PM_{2.5}$) with a resulting decay rate of $1.01 \pm 0.43 \text{ h}^{-1}$. Decay rates for elements associated with the fine fraction were generally lower than for elements associated with the coarse fraction, as would be expected, due to their lower settling velocities. For example, sulfur, which is associated with the fine fraction of aerosols in the form of sulfate, had calculated decay rates of 0.16 ± 0.04 and $0.21 \pm 0.04 \text{ h}^{-1}$ for $PM_{2.5}$ and PM_{10} fractions, respectively. The crustal elements

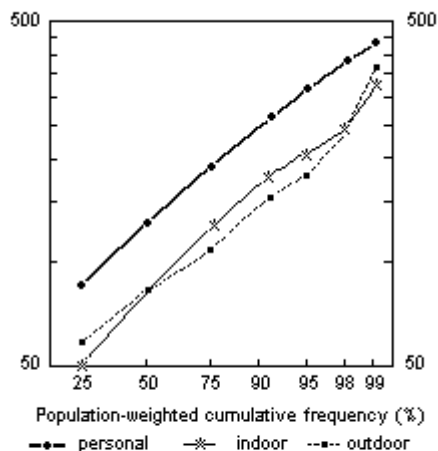


Fig. 37. PM₁₀: Daytime levels, PTEAM study, Riverside, California (from Thomas et al., 1993a)

(calcium, aluminium, manganese, iron) on the other hand, had decay rates ranging from 0.6 to 0.8 h⁻¹. Each cigarette emitted 22 ± 8 mg of PM₁₀ on average, about two-thirds of which (14 ± 4 mg) was in the fine fraction. Cooking emitted 4.1 ± 1.6 mg/min of PM₁₀ particles, of which about 40% (1.7 ± 0.6 mg/min) was in the fine fraction. All elements emitted by cooking were limited almost completely to the coarse fraction; presumably carbon or other elements not measured by XRF were contained in the fine fraction. Sources other than cooking and smoking emitted about 5.6 ± 3.1 mg/h of PM₁₀, of which only about 1.1 mg/h ± 1.0 (20%) was in the fine fraction (see Figs. 38 and 39).

Based on the mass-balance model, outdoor air was the major source of indoor particles in Riverside, providing about 75% of fine particles and 65% of inhalable particles in the typical home. It was also the major source for most elements, providing 70-100% of the observed indoor concentrations for 12 of the 15 elements. Unidentified indoor sources accounted for most of the remaining particle and elemental mass collected on the indoor monitors. The nature of these sources is not yet understood. They do not include smoking, other combustion sources, cooking, dusting, vacuuming, spraying or cleaning, since all these sources together account for less than the unidentified sources. For example, the unidentified sources accounted for 26% of the average indoor PM₁₀ particles, whereas smoking accounted for 4%, and cooking for 5%. Of the identified indoor sources, the two most important were smoking and cooking. Smoking was estimated to increase 12-h average indoor concentrations of PM₁₀ and PM_{2.5} by 2 and 1.5 $\mu\text{g}/\text{m}^3$ per cigarette, respectively. Most of this increase was in the fine fraction. Cooking increased indoor concentrations of PM₁₀ by about 6 $\mu\text{g}/\text{m}^3$ per min of cooking, with most of the increase in the coarse particles. Other household activities such as vacuuming and dusting appeared to make smaller contributions to indoor particle levels. An interesting finding was that commuting and working outside the home resulted in lower daytime particle exposures than for persons staying at home.

Multivariate calculations in two separate studies resulted in

rather similar estimates of the effect of smoking on indoor fine particle concentrations. Spengler et al. (1981) estimated an increase of about $20 \mu\text{g}/\text{m}^3$ per smoker, or $25 \mu\text{g}/\text{m}^3$ per smoking home, based on 55 residences monitored over a year in 6 US cities. In another study, a smoking effect of about $32 \mu\text{g}/\text{m}^3$ was estimated for smoking homes based on data collected in Tennessee, USA (Spengler et al., 1985).

12.3.2 Carbon monoxide

The largest personal monitoring study of carbon monoxide exposures was carried out by US EPA in Washington, DC and Denver, Colorado in the winter of 1982-1983 (Johnson, 1983; Hartwell et al.,

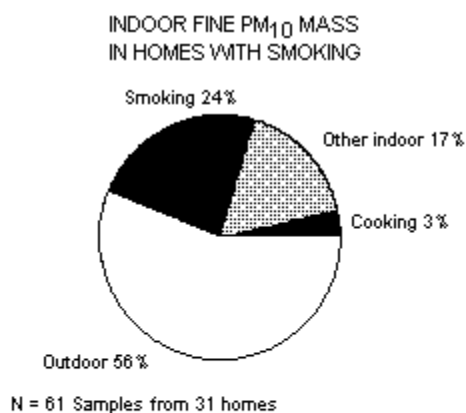
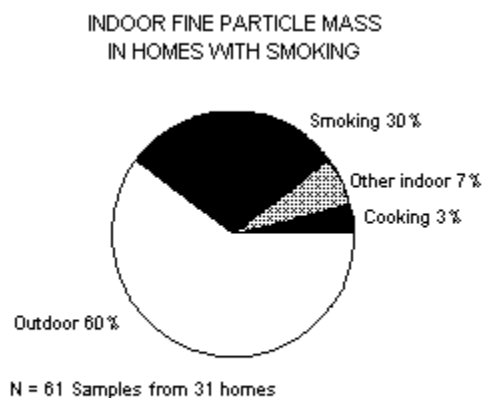


Fig. 38. Sources of fine ($\text{PM}_{2.5}$) Particles (top) and inhalable (PM_{10}) particles (bottom) in 31 homes with smoking

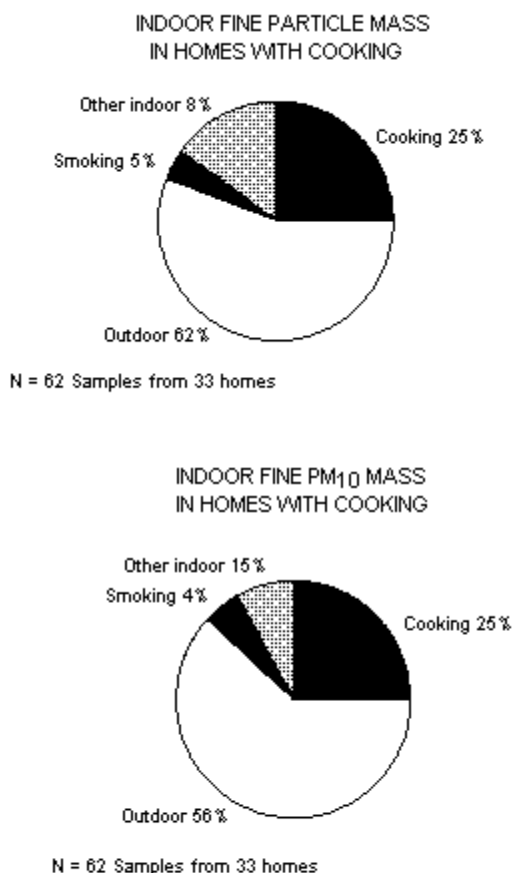


Fig. 39. Sources of fine (PM_{2.5}) particles (top) and inhalable (PM₁₀) particles (bottom) in 33 homes with cooking

1984; Akland et al., 1985; Johnson et al., 1986). About 800 people in DC and 450 in Denver were monitored for 24 h (48 h in Denver) using electrochemical carbon monoxide monitors with specially designed data loggers. The data loggers were capable of sampling the current from the monitor about 4 times a second. They were equipped with buttons that the subject could press when one activity ended and the next began; at that point, the logger would average all preceding values from the time the activity began. (There was also an automatic averaging every hour.) The result was an extraordinarily rich database, with approximately 1200 people averaging 40 activities per day, each with an associated average carbon monoxide level. At the end of the monitoring period, each subject provided a breath sample. Major findings of the study included the following:

- * Commuters had the highest exposures to carbon monoxide in general, averaging up to 13 $\mu\text{g/g}$. Parking garages had the highest carbon monoxide levels of any microenvironment, with churches and schools among the lowest.
- * The main indoor sources of carbon monoxide were gas stoves and cigarettes. Gas stoves increased levels by about 2.5 $\mu\text{g/g}$ when being used; homes with smokers had increases of about 1.5 $\mu\text{g/g}$ on average.

- * Personal exposures were higher than would be predicted by measurements at fixed monitoring stations. About 10% of DC residents appeared to exceed the 8-h standard of 9 µg/g, as determined by their breath concentrations, although only 1 of the 11 fixed stations exceeded the standard during the monitoring period.

A study of California homes (Wilson et al., 1993a,b, 1995; Colome et al., 1994), each monitored for 48 h, indicated that 13 of 277 homes (about 5%) had indoor 8-h averages exceeding 9 µg/g (the outdoor standard). Since the outdoor standard is to be exceeded only once per year, it is clear that the fraction of homes with 8-h indoor averages exceeding 9 µg/g more than once per year would be larger than the 5% observed in the single 48-h monitoring period. Homes with gas stoves and gas furnaces had indoor source levels for carbon monoxide that were about 3 times higher than homes without such sources. Homes with wall furnaces had higher levels of carbon monoxide than homes with forced-air gas furnaces. Homes with smokers (*n* = 85) had levels of carbon monoxide about 0.5 µg/g higher than homes without smokers (*n* = 190). Malfunctioning gas furnaces were a major cause of elevated concentrations of carbon monoxide. However, the homes with the highest carbon monoxide levels also included some with electric cooking stoves and electric heat, suggesting that other sources of carbon monoxide were present in these homes. Such sources could include cars idling in attached garages or unvented gas or kerosene space heaters.

12.3.3 Nitrogen dioxide

Nitrogen dioxide is a ubiquitous respiratory irritant for which air quality standards have been established in many countries (WHO, 1997d). It is emitted by industrial processes and mobile sources, but also by indoor combustion appliances such as gas cooking stoves and furnaces. Several studies in the 1970s suggested that children in homes with gas stoves suffered more infectious disease than children in homes with electric stoves; a possible connection with nitrogen dioxide (in lowering resistance) was postulated (Samet & Spengler, 1991). Also, exposure is likely to be higher for those living closer to roadways.

A study in Helsinki, Finland, explored weekly nitrogen dioxide exposure of preschool children as well as between- and within-children variances of repeated personal exposure measurements. The study tested the hypothesis that exposure to the low levels of nitrogen dioxide in Helsinki increases the risk of respiratory symptoms in preschool children (Mukala et al., 1996).

The parents of 246 children, aged 3-6 years, returned a letter of consent to participate in a personal nitrogen dioxide exposure study. The children spent their days at one of three daycare centres, two located in the downtown area and one in a suburban area. All children carried personal Palmes tubes on outdoor clothing one week at a time during six consecutive weeks in winter (14 January-4 March 1991) and seven consecutive weeks in spring (8 April-27 May 1991). Weekly concentrations of nitrogen dioxide were also measured inside and outside each daycare centre to assess the usefulness of the stationary measurements in estimating the variation of exposures. Ambient concentrations of nitrogen dioxide were monitored at three fixed sites of the Helsinki Metropolitan Area council network with

chemiluminescence monitors. The distance from each daycare centre to the nearest monitoring site varied from 0.5 to 11 km.

The geometric mean of personal nitrogen dioxide exposure levels of in the total 13-week period was 26.5 $\mu\text{g}/\text{m}^3$ in the downtown area and 17.5 $\mu\text{g}/\text{m}^3$ in the suburban area. These exposure levels were significantly lower than ambient air levels of nitrogen dioxide in the same areas. Gas cooking stove or/and smoking at home significantly increased personal exposure to nitrogen dioxide. The weekly exposures averaged over all children in each daycare centre correlated poorly with the fixed site ambient air levels ($r^2 = 0.37$), but much better with the nitrogen dioxide levels inside and outside the daycare centres ($r^2 = 0.88$ and 0.86 , respectively). In the suburban and downtown groups the between-child variances in nitrogen dioxide exposures were only 14% and 28% of the total variances, which were dominated by the within-child variances.

Stationary measurements at the ambient air fixed sites and inside and outside the daycare centres explained the variations in personal nitrogen dioxide exposures of the children well during the spring, but not during the winter. A statistical model, where data from outside daycare centre measurements, fixed ambient air monitors, residential area and home characteristics (i.e., gas cooking stove, smoking inside at home, type of dwelling) were included, explained only 32% of the personal exposure variations in winter, but 67% in spring.

There were significantly more days with stuffed nose (26% versus 20%) and cough (18% versus 15%) in the downtown area than in the suburban area. The observed risk of cough was highest and statistically significantly increased compared to the levels of personal nitrogen dioxide. Also, when using daycare centre measurements or fixed site ambient air data for exposure assessment, there was a positive trend between nitrogen dioxide exposure and cough in winter these associations were, however, weaker and non-significant.

According to the result of the study, exposure to nitrogen dioxide should be measured using personal exposure measurements when studying health effects of the gas in non-symptomatic children in areas with low nitrogen dioxide levels. Even personal exposure measurements using weekly averages, however, may not adequately reflect all biologically relevant exposure, e.g., short-term peak concentrations. The most significant determinants of the personal nitrogen dioxide exposures of the children in Helsinki are living in downtown rather than in a suburban area, gas versus electric cooking stove and smoking in the home. However, even all risk factors together did not increase the personal exposures of downtown children up to suburban outdoor air levels.

12.3.4 Ozone

The UC Berkeley Ozone project (USA) is an example of an epidemiological study addressing long-term effects of lifetime ambient oxidant pollution on pulmonary function (Tager et al., 1998a,b). A major purpose was to address the feasibility of improving ozone exposure assignment by means of collecting lifetime information on relevant time-activity patterns to exposure, in combination with fixed site ambient air monitoring data. Individual factors considered to be relevant for exposure were:

- * lifetime residential history
- * time spent outdoors in different age periods
- * time spent in outdoor physical activities in each lifetime residence.

To test the reliability of the retrospective assessment, a test-retest design was chosen. The study included a convenience sample of 168 non-smoking UC Berkeley college freshmen who had to be lifetime California (USA) residents (San Francisco Bay Area or Los Angeles Basin). It was shown that retrospective lifetime residential history is highly reliable (Künzli et al., 1996). Using pollution monitor

data, averaged over lifetime across all respective residential locations, may in fact improve the health effects assessment., compared with mere reliance on the ambient monitor data from the last or actual residence only (Künzli et al., 1997a). Three retrospective approaches to assess outdoor physical activity patterns have been tested and two methods gave rather reliable overall estimates for time spent in outdoor heavy or moderate activities, during summer. For the activity table format (see Fig. 19), only 13% of the total variance was attributed to reporting variability (test-retest). The categorization into heavy and moderate activities based on published data regarding energy expenditure (Ainsworth et al., 1993). Ambient long-term mean daytime concentrations of ozone were weighted by the duration and exertion level of the reported long-term average outdoor physical activity. This "effective exposure", therefore, may be considered a surrogate measure of ozone dose. Although the study had some promising results regarding the feasibility of retrospectively assessing exposure relevant surrogates over long periods of time, validity of the time-activity data cannot be directly assessed. Neither could the study answer the open question of whether time-activity data may be needed in the assessment of long-term effects of air pollution (Künzli et al., 1997a).

12.3.5 Combined exposure studies

The WHO, in a number of studies termed the Global Environmental Monitoring System (GEMS), sponsored several studies of combustion related air pollutants. GEMS, now renamed as the Air Management Information System (AMIS), continues to coordinate the gathering of data on levels of ambient air pollution in cities around the world. GEMS also conducted a series of exposure studies to examine the assumptions that fixed ambient monitoring accurately reflected personal exposures. Studies were carried out in Toronto, Canada (WHO, 1982b); Beijing, China (WHO, 1985c); Zagreb, Croatia (WHO, 1982a); and Bombay, India (WHO, 1984).

Through the GEMS, WHO and UNEP later formed the HEAL project. The goal was to improve exposure monitoring internationally, using direct measurements of human exposure with activity information, and provide guidelines for techniques that could be used uniformly around the world. Another goal was to increase the accuracy of risk assessment studies with the goal of better protection of human health.

A study in Kenya was carried out to attempt to determine the risk of acute respiratory infection by quantifying indoor air pollution levels caused by home combustion sources (WHO, 1987). The study was

carried out in 36 randomly chosen households that used biomass as fuel. It compared concentrations of particles, carbon monoxide, nitrogen dioxide and formaldehyde inside the home with outdoor pollution levels.

The mean 24-h concentration of respirable particles was $1400 \mu\text{g}/\text{m}^3$, and the estimated levels in areas where cooking and heating fires were used was $3000\text{-}4000 \mu\text{g}/\text{m}^3$. Although elevated levels of carbon dioxide and nitrogen dioxide were found in the homes, the levels were below those found in previous studies of indoor air pollution in developing countries. Little correlation was seen between indoor and outdoor levels, confirming that the source of the excess levels was combustion.

The excessive levels of particulate, which included a large concentration of PAHs, suggested that individuals spending a significant amount of time indoors (e.g., women and small children) were at greater risk owing to exposure to smoke. Because the levels observed were homogeneous across the samples, leaving no unexposed control group, the researchers were unable to reach conclusions about the effect of the levels on occurrence of acute respiratory infections.

12.3.6 Assessing ambient pollution impacts indoors

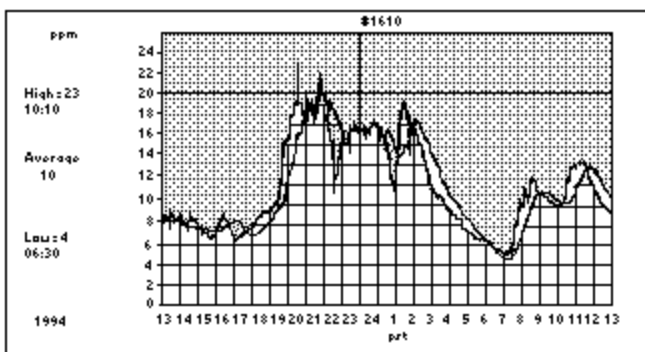
Santiago, Chile, a city of 5.2 million inhabitants in 1997 (40% of the Chilean population), has chronic high concentrations of certain air pollutants. For example, in 1995 the Chilean air quality standards for PM_{10} , carbon monoxide and ozone were exceeded on more than 200 days. Annual PM_{10} levels surpassed $100 \mu\text{g}/\text{m}^3$ in the 1990s and levels of $300 \mu\text{g}/\text{m}^3$ are common during the winter, especially when an inversion layer is formed.

In many countries when pollutants in the outdoor air exceed standards, the population is advised to remain indoors, but if infiltration occurs and indoor sources are generating pollutants, indoor air quality (IAQ) might be even worse than outdoors. A study was designed to evaluate the contribution of outdoor pollution to IAQ in Santiago and in a small rural town (Curocori). Carbon monoxide, PM_5 and PAHs were monitored simultaneously indoors and outdoors along heavy traffic roadways in Curocori and in Santiago. The methodology used is described in Gil & Adonis (1997).

In downtown Santiago, carbon monoxide concentrations ranged from 1.9 to $73 \mu\text{g}/\text{g}$ outdoors; indoor levels were $0.5\text{-}93 \mu\text{g}/\text{g}$. Although levels were slightly higher indoors (but not significant, $p > 0.05$) than outdoors, changes in outdoor levels (which were always related to vehicular traffic) simultaneously produced changes in indoor levels. A typical carbon monoxide profile is shown in Fig. 40 for outdoor and indoor levels in an office. Outdoor and indoor levels showed a high correlation ($r = 0.89$) with the higher values occurring during the rush hour.

Interior

Title: CiTical #1610



Exterior

Title: CiTical #1607

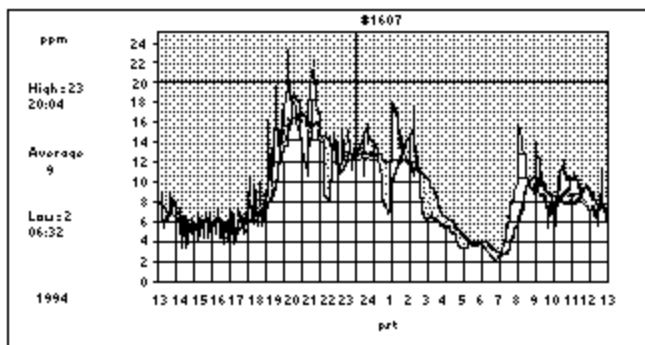


Fig. 40. Carbon monoxide indoor and outdoor levels in Santiago (Chile) on 14-15 July 1994

Levels of total PAHs, carcinogenic PAHs and PM_{5} were very high and showed no statistically significant differences indoors and outdoors ($p > 0.05$). Highest PM_{5} levels were 260 and 280 $\mu\text{g}/\text{m}^3$ for indoors and outdoors respectively. Levels of benzo [a]pyrene indoors and outdoors were highly correlated ($r = 0.869$). For restaurants which usually work with open doors, the correlation between indoor and outdoor levels was even higher ($r = 0.99$). In Curocori, levels (a town with little vehicular traffic) were almost identical indoors and outdoors. Levels of carbon monoxide PM_{5} , total PAHs and carcinogenic PAHs were considerably lower in this rural town and indoor/outdoor correlations were also much lower than those obtained in Santiago.

These results confirm the importance of ambient pollution to population exposures when outdoor pollution levels are high. Only when the contribution of penetrating ambient pollution is lowered can the indoor contributions be more readily assessed.

12.3.7 Volatile organic compounds

Human exposure to VOCs occurs mainly through inhalation, although some VOCs are ingested as contaminants in drinking-water, food and

beverages. Some hydrocarbons are known carcinogens or mutagens (e.g., benzene). Almost all cause eye irritation, coughing, drowsiness, clumsiness and loss of alertness. Acute effects from industrial exposures at the parts per million ($\mu\text{g/g}$) level include skin reactions, dizziness and fainting. Sick building syndrome (SBS) and multiple chemical sensitivity (MCS) have been associated with relatively low (ng/g , parts per billion) concentrations of VOCs.

Between 1979 and 1987, the US EPA carried out the TEAM studies to measure personal exposures of the general public to VOCs in several geographic areas in the USA (Pellizzari et al., 1987; Wallace et al., 1987a). About 20 target VOCs were included in the studies, which involved about 750 people, representing 750 000 residents of the areas. Each participant carried a personal air quality monitor containing 1.5 g Tenax. A small battery-powered pump pulled about 20 litres of air across the sorbent over a 12-h period. Two consecutive 12-h personal air samples were collected for each person. Concurrent outdoor air samples were also collected in the participants' backyards. In the 1987 studies, fixed indoor air samplers were also installed in the living room of their homes.

The initial TEAM pilot study (Wallace et al., 1982) in Beaumont, Texas and Chapel Hill, North Carolina indicated that personal exposures to about a dozen VOCs exceeded outdoor air levels, even though Beaumont has major oil producing, refining and storage facilities. These findings were supported by a second pilot study in Bayonne-Elizabeth, New Jersey (another major chemical manufacturing and petroleum refining area) and Research Triangle Park, North Carolina (Wallace et al., 1984a). A succeeding major study of 350 people in Bayonne-Elizabeth (Wallace et al., 1984b) and an additional

50 people in a non-industrial city and a rural area (Wallace et al., 1987a) reinforced these findings (Table 39). A second major study in Los Angeles and in Antioch-Pittsburgh, California (Wallace et al., 1988), with a follow-up study in Los Angeles in 1987 (Wallace et al., 1991a,b) added a number of VOCs to the list of target chemicals with similar results (Table 40). Major findings of these TEAM studies included the following:

- * Personal exposures exceeded median outdoor air concentrations by factors of 2-5 for nearly all of the 11 prevalent VOCs (Fig. 41). The difference was even larger (factors of 10 or 29) when the maximum values were compared. This is so despite the fact that most of the outdoor samples were collected in areas with heavy industry (New Jersey) or heavy traffic (Los Angeles).
- * Major sources are consumer products (bathroom deodorizers, moth repellents); personal activities (smoking, driving); and building materials (paints and adhesives). In the USA, one chemical (carbon tetrachloride) has been banned from consumer products and exposure is thus limited to the global background of about $0.7 \mu\text{g/m}^3$.
- * Traditional sources (automobiles, industry, petrochemical plants) contributed only 20-25% of total exposure to most of the target VOCs (Wallace, 1991a,b). No difference in exposure was noted for persons living close to chemical manufacturing plants or petroleum refineries.

The results of the VOC TEAM study encouraged investigators to explore the causes for higher personal exposures. In a study designed

to better understand the VOC contributions of specific sources, Wallace et al. (1989) had 7 volunteers undertake about 25 activities. A number of these activities (using bathroom deodorizers, washing dishes, cleaning an automobile carburettor) resulted in 10-1000-fold increases in 8-h exposures to certain VOCs.

A recent study of benzene and toluene in 293 California homes (Wilson et al., 1993a, b; 1995; Colome et al., 1994) resulted in some interesting differences between the two agents. For benzene, 48-h average indoor concentrations correlated fairly well with outdoor levels, but for toluene almost no correlation was observed. This is probably due to the much wider use of toluene in consumer products. Major variables associated with higher net indoor benzene levels were presence of a gas heating furnace and having two cars parked in an attached garage. For toluene, a particular brand of furnace had the highest partial correlation with net indoor toluene concentrations; apartments also had higher concentrations.

A study of 170 homes in Avon, England found mean indoor levels of benzene to be 8 $\mu\text{g}/\text{m}^3$, compared to outdoor concentrations of 5 $\mu\text{g}/\text{m}^3$ (Brown & Crump, 1996). The study employed passive Tenax tubes to collect 28-day indoor and outdoor samples. These results were in good agreement with the levels of 10 $\mu\text{g}/\text{m}^3$ indoors and 6 $\mu\text{g}/\text{m}^3$ outdoors at 50 homes in Los Angeles measured over two seasons in 1987 (Wallace et al., 1991).

Table 39. Weighted estimates of air and breath concentrations of 11 prevalent residents (fall 1981); 110 000 residents (summer 1982); and 49 000 re

Compound	Personal air (n = 340)	Fall outdoor air (86)	Breath (300)	Personal air (150)	Summer outdoor air (60)
1,1,1-Trichloroethane	94 ^a	7.0 ^a	15 ^b	67	12
m,p-Dichlorobenzene	45	1.7	8.1	50	1.3
m,p-Xylene	52	11	9.0	37	10
Tetrachloroethylene	45	6.0	13	11	6.2
Benzene	28	9.1	19	NC ^c	NC
Ethylbenzene	19	4.0	4.6	9.2	3.2
o-Xylene	16	4.0	3.4	12	3.6
Trichloroethylene	13	2.2	1.8	6.3	7.8
Chloroform	8.0	1.4	3.1	4.3	13
Styrene	8.9	0.9	1.2	2.1	0.7
Carbon tetrachloride	9.3	1.1	1.34	1.0	1.0

Total 11 (compounds) 338 48 80 200 59

- a Average of arithmetic means of day and night 12-h samples ($\mu\text{g}/\text{m}^3$).
 b Arithmetic mean.
 c Not calculated-high background contamination.
 d Not detected in most samples.

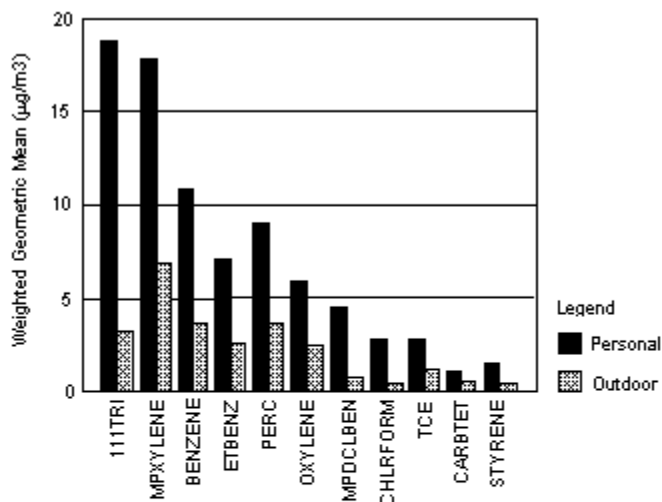


Fig. 41. Estimated geometric means of 11 toxic compounds in daytime (6 am-6 pm) air samples for the target population (128 000) of Elizabeth and Bayonne, New Jersey, between September and November 1981. Personal air estimates based on 340 samples; outdoor air estimates based on 88 samples. (1,1,1 TRI, 1,1,1-trichloroethane; MPXYLENE, = m,p-xylene; ETBENZENE, ethylbenzene; PERC, tetrachloroethylene; OXELENE, o-xylene; MPDCLBEN, m,p-dichlorobenzene; CHLRFORM, chloroform; TCE, trichloroethylene; CARBTET, carbon tetrachloride (from Wallace, 1987)

Another study of benzene in four New Jersey homes was focused on the extent of contamination from attached garages (Thomas et al., 1993b). Each home was monitored for either 6 or 10 consecutive 12-h periods. At all four homes, garage levels of benzene were higher than outdoors, and at three of the four homes the garage levels were higher than in the living area. Air exchange measurements made it possible to calculate the amount of benzene transferred from the garage to the living area in the four homes; in the home without elevated benzene levels in the garage, the total air flow between the garage and the living area was extremely small. Benzene concentrations in the garages ranged from 5 to 200 $\mu\text{g}/\text{m}^3$, and the 12-h average source strength estimates ranged from 730 to 26 000 $\mu\text{g}/\text{h}$. The mere presence of an attached garage was not a significant factor in affecting benzene concentrations in the living area. However, the total number of hours the car was parked in the garage had a significant effect on living-area benzene concentrations, as did the mass flow rate of benzene from the garage to the home.

In 1991 a subsample of the German Environmental Survey (see Chapter 2.6) of 113 people took part in a study to assess exposure to VOCs by personal sampling. The subjects wore passive samplers (OVM-3500, 3M Company) for 7 consecutive days and simultaneously

documented the length of time spent indoors, the room characteristics and any specific exposure such as that caused by renovation activities. Seventy-four VOCs were analysed by gas chromatography (Ullrich, 1992).

The results of personal sampling showed, for example, that from the various types of environments the workplace has the highest impact on exposure to C₈- and C₉-aromatic hydrocarbons (Figs. 42 and 43). Other important factors that need to be considered are renovation activities, use of paints and lacquers and the frequent reading of newspapers and journals (printing inks contain many VOCs). Smoking contributes significantly to human VOC exposure. In the case of benzene, the multivariate model contained five variables: two related to smoking exposure indoors, two related to vehicle traffic and the residential density (Fig. 44). The two smoking variables alone accounted for 20% out of a total variance of 40% that could be explained (Hoffmann et al., 1996; Ullrich et al., 1996).

Three large studies of VOCs, involving 300-800 homes, have been carried out in the Netherlands (Lebret et al., 1986), Germany (Krause et al., 1987) and the USA (Wallace, 1987). A small study of 15 homes was carried out in Northern Italy (De Bortoli et al., 1986). Observed concentrations were remarkable similar for most chemicals, indicating similar sources in these countries. One exception is chloroform, present at typical levels of 1-4 µg/m³ in the USA but not found in European homes. This is to be expected, since the likely source is volatilization from chlorinated water (Wallace et al., 1982; Andelman, 1985a,b); Germany and the Netherlands do not chlorinate their water.

12.3.8 Commuter exposures

In crowded urban areas it is not uncommon to find substantial populations living near busy roads. Still others make their living working among cars or vending goods along busy streets. Around the world the routine of commuting between home and workplace exposes most of the urban population to motor vehicle exhaust (carbon monoxide, oxides of nitrogen, PAHs, VOCs and lead, in many cases) on a daily basis. There have been several studies designed to assess exposures to vehicle exhaust.

In a study conducted in Stockholm, Sweden, Bostrom et al. (1991) demonstrated that nitrogen oxides can be used as tracers for VOCs originating from vehicular traffic. The most important sources of VOCs in Swedish cities are motor vehicles. Also, some 80-90% of NO_x (nitric oxide and nitrogen dioxide) in large Swedish cities originates from motor vehicle traffic. Quantitative relationships were developed between NO_x and individual hydrocarbons, independent of traffic intensity and time of year. For instance, a PAH/NO_x ratio of 2.0 × 10⁻² was reported for Gothenburg, Sweden, and a benzene/NO_x ratio of 0.16 was reported for Stockholm.

Chan et al. (1991) assessed in-vehicle levels of carbon monoxide in Raleigh, North Carolina, USA during the summer of 1988. The ratio

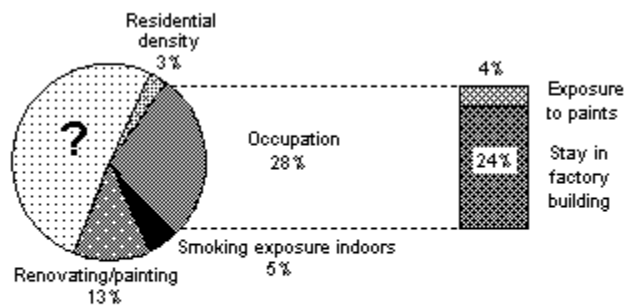


Fig. 42. Sources of exposure to C₉-aromatic hydrocarbons (modified from Hoffmann et al., 1996)

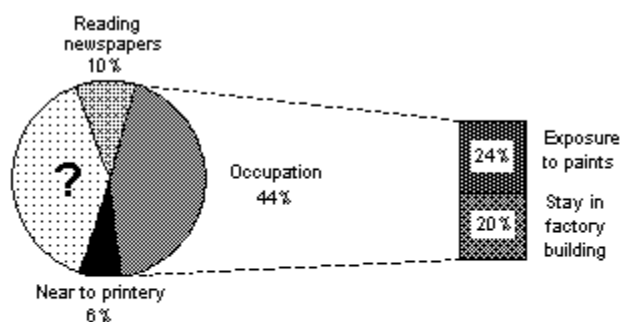


Fig. 43. Sources of exposure to C₈-aromatic hydrocarbons (modified from Hoffmann et al., 1996)

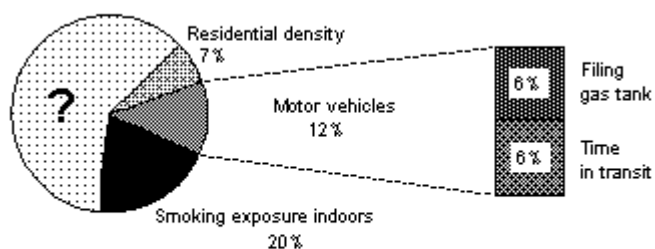


Fig. 44. Sources of exposure to benzene (modified from Hoffmann et al., 1996)

of mean concentrations of carbon monoxide inside and outside the vehicle was 1 : 1, and the ratio of mean concentrations inside the vehicle to a fixed-site location was about 5. The ratio of in-vehicle concentrations under three different driving conditions, urban/interstate/rural, was roughly 3.3 : 2.8 : 1. An investigation of carbon monoxide concentrations inside private and public transport vehicles in Mexico City in 1993 (Fernandez-Bremauntz & Ashmore, 1995a,b) found an average ratio of in-vehicle : ambient concentrations

of 2 : 1 for the metro and 5 : 2 for cars.

Liu et al. (1994b) conducted a study of carbon monoxide exposure among Taipei commuters (adults and students) in 1990. Roadside and in-vehicle measurements were made at the same time that commuters' personal exposure was assessed. Concentrations of carbon monoxide were measured for three transportation modes (bus, private car and motorcycle) and three times of day (morning rush hour, midday and evening rush hour). The ratio of in-vehicle to ambient concentrations of carbon monoxide was roughly 6 : 5, overall.

As part of their study of carbon monoxide exposure, Liu et al. performed a survey of commuting patterns in Taipei, for students and adults. Adults had a significantly longer average commuting time than students (1.4 h versus 0.8 h). Students commuted typically by walking (58%) or by riding on public buses (29%). Adults commuted to work by motorcycle (28%), public bus (26%), or in private cars (26%). Commuters using public buses had the longest commuting times (1.8 h for adult workers, and 1.2 h for students).

WHO recommended guidelines for carbon monoxide are 30 mg/m³ as a 1-h mean, 60 mg/m³ for a 30-min mean, and 100 mg/m³ as a 15-min mean. These guidelines are designed to prevent carboxy-haemoglobin levels in the bloodstream from surpassing 2.5-3.0% in the non-smoking population, and to protect people who are prone to heart problems. According to the 1992 UNEP report of air pollution in megacities of the world, the 1-h WHO guideline is routinely exceeded by a factor of 2-3 times in several cities in Asia (Amman, Bangkok, Jakarta, Peshawar, Shanghai) and Latin America (Mexico City, Santiago, Lima) (UNEP/WHO, 1992). Considering the exposure studies conducted in Mexico City and Taipei, the stationary monitors are an underestimate of the population at risk of elevated carbon monoxide levels.

12.4 Exposures and biomarkers

12.4.1 Exposure to lead and cadmium

Dose-response relationships exist for lead toxicity in children and adults, and demonstrate that subtle effects begin at levels as low as 1 µg/dl of lead in blood. Severe toxicity is associated with blood-lead levels of 70 µg/dl or higher in children, and 100 µg/dl or higher in adults. Toxicity symptoms include poisoning of the central nervous system, causing convulsions, coma, and deep, irreversible mental retardation. Functional changes in the peripheral nervous system and anaemia can also occur at levels below 40 µg/dl.

Particulate lead present in gasoline (from the octane enhancer tetraethyl lead) and bromine (from the lead scavenger ethylene dibromide) have traditionally been used as tracers for mobile sources. The WHO recommended ambient air quality guideline for lead is 1 µg/m³, a level routinely exceeded in many large Asian cities today where lead is still permitted in gasoline. This guideline value is based on the assumption that 98% of the general population will be maintained below a blood level of 20 µg/litre, which is considered the maximum acceptable concentration in blood.

Jimenez & Velasquez (1989) conducted a study in Manila, Philippines to measure blood lead concentrations in children. In a sample of 544 children, the average blood lead level was 22.8 µg/dl, with approximately 8% of the children having levels greater than

30 µg/dl. The study also found a significant correlation between high blood lead levels and proximity of the household to dense traffic. In a 1990-1991 study of exposure to lead among schoolchildren in Manila, Subida & Torres (1991) found that mean blood lead concentrations were 14 µg/dl (*n* = 387), with 10% having levels over 10 µg/dl. The same study measured blood lead levels among child street vendors. Mean blood lead level for a sample of 101 vendors was 17.8 µg/dl, with 33% having levels over 20 µg/dl.

Muangnoicharon (WHO, 1995b) reports on a lead exposure study of bus drivers in Bangkok. The study was a cooperation between the WHO HEAL Project and the Department of Medical Science, Ministry of Public Health of Thailand and was designed to assess exposure in a high risk group. Subjects were bus drivers assigned to traffic routes in Bangkok where ambient lead levels exceeded 1 µg/m³. Lead was analysed in 24-h air samples, duplicate food for each meal for 6 days and faeces for 5 days, as well as blood collected on the day 7.

Average personal air exposures were 0.117 µg/m³, which yielded an estimated 0.936 µg/day absorption by inhalation at an estimated absorption rate of lead via inhalation of 40% and 20 m³/day respiratory air. Intake by food was 87.92 µg/day (27.32 SD). Thus, the estimated average lead absorption from air, food and water was 13.325 µg/day at an estimated absorption rate via ingestion of 10%. Researchers suggested that meals consumed from roadside restaurants and food stands resulted in higher than expected lead levels in food. Blood lead levels for bus drivers ranged between 5 and 12 µg/dl.

The results for the Thai study were compared to other HEAL sponsored studies in China, Sweden and Yugoslavia (Table 41).

One of the HEAL projects investigated lead and cadmium exposure among small groups of non-smoking women (Vahter & Slorach, 1990). Subjects kept activity diaries. Duplicate portions of food and corresponding faeces samples were collected along with personal air samples. Food was found to be the main source of both lead and cadmium. Faecal concentrations could be used for validation of the duplicate portion samples because of the low uptake in the

Table 40. Weighted estimates of air and breath concentrations of 19 prevalent residents (February 1984); 330 000 Los Angeles residents (May 1984); (June 1984)

Compound	LA1 (February)			LA2 (May)		
	Personal air (<i>n</i> = 110)	Outdoor air (24)	Breath (110)	Personal air (50)	Outdoor air (23)	B (
1,1,1-Trichloroethane	96 ^a	34 ^a	39 ^b	44	5.9	23
m,p-Xylene	28	24	3.5	24	9.4	2
m,p-Dichlorobenzene	18	2.2	5.0	12	0.8	2
Benzene	18	16	8.0	9.2	3.6	8
Tetrachloroethylene	16	10	12	15	2.0	9
o-Xylene	13	11	1.0	7.2	2.7	0
Ethylbenzene	11	9.7	1.5	7.4	3.0	1
Trichloroethylene	7.8	0.8	1.5	6.4	0.1	1

n-Octane	5.8	3.9	1.0	4.3	0.7	1
n-Decane	5.8	3.0	0.8	3.5	0.7	0
n-Undecane	5.2	2.2	0.6	4.2	1.0	0
n-Dodecane	2.5	0.7	0.2	2.1	0.7	0
alpha-Pinene	4.1	0.8	1.5	6.5	0.5	1
Styrene	3.6	3.8	0.9	1.8	no data	n
Chloroform	1.9	0.7	0.6	1.1	0.3	0

^a Average of arithmetic means of day and night 12-h samples ($\mu\text{g}/\text{m}^3$).

^b Arithmetic mean.

Table 41. Results of lead HEAL exposure pilot studies in Bangkok, Thailand; Beijing, China; Stockholm, Sweden and Zagreb, Croatia

Sample	Unit	Thailand (n = 24)	China (n = 10)	Sweden (n = 15)	Croatia ^a (n = 17)
Breathing zone	$\mu\text{g}/\text{m}^3$	0.117	0.116	0.064	0.412
Food	$\mu\text{g}/\text{day}$	89.72	46.0	26.0	15.0
Faeces	$\mu\text{g}/\text{day}$	60.57	42.0	23.0	49.0
Blood	$\mu\text{g}/\text{dl}$	8.83	7.3	2.9	5.0

gastrointestinal tract. Inhalation was found to account for a few percent of the total exposures of cadmium. Inhalation contributed more than 70% of total lead exposure. On the other hand, where air lead levels were high, as in Zagreb, Croatia, inhalation contributed twice as much to total exposure as the ingestion route (see Fig. 45).

These pilot studies illustrated that without thorough analytical QC it was not possible to compare results between countries. The pilot study, although expensive, identified problems in collection and analysis. The need to exchange standards in the various media and training in analytical methods and procedures were important components for the success of the studies.

In a study conducted on Swedish women the bioavailability of dietary cadmium was contrasted for different diets. Dietary intake and uptake of cadmium were studied in non-smoking women, 20-50 years of age, consuming a mixed diet low in shellfish ($n = 34$), or with shellfish once a week or more ($n = 17$), or a vegetarian diet rich in fibre ($n = 23$) (Berglund et al., 1994b; Vahter et al., 1996). The objectives were to identify important factors, dietary and other, influencing cadmium exposure and dose.

Duplicate portions and corresponding faeces (using a coloured marker to indicate start and end of duplicate portion collection) were collected for four consecutive days (including weekdays and weekends), for the determination of cadmium intake. Blood and 24-h urine samples were collected for determination of total cadmium exposure. The women kept detailed dietary records for identification of significant sources.

The shellfish diets contained twice as much cadmium (22 $\mu\text{g}/\text{day}$) as the mixed diets (10 $\mu\text{g}/\text{day}$). The high fibre diets were intermediate (13 $\mu\text{g}/\text{day}$). The content in faeces were on the average 100%, 99% and 98% of intake in the shellfish group, the mixed diet group and the fibre group, respectively, indicating a low average absorption of dietary cadmium. Despite the differences in cadmium intake there were

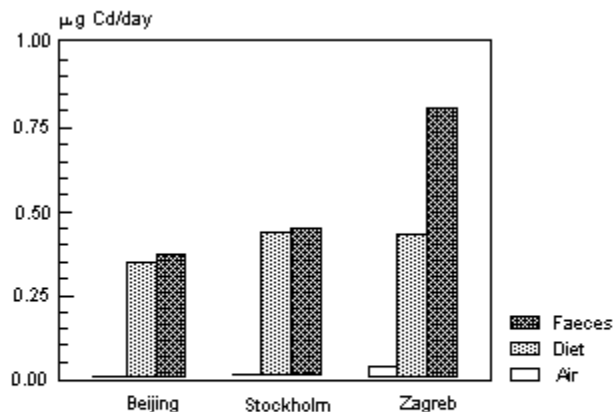


Fig. 45. Daily absorption of lead and cadmium estimated from the amounts in air, duplicate diets and faeces (UNEP/WHO, 1990)

no significant differences in blood cadmium (about 0.25 $\mu\text{g}/\text{litre}$) or urine (0.1 $\mu\text{g}/\text{litre}$), indicating a lower absorption of cadmium in shellfish and in high fibre foods compared to the mixed diet (low in shellfish and cereals) or a difference in the kinetics. A higher cadmium absorption in the mixed diet and the fibre diet group compared to the shellfish group could partly be explained by lower body iron stores (measured as serum ferritin). Low body iron stores in women of reproductive age are very common. Serum ferritin levels were negatively correlated with blood cadmium concentration, indicating an increased absorption of cadmium at reduced body iron stores (defined as serum ferritin below 30 $\mu\text{g}/\text{litre}$).

12.4.2 Exposure to furans, dioxins and polychlorinated biphenyls

Dioxins, furans and PCBs are persistent compounds found in industrial discharges and incinerator air emissions, and as trace contaminants in many products. These compounds accumulate in fat and undergo amplification in marine and terrestrial food chains. People consuming large amounts of contaminated seafood may have higher concentrations of organochlorine compounds in their tissues than the general population.

For 35 years a magnesium-producing factory in the inner part of a fjord in southern Norway had discharged 50-100 kg TCDD toxic equivalents (TEQ) to the fjord area. PCDDs/Fs and PCBs were monitored in sediments and marine organisms in 1986, 1989-1990 and 1992. In spite of a reduction by >98% in the discharge from 1990 to 1992,

levels were still very high. Restrictions in commercial fishing and advice to the general public regarding consumption were established.

Some residents still catch and consume considerable amounts of local fish and shellfish, particularly crabs, during summer and autumn. The crabs contain high concentrations of PCDDs/Fs with a predominance of tetra- and hexa-CDFs and PCB-209.

In the study by Johansen et al. (1996), 24 male crab consumers were recruited non-randomly from news announcements and 10 controls were drawn randomly from the population register. PCDDs/Fs and PCBs were measured in blood samples. Information on crab and fish consumption and intake of fatty food items were collected and the fishing site reported. The study was designed to determine if consumption of crabs from the contaminated fjord area led to increased body burden of PCDDs/Fs and PCBs. From the patterns of PCDDs/Fs and PCBs congeners in crabs, can congeners in blood be inferred sources? Finally, can exposure estimates based on blood levels be predicted by reported crab intake of location? A considerable increase of PCDDs/Fs in blood was found upon consumption of contaminated crabs. A direct relationship was found between blood level and the number of crabs times contamination level. See Fig. 46 from Johansen et al. (1996). The PCDD/F profile in the high intake group clearly reflected the profile found in the crab hepatopancreas. PCB-209 does not appear to be absorbed since it did not increase after crab consumption.

Using a simplified toxicokinetic calculation, good correlation ($r = 0.61$) was reported between estimated yearly intake based on blood values and intake based on reported intake and the fishing site. The intake calculated for the controls was 9.7 pg TEQ/kg body weight per week, in good agreement with estimated intake from food in Norway (8-10 pg TEQ/kg body weight per week). The average exposures of the moderate and high-intake groups were 31 (10-61) pg/kg body weight per week and 62 (24-114) pg/kg body weight per week. Most individuals in the high-intake group exceeded the recommended Nordic tolerable weekly intake (TWI) of 35 pg/kg body weight per week

12.4.3 Exposure to volatile organic compounds and urinary metabolites

In Tokyo, Nakahama et al. (1997) measured personal VOC exposures over 12 h and the metabolites in urine. Thirteen men and 17 women participated. The VOCs 1,1,1-trichloroethane, trichloroethylene and tetrachloroethylene were sampled with passive absorbent badges. Trichloroethanol and trichloroacetic acid corrected for creatinine were measured in urine. Personal exposures were well correlated ($r = 0.80$) with urinary metabolites. Interestingly, women inhaled twice as much VOCs as men, perhaps because of increased exposure to household chemicals and cosmetics.

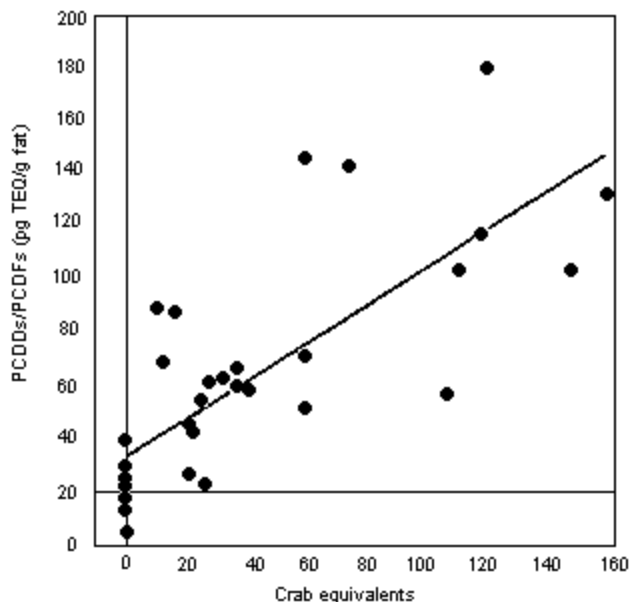


Fig. 46. Relationship between intake of crab equivalents and blood concentrations of PCDDs and PCDFs (pg TEQ/g fat) in 34 subjects ($r = 0.75$) (from Johansen et al., 1996)

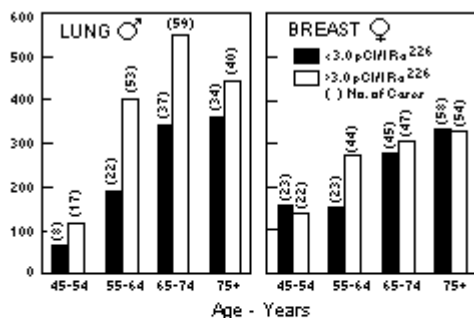


Fig. 47. Age-specific incidence rates of cancer of the lung among men and of the breast among women in municipalities in Iowa, 1969-1978, classified according to mean radium-226 in the water supply (Bean et al., 1982)

12.5 Exposure to contaminants in drinking-water

The health effects of exposure to natural background radiation, specifically radon, through inhalation have been explored, but drinking-water is another source of natural background radiation that may contribute to cancer incidence. Elevated rates of bone cancer have been hypothesized as potential outcomes of exposure to radium-226 and radium-228 because of their accumulation in the bone (Bean et al., 1982). These two isotopes are found in some deep aquifers. Previous to the study 300 000 residents of Iowa were found to have levels of radium-226 in their municipal drinking water that exceeded the US

Public Health Service's 1962 drinking water standard of 3 pCi/litre. The time periods 1969-1971 and 1973-1978 were studied for all 28 municipalities in Iowa. After testing each town for radium-226 levels, the towns were divided into three groups, with respectively 0-2, 2-5 and >5 pCi/litre of radium-226 in the water supply. In towns level > 5.0 pCi/litre, the incidence of lung and bladder cancer in men and lung and breast cancers among women was higher (Fig. 47). Although 77% of the individuals in the study had been on the same water supply for at least 10 years, misclassification due to uncertainties about past concentrations and past residential histories create problems for the study.

A Taiwanese study of a population that used artesian wells suggests that there may be a link between high arsenic levels in drinking water and the incidence of internal cancers, particularly bladder cancer (Chiou et al., 1995). Levels above the maximal permitted level of 50 µg/litre occur in some locations in the western USA. In 1978 a study was done in Utah of individuals between the ages of 21 and 84. Concentrations of arsenic in the water ranged from 0.5 to 160 µg/litre (mean 5.0 µg/litre). Two indexes of exposure were used, both of them assuming constant past levels in the water supply:

- * total cumulative exposure was calculated using the duration of time spent in the town, the rate of water consumption, and the 1978 levels of arsenic in the drinking-water
- * intake concentration was calculated using the above measurements, as well as the total fluid intake, to approximate the arsenic concentration in the urine to which the bladder is exposed (Bates et al., 1995).

Overall, no association between arsenic exposure and bladder cancer was seen with either index (Table 42). The only odds ratio (3.32) significantly different from 1 was for smokers with a cumulative dose greater than 53 mg. This suggests that smoking potentiates the relationship between arsenic and bladder cancer.

That drinking-water can be a main source of exposure could be shown in the framework of German Environmental Survey (see Chapter 2.6). Drinking-water (first draw and grab samples, see Chapter 7.3.2) was analysed in approximately 4000 German households. A significant correlation was observed between the lead content in drinking water and the lead content in the blood of the population (Nöllke et al., 1995; Becker et al., 1997).

12.6 Exposure to microbes

Examination of biological contamination involves a different approach, as discussed in Chapter 9. Bioaerosol samples are widely used and rely on impaction on to culture medium. The cut-off size of the samplers limits the ability to capture all bioaerosols, and no one culture medium and growth temperature is appropriate for all viable bacteria in the air. Therefore, the numbers from the impactor will be less than those actually present in the air because of limited power of detection. Chemical assay for endotoxin is independent of the ability to grow the bacteria, but it is sensitive to sampling and storage procedures.

Previous studies of bioaerosols in the occupational setting have examined levels of airborne bacteria. A study of bioaerosols at water

treatment plants was planned to go beyond previous studies and examine concentrations of both bacteria and endotoxin (Laitinen et al., 1994). Endotoxin (bacterial toxin not freely liberated into the surrounding medium) can cause fever, eye inflammation, fatigue and/or respiratory difficulties if inhaled, and may be a more reliable measure of

Table 42. Adjusted odds ratios (OR) and 90% confidence intervals (CI) for b enrolled into the National Bladder Cancer Study in Utah in 1978 who h living in study towns (Bates et al., 1995)

Exposure ^a	All subjects				Never smoked			
	Cases	Controls	OR ^b	90% CI	Cases	Controls	OR ^b	90% CI
Exposure index (cumulative dose (mg))								
<19	14	47	1.00		10	25	1.00	
19-< 33	21	36	1.56	0.8-3.2	10	19	1.09	
33-< 53	17	39	0.95	0.4-2.0	7	20	0.68	
„53	19	38	1.41	0.7-2.9	4	17	0.53	
Exposure index (mg/litre × year)								
<33	18	42	1.00		11	19	1.00	
33-< 53	16	42	0.69	0.3-1.5	3	19	0.21	
53-< 74	16	40	0.54	0.3-1.2	6	24	0.25	
≥74	21	36	1.00	0.5-2.1	11	19	0.91	

^a Cut-points based on exposure quartiles of all subjects in the table.

^b Adjusted for sex, age, smoking, (all subjects and smokers only), years of exposure of bladder infection, educational level, urbanization of the place of longest high-risk occupation.

biological exposure because it is independent of the ability to culture the microorganism.

The treatment area, control room and outside were sampled at nine industrial waste water treatment plants. Bacteria were collected using an impactor which sampled on to agar plates. After incubation for 2 days, the number of colonies of each plate were counted, and translated into numbers of CFU/m³ of air. Endotoxin was sampled on to sterile filters using a suction pump, and was reported as ng/m³. Levels of bacteria and endotoxin were correlated. Concentrations of endotoxins in the work areas of the treatment plant were assessed by collection on to glass fibres that were then tested using the *Limulus* endotoxin assay. The measured levels of endotoxin ranged between 0.1 and 350 ng/m³, and the 8-h time-weighted average

concentration was greater than the exposure limit of 30 ng/m³ at some of the plants. Bacterial levels were between 10 and 10⁵ CFU/m³ (Table 43).

Sixteen male workers with a mean exposure duration of 10 years were examined for symptoms related to exposure to bacteria and endotoxin. The workers' occupational history and symptoms were evaluated using written questionnaires. Symptoms were found in 6 workers; 4 reported fever, shivering and eye irritation, and 3 a cough. Although the number of subjects was too low for epidemiological conclusions based on the symptoms, the levels in some locations were high. Excessive levels of contamination were restricted to certain areas of the plant, suggesting that exposure levels should be minimized by changing the physical layout of those work areas and improving hygienic practices by individuals after working in those locations.

Previous work has established that both settled and airborne house dust contains allergens such as dust mites, animal dander, and fungi. The connection between home dampness, fungus levels and respiratory symptoms was investigated in 60 homes as part of a Netherlands case-control study (Verhoeff et al., 1994b). A relationship between dust levels and exposure to moulds was hypothesized, as was a relationship between characteristics of homes (e.g., dampness and type of flooring).

The level of viable fungal propagules present in settled dust was chosen as the sampling parameter; dust was collected from the floor and mattresses using a vacuum cleaner with a cellulose fibre filter. The presence and number of fungal propagules was determined by plating the dust on to agar growth medium. A checklist and a questionnaire on the residence type and occupant behaviour were filled out for each home.

The geometric mean of the number of dust sampled from the floor was 8990 CFU/g and it was significantly higher in samples from carpeted floors (12 880 CFU/g) than from smooth floors (3550 CFU/g). The level from mattresses was 7660 CFU/g. In rooms where damp spots

Table 43. Concentrations of endotoxin and bacteria (Laitinen et al., 1994)

Phase	Endotoxin (ng/m ³)			Gram-negative bacteria (10 ³ CFU/m ³)		
	AM	MD	Range	AM	MD	Range
Wastewater pumping	16	18	<0.04-30	0.56	0.08	0.01-1.6
Screening	30	31	3.6-55	5.0	6.3	0.63-7.9
Wastewater entering sedimentation basin	130	140	100-140	7.5	6.3	6.3-10
Sedimentation basin (indoor)	7.1	1.6	1.0-19	0.5	0.2	0.05-1.3
Aeration basin (indoor)	73	83	17-110	11	5.6	1.0-32

Aeration basin (outdoor)	8.7	1.7	0.8-36	1.8	0.5	0.1-6.3
Biofilter tower	38	38	4.8-71	13	13	10-16
Sludge treatment	140	97	9.2-350	25	13	1.3-63
Control room	3.5	1.4	<0.04-13	0.17	0.2	<0.002-0
Outdoors	0.6	0.3	<0.04-3.0	0.02	0.01	<0.002-0

were observed the levels were higher, but not significantly, and the number was not related to the average relative indoor humidity. The hypothesized association between the presence of fungi in the dust and respiratory symptoms was not observed. Home characteristic and occupant behaviour were therefore seen as poor predictors of fungal levels, with the exception of floor type.

12.7 Exposure studies and risk assessment

12.7.1 The German Environmental Survey

Much of the research into better exposure assessment strategies has come from the desire to more accurately estimate risks associated with environmental exposure in order to better protect human health: for instance, the HEAL studies, including the development of personal monitors and the use of biomarkers. The German Environmental Survey is a unique study providing a database of exposures to pollutants on a representative basis for the general population in Germany. The results of human biomonitoring provide important reference data for evaluating results of smaller studies addressing specific problems. The data of the study were also used for a number of risk assessments, for example in the case of liver cirrhosis in early childhood caused by copper in drinking water (Becker et al., 1997).

Using the German Environmental Survey data and multiple regression analysis it was possible to identify relevant factors that influence the body burden of pollutants of the general population.

12.7.2 The National Human Exposure Assessment Survey

The National Human Exposure Assessment Survey (NHEXAS) was created in order to design an exposure surveillance programme covering the population of the USA (Sexton et al., 1995c). NHEXAS is concerned with policy issues that include differentiation between high and low risk exposure groups and individuals in society. Understanding expected values in the "normal" population is essential for use in comparing to contaminant levels for those who live in a polluted area.

NHEXAS is conducted by researchers in the academic, private and governmental areas of science working in cooperation. The studies are coordinated; they share a common questionnaire on activity and sociodemographics, examine the same exposure sources and send samples for analysis to the same laboratory. The studies are unique in the degree of characterization of exposures of individuals. Multiple chemicals, chemical classes, exposure pathways and routes will be examined for each individual for each study. NHEXAS is conducted as four projects:

- * Population study in Arizona of exposures to metals, VOCs and pesticides carried out by the University of Arizona, Batelle Columbus and the Illinois Institute of Technology.
- * A study of population exposure measurements of metals, pesticides, PAHs and VOCs in two random populations drawn from the EPA's region 5, which includes the industrial northern states of the USA.
- * The relationship between long-term and short-term exposures of individuals to metals, PAHs, pesticides and VOCs is being studied on a population of 50 urban and suburban residents in the Baltimore, Maryland area.
- * Parallel to the field studies is a modelling exercise, where existing information is used in Monte Carlo simulation routines to estimate exposure distributions. A preliminary study of the regions in the first two projects for exposure to pesticides, metals and VOCs is being carried out by the Harvard School of Public Health.

12.7.3 Windsor, Canada exposure and risk study

The Ontario Ministry of Environment in Canada conducted a pioneering study to assess air pollution exposure risks to populations living in Southern Ontario downwind of Detroit, Michigan, a large city in the USA.

Windsor, Canada has a long history of air pollution monitoring dating back to the 1940s. The city's environmental concerns increased when an incinerator was built in Detroit, Michigan. At that time, Detroit had several steel mills in operation. Concern for transboundary transport of pollutants continues today.

The Ontario government performed a study between 1991 and 1993 in order to determine the level of risk associated with air pollution and to limit the exposure of residents of Windsor to airborne toxics (Bell et al., 1994). After examination of concentrations of local airborne toxic pollutants, 10 compounds were chosen for study due to their persistence, bioaccumulation, and toxicity in the environment:

- * metals: cadmium, chromium (VI), mercury
- * VOCs: benzene, 1,3-butadiene, carbon tetrachloride, 1,4-dichlorobenzene, formaldehyde
- * PAHs: benzo [a]pyrene
- * SVOCs: dioxins, furans.

The study first identified the exposure levels by emissions monitoring, fixed site ambient air monitoring, mobile air monitoring, personal exposure measurements, and soil and garden produce survey. Data on emissions from fixed, area, and mobile sources were placed on to a grid with 1 km × 1 km squares, including both the Windsor and the Detroit areas. Ambient monitors in the Windsor area showed levels for most of the toxics to be lower than federal guidelines, with the exception of benzo [a]pyrene. Dioxin and furan levels were below regulatory levels, but were higher than in other Canadian cities. A

mobile monitoring system travelled to find potential hot spots

downwind of potential sources of toxins. The toxins were found to be below regulatory levels, with the exception of hydrogen fluoride and hydrogen chloride.

Fifty-six VOCs and 8 airborne trace metals were sampled at residences, office, cars and recreation areas. Each personal exposure study had a 24-h exposure profile prepared using the concentrations in each environment and the time spent in that environment. It was found that the period of highest exposure to VOCs was during the commute, with outdoors the lowest. The highest exposure to heavy metals was inside the home.

Heavy metal concentrations in garden produce and soil were below regulatory limits, but cadmium and mercury levels were higher in the Windsor area than in rural areas. Indoor air exposure had disproportionately higher health risk than did outside air. Inhalation was found to be more important than dermal absorption and ingestion for these compounds.

The exposures to dioxins and furans were each less than one quarter of the tolerable daily dose. Mercury was 60% of the tolerable daily dose, and could be a health risk because of its persistence in the environment and bioaccumulation. The additive risks for all of the studied air pollutants were approximately 1×10^{-5} .

12.7.4 Pesticide exposure study

The Non-Occupational Pesticide Exposure Study (NOPES) was designed to examine human exposure to 32 pesticides and pesticide degradation products in two cities in the USA: Springfield, Massachusetts and Jacksonville, Florida (Whitemore et al., 1994). The two goals of the project were to develop instrumentation, laboratory procedures and surveys needed for a study of non-occupational exposure to pesticides and to determine non-occupational exposure to pesticides.

The NOPES study used TEAM in determining exposure levels. A probability sampling design was used to make statistical conclusions on the health risks of the pesticides. More participants were chosen from high-exposure groups in order to facilitate estimation of risk levels. Jacksonville was chosen as the high-use region and Springfield as the low-use area. The two sites were studied during the summer of 1986 (Jacksonville only), the spring of 1987 and the winter of 1988. The study population varied between 49 and 72 people. The study examined skin, food and water as routes of exposure, but focused on air as the primary route of exposure. Twenty-four-hour personal, indoor and outdoor samples were collected on polyurethane foam and analysed by gas chromatography/mass spectrometry and gas chromatography/electron capture detection. Personal samples were used as well as fixed monitors inside and outside the home. A questionnaire was administered after the end of the 24-h period to determine the activities of the subjects.

The lowest concentrations were found in the winter and the highest concentrations in the summer, with the spring levels intermediate. Readings from the indoor monitors were correlated with personal monitors, but neither was comparable to the lower measurements from the outdoor monitors. The relative importance of dietary and respiratory routes of exposure varied between pesticides: most of the chemicals had the diet as the main routes of uptake, but

pesticides used indoors were mainly taken via inhalation.

The chlorinated hydrocarbons chlordane, heptachlor, aldrin and dieldrin were calculated to have the largest risk for health effects, although all but heptachlor and aldrin had negligible risks. Heptachlor and aldrin had excess lifetime cancer risks of 2×10^{-4} and 1×10^{-4} respectively in Jacksonville, despite having been banned for many years.

12.7.5 Czech study of air pollution impact on human health

The aim of the Teplice programme has been to conduct a multi-end-point air monitoring and human biomonitoring study to assess the impact of air pollution on population health in the district of Teplice, Czech Republic (Sram et al., 1996). Particulate and gaseous air pollutants were measured in Teplice and in the control region Prachatice. $PM_{2.5}$ and PM_{10} composition and toxic metals as well as concentrations of PAHs were measured daily in winter and periodically during the spring/summer season. The concentrations of all pollutants measured were significantly higher in winter compared to spring and summer. Average fine particle mass in Teplice was $122 \mu\text{g}/\text{m}^3$ compared to $44 \mu\text{g}/\text{m}^3$ in Prachatice during the winter of 1993, and $28.7 \mu\text{g}/\text{m}^3$ and $17 \mu\text{g}/\text{m}^3$ respectively, in spring/summer. Total PAH concentrations in Teplice in winter were approximately twice as high as in Prachatice (278 versus $163 \text{ ng}/\text{m}^3$). Evaluation of the benzo [*a*]pyrene to lead ratio in Teplice over time indicated the presence of at least two sources of PAHs. During the summer when mobile sources are the major contributor to benzo [*a*]pyrene, the ratio was about 0.01. During winter, when the ratio was 0.05 to 0.15, emission from inefficient combustion of brown coal in domestic heating systems is considered to be the most likely source of PAHs.

Personal exposure and biomarkers were measured with the objective of simultaneously evaluating personal exposure to air pollution and internal measures of dose and genetic effects and susceptibility using a series of biomarkers. PAHs were selected as the pollutant marker for monitoring personal exposure. A group of 30 women working outdoors in Teplice district was compared with a group of 30 women from the Prachatice district. Personal exposure monitoring ($PM_{2.5}$) was conducted for the 24-h period prior to collection of blood and urine. High correlation were observed between the mass of fine particles and personal exposure to total carcinogenic PAHs and benzo [*a*]pyrene. Significant correlations were observed between the personal exposures to $PM_{2.5}$ or carcinogenic PAHs and blood lead and blood selenium. The urinary PAH metabolites, adjusted for creatinine content, were also significantly correlated with $PM_{2.5}$ or PAHs. Significant correlations were found between personal exposure to carcinogenic PAHs and white blood cell DNA adduct level.

The results consistently suggested that elevated levels of airborne fine particle pollution could result in measurable uptake, metabolism and cellular DNA damage in a population exposed to high concentrations, even for a short-term winter inversion period.

REFERENCES

ACGIH (1989) Guidelines for the assessment of bioaerosols in the indoor environment. Cincinnati, Ohio, American Conference of

Governmental Industrial Hygienists.

ACGIH (1991) Documentation of the threshold limit values and biological exposure indices, 6th ed. Cincinnati, Ohio, American Conference of Governmental and Industrial Hygienists.

ACGIH (1995) Air sampling instruments for evaluation of atmospheric contaminants, 8th ed. Cincinnati, Ohio, American Conference of Governmental Industrial Hygienists.

Adair J & Spengler JD (1989a) In: Starks ed. Assessing activity patterns for air pollution exposure research -- Proceedings of the Research Planning Conference on Human Activity Patterns. Las Vegas, Nevada, US Environmental Protection Agency (EPA/600/4-89/004).

Adair J & Spengler JD (1989b) Time/activity and exposure assessment: The six city indoor air quality experience -- Proceeding of the 82nd Annual Meeting of the Air and Waste Management Association. Anaheim, California, Air and Waste Management Association.

AIHC (1994) Exposure factors source book. Washington, DC, American Industrial Health Council.

Ainsworth B, Haskell W, Leon A, Jacobs DR Jr, Montoye HJ, Sallis JF, & Paffenbarger RS Jr (1993) Compendium of physical activities: classification of energy costs of human physical activities. Med Sci Sports Exerc, 25: 71-80.

Aitio A (1994) Biological monitoring today and tomorrow. Scand J Work Environ Health, 20(special issue): 46-58.

Aitio A & Järvisalo J (1984) Collection, processing and storage of specimens for biological monitoring of occupational exposure to toxic chemicals. Pure Appl Chem, 56: 549-566.

Akland G, Hartwell TD, Johnson TR, & Whitmore R (1985) Measuring human exposure to carbon monoxide in Washington, DC, and Denver, CO during the winter of 1982-83. Environ Sci Technol, 19: 911-918.

Alessio L (1993) Reference values for the study of low doses of metals. Int Arch Occup Environ Health, 65: S23-S27.

Andelman JB (1985a) Human exposures to volatile halogenated organic chemicals in indoor and outdoor air. Environ Health Perspect, 62: 313-318.

Andelman JB (1985b) Inhalation exposure in the home to volatile organic contaminants of drinking water. Sci Total Environ, 47: 443-460.

Anglov T, Holst E, & Christensen M (1993) Danish external quality assessment scheme: an interlaboratory comparison study on lead, cadmium and chromium in lyophilized human blood concentrate. Int Arch Occup Environ Health, 64: 431-438.

AOAC (1991) In: Garfield FM ed. Quality assurance principles for analytical laboratories. Washington, DC, Association of Official Analytical Chemists.

Armstrong RW (1985) The geography of specific environments of patients

and nonpatients in cancer studies, with a Malaysian example. *Econ Geogr*, 52: 161-167.

Aschengrau A, Beiser A, Bellinger A, Copenhafer D, & Weitzman M (1994) The impact of soil lead abatement on urban children's blood lead levels: Phase II results from the Boston lead-in-soil demonstration project. *Environ Res*, 67(2): 125-148.

ASTM (1993) Standard practice for collection of dust from carpeted floors for chemical analysis, Method D 5438-93. Philadelphia, Pennsylvania, American Society for Testing and Materials.

Aurand K, Drews M, & Seifert B (1983) A passive sampler for the determination of the heavy metal burden of indoor environments. *Environ Technol Lett*, 4, 4333-4440.

Baselt RC (1988) Biological monitoring methods for industrial chemicals, 2nd ed. Littleton, Massachusetts, PSG Publishing Company Inc.

Bates MN, Smith AH, & Cantor KP (1995) Case-control study of bladder cancer and arsenic in drinking water. *Am J Epidemiol*, 141(6): 523-530.

Beaglehole R, Bonita R, & Kjellstrom T (1993) Basic epidemiology. Geneva, World Health Organization.

Bean J-JA, Isacson P, Hahne RM, & Kohler J (1982) Drinking water and cancer incidence in Iowa. II. Radioactivity in drinking water *Am J Epidemiol*, 116: 924-932.

Bear J & Verruijt A (1987) Modelling groundwater flow and pollution. Dordrecht, The Netherlands, Reidel D. Publishing Company.

Becker K, Müsslig-Zufika M, Hoffmann K, Krause C, Meyer E, Nöllke P, Schulz C, & Seiwert M (1997) [Environmental survey (GerES) 1990/92 -- Volume V. Drinking water: Trace elements in drinking water used by the German population.] Berlin, Institute for Water, Soil and Air Hygiene (in German).

Bell RW, Chapman RE, Kruschel BD, & Spencer MJ (1994) Windsor air quality study: personal exposure survey results. Windsor, Ontario, Queen's Printer.

Bellinger D, Leviton A, Rabinowitz M, Needleman H, & Waternaux C (1986) Correlates of low level lead exposure in urban children. *Pediatrics*, 77: 826-833.

Bencko V (1991) Biological monitoring of environmental pollution and resulting human exposure to trace metals by hair analysis. In: Dillon HK & Ho MH ed. Biological monitoring of exposure to chemicals: Metals. New York, John Wiley & Sons, pp 243-254.

Bencko V (1995) Use of human hair as a biomarker in the assessment of exposure to pollutants in occupational and environmental settings. *Toxicology*, 101: 29-39.

Bencko V, Geist T, Arbetova D, Dharmadikari DM, & Svandova E (1986) Biological monitoring of environmental pollution and human exposure to some trace elements. *J Hyg Epidemiol Microbiol Immunol*, 30: 1-10.

- Bercini DH (1992) Pretesting questionnaires in the laboratory: an alternative approach. *J Expo Anal Environ Epidemiol*, 2(2): 241-248.
- Berglund M, Braback L, Bylin G, Jonson JO, & Vahter M (1994a) Personal NO₂ exposure monitoring shows high exposure among ice-skating schoolchildren. *Arch Environ Health*, 49: 17-24.
- Berglund M, Akesson A, Nermell B, & Vahter M (1994b) Intestinal absorption of dietary cadmium in women depends on body iron stores and fiber intake. *Environ Health Perspect*, 102: 1058-1066.
- Bernard AM (1995) Biokinetics and stability aspects of biomarkers: recommendations for applications in population studies. *Toxicology*, 101: 65-71.
- Bernard AM & Lauwerys RR (1986) Assessment of human exposure to chemicals through biological monitoring. In: Kopfler FC & Craun GF ed. *Environmental epidemiology*. Chelsea, Michigan, Lewis Publishers Inc., pp 17-28.
- Berry M (1992) Strategy for a dietary exposure research program. *J Expo Anal Environ Epidemiol*, 1(suppl): 97-110.
- Bevington PR (1969) *Data reduction and error analysis for the physical sciences*. New York, McGraw-Hill, pp 57-65.
- Bihl DE, Buschbom RL, & Sula MJ (1993) Experience with a routine fecal sampling program for plutonium workers. *Health Phys*, 65: 550-5.
- Binder S, Sokal D, & Maughan D (1986) Estimating soil ingestion: The use of tracer elements in estimating the amount of soil ingested by young children. *Arch Environ Health*, 41: 341-345.
- Binkova B, Lewtas J, Miskova I, Lenicek J, & Sram R (1995) DNA adducts and personal air monitoring of carcinogenic polycyclic aromatic hydrocarbons in an environmentally exposed population. *Carcinogenesis*, 16(5):1037-1046.
- Bischoff ERC, Fischer A, & Liebenberg B (1992) Assessment of mite numbers: new methods and results. *Exp Appl Acarol*, 16: 1-14.
- Bogen KT & Spear RC (1987) Integrating uncertainty and interindividual variability in environmental risk assessment. *Risk Anal*, 7(4): 427-436.
- Bond JA, Wallace LA, Osterman-Golkar S, Lucier GW, Buckpitt A, & Henderson RF (1992) Assessment of exposure to pulmonary toxicants: Use of biological markers. *Fundam Appl Toxicol*, 18: 161-174.
- Bookout RL, Quinn DW, & McDougal JN (1997) Parallel dermal subcompartments for modelling chemical absorption. *SAR QSAR Environ Res*, 7(1-4): 259-279.
- Bornschein RL, Succop P, Dietrich KN, Clark CS, Que Hee S, & Hammond PB (1985) The influence of social and environmental factors on dust lead, hand lead, and blood lead levels in young children. *Environ Res*, 38(1): 108-118.
- Bostrom C, Spengler JD, Özkaynak H, & Lefkopoulou M (1991) Commuter exposures to VOCs in Boston, Massachusetts. *J Air Waste Manage Assoc*,

41: 1594-1600.

Boudet C, Künzli N, Zmirou D, Oglesby L, & Expolis Team (1997) Subjects adapt time-activity patterns during participation in a personal exposure assessment study. Proceedings of the Annual Meeting of the International Society of Exposure Analysis (ISEA), Research Triangle Park, North Carolina, USA.

Brown SL (1987) Exposure assessment. In: Tardiff RG & Rodricks JV ed. Toxic substances and human risk. New York, Plenum Press, pp 377-390.

Brown SK (1994) Optimization of a screening procedure for house dust mite numbers in carpets and preliminary applications to buildings. *Exp Appl Acarol*, 18: 423-434.

Brown VM & Crump DR (1996) Volatile organic compounds. In: Berry RW, Brown VM, Coward SKD, Crump DR, Gavin M, Grimes CP, Higham DF, Hull AV, Hunter CA, Jeffery LG, Lea RG, Llewellyn JW, & Raw GJ ed. Indoor air quality in homes -- Part I: The building research establishment indoor environment study. London, Construction Research Communication.

Bruaux EP & Svartengren M (1985) Global environmental monitoring assessment (GEMS) -- Assessment of human exposure to lead: Comparison between Belgium, Malta, Mexico and Sweden. Stockholm, Sweden, National Institute of Environmental Medicine and Department of Environmental Hygiene, Karolinska Institute/Brussels, Belgium, Institute of Hygiene and Epidemiology, Ministry of Health.

Brunekreef B, Noy D, Biersteker K, & Boleij J (1983) Blood lead levels of Dutch city children and their relationship to lead in the environment. *J Air Pollut Control Assoc*, 33: 872-876.

Bullock DG, Smith NJ, & Whitehead TP (1986) External quality control of assays of lead in blood. *Clin Chem*, 32(10): 1884-1889

Burge HA (1990) Bioaerosols: prevalence and health effects in the indoor environment. *J Allergy Clin Immunol*, 86: 687-701.

Burge HA ed. (1995) Bioaerosols. Boca Raton, Florida, Lewis Publishers.

Burge HA & Solomon WR (1987) Sampling and analysis of biological aerosols. *Atmos Environ*, 21: 451-456.

Burke T, Anderson H, Beach N, Colome S, Drew RT, Firestone M, Hauchman FS, Miller TO, Wagener DK, Zeise L, & Tran N (1992) Role of exposure databases in risk management. *Arch Environ Health*, 47(6): 421-429.

Bustueva KA, Revich BA, & Bezpalka LE (1994) Cadmium in the environment of three Russian cities and in human hair and urine. *Arch Environ Health*, 49: 284-288.

Calabrese EJ, Pastides H, Barnes R, Edwards C, KostECKI P, Stanek E, Venman P, & Gilbert CE (1989) How much soil do children ingest: An epidemiologic study. *Regul Toxicol Pharmacol*, 10: 1-15.

Calabrese EJ, Stanek EJ, Gilbert CE, & Barnes RM (1990) Preliminary adult soil ingestion estimates: Results of a pilot study. *Regul Toxicol Pharmacol*, 12: 88-95.

Callahan MA & Bryan EF (1994) Exposure assessment. In: Milman HA & Weisburger EK ed. Handbook of carcinogen testing. Park Ridge, New Jersey, Noyes Publications, pp 651-671.

Callahan MA, Clickner RP, Whitmore RW, Kalton G, & Sexton K (1995) Overview of important design issues for a national human exposure assessment survey. *J Exp Anal Environ Epidemiol*, 5(3): 257-282.

Camus M, Siemiatycki J, & Meek B (1998) Nonoccupational exposure to chrysotile asbestos and the risk of lung cancer. *N Engl J Med*, 338: 1565-1571.

Carlin B & Louis T (1996) Bayes and empirical methods for data analysis. London, Chapman & Hall.

Carrano AV & Natarajan AT (1988) Considerations for population monitoring using cytogenetic techniques (ICPEMC Publication No. 14). *Mutat Res*, 204: 379-406.

CDC (1991) Strategic plan for the elimination of childhood lead poisoning. Atlanta, Georgia, US Department of Health and Human Services, Public Health Service, Centers for Disease Control.

Chan C, Özkaynak H, Spengler JD, & Sheldon L (1991) Driver exposure to volatile organic compounds, CO, ozone and NO₂ under different driving conditions. *Environ Sci Technol*, 25(5): 964-972.

Chapin FS Jr (1974) Human activity patterns in the city. New York, John Wiley & Sons.

Chapman MD, Aalberse RC, Brown MJ, & Platts-Mills TAE (1988) Monoclonal antibodies to the major feline allergen Fel d I. II. Single step affinity purification of Fel d I, N-terminal sequence analysis, and development of a sensitive two-site immunoassay to assess Fel d I exposure. *J Immunol*, 140: 812-818.

Charney E, Sayre J, & Coulter M (1980) Increased lead absorption in inner-city children: Where does the lead come from. *Pediatrics*, 65: 226-231.

Chase KM & Shields PG (1990) Medical surveillance of hazardous waste site workers exposed to polychlorinated biphenyls (PCBs). *Occup Med State Art Rev*, 5: 33-37.

Chavalitnitikul C & Levin L (1984) A laboratory evaluation of wipe testing based on lead oxide surface contamination. *Am Ind Hyg Assoc J*, 45(5): 311-317.

Chiou HY, Hsueh YM, Liaw KF, Horng SF, Chiang MH, Pu YS, Lin JS, Huang CH, & Chen CJ (1995) Incidence of internal cancers and ingested inorganic arsenic: a seven-year follow-up study in Taiwan. *Cancer Res*, 55(6): 1296-1300.

Christensen JM, Poulsen OM, & Anglov T (1994) Method evaluation, quality control, and external quality assurance systems of analytical procedures. In: Seiler HG, Sigel A, & Sigel H ed. Handbook on metals in clinical and analytical chemistry. New York, Basel, Hong Kong, Marcel Dekker, Inc.

Cleveland W (1993) Visualizing data. Murray Hill, New Jersey, Hobart

Press.

Cochran WG (1977) Sampling techniques, 3rd ed. New York, John Wiley & Sons.

Cohen Y & Ryan PA (1985) Multimedia modelling of environmental transport: Trichloroethylene test case. *Environ Sci Technol*, 9: 412-417.

Cohen Y, Tsai W, Chetty SL, & Mayer GL (1990) Dynamic partitioning of organic chemicals in regional environments: A multimedia screening-level approach. *Environ Sci Technol*, 24: 1549-1558.

Colloff MJ (1991) Practical and theoretical aspects of the ecology of house dust mites (Acari: Pyroglyphidae) in relation to the study of mite-mediated allergy. *Rev Med Vet Entomol*, 79: 611-630.

Colome SC, Wilson AL, & Tian Y (1994) California residential indoor air quality study -- Volume 2: Carbon monoxide and air exchange rate: a univariate and multivariate analysis. Irvine, California, Integrated Environmental Services.

Connell DW, Hawker DW, Warne MS, & Vowles PP (1997) Basic concepts of environmental chemistry. Boca Raton, Florida, CRC Press Inc.

Cooke TF (1991) Indoor air pollutants: A literature review. *Rev Environ Health*, 9(3): 137-160.

Cox LA (1996) Reassessing benzene risks using internal doses and Monte Carlo uncertainty analysis. *Environ Health Perspect*, 104(suppl 6): 1413-1429.

Cullen MR (1989) The role of clinical investigations in biological markers research. *Environ Res*, 50: 1-10.

Dabbs JM (1991) Salivary testosterone measurements: collecting, storing, and mailing saliva samples. *Physiol Behav*, 49: 815-817.

Dabbs JM (1993) Salivary testosterone measurements in behavioral studies. *Ann NY Acad Sci*, 694: 177-183.

Daisey JM, Cheney JL, & Liroy PJ (1986) Profiles of organic particulate emissions from air pollution sources: status and needs for receptor source apportionment modelling. *J Air Pollut Control Assoc*, 36(1): 17-33.

Davies D & Mes J (1987) Comparison of the residue levels of some organochlorine compounds in breast milk of the general and indigenous Canadian populations. *Bull Environ Contam Toxicol*, 39: 743-749.

Davies DJA, Thornton I, Watt JM, Culbard EB, Harvey PG, Delves HT, Sherlock JC, Smart GA, Thomas JFA, & Quinn MJ (1990) Lead intake and blood lead in two-year-old UK urban children. *Sci Total Environ*, 90: 13-29.

Dean AG, Dean JA, Coulombier D, Brendel KA, Smith DC, Burton AH, Dicker RC, Sullivan K, Fagan RF, & Arner TG (1995) Epi Info, version 6: A word-processing, database, and statistics program for public health on IBM-compatible microcomputers. Atlanta, Georgia, US Department of Health and Human Services, Public Health Service,

Centers for Disease Control. Atlanta, Georgia, Centers for Disease Control and Prevention.

De Blay F, Chapman MD, & Platts-Mills TAE (1991) Airborne cat allergen (Fel d I): Environmental control with the cat in situ. *Am Rev Respir Dis*, 143: 1334-1339.

De Bortoli M, Knoeppel M, Pecchio E, Peil A, & Rogora L (1986) Measurement of indoor air quality and comparison with ambient air: A study in 15 homes in Northern Italy. *Gov Rep Announc Index*, 8.

DeRosa CT, Stevens Y-W, Wilson JD, Ademoyero AA, Buchanan SD, Cibulas W Jr, Duerksen-Hughes PJ, Mumtaz MM, Neft RE, Pohl HR, & Williams-Johnson MM (1993) The Agency for Toxic Substances and Disease Registry's role in development and application of biomarkers in public health practice. *Toxicol Ind Health*, 9: 979-994.

Diemel JAL, Brunekreef B, Boleij JSM, Biersteker K, & Veenstra SJ (1981) The Arnhem lead study. II. Indoor pollution, and indoor/outdoor relationships. *Environ Res*, 25: 449-456.

DiVincenzo GD, Giordano CJ, & Schriever LS (1985) Biologic monitoring of workers exposed to silver. *Int Arch Occup Environ Health*, 56: 207-215.

Doi R, Raghupathy L, Ohno H, Naganuma A, Imura N, & Harada M (1988) A study of the sources of external metal contamination of hair. *Sci Total Environ*, 77: 153-161.

Douglas A (1973) Home-based trip end models -- A comparison between category analysis and regression analysis procedures. *Transportation*, 2: 53-70.

Douwes J, Versloot P, Hollander A, Heederik D, & Doekes G (1995) Influence of various dust sampling and extraction methods on the measurement of airborne endotoxin. *Appl Environ Microbiol*, 61: 1763-1769.

Dreborg S, Einarsson R, Lau S, Munir AKM, & Wahn U (1995) Dust sampling for determination of allergen content. *Allergy*, 50: 188-189.

Driver JH, Konz JJ, & Whitmyre GK (1989) Soil adherence to skin. *Bull Environ Contam Toxicol*, 43(6): 814-820.

Droz PO (1992) Quantification of biological variability. *Ann Occup Hyg*, 36: 295-306.

Droz PO (1993) Pharmacokinetic modelling as a tool for biological monitoring. *Int Arch Occup Environ Health*, 65: S53-S59.

Droz PO & Wu MM (1991) Biological monitoring strategies. In: Rappaport SM & Smith TJ ed. *Exposure assessment for epidemiology and hazard control*. Chelsea, Michigan, Lewis Publishers, pp 251-270.

Duan N (1982) Models for human exposure to air pollution. *Environ Int*, 8: 305-309.

Dybdal T, Vik H, & Elsayed S (1989) Dust from carpeted and smooth floors: II. Antigenic and allergenic content of dust vacuumed from carpeted and smooth floors under routine cleaning schedules. *Allergy*,

44: 401-411.

EC (1993) European collaborative action indoor air quality and its impact on man: Biological particles in indoor environments. Luxembourg, Office for Official Publications of the European Commission (ECSC-EEC-EAEC) (Report No. 12).

EC (1996) Technical guidance documents in support of the Commission Directive 93/67/EEC on risk assessment for new and notified substances and the Commission Regulation (EC) 1488/94 on risk assessment for existing substances. Luxembourg, Office for Official Publications of the European Community (Publication No. EC/CR-48-96-001/002/003/004-EN-C)

EC (1997a) Report on tasks for scientific cooperation: Improvement of knowledge of food consumption with a view to protection of public health by means of exchanges and collaboration between database managers. Luxembourg, Office for Official Publications of the European Commission (ISBN No. 92-827-9716-3).

EC (1997b) EUSES - the European Union system for the evaluation of substances. Ispra, Italy, European Commission, European Chemicals Bureau, Joint Research Centre.

Edgerton SA & Shah JJ (1991) Assessing total exposure to gasoline vapor using the source exposure model. *J Exp Anal Environ Epidemiol*, 2(1): 109-115.

Eisenberg JNS & McKone TE (1998) Decision tree method for the classification of chemical pollutants: Incorporation of across-chemical variability and within-chemical uncertainty. *Environ Sci Technol*, 32(21): 3396-3404.

Elkins HB (1954) Analyses of biologic materials as indices of exposure to organic solvents. *Arch Ind Hyg Occup Med*, 9: 212-222.

Elkins HB (1967) Excretory and biological threshold limits. *Am Ind Hyg Assoc J*, 128: 305-314.

Elkins ER (1989) Effect of commercial processing on pesticide residues in selected fruits and vegetables. *J Assoc Off Anal Chem*, 72 (3): 533-535.

Ellegard A (1997) Tears while cooking: an indicator of indoor air pollution and related health effects in developing countries. *Environ Res*, 75(1): 12-22.

Faegri K & Iversen J (1989) Textbook of pollen analysis. New York, John Wiley & Sons, p 327.

FAO/WHO (1995a) Recommendations for the revision of guidelines for predicting dietary intake of pesticide residues. Report of the Joint FAO/WHO Expert Consultation, Geneva, Switzerland, 13-17 March 1995. Geneva, World Health Organization.

FAO/WHO (1995b) Application of risk analysis to food standard issues. Report of a Joint FAO/WHO Consultation, York, UK, 2-6 May 1995. Geneva, World Health Organization (Document WHO/FNU/FOS/95.11).

FAO/WHO (1996) Preparation and use of food-based dietary guidelines.

Report of a Joint FAO/WHO Consultation, Nicosia, Cyprus, 2-7 March 1995. Geneva, World Health Organization (Document WHO/FNU/NUT/96.6).

FAO/WHO (1997) Report of the Joint FAO/WHO Consultation on Food Consumption and Exposure Assessment of Chemicals, Geneva, 10-14 February 1997. Geneva, World Health Organization (Document WHO/FSF/FOS/97.5).

Farfel MR & Rhode CA (1995) Determination of environmental lead, using compositing of house dust samples. In: Breen JJ & Stroup CR ed. Lead poisoning -- exposure, abatement, and regulation. Boca Raton, Florida, CRC Press Inc., chapter 26.

Farfel MR, Lees PSJ, Bannon D, Lim BS, & Rohde CA (1994) Comparison of two cyclone-based collection devices for the evaluation of lead-containing residential dusts. *Appl Occup Environ Hyg J*, 9(3): 212-217.

Feather IH, Warner JA, Holgate ST, Thompson PJ, & Stewart GA (1993) Cohabiting with domestic mites. *Thorax*, 48: 5-9.

Fenske RA (1993) Dermal exposure assessment techniques. *Ann Occup Hyg*, 37(6): 687-706.

Fenske RA, Leffengwell JT, & Spear RC (1986a) A video imaging technique for assessing dermal exposure: I. Instrument design and testing. *Am Ind Hyg Assoc J*, 47: 764-770.

Fenske RA, Leffengwell JT, & Spear RC (1986b) A video imaging technique for assessing dermal exposure: II. Fluorescent tracer method. *Am Ind Hyg Assoc J*, 47: 771-775.

Fenske RA, Curry PB, Wandelmaier F, & Ritter L (1991) Development of dermal and respiratory sampling procedures for human exposure to pesticides in indoor environments. *J Expo Anal Environ Epidemiol*, 1(1): 11-30.

Fernández-Caldas E, Trudeau WL, & Ledford DK (1994) Environmental control of indoor biological agents. *J Allergy Clin Immunol*, 94: 404-412.

Fernandez-Bremauntz A & Ashmore MR (1995a) Exposure of commuters to carbon monoxide in Mexico City II: Comparison of in-vehicle and fixed-site concentrations. *J Exp Anal Environ Epidemiol*, 5(4): 497-510.

Fernandez-Bremauntz A & Ashmore MR (1995b) Exposure of commuters to carbon monoxide in Mexico City: II. Measurement of in-vehicle concentrations. *Atmos Environ*, 29(4): 525-532.

Finley BL, Scott PK, & Mayhall DA (1994a) Development of a standard soil-to-skin adherence probability density function for use in Monte Carlo analyses of dermal exposure. *Risk Anal*, 14(4): 555-569.

Finley BL, Proctor D, Scott P, Harrington N, Paustenbach D, & Price P (1994b) Recommended distributions for exposure factors frequently used in health risk assessment. *Risk Anal*, 14(4): 533-553.

Fiserova-Bergerova V (1987) Development of biological exposure indices (BEIs) and their implementation. *Appl Ind Hyg*, 2: 87-92.

- Fowle JR & Sexton K (1992) EPA priorities for biologic markers research in environmental health. *Environ Health Perspect*, 98: 235-241.
- Fox MB (1983) Working women and travel: The access of women to work and community facilities. *J Am Plan Assoc*, 49: 156-170.
- Freeman NC, Ettinger A, Berry M, & Rhoads G (1997) Hygiene and food related behaviors associated with blood lead levels of young children from lead-contaminated homes. *J Expo Anal Environ Epidemiol*, 7(1): 103-118.
- Freeze RA & Cherry JA (1979) *Groundwater*. Englewood Cliffs, New Jersey, Prentice-Hall.
- Friberg L (1985) The rationale of biological monitoring of chemicals -- with special reference to metals. *Am Ind Hyg Assoc J*, 46: 633-642.
- Fries GF (1995) A review of the significance of animal food products as potential pathways of human exposures to dioxins. *J Anim Sci*, 73(6): 1639-1650.
- Garland M, Morris JS, Rosner BA, Stampfer MJ, Spate VL, Baskett CJ, Willett WC, & Hunter DJ (1993) Toenail trace element levels as biomarkers: reproducibility over a 6-year period. *Cancer Epidemiol Biomarkers Prev*, 2: 493-497.
- Garrett MH (1996) *Indoor environment and asthma in children*. Victoria, Australia, Monash University, School of Applied Science (Ph.D Thesis).
- Geno PW, Camann DE, Harding HJ, Villalobos K, & Lewis RG (1996) Handwipe sampling and analysis procedure for the measurement of dermal contact with pesticides. *Arch Environ Contam Toxicol*, 30: 132-138.
- Georgopoulos PG & Liroy PJ (1994) Conceptual and theoretical aspects of human exposure and dose assessment. *J Exp Anal Environ Epidemiol*, 4: 253-285.
- Gifford FA & Hanna SR (1973) Modelling urban air pollution. *Atmos Environ*, 7: 131-136.
- Gil L & Adonis M (1997) Influence of atmospheric air pollution on indoor air quality: comparison of chemical pollutants and mutagenicity levels in Santiago (Chile). *Indoor Built Environ*, 6: 320-330.
- Gilbert RO (1987) *Statistical methods for environmental pollution monitoring*. New York, Van Nostrand Reinhold Company.
- Glantz SA (1987) *Primer of biostatistics*. New York, McGraw-Hill Book Co., pp 287-330.
- Glover DM, Hopke PK, Vermette SJ, Landsberger S, & D'Auben DR (1991) Source apportionment with site specific source profiles. *J Air Waste Manage Assoc*, 41(3): 294-305.
- Goldman LR, Gomez M, Greenfield S, Hall L, Hulka BS, Kaye WE, Lybarger JA, McKenzie DH, Murphy RS, Wellington DG, & Woodruff T (1992) Use of exposure databases for status and trends analysis. *Arch Environ Health*, 47(6): 430-438.

- Goldstein IF, Hartel D, Andrews LR, & Weinstein AL (1986) Indoor air pollution exposure of low-income inner-city residents. *Environ Int*, 12: 211-219.
- Goldstein IF, Andrews LR, & Hartel D (1988) Assessment of human exposure to nitrogen dioxide, carbon monoxide, and respirable suspended particulates in New York City residents. *Atmos Environ*, 22: 2127-2139.
- Gordon SM, Wallace LA, Callahan PJ, Kenny DV, & Brinkman MC (1998) Effect of water temperature on dermal exposure to chloroform. *Environ Health Perspect*, 106(6): 337-345.
- Goto S, Sugita K, Endo O, Takagi Y, Matsushita H, & Lewtas J (1997) Method of determining the inhalation deposition of mutagenic components in environmental tobacco smoke aerosol. *Jpn J Toxicol Environ Health*, 43: 123-128.
- Graham J, Walker KD, Berry M, Bryan EFM, Callahan MA, Fan A, Finley B, Lynch J, McKone T, Ozkaynak H, & Sexton K (1992) Role of exposure databases in risk assessment. *Arch Environ Health*, 47(6): 408-420.
- Grandjean P (1986) Reference intervals for toxic metals: Problems and prospects. *Ann Clin Lab Sci*, 16: 67-74.
- Grandjean P, Brown SS, Reavey P, & Young DS (1994) Biomarkers of chemical exposure: State of the art. *Clin Chem*, 40: 1360-1362.
- Grassman J & Haas R (1993) Development of an immunoassay to detect hemoglobin adducts formed by benzene exposure. *Int Arch Occup Environ Health*, 65: S147-S150.
- Graziano JH (1994) Validity of lead exposure markers in diagnosis and surveillance. *Clin Chem*, 40: 1387-1390.
- Griffith J, Duncan RC, & Hulka BS (1989) Biochemical and biological markers: Implications for epidemiologic studies. *Arch Environ Health*, 44: 375-381.
- Haan M, Kaplan GA, & Camacho T (1987) Poverty and health: Prospective evidence from the Alameda County study. *Am J Epidemiol*, 125(6): 989-998.
- Hall JV, Winer AM, Kleinman MT, Lurmann FW, Brajer V, & Colome SD (1992) Valuing the health benefits of clean air. *Science*, 255: 812-817.
- Hamilton RG, Chapman MD, Platts-Mills TAE, & Adkinson NF (1992) House dust aeroallergen measurements in clinical practice: a guide to allergen-free home and work environments. *Immunol Allergy Pract*, 14: 58-74.
- Hansen MH, Hurwitz WN, & Madow WG (1953) *Sample survey methods and theory*. New York, John Wiley & Sons.
- Hanson S & Hanson P (1981) The travel-activity patterns of urban residents: Dimensions and relationships to sociodemographic characteristics. *Econ Geogr*, 57: 332-347.

Harris CC, Weston A, Willey JC, Trivers GE, & Mann DL (1987) Biochemical and molecular epidemiology of human cancer: Indicators of carcinogen exposure, DNA damage, and genetic predisposition. *Environ Health Perspect*, 75: 109-119.

Hart ML, Wentworth JE, & Bailey SD (1994) The effects of trap height and weather variables on recorded pollen concentration at Leicester. *Grana*, 33: 100-103.

Hartwell TD, Clayton CA, Michie RM, Whitmore RW, Zelon HS, & Whithurst DA (1984) Study of carbon monoxide exposure of residents in Washington, DC and Denver, CO. Research Triangle Park, North Carolina, US Environmental Protection Agency (EPA-600/4-84-031).

Hatch M & Thomas D (1993) Measurement issues in environmental epidemiology. *Environ Health Perspect*, 101(suppl 4): 49-57.

Hattis DB (1986) The promise of molecular epidemiology for quantitative risk assessment. *Risk Anal*, 6: 181-193.

Hauser R, Elreedy S, Hoppin JA, & Christiani DC (1995) The upper airway response in workers exposed to fuel oil ash: nasal lavage analysis. *Occup Environ Med*, 52: 353-358.

Hawley JK (1985) Assessment of health risk from exposure to contaminated soil. *Risk Anal*, 5: 289-302.

Heddle JA, Cimino MC, Hayashi M, Romagna F, Shelby MD, Tucker JD, Vanparys P, & MacGregor JT (1991) Micronuclei as an index of cytogenetic damage: past, present, and future. *Environ Mol Mutagen*, 18(4): 277-291.

HEI (1991) Asbestos in public and commercial buildings: a literature review and synthesis of current knowledge. Cambridge, Massachusetts, Health Effects Institute.

Hemminki K (1992) Use of chemical, biochemical, and genetic markers in cancer epidemiology and risk assessment. *Am J Ind Med*, 21: 65-76.

Henderson RF, Bechtold WE, Bond JA, & Sun JD (1989) The use of biological markers in toxicology. *Crit Rev Toxicol*, 20: 65-82.

Hickman JR, McBain DC, & Armstrong (1982) The contribution of drinking water to exposure to toxic substances in Canada. *Environ Monit Assess*, 2: 71-83.

Hinds WC (1982) Aerosol technology: properties, behavior, and measurement of airborne particles. New York, John Wiley & Sons.

Hinton D (1990) Wearable personal activity logger. Proceedings of the First International Symposium on Total Exposure Assessment Methodology: A new horizon, Las Vegas, Nevada, 1989. Pittsburgh, Pennsylvania, Air and Waste Management Association.

Hoffman FO & Hammonds JS (1994) Propagation of uncertainty in risk assessments: the need to distinguish between uncertainty due to lack of knowledge and uncertainty due to variability. *Risk Anal*, 14(5):707-712.

Hoffmann K, Schwabe R, Krause C, Schulz C, Seifert B, & Ullrich D

- (1996) [Environmental survey (GerES) 1990/91- Volume IV: Personal exposure to volatile organic compounds in West Germany.] Berlin, Institute for Water, Soil and Air Hygiene (WaBoLu No. 4/1996) (in German).
- Hoppin JA, Aro ACA, Williams PL, Hu H, & Ryan PB (1995) Validation of K-XRF bone lead measurement in young adults. *Environ Health Perspect*, 103: 78-83.
- Horne RA (1978) *The chemistry of our environment*. New York, Wiley-Interscience, pp 596-593.
- Horner WE, Lehrer SB, & Salvaggio JE (1994) Fungi. *Immunol Allergy Clin North Am*, 14: 551-556.
- Houeto P, Bindoula G, & Hoffman JR (1995) Ethylenebisdithiocarbamates and ethylenethiourea: possible human health hazards. *Environ Health Perspect*, 103(6): 568-573.
- Hoyet C, Bessot JC, Le Mao J, Quoix E, & Pauli G (1991) Comparison between Der p I plus Der f I content determinations and guanine measurements in 239 house dust samples. *J Allergy Clin Immunol*, 88: 678-680.
- Hu H, Aro ACA, & Rotnitsky A (1995) Bone lead measured by X-ray fluorescence: epidemiologic methods. *Environ Health Perspect*, 103(suppl 1): 105-110.
- Hulka B (1991) Epidemiological studies using biological markers: Issues for epidemiologists. APSO Distinguished achievement award lecture. *Cancer Epidemiol Biomarkers Prev*, 1: 13-19.
- Hulka BS & Margolin BH (1992) Methodological issues in epidemiologic studies using biologic markers. *Am J Epidemiol*, 135: 200-209.
- Hulka BS & Wilcosky T (1988) Biological markers in epidemiologic research. *Arch Environ Health*, 43: 83-89.
- Hyvarinen AM, Martikainen PJ, & Nevalainen AI (1991) Suitability of poor medium in counting total viable airborne bacteria. *Grana*, 30: 414-417.
- IAEA (1989) *Evaluating the reliability of predictions made using environmental transfer models*. Vienna, International Atomic Energy Agency (Safety Series No. 100).
- IAEA (1995) *Survey of reference materials -- Volume 1: Biological and environmental reference materials for trace elements, nuclides and microcontaminants*. A report prepared by the International Atomic Energy Agency in co-operation with the United Nations Environment Programme. Vienna, International Atomic Energy Agency (Document IAEA-TECDOC-854).
- IAEA (1996) *Survey of reference materials -- Volume 2: Environmentally related reference materials for trace elements, nuclides and microcontaminants*. A report prepared by the International Atomic Energy Agency in co-operation with the United Nations Environment Programme. Vienna, International Atomic Energy Agency (Document IAEA-TECDOC-880).

Iman RL & Helton JC (1988) An investigation of uncertainty and sensitivity analysis techniques for computer models. *Risk Anal*, 8(1): 71-90.

IPCS (1992) Environmental health criteria 141: Quality management for chemical safety testing. Geneva, World Health Organization, International Programme on Chemical Safety.

IPCS (1993) Environmental health criteria 155: Biomarkers and risk assessment: Concept and principles. Geneva, World Health Organization, International Programme on Chemical Safety.

IPCS (1994) Environmental health criteria 170: Assessing human health risks of chemicals: The derivation of guidance values for health-based exposure limits. Geneva, World Health Organization, International Programme on Chemical Safety.

IPCS (1997d) Environmental health criteria 188: Nitrogen dioxide, 2nd edition. Geneva, World Health Organization, International Programme on Chemical Safety.

ISO (1991) International standard 8258: Shewhart control charts. Geneva, International Organization for Standardization.

ISO (1993) International standard 7870: Control charts -- General guide and introduction. Geneva, International Organization for Standardization.

ISO (1994) International standard 5725: Accuracy (trueness and precision) of measurement methods and results -- Part 1: General principles and definitions. Geneva, International Organization for Standardization.

ISO (1997) International standard 7871: Cusum charts. Geneva, International Organization for Standardization.

Ito Y (1993) [The history of the investigating group on the per capita intake/day of food additives in Japan.] *Foods Food Ingrid J*, 157: 4-21 (in Japanese).

James IR & Knuiman MW (1987) An application of Bayes methodology to the analysis of diary records from a water use study. *J Am Stat Assoc*, 82(399): 705-711.

Jantunen M, Hänninen O, Katsouyanni K, Knöppel H, Künzli N, Lebet E, Maroni M, Saarela K, Sram R, & Zmirou D (1998) Air pollution exposure in European cities: The EXPOLIS-Study. *J Expo Anal Environ Epidemiol*, 8(4): 495-518.

Jenkins P, Phillips TJ, Mulberg EJ, & Hui SP (1992) Activity patterns of Californians: Use of and proximity to indoor pollutant sources. *Atmos Environ*, 26A.

Jensen H (1992) Lead in household dust. *Sci Total Environ*, 114: 1-6.

Jensen J, Poulsen K, Mygind K, Weeke ER, & Weeke B (1989) Immunochemical estimations of allergenic activities from outdoor aero-allergens, collected by a high-volume sampler. *Allergy*, 44: 52-59.

- Jimenez RD & Velasquez A (1989) Metropolitan Maniza: A framework for its sustained development. *Environ Urban*, 1(1): 51-58.
- Johansen HR, Alexander J, Rosslund OJ, Planting S, Lovik M, Gaarder PI, Gdynia W, Bjerve KS, & Becher G (1996) PCDDs, PCDFs, and PCDs in human blood in relation to consumption of crabs from a contaminated fjord area in Norway. *Environ Health Perspect*, 104: 756-764.
- Johnson T (1983) A study of personal exposures to carbon monoxide in Denver, CO -- Final report (US EPA Contract No. 68-02-3755). Research Triangle Park, North Carolina, US Environmental Protection Agency.
- Johnson T (1984) A study of personal exposure to carbon monoxide in Denver, CO. Research Triangle Park, North Carolina, US Environmental Protection Agency (EPA-600/4-84-014).
- Johnson T (1989) Human activity patterns in Cincinnati, Ohio. Palo Alto, California, Electric Power Research Institute (Report EPRI EN-6204, Project 940-6).
- Johnson NL & Kotz S (1970a) Continuous univariate distributions: I. Boston, Massachusetts, Houghton Mifflin Co.
- Johnson NL & Kotz S (1970b) Continuous univariate distributions: II. New York, John Wiley & Sons.
- Johnson T, Capell J, & Wijnberg L (1986) Selected data analyses relating to studies of personal carbon monoxide exposure in Denver and Washington, DC -- Final report (US EPA Contract No. 68-02-3496). Research Triangle Park, North Carolina, US Environmental Protection Agency.
- Johnson T, Paul RA, Capel JE, & McCurdy T (1990) Estimation of ozone exposure in Houston using a probabilistic version of NEM: Proceedings of the 83rd Annual Meeting of the Air and Waste Management Association. Pittsburgh, Pennsylvania, Air and Waste Management Association (Paper 90-150.1).
- Jury W, Spencer W, & Farmer W (1983) Behavior assessment model for trace organics in soil: I. Model description. *J Environ Qual*, 12: 558-564.
- Juster FT (1985a) Conceptual and methodological issues involved in the measurement of time use. In: Juster FT & Stafford FP ed. *Time, goods, and well being*, pp 19-32.
- Juster FT (1985b) The validity and quality of time use estimates obtained from recall diaries. In: Juster FT & Stafford FP ed. *Time, goods, and well being*, pp 63-91.
- Kalton G (1983) *Introduction to survey sampling*. New York, John Wiley & Sons.
- Kalton G & Kasprzyk D (1986) The treatment of missing survey data. *Surv Methodol*, 12: 1-16.
- Kamphuis HJ, Notermans SHW, Veeneman GH, Van Boom JH, & Rombouts FM (1991) Extracellular polysaccharides of moulds and their immunological activity. In: *Fungal cell wall and immune response*. Berlin, Heidelberg, New York, Springer-Verlag, vol H35, pp 157-167.

- Kaye WE, Novotny TE, & Tucker M (1987) New ceramics-related industry implicated in elevated blood lead levels in children. *Arch Environ Health*, 42(2): 161-164.
- Kelsey KT (1990) Cytogenetic techniques for biological monitoring. *Occup Med*, 5: 39-47.
- Kemper FH (1993) Human organ specimen banking: 15 years of experience. *Sci Total Environ*, 139/140: 13-25.
- Kish L (1965) Survey sampling. New York, John Wiley & Sons.
- Kissel JC, Richter KY, & Fenske RA (1996) Factors affecting soil adherence to skin in hand-press trials. *Bull Environ Contam Toxicol*, 56(5): 722-728.
- Klein J, Chitayat D, & Koren G (1993) Hair analysis as a marker for fetal exposure to maternal smoking. *N Engl J Med*, 328: 66-67.
- Kleinbaum DG, Kupper LL, & Muller KE (1988) Applied regression analysis and other multivariable methods. Boston, Massachusetts, PWS-Kent Publishing Co., pp 88-90.
- Kohlmeier L & Kohlmeier M (1995) Adipose tissue as a medium for epidemiologic exposure assessment. *Environ Health Perspect*, 103 (suppl 3): 99-106.
- Kollander M (1993) Guidance on survey design for human exposure assessment location (HEAL) studies. Geneva, World Health Organization (Document WHO/PEP/92.6)
- Kompaore F & Tsuruta H (1993) *In vivo* differences between Asian, Black and White in the stratum corneum barrier function. *Int Arch Occup Environ Health*, 65: S223-S225.
- Koning de HW (1988) Air pollution in African villages and cities. Geneva, World Health Organization
- Korsgaard J & Iversen M (1991) Epidemiology of house dust mite allergy. *Allergy*, 46 (suppl 11): 14-18.
- Koutrakis P & Sioutas C (1996) Physico-chemical properties and measurement of ambient particles. In: Wilson R & Spengler J ed. *Particles in our air: Concentrations and health effects*. Cambridge, Massachusetts, Harvard University Press, pp 15-40.
- Koutrakis P, Briggs SLK, & Leaderer BP (1992) Source apportionment of indoor aerosols in Suffolk and Onondaga counties, New York. *Environ Sci Technol*, 26(3): 521-527.
- Krause C, Mailahn W, Nagel R, Schulz C, Seifert B, & Ulrich D (1987) Occurrence of volatile organic compounds in the air of 500 homes in Federal Republic of Germany. In: *Proceedings of the 4th International Conference on Indoor Air Quality and Climate*. Berlin, Institute for Water, Soil and Air Hygiene, vol I, pp 102-106.
- Krause C, Chutsch M, Henke M, Leiske M, Schulz C, Schwarz E, & Seifert B (1992) Heavy metals in the blood, urine and hair of a representative population sample in the Federal Republic of Germany 1985/86. In:

- Seemayer NH & Hadnagy W ed. Environmental hygiene -- Volume III: Proceedings of the 3rd European Meeting of Environmental Hygiene, Düsseldorf, 25-27 June 1991. Berlin, Heidelberg, New York, Springer Verlag, pp 159-162.
- Künzli N, Lurman F, Segal M, Ngo L, Balmes J, & Tager I (1996) Reliability of life-time residential history and activity measures as elements of cumulative ambient ozone exposure assessment. *J Exp Anal Environ Epidemiol*, 6: 289-310.
- Künzli N, Lurman F, Segal M, Ngo L, Balmes J, & Tager I (1997a) Association between life-time ambient ozone exposure and pulmonary function in college freshman: Results of a pilot study. *Environ Res*, 72: 8-23.
- Künzli N, Kelly T, Balmes J, & Tager IB (1997b) Reproducibility of retrospective assessment of outdoor time-activity patterns as an individual determinant of long-term ambient ozone exposure. *Int J Epidemiol*, 26: 1258-1271.
- Laitinen S, Kangas J, Kotimaa M, Liesivuori JM, Martikainen PJ, Nevalainen A, Sarantila R, & Husman K (1994) Workers' exposure to airborne bacteria and endotoxins at industrial wastewater treatment plants. *Am Ind Hyg Assoc J*, 55: 1055-1060.
- Lanphear BP & Roghmann KJ (1997) Pathways of lead exposure in urban children. *Environ Res*, 74(1):67-73.
- Lanphear BP, Emond M, Jacobs DE, Weitzman M, Tanner M, Winter NL, Yakir B, & Eberly S (1995) The relationship of lead-contaminated house dust and blood lead levels among urban children. *Environ Res*, 68(2): 114-123.
- Laporte RE, Montage HJ, & Caspersen CJ (1985) Assessment of physical activity in epidemiologic research: Problems and prospects. *Public Health Rep*, 100: 131-146.
- Lau S, Rusche A, Weber A, Werthmann I, Büttner-Götz P, & Wahn U (1990) [Comparison of the determination of house dust mite allergens ELISA and guanine.] *Allergologie*, 13: 12-15 (in German).
- Lauwerys RR (1983) Industrial chemical exposure: Guidelines for biological monitoring. Davis, California, Biomedical Publications.
- Laxen DPH, Raab GM, & Fulton M (1987) Children's blood lead and exposure to lead in household dust and Water: A basis for an environmental standard for lead in dust. *Sci Total Environ*, 66: 235-244.
- Lebowitz D, Quackenboss JJ, Kollander M, Soczek ML, & Colome S (1989) The new standard environmental inventory questionnaire for estimation of indoor concentrations. *J Air Pollut Control Assoc*, 39: 1411-1419.
- Lebret E, Van de Weil HJ, Noji D, & Boleij JSM (1986) Volatile hydrocarbons in Dutch homes. *Environ Int*, 12(1-4): 323-332.
- Lehrer SB, Horner WE, Menon P, & Stankus RB (1991) Comparison of cockroach allergenic activity in whole body and fecal extracts. *J Allergy Clin Immunol*, 87(2): 574-580.

- Lehtimäki M & Willeke K (1993) Measurement methods. In: Willeke K & Baron P ed. *Aerosol measurement: Principles, techniques and applications*. New York, Van Nostrand Reinhold, pp 112-129.
- Le Mao J, Pauli G, Tekaiia F, Hoyet C, Bischoff E, & David B (1989) Guanine content and *Dermatophagoides pteronyssinus* allergens in house dust samples. *J Allergy Clin Immunol*, 83: 926-933.
- Lemeshow S, Hosmer DW Jr, Klar J, & Lwanga SK (1990) Adequacy of sample size in health studies. New York, John Wiley & Sons.
- Lepow ML, Bruckman L, Gillette M, Markowitz S, Robino RA, & Kapish J (1975) Investigations into sources of lead in the environment of urban children. *Environ Res*, 10(3): 415-426.
- Lepow ML, Bruckman L, Rubino RA, Markowitz S, Gillette M, & Kapish J (1974) Role of airborne lead in increased body burden of lead in Hartford children. *Environ Health Perspect*, 7: 99-102.
- Leuenberger P, Schwartz J, Ackermann-Lieblich U, Blaser K, Bolognini G, Bongard JP, Brandli O, Braun P, Bron C, & Brutsche M (1994) Passive smoking exposure in adults and chronic respiratory symptoms (SAPALDIA study). Swiss study on air pollution and lung diseases in adults, SAPALDIA team. *Am J Respir Crit Care Med*, 150: 1222-1228.
- Levallois P, Lavoie M, Goulet L, Nantel AJ, & Gingras S (1991) Blood lead levels in children and pregnant women living near a lead-reclamation plant. *Can Med Assoc J*, 144(7): 877-885.
- Levesque B, Ayotte P, LeBlanc A, Dewailly E, Prud'Homme D, Lavoie R, Allaire S, & Levallois P (1994) Evaluation of dermal and respiratory chloroform exposure in humans. *Environ Health Perspect*, 12: 1082-1087.
- Lewis RG, Fortman RC, & Camann DE (1994) Evaluation of methods for monitoring the potential exposure of small children to pesticides in the residential environment. *Arch Environ Contam Toxicol*, 26: 1-10.
- Lichtenstein CH, Roth HD, & Wyzga RE (1989) In: Starks TH ed. *An activity pattern survey for asthmatics: Proceedings of the Research Planning Conference on Human Activity Patterns*. Las Vegas, Nevada, US Environmental Protection Agency (EPA/600/4-89/004).
- Lind B, Elinder C-G, Friberg L, Nilsson B, Svartengren M, & Vahter M (1987) Quality control in the analysis of lead and cadmium in blood. *Fresenius Z Anal Chem*, 326: 647-655
- Linet MS, Hatch EE, Kleinerman RA, Robinson LL, Kaune WT, Friedman DR, Severson RK, Haines CM, Hartsock CT, Shelley N, Wacholder S, & Tarone RE (1997) Residential exposure to magnetic fields and acute lymphoblastic leukemia in children. *N Engl J Med*, 337(1): 1-7.
- Lioy PJ, Wainman T, & Weisel C (1993) A wipe sampler for the quantitative measurement of dust on smooth surfaces: Laboratory performance studies. *J Expo Anal Environ Epidemiol*, 3(3): 315-330.
- Liu L-JS, Olson MP III, Allen GA, & Koutrakis P (1994a) Evaluation of the Harvard ozone passive sampler on human subjects indoors. *Environ Sci Technol*, 28(5): 915-923.
- Liu J, Chan C, & Jeng F (1994b) Predicting personal exposure levels to

carbon monoxide (CO) in Taipei, based on actual CO measurements in microenvironments and Monte Carlo simulation method. *Atmos Environ*, 28(14): 2361-2368.

Lodge JP Jr (1988) *Methods of air sampling and analysis*. Boca Raton, Florida, Lewis Publishers.

Luczynska CM, Li Y, Chapman MD, & Platts-Mills TAE (1990) Airborne concentrations and particle size distribution of allergen derived from domestic cats (*Felis domesticus*): Measurements using cascade impactor, liquid impinger, and a two-site monoclonal antibody assay for Fel d I. *Am Rev Respir Dis*, 141: 361-367.

Lyman WJ, Reehl WF, & Rosenblatt DH (1990) *Handbook of chemical property estimation methods: Environmental behavior of organic compounds*. Washington, DC, American Chemical Society.

McCullagh P & Nelder J (1990) *Generalized linear models*, 2nd ed. London, Chapman & Hall.

MacIntosh DL, Suter GW, & Hoffman FO (1994) Uses of probabilistic exposure models in ecological risk assessments of contaminated sites. *Risk Anal*, 14(4): 405-420.

MacIntosh DL, Xue J, Ozkaynak H, Spengler JD, & Ryan PB (1995) A population-based exposure model for benzene. *J Expo Anal Environ Epidemiol*, 5(3): 375-403.

MacIntosh DL, Spengler JD, Ozkaynak H, Tsai L, & Ryan PB (1996) Dietary exposures to selected metals and pesticides. *Environ Health Perspect*, 104(2): 202-209.

MacIntosh DL, Williams PL, Hunter DJ, Sampson LA, Morris SC, Willett WC, & Rimm EB (1997) Evaluation of a food frequency questionnaire-food composition approach for estimating dietary intake of inorganic arsenic and methylmercury. *Cancer Epidemiol Biomarkers Prev*, 6(12):1043-1050.

Mackay D (1979) Finding fugacity feasible. *Environ Sci Technol*, 13: 1218-1223.

Mackay D (1991) *Multimedia environmental models, the fugacity approach*. Chelsea, Michigan, Lewis Publishers.

Mackay D & Paterson S (1981) Calculating fugacity. *Environ Sci Technol*, 15: 1006-1014.

Mackay D & Paterson S (1982) Fugacity revisited. *Environ Sci Technol*, 16: 654-660.

McKone TE & Layton DW (1986) Screening the potential risk of toxic substances using a multimedia compartment model: estimation of human exposure. *Regul Toxicol Pharmacol*, 6: 359-380.

McKone TE, Gratt LB, Lyon MJ, & Perry BW (1987) *GEOTOX multimedia compartment model user's guide*. Livermore, California, Lawrence Livermore National Laboratory (UCRL-15913).

Madden NA, Russo DC, & Cataldo MF (1980) Environmental influences of mouthing in children with lead intoxication. *J Pediatr Psychol*,

5: 207-216.

Mamane Y (1992) Characterization of PTEAM indoor aerosol samples (electron microscopy analysis). Research Triangle Park, North Carolina, Atmospheric Research and Exposure Assessment Laboratory.

Masters GM (1991) Introduction to environmental engineering and science. New York, Van Nostrand Reinhold.

Matanoski G, Selevan SG, Akland G, Bornschein RL, Dockery D, Edmonds L, Greife A, Mehlman M, Shaw GM, & Elliott E (1992) Role of exposure databases in epidemiology. Arch Environ Health, 47(6): 439-446.

Matsushita H & Tanabe K (1991) WHO/UNEP Global Environment Monitoring System: Exposure monitoring of nitrogen dioxide -- An international pilot study within the WHO/UNEP Human Exposure Assessment Location (HEAL) project. Geneva, World Health Organization.

Mercier MJ & Robinson AG (1993) Use of biologic markers for toxic end points in assessment of risks from exposure to chemicals. Int Arch Occup Environ Health, 65: S7-S10.

Milkovic-Kraus S, Restek-Samarzija N, Samarzija M, & Kraus O (1997) Individual variation in response to lead exposure: A dilemma for the occupational health physician. Am J Ind Med, 31: 631-635.

Miller JD, Laflamme AM, Sobol Y, Lafontain P, & Greenhalg R (1988) Fungi and fungal products in some Canadian houses. Int Biodeter Biodegrad, 24: 103-120.

Milton DK (1992) Endotoxin in metal working fluids: Report to United Auto Workers, General Motors Joint National Committee on Occupational Health and Safety.

Milton DK (1995) Endotoxin. In: Burge HB ed. Bioaerosols. Boca Raton, Florida, Lewis Publishers, pp 77-86.

MMWR (1997) Update: blood lead levels - United States, 1991-1994. Morbidity Mortality Wkly Rep, 46(7): 141-146.

Moffat WE (1989) Blood lead determinants of a population living in a former lead mining area in southern Scotland. Environ Geochem Health, 11(1): 3-8.

Monster AC & Zielhuis RL (1991a) Biological exposure and/or effect limits, facts, fallacies and uncertainties: General principles. J Soc Occup Med, 41: 55-59.

Monster AC & Zielhuis RL (1991b) Biological exposure and/or effect limits, facts, fallacies, and uncertainties: Practical aspects. J Soc Occup Med, 41: 60-63.

Morgan MG & Henrion M (1990) Uncertainty: a guide to dealing with uncertainty in quantitative risk analysis. Cambridge, United Kingdom, Cambridge University Press.

Moschandreas D & Relwani S (1991) The shadow sensor: An electronic activity pattern sensor. J Expo Anal Environ Epidemiol, 1: 357-367.

Mosteller F & Rourke R (1973) Sturdy statistics: nonparametrics and

order statistics. Reading, Massachusetts, Addison-Wesley.

Mukala KJ, Pekkanen P, Tiittanen P, Alm S, Salonen RO, Jantunen M, & Tuomisto J (1996) Seasonal exposure to NO₂ and respiratory symptoms in preschool children. *J Expo Anal Environ Epidemiol*, 6: 197-210.

Munir AK, Einarsson R, Kjellman N-IM, & Bjorksten B (1993) Mite (Der p I, Der f I) and cat (Fel d I) allergens in the homes of babies with a family history of allergy. *Allergy*, 48: 158-163.

Mushak P & Crocetti AF (1995) Risk and revision in arsenic cancer risk assessment. *Environ Health Perspect*, 103(7-8): 684-689.

Nakahama T, Fukuhara M, & Inouye Y (1997) Volatile halogenated hydrocarbons in ambient air and the metabolites in human urine in an urban area. *Jpn J Toxicol Environ Health*, 43(5): 280-284.

Nessel CS, Butler JP, Post GB, Held JL, Gochfeld M, & Gallo MA (1991) Evaluation of the relative contribution of exposure routes in a health risk assessment of dioxin emissions from a municipal waste incinerator. *J Expo Anal Environ Epidemiol*, 1(3): 283-307.

Nevalainen A, Pastuszka J, Liebhaber F, & Willeke K (1992) Performance of bioaerosol samplers: collection characteristics and sampler design considerations. *Atmos Environ*, 26A: 531-540.

Niessen KH, Ramolla J, Binder M, Brugmann G, & Hofmann U (1984) Chlorinated hydrocarbons in adipose tissue of infants and toddlers: Inventory and studies on their association with intake of mother's milk. *Eur J Pediatr*, 142: 238-243.

Nigg HN & Wade SE (1992) Saliva as a monitoring medium for chemicals. *Rev Environ Contam Toxicol*, 129: 95-119.

Nilsson S & Praglowski J (1992) Erdtman's handbook of palynology. Copenhagen, Denmark, Munksgaard, 580 pp.

NIOSH (1979) Chemical reference laboratory proficiency analytical testing program. Cincinnati, Ohio, National Institute for Occupational Safety and Health (Publication No. 79-128).

NIOSH (1994) Para-occupational bibliography. Cincinnati, Ohio, National Institute for Occupational Safety and Health.

Nöllke P, Becker K, Bernigau W, Hoffmann K, Krause C, Seiwert M, Schulz C, & Schwabe R (1995) Trace elements in domestic tap water in the FRG. *Environ Surv Epidemiol*, 6(4): 23.

Noren K (1993) Contemporary and retrospective investigations of human milk in the trend studies of organochlorine contaminants in Sweden. *Sci Total Environ*, 139-140: 347-355.

Ogden EC, Hayes JV, & Raynor GS (1969) Diurnal patterns of pollen emission in *Ambrosia*, *Phleum*, *Zea* and *Ricinus*. *Am J Bot*, 56(1): 16-21.

Oglesby L, Krütli P, Künzli N, & Jantunen M (1998) Better air -- better participation? Evaluation of selection bias in the European Air Pollution Exposure Study EXPOLIS. *Epidemiology*, July (abstract).

Oliver J, Birmingham K, Crewes A, Weeks J, & Carswell F (1995)

Allergen levels in airborne and surface dust. *Int Arch Allergy Immunol*, 107: 452-453.

O'Rourke MK & Lebowitz (1984) A comparison of regional atmospheric pollen with pollens collected at and near homes. *Grana*, 23: 55-64.

Osterman-Golkar S, Ehrenberg L, Segerback D, & Hallstrom I (1976) Evaluation of genetic risks of alkylating agents: II. Haemoglobin as a dose monitor. *Mutat Res*, 34: 1-10.

Ott W (1989) In: Starks TH ed. *Human activity patterns: A review of the literature for estimating time spent indoors, outdoors, and in-transit*. Proceedings of the Research Planning Conference on Human Activity Patterns. Las Vegas, Nevada, US Environmental Protection Agency (EPA/600/4-89/004).

Ott WR (1990) Total human exposure: Basic concepts -- EPA field studies, and future research needs. *J Air Waste Manage Assoc*, 40(7): 966-975.

Ott W (1995) *Environmental statistics and data analysis*. Boca Raton, Florida, CRC Press Inc.

Ott WR & Roberts JW (1998) Everyday exposure to toxic pollutants. *Sci Am*, 2: 1-7.

Ott WR, Thomas J, Mage D, & Wallace L (1988) Validation of the simulation of human activity and pollutant exposure (SHAPE) model using paired days from the Denver, Colorado, carbon monoxide field study. *Atmos Environ*, 22: 2101-2113.

Ozkaynak H, Xue J, Spengler JD, Wallace L, Pellizzari E, & Jenkins P (1996) Personal exposure to airborne particles and metals: results from the particle TEAM study in Riverside, California. *J Expo Anal Environ Epidemiol*, 6(1): 57-78.

Ozolins G (1989) Global efforts to produce accurate human exposure data: the challenge ahead. In: US EPA/Air and Waste Management Association Symposium on Total Exposure Assessment Methodology. Las Vegas, Nevada, US Environmental Protection Agency, pp 11-16.

Pasquill F (1961) The estimation of the dispersion of windborne material. *Meteorol Mag*, 90: 33-49.

Pastuska JS (1988) Inertial impaction. In: Spurny K ed. *Advances in aerosol filtration science*. Boca Raton, Florida, CRC Press Inc.

Patterson DG, Hoffman RE, Needham LL, Roberts DW, Bagby JR, Pirkle JL, Falk H, Sampson EJ, & Houk VN (1986) 2,3,7,8-Tetracholorodibenzo-p-dioxin levels in adipose tissue of exposed and control persons in Missouri: An interim report. *J Am Med Assoc*, 256: 2683-2686.

Pauli G, de-Blay F, Le Mao J, & Bessot JC (1995) Importance of measuring exposure to principal indoor allergens in allergic asthma. *Bull Natl Acad Med*, 179(1): 67-75 (discussion 75-77).

Pellizzari ED, Perritt K, Hartwell TD, Michael LC, Whitmore R, Handy RW, Smith D, & Zelon H (1987) Total exposure assessment methodology (TEAM) study: Volume II -- Elizabeth and Bayonne, New Jersey; Devils

Lake, North Dakota; and Greensboro, North Carolina. Washington, DC, US Environmental Protection Agency.

Pellizzari ED, Zweidinger RA, & Sheldon LS (1988) Methods for industrial and ambient monitoring: Method 4 -- Breath sampling. Lyon, International Agency for Research on Cancer, pp 255-266 (IARC Scientific Publications No. 85).

Pellizzari E, Liroy P, Quackenboss J, Whitmore R, Clayton A, Freeman N, Waldman J, Thomas K, Rhodes C, & Wilcosky T (1995) Population-based exposure measurements in EPA region 5: A phase I field study in support of the national human exposure assessment survey. *J Expo Anal Environ Epidemiol*, 5(3): 327-358.

Pennington J (1992) The 1990 revision of the FDA total diet study. *J Nutr Educ*, 24 (4): 173-178.

Pennington J & Gunderson EL (1987) History of the food and drug administration's total diet study-1961 to 1987. *J Assoc Off Anal Chem*, 70(5): 772-782.

Perera FP (1987) Molecular cancer epidemiology: a new tool in cancer prevention. *J Natl Cancer Inst*, 78: 887-898.

Perera FP & Weinstein IB (1982) Molecular epidemiology and carcinogen-DNA adduct detection: New approaches to studies of human cancer causation. *J Chron Dis*, 35: 581-600.

Perera FP, Hemminki K, Young TL, Brenner D, Kelly G, & Santella RM (1988) Detection of polycyclic aromatic hydrocarbon-DNA adducts in white blood cells of foundry workers. *Cancer Res*, 48: 2288-2291.

Periago JF, Luna A, Morente A, & Zambudio A (1992) Design and evaluation of an exhaled breath sampler for biological monitoring of organic solvents. *J Appl Toxicol*, 12: 91-96.

Phoon W, Lee HS, & Ho CK (1990) Biological monitoring of workers exposed to inorganic lead in Singapore. *Singap Med J*, 31(2):127-130.

Pizzichini E, Pizzichini MM, Efthimiadis A, Dolovich J, & Hargreave FE (1997) Measuring airway inflammation in asthma: Eosinophils and eosinophilic cationic protein in induced sputum compared with peripheral blood. *J Allergy Clin Immunol*, 99(4): 539-544

Platts-Mills TAE & De Weck AL (1989) Dust mite allergens and asthma: a world wide problem. International workshop report. *J Allergy Clin Immunol*, 83: 416-427.

Platts-Mills TAE, Hayden ML, Chapman MD, & Wilkins SR (1987) Seasonal variation in dust mite grass-pollen allergens in dust from the houses of patients with asthma. *J Allergy Clin Immunol*, 79: 781-791.

Platts-Mills TAE, Thomas WR, Aalberse RC, Vervloet D, & Chapman MD (1992) Dust mite allergens and asthma: report of a second international workshop. *J Allergy Clin Immunol*, 89: 1046-1060.

Pleil JD & Lindstrom AB (1995) Measurement of volatile organic compounds in exhaled breath as collected in evacuated electropolished canisters. *J Chromatogr Biomed Appl*, B665(2): 271-279.

Pollart SM, Mullins DE, Vailes LD, Hayden ML, Platts-Mills TAE, Sutherland WM, & Chapman MD (1991a) Identification, quantification and purification of cockroach allergens using monoclonal antibodies. *J Allergy Clin Immunol*, 87: 935-946.

Pollart SM, Smith TF, Morris EC, Gelder LE, Platts-Mills TAE, & Chapman MD (1991b) Environmental exposure to cockroach allergens: Analysis with monoclonal antibody-based enzyme immunoassays. *J Allergy Clin Immunol*, 87: 505-510.

Pope AM, Patterson R, & Burge H (1993) *Indoor allergens: Assessing and controlling adverse health effects*. Washington, DC, National Academic Press.

Price JA, Pollock I, Little SA, Longbottom JL, & Warner JO (1990) Measurement of airborne mite antigen in homes of asthmatic children. *Lancet*, 336: 895-897.

Prpic-Majic D, Pongracic J, Hrsak J, & Pizent A (1992) A follow-up study in a lead smelter community following the introduction of an effective pollution control system. *Isr J Med Sci*, 28(8-9): 548-556.

Quackenboss JJ & Lebowitz MD (1989) The utility of time/activity data for exposure assessment: Summary of procedures and research needs. In: *Proceedings of the 82nd Annual Meeting of the Air and Waste Management Association*. Pittsburgh, Pennsylvania, Air and Waste Management Association, pp 89-100.

Quackenboss JT, Spengler JD, Kanaek MS, Letz R, & Duffy CP (1986) Personal exposure to NO₂: Relationship to indoor/outdoor air quality and activity patterns. *Environ Sci Technol*, 20: 775-783.

Que Hee SS (1993) *Biological monitoring: An introduction*. New York, Van Nostrand Reinhold.

Que Hee SS, Peace B, Clark CS, Boyle JR, Bornsheim RL, & Hammond PB (1985) Evolution of efficient methods to sample lead sources, such as house dust and hand dust, in the homes of children. *Environ Res*, 38: 77-95.

Rabinowitz MB (1991) Toxicokinetics of bone lead. *Environ Health Perspect*, 91: 33-37.

Rabinowitz MB & Bellinger DC (1988) Soil lead -- blood lead relationship among Boston children. *Bull Environ Contam Toxicol*, 41: 791-797.

Rabinowitz M, Leviton A, Needleman H, Bellinger D, & Waternaux C (1985) Environmental correlates of infant blood lead levels in Boston. *Environ Res*, 38: 96-107.

Rabinowitz MB, Leviton A, & Bellinger DC (1989) Blood lead -- tooth lead relationship among Boston children. *Bull Environ Contam Toxicol*, 43: 485-492.

Raghupathy L, Harada M, Ohno H, Naganuma A, Imura N, & Doi R (1988) Methods of removing external metal contamination from hair samples for environmental monitoring. *Sci Total Environ*, 77: 141-151.

Raizenne ME & Spengler JD (1989) Dosimetric model of acute health

effects of ozone and acid aerosols in children. In: Atmospheric ozone research and policy implications. Amsterdam, Oxford, New York, Elsevier Science Publishers, pp 319-329.

Rao HV & Ginsberg GL (1997) A physiologically-based pharmacokinetic model assessment of methyl t-butyl ether in groundwater for a bathing and showering determination. *Risk Anal*, 17(5): 583-598.

Rappaport SM, Kromhout H, & Symanski E (1993) Variation of exposure between workers in homogeneous exposure groups. *Am Ind Hyg Assoc J*, 54: 654-662.

Rees N & Tennant D (1993) Estimating consumer intakes of food chemical contaminants. In: Watson D ed. *Safety of chemicals in food*. London, Ellis Horwood.

Rees N & Tennant D (1994) Estimation of food chemical intake. In: Kotsons FN, Mackey M, & Hjelle J ed. *Nutritional toxicology*. New York, Raven Press Ltd.

Reiss R, Ryan PB, Tibbetts SJ, & Koutrakis P (1995) Measurement of organic acids, aldehydes, and ketones in residential environments and their relationship to ozone. *J Air Waste Manage Assoc*, 45(10): 811-822.

Reponen T (1994) *Viable fungal spores as indoor aerosols*. Kuopio, Finland, Kuopio University, Natural and Environmental Sciences (Academic Dissertation C25).

Rimm EB, Giovannucci EL, Stampfer MJ, Colditz GA, Litin LB, & Willett WC (1992) Reproducibility and validity of an expanded self-administered semiquantitative food frequency questionnaire among male health professionals. *Am J Epidemiol*, 135: 1114-1126.

Rinehart RD & Yanagisawa Y (1993) Para-occupational exposures to Pb and Sn carried by electric cable splicers. *Am Ind Hyg Assoc J*, 54(120): 593-599.

Roberts JW & Dickey P (1995) Exposure of children to pollutants in house dust and indoor air. *Rev Environ Contam Toxicol*, 143: 59-78.

Roberts JW, Budd WT, Ruby MG, Bond AE, Lewis RG, Weiner RW, & Camann DE (1991) Development and field testing of a high volume sampler for pesticides and toxins in dust. *J Expo Anal Environ Epidemiol*, 1(2): 143-155.

Roberts JW, Budd WT, Ruby MG, Camann DE, Fortmann RC, Lewis RG, Wallace LA, & Spittler TM (1992) Human exposure to pollutants in the floor dust of homes and offices. *J Expo Anal Environ Epidemiol*, 1(suppl): 127-146.

Robinson J (1977) *How Americans use time: A social psychological analysis of everyday life*. Ann Arbor, Michigan, University Microfilms (Monograph Series).

Robinson J (1985) Validity and reliability of diaries versus alternative time use measures. In: Juster FT & Stafford FP ed. *Time, goods, and well being*, pp 33-62.

Robinson J (1988) *Time-diary research and human exposure assessment*:

Some methodological considerations. *Atmos Environ*, 22: 2085-2092.

Roels M, Buchet JP, & Lauwerys RR (1980) Exposure to lead by the oral and pulmonary route of children living in the vicinity of a primary lead smelter. *Environ Res*, 22: 81-94.

Rogan WJ, Bagniewska A, & Damstra T (1980) Pollutants in breast milk. *N Engl J Med*, 302: 1450-1453.

Rogan WJ, Gladen BC, McKinney JD, Carreras N, Hardy P, Thullen J, Tingelstad J, & Tully M (1986) Polychlorinated biphenyls (PCBs) and dichlorophenyl dichloroethene (DDE) in human milk: Effects of maternal factors and previous lactation. *Am J Public Health*, 76: 172-177.

Roseberry AM & Burmaster D (1992) Lognormal distributions for water intake by children and adults. *Risk Anal*, 12(1): 99-104.

Ryan PB, Spengler JD, Schwab M, & Soczek ML (1990) Personal monitoring for nitrogen dioxide: Boston personal monitoring. Proceedings of the First International Symposium on Total Exposure Assessment Methodology: A New Horizon, Las Vegas, Nevada, November 1989. Pittsburgh, Pennsylvania, Air and Waste Management Association.

Rylander R, Persson K, Goto H, Yuasa K, & Tanaka S (1992) Airborne beta-1,3-glucan may be related to symptoms in sick buildings. *Indoor Environ*, 1: 190-193.

Sachs L (1986) A guide to statistical methods and to the pertinent literature. Berlin, Heidelberg, New York, Springer Verlag.

Sakaguchi M, Inouye S, Irie T, Miyazawa H, Watanabe M, Yasueda H, Shida T, Nitta H, Chapman MD, Schou C, & Aalberse RC (1993) Airborne cat (Fel d I), dog (Can f I), and mite (Der I and Der II) allergen levels in the homes of Japan. *J Allergy Clin Immunol*, 92: 797-802.

Saltzman BE (1988) Linear pharmacokinetic models for evaluating unusual work schedules, exposure limits and body burden of pollutants. *Am Ind Hyg Assoc J*, 49: 213-225.

Samet JS & Spengler JD ed. (1991) *Indoor air pollution: A health perspective*. Baltimore, London, The John Hopkins University Press.

Samet JM, Lambert WE, Skipper BJ, Cushing AH, McLaren LC, Schwab M, & Spengler JD (1992) A study of respiratory illnesses in infants and NO₂ exposure. *Arch Environ Health*, 47: 57-63.

Sampson EJ, Needham LL, Pirkle JL, Hannon WH, Miller DT, Patterson DG, Bernert JT, Ashley DL, Hill RH, Gunter EW, Paschal DC, Spierto FW, & Rich MJ (1994) Technical and scientific developments in exposure marker methodology. *Clin Chem*, 40: 1376-1384.

Santella RM, Hemminki K, Tang D-L, Paik M, Ottman R, Young TL, Savela K, Vodickova L, Dickey C, Whyatt R, & Perera FP (1993) Polycyclic aromatic hydrocarbon -- DNA adducts in white blood cells and urinary 1-hydroxypyrene in foundry workers. *Cancer Epidemiol Biomarkers Prev*, 2: 59-62.

Santos PL, Gouvea RC, & Dutra IR (1994) Concentrations of ²¹⁰Pb and ²¹⁰Po in hair and urine of workers, of the uranium mine at Pocos de Caldas (Brazil). *Sci Total Environ*, 148: 61-65.

- Saraf A, Larsson L, Burge H, & Milton D (1997) Quantification of ergosterol and 3-hydroxy fatty acids in settled house dust by gas chromatography-mass spectrometry: comparison with fungal culture and determination of endotoxin by *Limulus* ameocyte lysate assay. *Appl Environ Microbiol*, 63(7): 2554-2559.
- Sato A (1993) Confounding factors in biological monitoring of exposure to organic solvents. *Int Arch Occup Environ Health*, 65: S61-S67.
- Schaller KH, Angerer J, & Lehnert G (1991) Internal and external quality control in the toxicological analysis of blood and urine sample in the Federal Republic of Germany. *Int Arch Occup Environ Health*, 62: 537-542.
- Schnoor JL (1981) Fate and transport of dieldrin in Coraville Reservoir: Residues in fish and water following a pesticide ban. *Science*, 211: 840-842.
- Schnoor JL & MacAvoy DC (1981) A pesticide transport and bioconcentration model. *J Environ Eng Div Am Soc Civil Eng*, 107: 1229-1245.
- Schou C, Fernandez-Caldas E, Lockey RF, & Lowenstein H (1991) Environmental assay for cockroach allergens. *J Allergy Clin Immunol*, 87: 828-834.
- Schou C, Hansen GN, Lintner T, & Lowenstein H (1992) Assay for the major allergen, Can f I: investigation of house dust samples and commercial dog extracts. *J Allergy Clin Immunol*, 88: 847-853.
- Schulte PA (1987) Methodologic issues in the use of biological markers in epidemiological research. *Am J Epidemiol*, 126: 1006-1016.
- Schulte PA (1989) A conceptual framework for the validation and use of biologic markers. *Environ Res*, 48: 129-144.
- Schulte PA (1991) Contribution of biological markers to occupational health. *Am J Ind Med*, 20: 435-446.
- Schulte PA (1992) Biomarkers in epidemiology: Scientific issues and ethical implications. *Environ Health Perspect*, 98: 143-147.
- Schulte PA & Talaska G (1995) Validity criteria for the use of biological markers of exposure to chemical agents in environmental epidemiology. *Toxicology*, 101: 73-88.
- Schulz C, Becker K, Bernigau W, Hoffmann K, Krause C, Nöllke P, Schwabe R, & Seiwert M (1995) The 1990/92 environmental survey in the old and new States of the Federal Republic of Germany. *Ann Clin Lab Sci*, 25: 561
- Schwab M, Colome SD, Spengler JD, Ryan PB, & Billick IH (1990) Activity patterns applied to exposure assessment: data from a personal monitoring study in Los Angeles. *J Toxicol Ind Health Expo Assess Sect*, 6: 517-532.
- Schwab M, Terblanche APS, & Spengler JD (1991) Self-reported exertion levels on time/activity diaries: Application to exposure assessment. *J Expo Anal Environ Epidemiol*, 1(3): 339-356.

Schwab M, McDermott A, & Spengler JD (1992) Using longitudinal data to understand children's activity patterns in an exposure context: Data from the Kanawha Valley Health Study. *Environ Int*, 18: 173-189.

Seiler F (1987) Error propagation for large errors. *Risk Anal*, 7(4): 509-518.

Sexton K (1992) The role of scientific research in risk assessment and risk management decisions. *Otolaryngol Head Neck Surg*, 106(6): 635-641.

Sexton K (1993) An introduction to risk-based priority setting: Toward a conceptual framework for analysis. In: *Proceedings of the Symposium on Comparative Risk Analysis and Priority Setting of Air Pollution Issues*, Keystone, CO, June 1993. Pittsburgh, Pennsylvania, Air and Waste Management Association

Sexton K & Ryan PB (1988) Assessment of human exposure to air pollution: Methods, measurements, and models. In: Watson AY, Bates RR, & Kennedy D ed. *Air pollution, the automobile, and public health*. Cambridge, Massachusetts, Health Effects Institute.

Sexton K, Selevan SG, Wagener DK, & Lybarger JA (1992) Estimating human exposures to environmental pollutants: Availability and utility of existing databases. *Arch Environ Health*, 47(6): 398-407.

Sexton K, Olden K, & Johnson BL (1993) "Environmental justice": The central role of research in establishing a credible scientific basis for informed decision making. *Toxicol Ind Hyg*, 9: 685-727.

Sexton K, Wagener DK, Selevan SG, Miller TO, & Lybarger JA (1994) An inventory of human exposure-related data bases. *J Expo Anal Environ Epidemiol*, 4(1): 95-109.

Sexton K, Callahan MA, & Ryan EF (1995a) Estimating exposure and dose to characterize health risks: the role of human tissue monitoring in exposure assessment. *Environ Health Perspect*, 103(suppl 3): 13-29.

Sexton K, Callahan MA, Ryan EF, Saint CG, & Wood WP (1995b) Informed decisions about protecting and promoting public health: rationale for a national human exposure assessment survey. *J Expo Anal Environ Epidemiol*, 5(3): 233-256.

Sexton K, Kleffman D, & Callahan M (1995c) An introduction to the national human exposure assessment survey and related phase I field studies. *J. Expo Anal. Environ Epidemiol*, 5: 229-232.

Shamoo DA, Johnson TR, Trim SC, Little DE, Linn WS, & Hackney JD (1991) Activity patterns in a panel of outdoor workers exposed to oxidant pollution. *J Expo Anal Environ Epidemiol*, 1(4): 423-428.

Shealy DB, Barr JR, Ashley DL, Patterson DG Jr, Camann DE, & Bond AE (1997) Correlation of environmental carbaryl measurements with serum and urinary 1-naphthol measurements in a farmer applicator and his family. *Environ Health Perspect*, 105(5): 510-513.

Sikorski R, Paszkowski T, Radomanski T, Niewiadowska A, & Semeniuk S (1990) Human colostrum as a source of organohalogen xenobiotics for a breast-fed neonate. *Reprod Toxicol*, 4: 17-20.

Silbergeld EK (1991) Lead in bone: Implications for toxicology during pregnancy and lactation. *Environ Health Perspect*, 91: 63-70.

Silbergeld EK (1993) New approaches to monitoring environmental neurotoxins. *Ann NY Acad Sci*, 694: 62-71.

Silbergeld EK & Davis DL (1994) Role of biomarkers in indexing and understanding environmentally induced disease. *Clin Chem*, 40: 1363-1367.

Silvers A, Florence BT, Rourke DL, & Lorimor RJ (1994) How children spend their time: A sample survey for use in exposure and risk assessments. *Soc Risk Anal*, 14: 931-944.

Sim MR & McNeil JJ (1992) Monitoring chemical exposure using breast milk: A methodological review. *Am J Epidemiol*, 136: 1-11.

Simcox NJ, Fenske RA, Wolz SA, Lee I, & Kalman DA (1995) Pesticides in household dust and soil: Exposure pathways for children of agricultural families. *Environ Health Perspect*, 103(12): 1126-1134.

Simonich SL & Hites RA (1997) Relationships between socioeconomic indicators and concentrations of organochlorine pesticides in tree bark. *Environ Sci Technol*, 31(4): 999-1003.

Skog K, Solyakov A, Arvidsson P, & Jagerstad M (1998) Analysis of nonpolar heterocyclic amines in cooked foods and meat extracts using gas chromatography-mass spectrometry. *J Chromatogr*, A803(1-2): 227-233.

Slorach SA & Vaz R (1983) Assessment of human exposure to selected organochlorine compounds through biological monitoring -- Report prepared for UNEP/WHO. Uppsala, Sweden, National Food Administration.

Smith KR (1995) Global environmental epidemiology network -- The potential of human exposure assessment for air pollution regulation. Geneva, World Health Organization (Document WHO/EHG/95.9).

Smith MT & Suk WA (1994) Application of molecular biomarkers in epidemiology. *Environ Health Perspect*, 102(suppl 1): 229-235.

Solomon RL & Hartford JW (1976) Lead and cadmium in dusts and soils in a small urban community. *Environ Sci Technol*, 10: 733-777.

Somerville LJ, Chettle DR, Scott MC, Tennant DR, McKiernan MJ, Skilbeck A, & Trethowan WN (1988) *In vivo* tibia lead measurements as an index of cumulative exposure in occupationally exposed subjects. *Br J Ind Med*, 45: 174-181.

Spengler JD, Dockery DW, Turner WA, Wolfson JM, & Ferris BG Jr (1981) Long-term measurements of respirable sulfates and particles inside and outside homes. *Atmos Environ*, 15: 23-30.

Spengler JD, Treitman RD, Tosteson TD, Maye DT, & Soczer MC (1985) Personal exposures to respirable particulates and implications for air pollution epidemiology. *Environ Sci Technol*, 19: 700-707.

Spengler JD, Schwab M, Ryan PB, Billick IH, Colome SD, & Becker E (1994) An overview of the Los Angeles personal monitoring study. *J Air*

Waste Manage Assoc, 44: 39-47.

Sram RJ, Benes I, Binkova B, Dejmek J, Horstman D, Kotesovec F, Otto D, Perreault SD, Rubes J, Selevan SG, Skalik I, Stevens RK, & Lewtas J (1996) Teplice program: The impact of air pollution on human health. *Environ Health Perspect*, 104(suppl 4):699-714.

Stark AD, Quah RF, Meigs JW, & DeLouise ER (1982) The relationship of environmental lead to blood-lead levels in children. *Environ Res*, 27: 372-383.

Steerenberg PA, Fischer PH, van Bree L, & van Loveren H (1997) Nasal lavage biomarkers in air pollution epidemiology. *Arch Toxicol*, 19(suppl): 207-216.

Strom G, Palmgren U, & Blomquist G (1987) Separation of organic dust from microorganism suspensions by partitioning in aqueous polymer two-phase systems. *Appl Environ Microbiol*, 53: 860-863.

Subida RD & Torres EB (1991) Epidemiology of chronic respiratory symptoms and illnesses among jeepney drivers, air conditioned bus drivers, and commuters exposed to vehicular emissions in metro Manila, 1990-91. Manila, University of the Philippines, School of Public Health.

Subramanian R (1991) Metals in hair as an indicator for metal burden of the body. In: Dillon HK & Ho MH ed. *Biological monitoring of exposure to chemicals: Metals*. New York, John Wiley & Sons, pp 255-261.

Sugita M, Harada A, Taniguchi M, Saito M, Imaizumi K, Kitamura M, Kodama Y, Mori Y, Wada O, & Ikeda M (1990) Quality control programme on biological monitoring by the Japan Federation of Occupational Health Organizations. *Int Arch Occup Environ Health*, 62: 569-577.

Sugita S, Goto S, Endo O, Machii K, Ishii T, Matsushita H, & Lewtas J (1997) Influence of respiratory depth on the deposition ratio of PAHs of airborne particles in the human respiratory tract. *J Jpn Soc Atmos Environ*, 32: 64-67.

Sukumar A & Subramanian R (1992) Trace elements in scalp hair of manufacturers of fireworks from Sivakasi, Tamil Nadu. *Sci Total Environ*, 114: 161-168.

Suzuki T, Watanabe S, & Matsuo N (1989) Comparison of hair with nail as index media for biological monitoring of mercury. *Sangyo Igaku*, 31: 235-238.

Swanson MC, Agarwal MK, & Reed CE (1985) An immunochemical approach to indoor aeroallergen quantitation with a new volumetric air sampler: studies with mite, roach, cat, mouse, and guinea pig antigens. *J Allergy Clin Immunol*, 76: 724-729.

Szalai A (1972) *The use of time: Daily activities of urban and suburban populations in twelve countries*. The Hague, Moughton Publishing Co..

Tager IB, Kunzli N, Lurmann F, Ngo L, Segal M, & Balmes J (1998) Methods development for epidemiologic investigations of the health effects of prolonged ozone exposure. Part II: An approach to

retrospective estimation of lifetime ozone exposure using a questionnaire and ambient monitoring data (California sites). Res Rep Health Eff Inst, 81: 27-78.

Tardiff RG & Goldstein BD ed. (1991) Methods for assessing exposure of human and non-human biota -- Prepared by the Scientific Group on Methodologies for the Safety Evaluation of Chemicals (SGOMSEC). Chichester, United Kingdom, Wiley.

Tarshis B (1981) The average American book. New York, New American Library, 191 pp.

Taylor A (1988) The use of internal quality control materials for the preparation and maintenance of reliable methods for the measurement of lead in blood. Fresenius Z Anal Chem, 332: 732-735.

Terblanche AP, Ozkaynak H, Spengler JD, & Butler D (1991) Relationship between self-reported activity levels and actual heart rates in teenagers. J Air Waste Manage Assoc, 41: 942-946.

Thibodeaux LJ (1996) Environmental chemodynamics- movement of chemicals in air, water and soil, 2nd ed. New York, John Wiley & Sons.

Thien FCK, Leung RCC, Czarny D, & Walters EH (1994) Indoor allergens and IgE-mediated respiratory illness. Immunol Allergy Clin North Am, 14: 567-590.

Thomas KW, Pellizzari ED, Clayton CA, Whitaker DA, Shores RC, Spengler JD, Özkaynak H, & Wallace LA (1993a) Particle total exposure assessment methodology (PTEAM) study: Method performance and data quality for personal, indoor, and outdoor aerosol monitoring at 178 homes in Southern California. J Expo Anal Environ Epidemiol, 3: 203-226.

Thomas KW, Pellizzari ED, Clayton CA, Perritt RL, Dietz RN, Goodrich TW, Nelson WC, & Wallace LA (1993b) Temporal variability of benzene exposure for residents in several New Jersey homes with attached garages or tobacco smoke. J Expo Anal Environ Epidemiol, 3: 49-73.

Thomas KW, Sheldon LS, Pellizzari ED, Handy RW, Roberts JM, & Berry MR (1997) Testing duplicate diet sample collection methods for measuring personal dietary exposures to chemical contaminants. J Expo Anal Environ Epidemiol, 7(1): 17-36.

Thornton I, Davies DJA, & Quinn MJ (1990) Lead exposure in young children from dust and soil in the United Kingdom. Environ Health Perspect, 89: 55-60.

Tomerlin JR, Berry, MR, Tran NL, Chew SB, Petersen BJ, Tucker KD, & Fleming KH (1996) Development of a dietary exposure potential model for evaluating dietary exposure to chemical residues in food. J Expo Anal Environ Epidemiol, 7(1): 81-101.

Tomita M & Nishimura M (1982) Using saliva to estimate human exposure to organic solvents. Bull Tokyo Dent Coll, 23: 175-188.

Tovey ER, Marks GB, Matthews M, Green WF, & Woolcock A (1992) Changes in mite allergen Der p I in house dust following spraying with tannic acid/acaricide solution. Clin Exp Allergy, 22: 67-74.

Tufte ER (1983) The visual display of quantitative information. Conn, Cheshire, Graphics Press.

Tufte ER (1997) Visual explanations: images and quantities, evidence and narrative. Conn, Cheshire, Graphics Press.

UK MAFF (United Kingdom -- Ministry of Agriculture, Fisheries and Food) (1985) Survey of aluminium, antimony, chromium, cobalt, indium, nickel, thallium and tin in food. London, United Kingdom, Her Majesty's Stationary Office (Food Surveillance Paper No. 15).

UK MAFF (United Kingdom -- Ministry of Agriculture, Fisheries and Food) (1989) Lead in food: Progress report. London, United Kingdom, Her Majesty's Stationary Office (Food Surveillance Paper No. 27).

UK NEQAS (1993) Report and directory. Sheffield, United Kingdom National External Quality Control Schemes.

Ullrich D (1992) Diffusive sampling of volatile organic compounds. In: Clean air at work: New trends in assessment and measurement for the 1990s. Proceedings of an international symposium, Luxembourg, September 1992. Cambridge, United Kingdom, Royal Society of Chemistry, pp 349-356 (Special Publication No. 108).

Ullrich D, Brenske K-R, Heinrich J, Hoffmann K, Ung L, & Seifert B (1996) Volatile organic compounds: Comparison of personal exposure and indoor air quality measurements. In: Indoor air '96: Proceedings of the International Conference on Indoor Air Quality and Climate, Nagoya, 21-26 July 1996. Tokyo, Japan, Institute of Public Health, vol 4, pp 301-306.

UNEP (United Nations Environment Programme) (1991) Environmental data report. Oxford, Blackwell Publications.

UNEP/WHO (1982) Global Environmental Monitoring System (GEMS) -- Estimating human exposures to air pollutants. Geneva, World Health Organization (Offset Publication No. 69).

UNEP/WHO (1986) Global Environmental Monitoring System (GEMS) -- Human Exposure Assessment Location (HEAL) project: Guidelines for integrated air, water, food and biological exposure monitoring. Geneva, World Health Organization (Document PEP/86.6).

UNEP/WHO (1988) Global Environmental Monitoring System (GEMS) -- Assessment of urban air quality. Geneva, United Nations Environment Programme and World Health Organization.

UNEP/WHO (1990) Global Environmental Monitoring System (GEMS) -- Exposure monitoring of lead and cadmium. Geneva, United Nations Environment Programme and World Health Organization.

UNEP/WHO (1991) Global Environmental Monitoring System (GEMS) -- Human exposure to pollutants: Report on the pilot phase of the Human Exposure Assessment Location (HEAL) project. Geneva, World Health Organization (Document PEP/HEAL/91.27).

UNEP/WHO (1992) Global Environmental Monitoring System (GEMS) -- Urban air pollution in mega cities of the world. Geneva, United Nations Environment Programme and World Health Organization.

UN ESCAP (1990) State of the environment in Asia and the Pacific. Bangkok, United Nations Economic and Social Commission for Asia and the Pacific (ESCAP).

US EPA (1983-1989) Methods for assessing exposure to chemical substances: Volumes 1-13. Washington, DC, US Environmental Protection Agency, Office of Toxic Substances, Exposure Evaluation Division.

US EPA (1984) Pesticide assessment guidelines, subdivision K -- Exposure: Reentry protection. Washington, DC, US Environmental Protection Agency, Office of Pesticide Programs (EPA/540/9-48/001 / PB-85-120962).

US EPA (1986a) Standard scenarios for estimating exposure to chemical substances during use of consumer products, Volumes 1 and II. Washington, DC, US Environmental Protection Agency, Office of Toxic Substances, Exposure Evaluation Division.

US EPA (1986b) Pesticide assessment guidelines, subdivision U -- Applicator exposure monitoring. Washington, DC, US Environmental Protection Agency, Office of Pesticide Programs (EPA/540/9-87/127 / PB-85-133286).

US EPA (1987) Selection criteria for mathematical models used in exposure assessments: Surface water models. Washington, DC, US Environmental Protection Agency, Exposure Assessment Group, Office of Health and Environmental Assessment (EPA/600/8-87/042, PB-88-139928/AS).

US EPA (1988a) Superfund exposure assessment manual. Washington, DC, US Environmental Protection Agency, Office of Emergency and Remedial Response (EPA/540/1-88/001, PB-89-135859).

US EPA (1988b) Selection criteria for mathematical models used in exposure assessments: groundwater models. Washington, DC, US Environmental Protection Agency, Exposure Assessment Group, Office of Health and Environmental Assessment (EPA/600/8-88/075, PB-88-248752/AS).

US EPA (1990) Methodology for assessing health risks associated with indirect exposure to combustor emissions. Washington, DC, US Environmental Protection Agency (EPA 600/6-90/003, PB-90-187055/AS).

US EPA (1991) Strategy for reducing lead exposures. Washington, DC, US Environmental Protection Agency.

US EPA (1992a) Guidelines for exposure assessment. Washington, DC, US Environmental Protection Agency, Office of Research and Development, Office of Health and Environmental Assessment (EPA/600/Z-92/001).

US EPA (1992b) Dermal exposure assessment: principles and applications. Washington, DC, US Environmental Protection Agency, Office of Health and Environmental Assessment (EPA/600/8-9/011F).

US EPA (1992c) Guidelines for exposure-related measurements. Fed Reg, 7: 22888-22938.

US EPA (1994) Estimating exposures to dioxin-like compounds. Washington, DC, US Environmental Protection Agency, Office of Research and Development (EPA/600/6-88/005Cb).

- US EPA (1995a) Settled dust sampling for lead: basic concepts and literature review. Washington, DC, US Environmental Protection Agency (EPA/747-R-95-007).
- US EPA (1995b) Laboratory evaluation of dust and dust lead recoveries for samplers and vacuum cleaners -- Volume 1: Objectives, methods, and results. Washington, DC, US Environmental Protection Agency (EPA/747-R-94-004A).
- US EPA (1996) Compendium of methods for the determination of inorganic compounds in ambient air. Washington, DC, US Environmental Protection Agency (EPA/625-R-96-010A).
- US FDA (1997a) Pesticide analytical manual -- Volume I: Multiresidue methods, 3rd ed. Washington, DC, US Food and Drug Administration (PB94-911899).
- US FDA (1997b) Pesticide analytical manual -- Volume II. Washington, DC, US Food and Drug Administration (PB92-911999).
- US Federal Highway Administration (1986) Personal travel in the US -- Volume I: 1983-1984 nationwide personal travel study. Washington, DC, US Department of Transportation.
- US Federal Highway Administration (1992) 1990 nationwide personal travel study. Washington, DC, US Department of Transportation.
- US HUD (1995) Guidelines for the evaluation and control of lead-based paint hazards in housing. Washington, DC, US Department of Housing and Urban Development.
- US NRC (US National Research Council) (1983) Risk assessment in the Federal Government: managing the process. Washington, DC, National Academy Press.
- US NRC (National Research Council) (1987) Biological markers in environmental health research by the Committee on Biological Markers. Environ Health Perspect, 74: 3-9.
- US NRC (US National Research Council) (1989) Biological markers in reproductive toxicology. Washington, DC, National Academy Press.
- US NRC (US National Research Council) (1991a) Frontiers in assessing human exposures to environmental toxicants. Washington, DC, National Academy Press.
- US NRC (US National Research Council) (1991b) Human exposure assessment for airborne pollutants, advances and opportunities. Washington, DC, National Academy Press.
- US NRC (US National Research Council) (1991c) Environmental epidemiology: Public health and hazardous wastes. Washington, DC, National Academy Press.
- US NRC (US National Research Council) (1993) Pesticides in the diets of infants and children. Washington, DC, National Academy Press, p 21.
- US NRC (US National Research Council) (1994) Science and judgement in risk assessment. Washington, DC, US National Academy of Sciences,

National Research Council.

Vahter M (1982) Assessment of human exposure to lead and cadmium through biological monitoring: Prepared for UNEP/WHO. Stockholm, Sweden, National Institute of Environmental Medicine and Department of Environmental Hygiene, Karolinska Institute.

Vahter M & Slorach S (1990) Global Environmental Monitoring System (GEMS) -- Exposure monitoring of lead and cadmium: An international pilot study within the WHO/UNEP Human Exposure Assessment Location (HEAL) project. Geneva, World Health Organization / Nairobi, United Nations Environment Programme..

Vahter M, Berglund M, & Lind B (1991) Personal monitoring of lead and cadmium exposure. A Swedish study with special reference to methodological aspects. *Scand J Work Environ Health*, 17: 65-74.

Vahter M, Berglund M, Nermell B, & Akesson A (1996) Bioavailability of cadmium from shellfish and mixed diet in women. *Toxicol Appl Pharmacol*, 136: 332-341.

Vailes L, Glime T, Pollart S, & Chapman MD. (1990) Cockroach washes -- a potent source of asthma associated allergens. *J Allergy Clin Immunol*, 85: 171 (abstract).

Vandenberg SA (1991) Maternal occupational molybdenum exposure: Is there risk to the breastfed infant? *J Hum Lact*, 7: 23-24.

Van Strien RT, Verhoeff AP, Brunekreef B, & Van Wijnen JH (1994) Mite antigen in house dust: relationship with different housing characteristics in the Netherlands. *Clin Exp Allergy*, 24: 843-853.

Van Veen MP (1996) A general model for exposure and uptake from consumer products. *Risk Anal*, 16(3): 331-338.

van Welie RTH, van Duyn P, & Permolen NPE (1991) Environmental and biological monitoring of non-occupational exposure to 1,3-dichloropropene. *Int Arch Occup Environ Health*, 63: 169-173.

Verberk MM (1995) Biomarkers of exposure versus parameters of external exposure; practical applications in estimating health risks. *Toxicology*, 101: 107-115.

Verhoeff AP, Van Wijnen JH, Boleij JSM, Brunekreef B, Van Reenen-Hoekstra ES, & Samson RA (1990) Enumeration and identification of airborne viable mould propagules in houses; a field comparison of selected techniques. *Allergy*, 45: 275-284.

Verhoeff AP, Van Wijnen JH, Brunekreef B, Fischer P, Van Reenen-Hoekstra ES, & Samson RA (1992) The presence of viable mould propagules in indoor air in relation to house damp and outdoor air. *Allergy*, 47: 83-91.

Verhoeff AP, Van Reenen-Hoekstra ES, Samson RA, Brunekreef B, & Van Wijnen JH (1994a) Fungal propagules in house dust: I. Comparison of analytic methods and their value as estimators of potential exposure. *Allergy*, 49: 533-539.

Verhoeff AP, van Wijnen J, van Reenen-Hoekstra E, Samson R, van Strien RM, & Brunekreef B (1994b) Fungal propagules in house dust: II.

Relation with residential characteristics and respiratory symptoms. *Allergy*, 49: 540-547.

Vostal JJ, Traves E, Sayre JW, & Charney E (1974) Lead analysis of house dust: A method for the detection of another source of lead exposure in inner city children. *Environ Health Perspect*, 7: 91-97.

Wagener DK, Selevan SG, & Sexton K (1995) The importance of human exposure information: A need for exposure-related data bases to protect and promote public health. *Annu Rev Public Health*, 16: 105-121.

Waldman JM, Liroy PJ, Greenberg A, & Butler JP (1991a) Analysis of human exposure to benzo(a)pyrene via inhalation and food ingestion in the total human environmental exposure study (THEES). *J Expo Anal Environ Epidemiol*, 1(2):193-225.

Waldman J, Bilder S, & Freeman NCG (1991b) Can a subject-worn datalogger be used to validate recall diary responses? Presented at the Conference on Measuring, Understanding, and Predicting Exposures in the 21st Century, Atlanta, Georgia, USA.

Wallace LA (1987) The total exposure assessment methodology (TEAM) study: Summary and analysis, Volume I. Washington, DC, US Environmental Protection Agency, Office of Research and Development.

Wallace JC & Hites RA (1996) Diurnal variations in atmospheric concentrations of polychlorinated biphenyls and endosulfan implications for sampling protocols. *Environ Sci Technol*, 30(2): 444-446.

Wallace LA & Ott WR (1982) Personal monitors: a state-of-the-art survey. *J Air Pollut Control Assoc*, 32: 601-610.

Wallace LA, Zweidinger RA, Erickson M, Cooper S, Whitaker D, & Pellizzari ED (1982) Monitoring individual exposure: Measurement of volatile organic compounds in breathing-zone air, drinking water, and exhaled breath. *Environ Int*, 8: 269-282.

Wallace LA, Pellizzari ED, Hartwell TD, Rosenzweig M, Erickson M, Sparacino C, & Zelon H (1984a) Personal exposure to volatile organic compounds: I. Direct measurement in breathing-zone air, drinking water, food, and exhaled breath. *Environ Int*, 35: 293-319.

Wallace LA, Pellizzari ED, Hartwell TD, Zelon H, Sparacino C, & Whitmore R (1984b) Analysis of exhaled breath of 355 urban residents for volatile organic compounds. In: *Indoor air -- Volume 4: Chemical characterization and personal exposure*. Stockholm, Swedish Council for Building Research, pp 15-20.

Wallace LA, Pellizzari E, Hartwell TD, Sparacino C, Sheldon LS, & Zelon H (1985) Personal exposures, indoor-outdoor relationships, and breath levels of toxic air pollutants measured for 355 persons in New Jersey. *Atmos Environ*, 19: 1651-1661.

Wallace LA, Pellizzari E, Hartwell TD, Whitmore R, Sparacino C, & Zelon H (1986) Total exposure assessment methodology (TEAM) study: Personal exposures, indoor-outdoor relationships, and breath levels of volatile organic compounds in New Jersey. *Environ Int*, 12: 369-387.

- Wallace LA, Pellizzari ED, Hartwell TD, Sparacino C, Whitmore R, Sheldon L, Zelon H, & Perritt R (1987a) The TEAM (total exposure assessment methodology) study: Personal exposures to toxic substances in air, drinking water, and breath of 400 residents of New Jersey, North Carolina, and North Dakota. *Environ Res*, 43: 290-307.
- Wallace LA, Pellizzari E, Hartwell TD, Perritt K, & Ziegenfus R (1987b) Exposures to benzene and other volatile organic compounds from active and passive smoking. *Arch Environ Health*, 43: 290-307.
- Wallace LA, Pellizzari ED, Hartwell TD, Whitmore R, Perritt R, & Sheldon L (1988) The California TEAM study: Breath concentrations and personal exposures to 26 volatile compounds in air and drinking water of 188 residents of Los Angeles, Antioch and Pittsburgh, CA. *Atmos Environ*, 22: 2141-2163.
- Wallace LA, Pellizzari ED, Hartwell TD, Davis V, Michael LC, & Whitmore RW (1989) The influence of personal activities on exposure to volatile organic compounds. *Environ Res*, 50: 37-55.
- Wallace LA, Nelson W, Ziegenfus R, Pellizzari E, Michael L, Whitmore R, Zelon H, Hartwell TD, Perritt R, & Westerdahl D (1991a) The Los Angeles TEAM study: Personal exposures, indoor-outdoor air concentrations, and breath concentrations of 25 volatile organic compounds. *J Expo Anal Environ Epidemiol*, 1: 157-192.
- Wallace LA, Nelson WC, Ziegenfus R, & Pellizzari ED (1991b) The Los Angeles TEAM study: Personal exposures, indoor-outdoor air concentrations, and breath concentrations of 25 volatile organic compounds. *J Expo Anal Environ Epidemiol*, 1(2): 37-72.
- Wallace JC, Basu I, & Hites RA (1996) Sampling and analysis artifacts caused by elevated indoor air polychlorinated biphenyl concentrations. *Environ Sci Technol*, 30(9): 2730-2734.
- Walters M, Milton D, Larsson L, & Ford T (1994) Airborne environmental endotoxin: a cross-validation of sampling and analysis techniques. *Appl Environ Microbiol*, 60: 996-1005.
- Ward E, Clapp D, Tolos W, & Groth D (1986) Efficacy of urinary monitoring for 4,4'-methylenebis(2-chloroaniline). *J Occup Med*, 28: 637-642.
- Watt J, Moorcroft S, Brooks K, Culbard E, & Thornton I (1983) Metal contamination of dusts and soils in urban and rural households in the United Kingdom, sampling and analytical techniques for households and external dusts. In: *Proceedings of the 17th Trace Substances in Environmental Health Conference, Columbia, 13-16 June 1983*. Columbia, Missouri, University of Missouri Press.
- Weber J-P (1988) An interlaboratory comparison programme for several toxic substances on blood and urine. *Sci Total Environ*, 71: 111-123.
- Weitzman M, Aschengrau A, Bellinger A, & Jones R (1993) Lead-contaminated soil abatement and urban children's blood lead levels. *J Am Med Assoc*, 269(13): 1647-1654.
- Wetmur JG (1994) Influence of the common human delta-aminolevulinic acid dehydratase polymorphism on lead body burden. *Environ Health Perspect*, 102(suppl 3): 215-219.

Whicker FW & Kirchner TB (1987) PATHWAY: a dynamic food-chain model to predict radionuclide ingestion after fallout deposition. Health Phys, 52: 717-737.

Whitmore RW (1988) The design of surveys for residential and personal monitoring of hazardous substances. Atmos Environ, 22: 2077-2084.

Whitmore RW, Immerman FW, & Camann DE (1993) Non-occupational exposures to pesticides for residents of two US cities. Arch Environ Contam Toxicol, 26: 1-13.

Whitmore RW, Immerman F, Camann D, Bond A, Lewis R, & Schaum J (1994) Non-occupational exposures to pesticides for residents of two US cities. Arch Environ Contam Toxicol, 26: 47-59.

WHO (1978) Guidelines for establishing or strengthening national food contamination monitoring programmes. Geneva, World Health Organization.

WHO (1982a) Human exposure to carbon monoxide and suspended particulate matter in Zagreb, Yugoslavia. Geneva, World Health Organization (Document EFP/82.33).

WHO (1982b) Human exposure to SO₂, NO₂ and suspended particulate matter in Toronto, Canada. Geneva, World Health Organization.

WHO (1984) Human exposure to suspended particulate matter and sulphate in Bombay, India. Geneva, World Health Organization.

WHO (1985a) Guidelines for the study of dietary intakes of chemical contaminants: Report prepared by UNEP/FAO/WHO. Geneva, World Health Organization (Offset Publication No. 87).

WHO (1985b) In: Bruaux P & Svartengren M ed. Assessment of human exposure to lead: Comparison between Belgium, Malta, Mexico and Sweden. Geneva, World Health Organization and United Nations Environment Programme.

WHO (1985c) Human exposure to carbon monoxide and suspended particulate matter in Beijing, People's Republic of China. Geneva, World Health Organization.

WHO (1986) Teaching health statistics. Geneva, World Health Organization.

WHO (1987) Air quality guidelines for Europe. Copenhagen, World Health Organization, Regional Office for Europe (WHO Regional Publications, European Series No. 23).

WHO (1992) GEMS/Water operational guide, 3rd ed. Geneva, World Health Organization (Document GEMS/W.92.1).

WHO (1993) Guidelines for drinking-water quality -- Volume 1: Recommendations, 2nd ed. Geneva, World Health Organization.

WHO (1995a) Global Environmental Epidemiology Network -- The potential of human exposure assessment for air pollution regulation. Geneva, World Health Organization, Office of Global and Integrated Environmental Health.

WHO (1995b) Global Environmental Epidemiology Network -- Human exposure to lead. Geneva, World Health Organization, Office of Global and Integrated Environmental Health (Document WHO/EHG/95.15).

WHO (1995c) Application of risk analysis to food standards issues: Report of the Joint FAO/WHO Consultation, York, UK, 2-6 May 1995. Geneva, World Health Organization (Document WHO/FNU/FOS/95.11).

WHO (1996a) Guidelines for drinking-water quality, 2nd ed. -- Volume 2: Health Criteria and other supporting information. Geneva, World Health Organization.

WHO (1996b) Levels of PCBs, PCDDs, and PCDFs in human milk: Second round of WHO-coordinated exposure study. Bilthoven, Copenhagen, Nancy, Rome, WHO European Centres for Environment and Health (Environmental Health in Europe No. 3).

WHO (1997a) Healthy city air management -- Information system AMIS 1.0 (CD-ROM). Geneva, World Health Organization.

WHO (1997b) In: Gantunen N, Jaakola JJK, & Krzyzanowski M ed. Assessment of exposure to indoor air pollutants. Copenhagen, World Health Organization, Regional Office for Europe (WHO Regional Publications, European Series No. 78).

WHO (1997c) Guidelines for predicting dietary intake of pesticides residues (revised). Prepared by GEMS/Food in collaboration with the Codex Committee on Pesticide Residues. Geneva, World Health Organization.

WHO/UNEP (1986) Global Environmental Monitoring Programme/Human Exposure Assessment Location (HEAL) project -- Guidelines for integrated air, water, food and biological exposure monitoring. Geneva, World Health Organization.

WHO/UNEP (1987) Global Environment Monitoring System/Human Exposure Assessment Location (HEAL) project -- Indoor air quality study Maragua Area, Kenya. Geneva, World Health Organization.

WHO/UNEP (1988) Global Environment Monitoring System/Human Exposure Assessment Location (HEAL) project -- Indoor air quality in the Basse Area, The Gambia. Geneva, World Health Organization

WHO/UNEP (1992a) An introductory guide to human exposure field studies: Survey methods and statistical sampling. Geneva, World Health Organization.

WHO/UNEP (1992b) Endemic fluorosis, a global health issue: A technical report for the Human Exposure Assessment Location (HEAL) project. Geneva, World Health Organization.

Wiley JA & Robinson J (1991) Activity patterns of California residents (Contract No. A6-177-33 with the University of California, Berkley). Sacramento, California, California Air Resources Board.

Wiley JA, Robinson JP, Cheng YT, Piazza T, Sork L, & Pladsen K (1991) Study of children's activity patterns (Contract No. A733-149). Sacramento, California, California Air Resources Board.

Wilhelm M, Lombeck I, Hafner D, & Ohnesorge FK (1989) Hair lead levels in young children from the FRG. *J Trace Elem Electrolytes Health Dis*, 3: 165-70.

Wilhelm M, Ohnesorge FK, & Hotzel D (1990) Cadmium, copper, lead, and zinc concentrations in human scalp and pubic hair. *Sci Total Environ*, 92: 199-206.

Wilhem M, Hafner D, Lombeck I, & Ohnesorge FK (1991) Monitoring of cadmium, copper, lead and zinc status in young children using toenails: Comparison with scalp hair. *Sci Total Environ*, 103: 199-207.

Wilson R & Spengler J ed. (1996) *Particles in our air*. Cambridge, Massachusetts, Harvard University Press, pp 41-62.

Wilson AL, Colome SC, & Tian Y (1993a) California residential indoor air quality study -- Volume I: Methodology and descriptive statistics. Irvine, California, Integrated Environmental Services.

Wilson AL, Colome SC, & Tian Y (1993b) California residential indoor air quality study -- Volume II: Appendix. Irvine, California, Integrated Environmental Services.

Wilson AL, Colome SD, & Tian Y (1995) California residential indoor air quality study -- Volume 3: Ancillary and exploratory analyses. Irvine, California, Integrated Environmental Services.

Witschi JC (1990) Short-term dietary recall and recording methods. In: Willett WC ed. *Nutritional epidemiology*. New York, Oxford University Press.

Wolff US, Rivera M, & Baker DB (1991) Detection limits of organochlorine pesticides and related compounds in blood serum. *Bull Environ Contam Toxicol*, 47: 499-503.

Wood P, Phillips L, Adenuga A, Koontz M, & Rector H (1997) Exposure factors handbook -- Volume 1: General factors (Final report). Washington, DC, US Environmental Protection Agency (EPA/600/P-97/002FA).

World Bank (1992) *World development report*. New York, Oxford University Press.

World Resources Institute (1992) *World resources 1992-93*. New York, Oxford University Press.

Yager JW, Paradisin WM, & Rappaport SM (1993) Sister-chromatid exchange in lymphocytes are increased in relation to longitudinally measured occupational exposure to low concentrations of styrene. *Mutat Res*, 319: 155-165.

Yli-Panula E & Rantio-Lehtimäki A (1995) Birch-pollen antigenic activity of settled dust in rural and urban homes. *Allergy*, 50: 303-307.

Zartarian VG, Streicker J, Rivera A, Cornejo CS, Molina S, Valadez OF, & Leckie JO (1995) A pilot study to collect micro-activity data of two- to four-year olds farm labor children in Salinas Valley, California. *J Expo Anal Environ Epidemiol*, 5: 21-33.

RÉSUMÉ

1. Définition de l'exposition

Pour qu'il y ait exposition, il faut qu'une substance toxique se trouve à l'instant t en un point donné de l'environnement et qu'une ou plusieurs personnes se trouvent également en ce point au même moment. En outre, la quantité de substance en contact avec le tégument entre également en ligne de compte.

Lorsqu'on a pris conscience de l'intérêt intrinsèque de cette notion, "l'analyse de l'exposition" s'est imposée comme un aspect important de l'investigation scientifique en santé publique, qui vient compléter les disciplines traditionnelles que sont la toxicologie et l'épidémiologie et constitue désormais un élément essentiel de toute décision éclairée dans le domaine de l'hygiène de l'environnement.

2. Usage des données relatives à l'exposition humaine

Toute analyse de l'exposition se caractérise par le ou les usages qu'on a l'intention d'en faire. Ainsi, les aspects de l'exposition qui sont à prendre en compte, la nature de l'information nécessaire, de même que la quantité et le niveau de qualité des données à réunir pourront varier selon que l'analyse est effectuée dans le cadre d'une enquête épidémiologique, d'une évaluation du risque, d'une analyse de tendance ou encore selon que l'on cherche à caractériser le risque ou à le maîtriser.

La connaissance de l'exposition humaine aux polluants présents dans l'environnement est importante dans ce type de démarche ou d'action. Elle permet d'établir le lien déterminant qui existe entre les sources de contamination, leur présence dans l'environnement et les effets qui peuvent en découler pour la santé humaine. Les informations de ce genre, si elles sont utilisées en vue d'une gestion de l'environnement visant à réduire le risque pour la santé humaine, vont faciliter le choix et l'analyse de stratégies qui se distinguent de l'approche traditionnelle, basée sur "le commandement et la conduite des opérations". La plupart des structures de gestion de l'environnement se fondent sur une exploitation directe des données relatives à la concentration des polluants dans les divers milieux pour juger de la qualité environnementale d'un site, évaluer le risque et voir dans quelle mesure les normes sont respectées. Même en pareil cas, la connaissance de l'exposition peut permettre de déterminer dans quelle mesure on peut protéger efficacement tel ou tel groupe de population plus sensible ou plus exposé au risque.

C'est ce lien direct qui fait que la mesure de l'exposition est d'une aide précieuse dans les études d'impact au niveau local, régional ou mondial.

3. Stratégies et protocoles pour l'évaluation de l'exposition

L'élément le plus important d'une évaluation de l'exposition est constitué par le protocole de l'étude. Ce protocole doit préciser la finalité et les objectifs de l'étude ainsi que les méthodes d'échantillonnage, de mesure et d'analyse statistique qui seront utilisées, sans oublier l'assurance de la qualité. La caractérisation de l'ampleur, de la durée et de la chronologie des contacts entre sujets humains et polluants de l'environnement peut se faire de

manière directe ou indirecte. Si l'on procède directement, on pourra par exemple effectuer des mesures aux points de contact et évaluer les marqueurs biologiques de l'exposition. Si l'on a recours à une méthode indirecte, elle pourra se fonder sur la surveillance de l'environnement, la modélisation ou l'usage de questionnaires. Toutes ces méthodes sont susceptibles d'être utilisées dans divers types d'études d'exposition caractérisées par la manière dont s'opère le choix de la population à étudier. Par exemple, il pourra s'agir d'études exhaustives portant sur la totalité de la population en cause, d'études descriptives sur un échantillon non aléatoire ou encore d'enquêtes basées sur un échantillon représentatif constitué d'individus tirés au sort.

4. Les méthodes statistiques utilisées dans l'évaluation de l'exposition

Ces méthodes constituent un outil essentiel pour les études d'exposition à vocation heuristique ou à caractère appliqué. Il est souhaitable qu'un statisticien intervienne à tous les stades de l'étude et notamment lors de la mise au point du protocole et de l'analyse des données. L'un des aspects importants de l'utilisation des méthodes statistiques est la détermination de la taille de l'échantillon à laquelle on procède lors du stade de planification de l'étude. On peut également récapituler les données d'exposition sous la forme de statistiques descriptives numériques ou graphiques et effectuer une analyse préliminaire des relations entre les diverses variables. Les données d'exposition ont souvent une distribution normale ou log-normale et on peut donc les soumettre immédiatement à une analyse statistique paramétrique avec estimation et tests d'hypothèses. On peut également avoir recours à d'autres modèles statistiques paramétriques tels que l'analyse de la variance, la régression linéaire et la régression logistique afin de quantifier les associations entre les diverses mesures de l'exposition. Lorsque le nombre d'observations est faible ou que les données ne peuvent pas être transformées pour leur faire adopter une distribution sensiblement normale, on peut utiliser des méthodes non paramétriques comme le test des signes, le test de Mann-Whitney ou celui de Kruskal-Wallis pour vérifier les hypothèses.

5. Profils temps-activités des sujets humains et évaluation de l'exposition

La connaissance du type d'activité des individus permet de mettre en évidence les déterminants de l'exposition mesurée, de déterminer *a priori* une exposition non mesurée ou non mesurable, d'établir les relations susceptibles d'exister entre exposition et état de santé ou encore de reconnaître les situations à haut risque justiciables d'une intervention par les autorités en charge de la santé publique.

Le coût relatif des prélèvements sur le terrain et des analyses en laboratoire dans le cas d'échantillons environnementaux ou biologiques fait ressortir l'intérêt potentiel des données temps-activités. Pour une évaluation à très long terme (par ex. sur toute la durée de la vie), on n'a parfois pas d'autre possibilité que l'utilisation de questionnaires temps-activités. Il existe diverses méthodes pour recueillir des informations sur les activités humaines: agendas, questionnaires, dispositifs mécaniques ou observation. Plus récemment, on a commencé à élaborer des méthodes permettant d'évaluer le rôle du profil temps-activités sur les voies d'exposition alimentaire, non alimentaire ou cutanée. On s'interroge cependant sur

le point de savoir si les méthodes de collecte des données garantissent la représentativité de l'activité effective et permettent de recueillir des informations valables, sans parler du problème des variations inter- et intraindividuelles, ce qui fait entrevoir les limites de l'utilisation des données temps-activités pour l'évaluation de l'exposition humaine. Cependant, au prix d'un bon programme d'assurance de la qualité, les profils temps-activités peuvent se révéler très précieux pour l'interprétation et la modélisation de l'exposition.

6. Exposition humaine et modélisation de la dose

Un modèle d'exposition est une représentation logique ou expérimentale qui permet l'estimation des paramètres d'exposition d'un individu ou d'une population à partir d'un certain nombre de données initiales. Les modèles d'exposition qui s'appuient sur de bonnes observations peuvent être utilisés pour évaluer l'exposition collective (moyenne pour une population par ex.) ou individuelle (par ex. la distribution de l'exposition parmi les membres d'une population). Ces modèles peuvent également servir à estimer l'exposition par le canal d'un seul ou de plusieurs milieux. Cette dernière possibilité est particulièrement utile pour comparer l'intensité de l'exposition imputable à divers milieux et fixer des priorités. Les modèles d'exposition peuvent être de nature déterministe ou statistique ou tenir des deux. Des méthodes probabilistes sont applicables aux trois types de modèles pour obtenir la distribution estimative de l'exposition dans une population, c'est-à-dire pour se faire une idée de sa variabilité selon les individus. En outre, ces méthodes peuvent être utilisées pour caractériser l'incertitude des paramètres initiaux d'un modèle en conservant ce caractère incertain jusqu'au point d'aboutissement

prévisible. Il est capital d'évaluer le degré d'exactitude d'un modèle avant de prendre une décision sur la base de ses résultats.

7. Mesure de l'exposition humaine aux substances chimiques présentes dans l'air, l'eau ou les aliments

Qu'il s'agisse de l'air, de l'eau ou des aliments, les mêmes considérations relatives aux limites de détection, aux interférences, à la commodité de mise en oeuvre et au coût se retrouvent lors du choix d'une méthode d'échantillonnage. Pour la surveillance passive ou active des gaz, des vapeurs, des aérosols, des produits organiques semi-volatils ou des gaz réactifs, on peut faire des prélèvements individuels, microenvironnementaux ou dans l'air ambiant.

Lorsqu'on se propose de déterminer la qualité d'une eau, plusieurs aspects sont à prendre en considération. Il y en a un notamment, qui a son importance - à savoir le fait que l'exposition à d'éventuels contaminants ne se limite pas à la voie digestive et que tout le monde n'a pas accès à un réseau de distribution délivrant de l'eau traitée. Le document fournit des indications relatives aux programmes d'échantillonnage et de surveillance.

Il existe un certain nombre de méthodes pour évaluer la consommation de nourriture et le degré de contamination des aliments. La méthode à adopter sera fonction des données disponibles, du groupe de population en cause, des effets - aigus ou chroniques- qui se manifestent, de l'utilisation que l'on se propose de faire des résultats et des ressources disponibles.

8. Mesure de l'exposition humaine à des contaminants chimiques présents dans le sol et la poussière déposée

Les contacts avec le sol et la poussière déposée peuvent constituer une source importante d'exposition humaine à des contaminants chimiques, notamment chez l'enfant. On a mis au point de nombreuses méthodes d'échantillonnage mais aucune d'entre elles ne s'est révélée supérieure aux autres. Il est donc difficile, dans ces conditions, de comparer les résultats d'études qui font appel à des techniques d'échantillonnage différentes. Lorsqu'on choisit une méthode d'échantillonnage, un certain nombre de facteurs importants sont à prendre en considération: l'efficacité de la collecte, les différences dans la nature des activités humaines, la variabilité des caractéristiques physiques du sol, l'évolution du taux de poussière dans le temps et l'espace, la surface et le substrat sur lesquels on effectue les prélèvements, le moment de la collecte et les méthodes d'analyse qui seront utilisées pour le dosage des produits toxiques en laboratoire.

9. Dosage des agents biologiques présents dans l'air et l'eau et auxquels l'Homme est exposé

Les aérosols biologiques contiennent divers microorganismes ou constituants de microorganismes aéroportés qui sont susceptibles d'être inhalés. Il s'agit notamment de virus, de bactéries, de pollens, de champignons, de protozoaires ou d'algues qui, lorsqu'ils sont viables, peuvent être la cause de maladies. Des fragments de bactéries ou de champignons, de même que les produits de leur métabolisme ou les structures protéiques que ces microorganismes contiennent ou encore des déjections ou des parties du corps d'animaux divers, comme des insectes ou des arachnides, sont capables de déclencher des réactions allergiques. Les aérosols biologiques les plus répandus que l'on trouve communément à l'intérieur des habitations contiennent des acariens, des champignons, des bactéries et des pollens.

L'évaluation de l'exposition microbiologique en est actuellement au même stade que celle de nombreux autres polluants atmosphériques. On n'a pas encore mis au point d'échantillonneurs individuels. De fait, nombre de techniques d'échantillonnage utilisées pour l'évaluation de l'exposition aux agents biologiques aéroportés sont des adaptations de techniques employées à d'autres fins. C'est un domaine qui progresse, maintenant que des organismes professionnels s'efforcent d'améliorer et de normaliser les méthodes de mesure et de culture, les protocoles d'analyse et la présentation des comptes rendus. Tous ces points sont d'une importance capitale pour la comparaison des résultats obtenus par les différents chercheurs.

De par leur nature même, les aérosols biologiques sont de composition et de concentration très variables. La croissance, la reproduction et la dispersion des microorganismes varient largement en fonction de la température, du degré d'humidité et de la présence de nutriments. Leurs interactions avec les activités humaines ou animales dépendent d'ailleurs de ces mêmes facteurs. Certains dispositifs mécaniques ou machines peuvent amplifier et disperser les aérosols biologiques. Il en résulte que l'exposition individuelle est passablement variable; dans ces conditions, de nombreux chercheurs ont été amenés à s'en remettre à des prélèvements d'air dans un secteur donné ou à un échantillonnage général. Par exemple, plutôt que de

chercher à mesurer l'exposition individuelle aux allergènes des acariens, il est recommandé de s'en tenir à des prélèvements sur la literie ou dans la poussière du sol. La "mesure" de l'exposition utilisée dans les enquêtes épidémiologiques est souvent effectuée sur des échantillons intradomiciliaires constitués de prélèvements d'air ou de poussière.

En définitive, si l'on veut que l'évaluation de l'exposition aérobiologique progresse suffisamment pour qu'on puisse l'utiliser en vue d'une estimation quantitative du risque, il va falloir déterminer avec une plus grande précision et pour de nombreux agents ou microorganismes, la dose nécessaire à la sensibilisation et à l'apparition de réactions.

10. Evaluation de l'exposition à partir de marqueurs biologiques

Les marqueurs biologiques constituent un moyen de mesurer l'exposition environnementale en caractérisant la dose totale de contaminant reçue par un sujet à partir de l'ensemble des sources d'exposition. Le principal avantage de cette stratégie réside dans le fait que l'on obtient une évaluation de l'exposition individuelle totale par une mesure qui intègre la contribution de toutes les sources d'exposition et qui dépend du comportement humain. On estime également que les marqueurs biologiques permettent une meilleure prévision des effets sur la santé que les mesures externes de l'exposition. Ils permettent aussi de répondre à plusieurs des exigences de l'évaluation:

- * caractérisation de l'exposition d'un individu ou d'une population
- * obtention de la distribution de la dose à l'intérieur de la population
- * mise en évidence des déterminants environnementaux et démographiques de l'exposition

Le principal inconvénient des marqueurs biologiques tient à la difficulté de caractériser individuellement les sources de pollution qui contribuent à l'exposition totale du sujet. Lorsqu'on met au point et que l'on utilise de tels marqueurs, il est capital de connaître la toxicocinétique du contaminant dans le système pour caractériser la variabilité biologique et déterminer si tel ou tel marqueur permet de déterminer valablement l'exposition à la substance en cause pour la concentration toxicologiquement intéressante. Les marqueurs biologiques ont joué un rôle capital dans la détermination de l'exposition humaine à certains polluants, comme le plomb. Il existe un grand nombre de méthodes non effractives pour la surveillance biologique et il faut s'efforcer, lorsque l'on se propose d'évaluer l'exposition à telle ou telle substance, de les inscrire dans les protocoles de surveillance de l'environnement élaborés à cet effet.

11. Assurance de la qualité des études d'exposition

L'assurance de la qualité consiste en un suivi indépendant du déroulement de l'étude destiné à faire en sorte que les responsables du laboratoire et les utilisateurs des données aient l'assurance que les installations, le matériel, le personnel, les méthodes, les pratiques, les dossiers et les contrôles sont bien conformes aux critères de qualité en la matière. Certaines erreurs dans l'évaluation de l'exposition s'expliquent par des variations dans les résultats des

analyses ou par des changements qui se produisent lors du prélèvement et de la manipulation des échantillons, de leur préparation et de leur conservation ou encore dans la tenue et l'enregistrement des données. Les variations dans les résultats des analyses peuvent se répartir en deux grandes catégories: celles qui concernent l'exactitude, c'est-à-dire la concordance entre le résultat du dosage et la quantité de substance effectivement présente dans la prise d'essai et celles

qui concernent la précision, c'est-à-dire la variabilité aléatoire ou la reproductibilité de la méthode.

Le plan de l'étude est le document le plus important à consulter pour obtenir des informations sur les éléments essentiels d'une enquête, c'est-à-dire le personnel responsable, le mode de collecte des données, la conservation des échantillons et leur traitement préliminaire, les méthodes d'analyse et l'analyse des résultats. Un mode opératoire normalisé est annexé au plan de l'étude. Il comporte des instructions détaillées sur la manière d'effectuer certaines tâches sur le terrain ou au laboratoire. On peut considérer le plan de l'étude et le mode opératoire normalisé comme des directives de gestion visant à faire en sorte que l'ensemble du personnel qui participe à l'étude se familiarise avec les diverses procédures et n'en utilise pas d'autres.

Le contrôle de qualité vise expressément la qualité des résultats de laboratoire. Il comporte deux volets. Le contrôle interne consiste en un ensemble de procédures utilisées par le personnel du laboratoire pour évaluer en continu les résultats qu'il obtient. Le contrôle de qualité externe est un système de vérification objective de la bonne exécution des analyses par un organisme indépendant. Dans le contrôle interne, on affiche les résultats sur des cartes de contrôle (par ex. cartes de contrôle de Sheward ou à sommes cumulées) et on se base sur les limites de contrôle pour prendre des mesures le cas échéant ou juger si l'ensemble de données comporte ou non un contrôle statistique. Le contrôle externe, par contre, donne des indications indépendantes sur la qualité du travail effectué par le laboratoire et sur la compétence de tel ou tel opérateur. Généralement, un laboratoire coordinateur distribue aux laboratoires participants des échantillons contenant le produit à doser à une concentration connue. Les laboratoires participants effectuent leurs dosages sur ces échantillons et soumettent leurs résultats au laboratoire coordinateur qui vérifie alors la bonne exécution des analyses. Dans les échantillons de référence utilisés pour les contrôles de qualité interne et externe la matrice et le polluant doivent être à la même concentration que dans l'échantillon réel. En outre, pour certaines substances, il peut être nécessaire de prendre en considération la forme chimique sous laquelle elles sont susceptibles de se trouver.

Enfin, les interactions avec la population humaine constituent un ensemble spécifique d'éléments à prendre en considération au niveau de la conception de l'étude et de l'assurance de la qualité, éléments qui doivent être soigneusement évalués en même temps que les questions plus traditionnelles relatives à l'échantillonnage, à l'analyse et aux modes opératoires.

RESUMEN

1. Definición de la exposición

El concepto de exposición implica la presencia de una sustancia

tóxica ambiental en un determinado punto del espacio y el tiempo, y la presencia simultánea de una persona o personas en el mismo lugar. Además, es necesario precisar la cantidad de la sustancia que entra en contacto con la superficie externa del cuerpo humano.

Tras reconocerse el valor intrínseco de la información relacionada con la exposición, el "análisis de la exposición" se ha convertido en un importante campo de investigación científica, que complementa las disciplinas tradicionales de la salud pública, como son la epidemiología y la toxicología, y constituye un componente esencial de la adopción de decisiones fundamentadas en materia de higiene del medio.

2. Usos de la información sobre la exposición humana

Las particularidades de un determinado análisis de la exposición dependerán del uso o usos previstos. Por ejemplo, los aspectos de la exposición que interese examinar, la naturaleza de la información requerida y la cantidad y calidad de los datos dependerán de si la evaluación de la exposición se inscribe en el contexto de una investigación epidemiológica, de una evaluación del riesgo, de la gestión de los riesgos o de un análisis de la situación y las tendencias.

El conocimiento del nivel de exposición humana a los contaminantes ambientales es un componente importante de la epidemiología ambiental, la evaluación de los riesgos, la gestión de los riesgos y el análisis de situaciones y tendencias. La información sobre la exposición proporciona el nexo decisivo entre las fuentes de contaminantes, su presencia en el medio y los posibles efectos para la salud humana. Esta información, empleada en el contexto de una gestión del medio basada en la reducción de los riesgos para el ser humano, facilitará la selección y el análisis de otras estrategias distintas del tradicional enfoque de "dirección y control". En todo el mundo, la mayoría de las estructuras de gestión del medio ambiente dependen directamente de las mediciones de los contaminantes presentes en diversos medios para estimar la calidad del entorno, inferir los riesgos e interpretar el grado de observancia de las normas. Incluso en estos casos, la información sobre la exposición permite evaluar la eficacia de las medidas de protección de los sectores de la población más vulnerables o en situación de mayor riesgo.

Es esa relación directa lo que hace de las mediciones de la exposición un arma inestimable a efectos de evaluación de las repercusiones para la higiene del medio a escala local, regional y mundial.

3. Estrategias y diseño de las evaluaciones de la exposición

El correcto diseño del estudio es el elemento más importante de cualquier evaluación de la exposición. Se deben especificar los fines y objetivos de la investigación, así como los métodos idóneos de muestreo, medición, análisis estadístico y aseguramiento de la calidad. Para caracterizar la magnitud, duración y distribución temporal del contacto humano con los contaminantes del medio se pueden emplear métodos directos o indirectos. Entre los primeros cabe citar las mediciones en el punto de contacto y las mediciones de marcadores biológicos de la exposición. Los métodos indirectos incluyen la vigilancia ambiental, las modelizaciones y los cuestionarios. Estos métodos pueden emplearse en estudios de la exposición basados en

distintas maneras de seleccionar a la población estudiada; se distinguen así, por ejemplo, los estudios amplios que abarcan a todos los miembros de la población analizada, los estudios descriptivos de una muestra no probabilística, o los estudios basados en muestras representativas de individuos, seleccionados al azar.

4. Métodos estadísticos de evaluación de la exposición

Los métodos estadísticos son un instrumento crítico de los estudios -- aplicados o de investigación -- de evaluación de la exposición. Se recomienda que participe siempre un estadístico en todos los aspectos de la investigación de la exposición, en especial durante las fases de diseño y de análisis de los datos. La determinación del tamaño de la muestra es una aplicación importante de la estadística durante la planificación de esos estudios. La estadística descriptiva numérica y gráfica permite resumir los datos de exposición y llevar a cabo análisis preliminares de las relaciones entre las variables determinantes de la exposición. En muchos casos los datos sobre ésta adoptan una distribución aproximadamente normal o log-normal, y se prestan pues fácilmente a ser analizados mediante los métodos paramétricos habituales de inferencia estadística, como las estimaciones y la verificación de hipótesis. Se pueden emplear además otros modelos estadísticos paramétricos, como el análisis de la varianza (ANOVA), la regresión lineal y la regresión logística, para cuantificar la relación entre los niveles de exposición medidos. Cuando el número de observaciones es pequeño o no es posible transformar los datos en una distribución aproximadamente normal, se pueden utilizar métodos no paramétricos, como las pruebas de signo de Mann-Whitney y de Kruskal-Wallis, para verificar las hipótesis.

5. Patrones temporales de la actividad humana y evaluación de la exposición

Se puede utilizar información sobre el perfil de actividades de la gente para identificar los determinantes de los niveles de exposición detectados, predecir exposiciones no medidas o no medibles, evaluar la relación entre la exposición y el estado de salud, e identificar situaciones de exposición de alto riesgo que puedan afrontarse con medidas de salud pública.

El costo relativo del muestreo sobre el terreno y de los análisis de laboratorio en las mediciones ambientales y biológicas subraya el valor potencial de los datos tiempo-actividad. La evaluación de los perfiles de actividad a largo plazo (p. ej., toda la vida) sólo puede hacerse a veces empleando cuestionarios de análisis de la relación tiempo-actividad. Para reunir información sobre las actividades humanas se emplean diversos métodos, entre ellos diarios y cuestionarios, dispositivos mecánicos y medidas de observación. Sólo recientemente se han empezado a desarrollar métodos para evaluar la influencia de los perfiles de tiempo-actividad en la ingestión alimentaria y no alimentaria y en la exposición cutánea. Las dudas albergadas respecto a la capacidad de los métodos de acopio de datos para reflejar fielmente las actividades y garantizar la validez de la información, así como respecto a las repercusiones de la variabilidad ínter e intrapersonal del comportamiento, imponen límites a la aplicación de los datos de tiempo-actividad a la evaluación de la exposición humana. Sin embargo, con unos programas adecuados de aseguramiento de la calidad, la información sobre los patrones temporales de la actividad puede ser de enorme utilidad para interpretar y modelizar la exposición.

6. Modelización de la exposición humana y de las dosis

Un modelo de exposición es un esquema lógico o empírico que permite estimar los parámetros de la exposición individual o poblacional a partir de una serie de datos. Los modelos de la exposición, cuando están basados en observaciones adecuadas, pueden emplearse para estimar exposiciones colectivas (p. ej., la media de una población) o individuales (p. ej., la distribución de la exposición entre los miembros de una población). Mediante esos modelos se puede estimar la exposición sufrida a través de uno o de varios medios. Esto último es especialmente útil para poder comparar la magnitud de las exposiciones previsibles a través de distintos medios, y por tanto para establecer las prioridades. Los modelos pueden ser estadísticos, deterministas, o una combinación de ambos. En los tres casos se pueden aplicar métodos probabilísticos para estimar la distribución de la exposición en la población, esto es, la variabilidad de la exposición entre los individuos. Además, los métodos probabilísticos pueden utilizarse para definir la incertidumbre de los parámetros introducidos en el modelo y propagar esa incertidumbre hasta la variable de evaluación sometida a predicción. La evaluación de la exactitud de los resultados del modelo es una condición fundamental para pasar a utilizarlos con fines de adopción de decisiones.

7. Medición de la exposición humana a productos químicos presentes en el aire, el agua y los alimentos

En la selección de los métodos de muestreo de productos químicos presentes en el aire, el agua y los alimentos intervienen consideraciones comunes relacionadas con los límites de detección, los factores de interferencia, la facilidad de manejo y los costos. Se

dispone de métodos de muestreo para personas, aire de microambientes y aire ambiente, para la vigilancia de gases y vapores -- tanto pasiva como activamente--, aerosoles, compuestos orgánicos semivolátiles y gases reactivos.

La evaluación de la calidad del agua obliga a considerar numerosos factores en relación con el muestreo. Una consideración importante es que la exposición a los contaminantes no se limita a las vías orales y que no todos los individuos tienen acceso al agua tratada que circula por los sistemas de distribución. Se proporciona orientación respecto al muestreo y los programas de vigilancia.

Existen varios métodos para estimar el consumo de alimentos y la contaminación de éstos. El método elegido dependerá de la información disponible, del grupo de población de interés, de que lo expresado sean los efectos agudos o crónicos del producto químico, del uso previsto de los resultados y de los recursos disponibles.

8. Medición de la exposición humana a los contaminantes químicos presentes en el suelo y en el polvo depositado

El contacto humano con el suelo y el polvo depositado puede ser una importante fuente de exposición a contaminantes químicos, sobre todo en los niños. Aunque se han desarrollado muchos métodos de muestreo, no se ha demostrado que ninguno de ellos sea superior a los otros, por lo que resulta difícil comparar los resultados de estudios realizados con diferentes métodos. Entre los factores que deben

tenerse en cuenta para seleccionar un método de muestreo cabe citar la eficiencia de la recogida de muestras, las diferencias entre los perfiles de actividad de las personas, la variabilidad física del suelo y de los niveles de polvo en el espacio y en el tiempo, las superficies y sustratos de muestra, el momento elegido para obtener las muestras y los métodos analíticos utilizados para medir las sustancias tóxicas en el laboratorio.

9. Medición de la exposición humana a agentes biológicos presentes en el aire y el polvo

Se consideran bioaerosoles diversos microorganismos, o componentes de los mismos, que pueden ser transportados por el aire e inhalados. Comprenden virus, bacterias, pólenes, hongos, protozoos y algas en forma de microorganismos viables potencialmente causantes de enfermedades. Diversos fragmentos o componentes metabólicos de las bacterias y los hongos, al igual que las estructuras proteicas presentes en esos microorganismos, así como en los excrementos y en distintas partes de los insectos, arácnidos y otros animales, pueden provocar reacciones alérgicas. Los bioaerosoles más extendidos en interiores y más implicados en las reacciones alérgicas son los ácaros, los hongos, las bacterias y el polen.

La evaluación de la exposición a agentes microbiológicos está tan avanzada en estos momentos como la de muchos contaminantes del aire. No se han desarrollado muestreadores de personas. De hecho, muchas de

las técnicas disponibles para obtener muestras de agentes aerobiológicos son adaptaciones de instrumentos diseñados con otros fines. Sin embargo, se observan progresos en el sector, a medida que diversas organizaciones profesionales intentan mejorar y normalizar sus métodos de medición, sus protocolos de cultivo y análisis y sus sistemas de notificación de datos, aspectos todos ellos decisivos para poder comparar los resultados de diferentes investigadores.

Por su propia naturaleza, los bioaerosoles varían mucho en lo que respecta a su composición y concentración. Las condiciones favorables para su crecimiento, reproducción y dispersión varían dentro de un amplio margen de condiciones de temperatura, humedad y presencia de nutrientes. Esos mismos factores se ven alterados por las actividades del ser humano y de los animales. Los aerosoles biológicos pueden verse difundidos y amplificados por sistemas mecánicos y máquinas de diverso tipo. Como resultado de ello, las exposiciones personales son bastante variables; esto, a su vez, ha llevado a muchos investigadores a obtener muestras del aire de la zona y/o de grandes cantidades de material. Por ejemplo, se recomienda medir de forma indirecta la exposición a los alérgenos de los ácaros a partir de muestras de polvo de la ropa de cama y el suelo. Esas muestras domésticas, ya sea de aire o de polvo, determinan a menudo el nivel de "exposición" empleado en las investigaciones epidemiológicas.

Por último, para que los progresos de los métodos de evaluación de la exposición a agentes aerobiológicos permitan aplicarlos a la evaluación cuantitativa de los riesgos, habrá que determinar mejor las dosis causantes de sensibilización y reactividad para muy diversos microorganismos y/o agentes.

10. Evaluación de la exposición mediante marcadores biológicos

Los marcadores biológicos permiten vigilar la exposición

ambiental determinando la dosis total de un contaminante recibida por un individuo a partir de todas las fuentes de exposición. La principal ventaja de esta estrategia es que permite evaluar la exposición total usando una medida que integra todas las fuentes de exposición y está influida por el comportamiento humano. Se considera además que los marcadores biológicos tienen un mayor valor predictivo de los efectos sanitarios que las medidas externas de la exposición. Con ellos se responde a varias exigencias de la evaluación de la exposición, como son las siguientes:

- * caracterización de la exposición de un individuo o población
- * determinación de la distribución de la dosis en la población
- * identificación de los determinantes ambientales y demográficos de la exposición

El principal inconveniente de los marcadores biológicos estriba en la dificultad para caracterizar las fuentes individuales que contribuyen a la exposición total del sujeto. Al poner a punto y emplear marcadores biológicos, el conocimiento de la toxicocinética del contaminante en el sistema es fundamental para caracterizar la variabilidad biológica y determinar si el marcador biológico es válido para poder evaluar la exposición a la concentración de interés. Los marcadores biológicos han sido cruciales para profundizar en el conocimiento de la exposición humana a ciertos contaminantes, como el plomo. Se dispone de numerosos métodos no invasivos para la vigilancia biológica, métodos que los asesores en materia de exposición deberían intentar incorporar al desarrollar protocolos de vigilancia del medio ambiente.

11. Aseguramiento de la calidad de los estudios de la exposición

El aseguramiento de la calidad (AC) implica una vigilancia independiente del estudio que garantice a los responsables de la gestión del laboratorio y a los usuarios de los datos que las instalaciones, el equipo, el personal, los métodos, las prácticas, los registros y los controles se atienen a principios aceptados de gestión de la calidad. Los errores en los datos de exposición se deben tanto a variaciones analíticas como a los cambios que pueden afectar a la obtención y el manejo de las muestras, la preparación y el almacenamiento de las mismas y el registro y conservación de los datos. La variación analítica depende de dos factores principales: la exactitud, que refleja la concordancia entre la cantidad de analito medido y la cantidad realmente presente, y la precisión, que refleja la variabilidad aleatoria o la reproducibilidad del método.

El protocolo es el documento más importante para detallar los componentes críticos de una investigación, como por ejemplo el personal encargado, el acopio de muestras, el almacenamiento de las muestras y el tratamiento preanalítico, los procedimientos analíticos y el análisis de los datos. Los procedimientos normalizados de utilización (PNU) que se añaden al protocolo contienen instrucciones escritas detalladas sobre la manera de llevar a cabo algunas actividades rutinarias sobre el terreno y en el laboratorio. El protocolo y los PNU pueden considerarse como directrices de gestión concebidas para asegurar que todo el personal que participe en las operaciones del estudio conozca y emplee correctamente los mismos procedimientos.

El control de la calidad (CC) atañe específicamente a la calidad de los resultados de laboratorio, y presenta dos componentes. El CC interno es el conjunto de procedimientos que emplea el personal de un laboratorio para evaluar continuamente los resultados a medida que se obtienen. El CC externo es un sistema de control objetivo del desempeño de un laboratorio por un organismo independiente. El CC interno comprende la presentación de los resultados correspondientes a muestras de control en gráficos especiales (por ejemplo los gráficos de Shewhard y las sumas acumuladas) y el uso de límites de control como criterio para intervenir, o para juzgar si un conjunto de datos incluye o no algún tipo de control estadístico. El CC externo, por otra parte, aporta pruebas independientes de la calidad del desempeño de los laboratorios y de la competencia de los analistas. Por lo general, un laboratorio coordinador distribuye entre los laboratorios participantes muestras de una concentración conocida. Los laboratorios analizan las muestras de referencia y envían los resultados al laboratorio coordinador para que evalúe el desempeño.

Las muestras de referencia de los CC interno y externo deben poseer una matriz y una concentración de contaminante similares a las de la muestra real. Además, a veces es necesario tener en cuenta las formas químicas que puede adoptar la sustancia.

Por último, las interacciones con las poblaciones humanas plantean una serie de consideraciones peculiares respecto al diseño y el CC del estudio, que deben ser detenidamente evaluadas junto con los aspectos tradicionales concernientes al muestreo, los análisis y los procedimientos.

See Also:

[Toxicological Abbreviations](#)