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Children's health and environment: A review of evidence

A joint report from the European Environment Agency
and the WHO Regional Office for Europe

Experts' corner

Edited by:
Giorgio Tamburlini
Ondine S. von Ehrenstein
Roberto Bertollini

WHO Regional Office for Europe

World Health Organization
Regional Office for Europe

European Environment Agency

Layout: Brandenborg a/s

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European Environment Agency
Kongens Nytorv 6
DK-1050 Copenhagen K
Tel.: (45) 33 36 71 00
Fax: (45) 33 36 71 99
E-mail: eea@eea.eu.int
Internet: http://www.eea.eu.int

World Health Organization
European Centre for Environment and Health
Rome Operational Division
Via Francesco Crispi, 10
I-00187 Rome
Tel: (39) 06 48 77 51
Fax: (39) 06 48 77 599
E-mail: ecehr@who.it
Internet: http://www.euro.who.int/ecehrome

Foreword

Children's health and environment needs to be high on the political agenda. It is not possible to talk about health and quality of life without taking into consideration, and paying special attention to the needs of children. We must never forget that a healthy environment is not a privilege but a basic human right — not least for our children.

'Environment and health' is one of four priority areas outlined in the 6th Environmental Action Programme, which defines the Community's environmental policy for the next ten years. The fundamental objective is to promote a quality environment where levels of man-made pollutants, including different types of radiation, do not have a significant impact on or pose a risk to human health. In this regard, the action programme calls for special attention to the more vulnerable groups in society, including children.

Children are, for a variety of reasons, particularly vulnerable to the impact of environmental pollution. They are often the first to pay the price for unsustainable development. Children and young people also have limited opportunity to influence the present or the future. They do not participate in the planning and decision-making process. We adults bear, therefore, a great burden of responsibility — a responsibility that we must take much more seriously in the future.

The first thing that we must achieve if we want to promote a 'child friendly' environment is to gain a better understanding of children's situation today and of the relationship between their health and the environment. We need much more information and research data. This is largely lacking at the moment. This publication, *Children's health and environment: A review of evidence* is therefore a very useful tool for gaining a clearer understanding of the major threats, challenges and opportunities that exist in the field of children's health and the environment.

Promoting a healthy environment for our children is a major task that will require all our energy and application. But we cannot achieve it on our own. If we are to succeed, all the parties involved must co-operate closely with each other. The World Health Organization and the European Environment Agency have given us a good example of how successful close co-operation can be. It's up to us to follow that example.

I hope that our joint efforts will succeed in promoting a more 'child friendly' environment and help us take another step along the road to sustainable development. What is good for our children is good for society as a whole. We need to give children a voice.

Margot Wallström
European Commissioner for the Environment

Foreword

Children's health and the environment lie at the centre of sustainable development. Failing to focus on this concept will amplify not only the health burden of today's children but also of future generations. There is no doubt that protecting children from environmental hazards *now* will be of benefit to the well-being of the population as a whole in the long term. We should not forget that the developing organism of a child is likely to be the most 'sensitive indicator' for the environmental health of populations. Can we afford to continue involving our children in this 'environmental experiment'?

The need to prioritize children's particular vulnerability was addressed by World Health Organization (WHO) Member States at the Third Ministerial Conference on Environment and Health in London, 1999. The European Member States recognized that 'exposure prevention is the most effective means of protecting children from environmental threats to health' and they committed to develop prevention-oriented policies and actions. At the same time, it became increasingly clear that scientific evidence on the specific needs and vulnerabilities of children, as well as scientific uncertainties have to be translated into environmental health policies, including cautionary policies when there is the risk of severe and irreversible damage. This joint publication of the WHO Regional Office for Europe and the European Environment Agency, which is based on the background documentation of the Third Ministerial Conference on Environment and Health, is a first step in this direction. The process leading to this publication has increased the collaboration between WHO, the European Environment Agency and other agencies and institutions in the field of children's health and environment. Moreover, it has strengthened WHO's technical support to governments that have committed to increase their efforts to protect children's health in a number of declarations and policy statements. The forthcoming Fourth Ministerial Conference on Environment and Health, which will be held in Budapest in 2004, will focus on the health of children and future generations in the broader context of sustainable development. This gives further emphasis to the importance of the need to implement the protection of children's health in environmental policies.

Improving the science basis for priority-setting and decision-making and increasing the effectiveness of the use of limited resources in the protection of children against environmental hazards is an important challenge for the future. This publication contributes to the capacity of European institutions and the governments of the WHO European Region to provide appropriate answers to the challenge of protecting children's health against environmental threats.

Marc Danzon
Regional Director,
WHO Regional Office for Europe

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Preface

This publication was prepared by the WHO European Centre for Environment and Health, Rome Operational Division, with support from the European Environment Agency, building on a collection of background papers prepared for the Third Ministerial Conference on Environment and Health in London in 1999. It provides an overview of the available evidence of the relationship between the physical environment and children's health, identifying both research needs and policy priorities to protect children's health from environmental hazards. The report aims to assist policy-makers and public health officials as they develop plans and strategies to address the most serious environmental health threats to children. It is also intended to promote a better understanding of children's environmental health issues within the scientific and professional communities involved in both child health and environmental protection.

The environment in which children live and play is an important determinant of their health and well being even if the extent of its importance is difficult to assess. Damage to children's health is also an important driver for the improvements to those parts of the environment that are associated with such ill health. It is therefore vital that there is close cooperation between environmental and health organisations, not least so as to minimise duplication of efforts.

Many publications on environmental health adopt a toxicant-centred approach, which is appropriate in view of the need to summarise the epidemiology, toxicology, risk assessment and risk-reduction interventions for each specific substance. This publication, which focuses on children rather than on toxicants, is aimed also at providing readers with different, yet equally important, perspectives on children's environmental health issues:

- the developmental perspective, which considers the risks in the different developmental stages, from preconception to adolescence;
- the environmental setting perspective, which considers the various risks that children may face in their different environments;
- the disease perspective, which considers the various health effects and the role played by various environmental hazards.

We hope that these complementary perspectives may help provide a comprehensive overview of risks and exposures as well as a basis for integrated prevention policies.

The chapters in this publication are grouped in four parts:

Part 1 provides an overall view of children's environmental health from a developmental and environmental setting perspective. It describes the biological and psychosocial factors that cause the particular vulnerability of children to environmental threats, from preconception to adolescence, and provides an overview of the environmental hazards in various settings where children live and grow.

Part 2 deals with the specific health effects of environmental contamination, such as asthma and atopic disorders, neurodevelopmental toxicity, cancer, birth defects, waterborne and foodborne gastrointestinal disorders, and injuries.

Part 3 addresses multiple health effects of environmental exposures such as tobacco smoke, pesticides, electromagnetic fields, and ultraviolet radiation. For each chapter current knowledge is summarised, data gaps are identified and actions needed to ensure adequate health protection for children are highlighted.

Part 4 is intended to offer the basis for the assessment and development of child-focused environment health policies. This part includes a discussion of the relevance of environmental justice issues. The methodological challenges relating to the risk assessment process are described, and approaches to decision-making, in the presence of scientific uncertainties, ignorance and multicausality, are proposed. Finally, the rationale and some guiding principles for developing and implementing environmental and health policies, specifically focusing on children, are provided.

This publication is intended to represent a starting point of a collaborative effort, involving experts as well as policy makers, aimed at improving the scientific basis of child-focused environment and health policies. Knowledge in this field is rapidly progressing: new information is continuously made available on old issues; new data are produced; innovative methodological and policy approaches are proposed; and new environmental threats emerge. A focus on emerging environmental threats to children may be particularly useful because children might be the 'canaries in the coalmines', the first ones to suffer from adverse health effects — with possible life long implications for both adults and children. The widespread distribution of endocrine disrupting chemicals in the environment might be such an emerging threat that not only impacts on children today but also on future generations. However, the risks to public health from exposure to endocrine disrupting substances are yet to be fully understood, particularly with regard to the timing of the dose. Due to the importance of this issue, the EEA and WHO will be providing a separate publication on endocrine disrupting chemicals and their importance for children's health later this year.

A cross-cutting issue is the question of how to assess and monitor children's health effects and how to identify and describe a possible association with environmental impacts, ultimately leading to the implementation of protective policies. Several international agencies, including the WHO and EEA, as well as expert groups from different countries, have already started to work in this field. Necessary steps in the establishment of such a monitoring and reporting system in the European Region include: identification of the most significant and sensitive check points in the system, taking into account possible critical pathways, multi-causal effects, synergies and additional factors such as changing diets, behavioural and lifestyle patterns; development of indicators on health outcomes in childhood and linked to relevant environmental exposures; the standardisation of a reporting system based on key indicators that are relevant for all countries in the region; performance of original research to improve the monitoring system and the timely identification of early warnings; and close collaboration between governments, international agencies and experts. The impact of environmental policies on children's health may be evaluated on the bases of key indicators, and the improvement of children's health should be one of the main measures of effective policies.

The evaluation of scientific evidence about the environmental causes of ill health is difficult, and, beyond the cancer and climate change fields, there have been few attempts to produce criteria for classifying evidence based on a 'strength of evidence' approach. A simple 'typology of causation' has been used in the chapter on birth defects (Chapter 6), where the evidence has been roughly sorted into 'very likely', 'likely' and 'possible' causes. This approach needs further development for application in this and other fields of environmental health.

Overall, there are many areas of uncertainty in children's health related to the environment, and consensus among experts may still be lacking on many issues. For all these reasons, we think that the best way to serve the cause of scientific evidence on children's environmental health would be to consider this publication as work in progress, to periodically update it, and to invite scientists involved in this area to contribute to this providing their comments and suggestions. We plan a specific web-site for this purpose.

This monograph is published as an Expert Corner in the EEA's environmental issues series of publications continuing the joint activities of EEA and WHO on children and environmental health that began in 1999. Such reports are designed to stimulate debate on issues that may contribute to the identification, framing and evaluation of environmental policy measures. This emerging and very cross-disciplinary issue poses considerable challenges to WHO and EEA, and hence the need for such an integrated approach and stock taking of expert knowledge. We trust that this will a be useful starting point from which improved reporting and policy support can develop.

Finally, it remains for us to thank all the authors, editors and other contributors who have made this report possible. The chapters in this monograph have been reviewed within the WHO network and we would therefore also like to express our thanks to all those experts involved.

Domingo Jiménez-Beltrán, Executive Director, EEA
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Introduction: Children's health and environment in Europe

Giorgio Tamburlini, Ondine S. von Ehrenstein, Roberto Bertollini

Investing in children's health and the environment

Investing in child health is essential to ensure human and economic development (WHO, 2001; World Bank, 1993). Healthy children have the best chances for future health and productive life, and they have the right to health protection and promotion as citizens of today's world and not just in view of their future contribution to society (UN General Assembly, 1989; UNICEF, 1994). Children's health is, at the same time, a basic human right and a determinant and indicator of economic and human development (UNDP, 1999). On the other hand, a healthy environment is an important determinant of population health and well-being, and nowhere is this more true than in the case of children. The health of children and their protection against environmental hazards lie at the very heart of sustainable development.

This publication is a first contribution to assess the extent of the impact of environmental quality on children's health, and stems primarily from the commitment to children's environmental health taken by the Third Ministerial Conference on Environment and Health, held in London in June 1999 (WHO, 1999a,b).

Child health in the European Region

Although, on the whole, the health of children in the 51 countries of the World Health Organization (WHO) European Region is satisfactory and shows continuous improvement, there are important reasons for concern. Warning signals concern the recrudescence of diseases previously under control, such as diphtheria and tuberculosis, the increase of chronic diseases such as asthma and allergies, and the emergence of new morbidity such as that due to substance abuse, injuries and mental disorders. The health gap between the rich and the less affluent is getting larger across nations and within nations: infant mortality is decreasing in most western European countries but shows little or no improvement in some of the less developed countries and in disadvantaged social groups. For countries and social groups with less favourable trends, the adverse factors involved include the disruption of welfare systems, the decline in public health systems, economic crisis, diminishing social cohesion, and increasing pollution and damage to the physical environment. The direct and indirect consequences of armed conflict and the emerging plague of child labour and sexual exploitation of minors also play a role in causing suffering and worsening health conditions for many children in the European Region.

Health and the physical environment

Health is influenced by a variety of factors, the main ones being genetic inheritance and the economic, social, psychological and physical environment. These factors interact in complex ways, which are specific for each disease and for specific individuals and population groups.

This publication addresses, in relation particularly to the European Region, one of today's major health concerns: the consequences for children's health of the contamination and deterioration of the physical environment. Children are at risk of exposure to more than 15 000 synthetic chemicals, nearly all of them developed over the past 50 years, and to a variety of physical agents. In addition, developing organisms are more vulnerable to environmental contaminants for several reasons, including greater and longer exposure and particular susceptibility windows. We are witnessing an unprecedented increase in the incidence of asthma; some childhood cancers also show an upward trend; injuries still represent a high burden for children and young adults; and there is increasing concern regarding the neurotoxicity, immunotoxicity and endocrine-disrupting properties of substances that are widely dispersed in the environment.

Addressing the physical environment as a determinant of disease and ill-health in children does not imply a clear-cut separation between what is environmental and what is not, and between what is 'physical' and what is not. On the contrary, by focusing on health effects that are at least partially attributable to the physical environment, we intend to contribute to a more comprehensive view of the complex

and multifactorial causal pathways of many diseases, and go beyond the widespread mechanistic and purely biological models of disease causation. For example, children's exposure to environmental hazards is not uniform across social strata, due to the frequent overlapping of poverty, poor housing conditions, polluted environment and restricted access to education, information, prevention and care in disadvantaged population groups. Education and the cultural background play a crucial role in determining exposure, and genetic heritage is often dependent on environmental factors to produce disease.

The physical environment is recognised as one of the factors that influence health, and a better understanding of its interactions with genetic, social and psychological factors is seen as a main challenge for the scientific community. Effective public health policies must reflect this holistic concept of health determinants and be based on multidisciplinary and multisectoral approaches, in which the community is seen as a fully participating partner.

The political background: an increased awareness of the importance of children's environmental health

The protection of children from environmental health threats is based on international agreements designed to ensure that children grow up and live in an environment that is conducive to the highest attainable level of health.

In 1989, the United Nations Convention on the Rights of the Child (UN, 1989) laid down basic standards for the protection of children and declared that they are entitled to special care and assistance. A year later, the World Summit for Children adopted a declaration on the survival, protection and development of children, in which the signatories agreed to work together on taking common measures to protect the environment, so that all children could enjoy a safer and healthier future.

In 1992, the United Nations Conference on Environment and Development (the Earth Summit) built on these achievements by adopting the World Summit for Children's health goals as the health goals for Agenda 21. The protection of children from the effects of a deteriorating environment was given prominence in several chapters of Agenda 21. Chapter 6, 'Protecting and promoting human health', emphasises the need to pay special attention to the protection and the education of vulnerable groups, in particular infants, young people, women, indigenous people and the poor. Agenda 21 urges governments to develop programmes to protect children from the effects of environmental and occupational toxic compounds (UNCED, 1992).

The 1997 Declaration of the Environmental Leaders of the Eight on Children's Environmental Health intensified their commitment to protect children's health from environmental hazards. The environment ministers of the G8 countries acknowledged the special vulnerability of children and committed their countries to take action on several specific environmental health issues such as chronic lead poisoning, microbiologically contaminated drinking-water, endocrine-disrupting chemicals, environmental tobacco smoke and poor air quality. They called on financial institutions, WHO, the United Nations Environment Programme (UNEP) and other international bodies to continue ongoing activities and to pay increasing attention to children's environmental health, in particular to the economic and social dimensions of children's health. The 1997 Declaration of the Environmental Leaders of the Eight on Children's Environmental Health includes the following policy approaches, which may contribute to the development of policies aimed at the protection of children in Europe:

- Preventing exposure is the most effective way of protecting children's health from environmental threats. Governments should therefore develop policies that seek to prevent childhood diseases by preventing exposures to environmental agents, on the basis of the precautionary principle.
- National policies should take into account the specific exposure pathways and dose-response characteristics of children when conducting environmental risk assessment and setting protective standards.
- Research should be promoted in order to gain a better understanding of the particular exposure and sensitivities of infants and children to environmental hazards. Exchange of information on research results and the development of regulatory systems should also be promoted.
- Awareness of the environment and health should be promoted, so as to enable

families to better protect their children's health.

In addition, the environment ministers of the G8 countries committed their countries to fulfilling and promoting the Organisation for Economic Co-operation and Development (OECD) declaration on risk reduction for lead (OECD, 1996).

The pan-European strategy to phase out leaded petrol (endorsed by the United Nations Economic Commission for Europe, UNECE, Fourth Ministerial Conference 'Environment for Europe' in 1998) and the declaration on the phasing-out of added lead in petrol (signed by representatives of 32 Member States of UNECE at that conference) committed countries to banning the use of added lead in petrol for general use by road vehicles by 1 January 2005.

The 1998 UNECE convention on access to information, public participation in decision-making and access to justice in environmental matters (the Aarhus Convention), recognises the important role of non-governmental organisations (NGOs) and the value of public awareness for environmental policy-making (UNECE,1998). In this context, it is important to acknowledge that children are not only consumers with rights, but also citizens who can play an active role in society for their own protection, and to remember that, in 1996, children were declared full citizens of the European Union.

The policy of health for all in Europe in the 21st century (WHO, 1999c), adopted by the European Member States of WHO in September 1998, emphasises the importance of considering the environmental determinants of human health and recommends strategic activities to ensure a healthy start in life. Specific recommendations are made in areas such as air quality, drinking-water and wastewater, solid waste and radiation. Target 10 in that policy states that, by the year 2015, people in the WHO European Region should live in a safer physical environment, with exposure to contaminants hazardous to health at levels not exceeding internationally agreed standards.

The Third Ministerial Conference on Environment and Health, held in London in June 1999, emphasised the importance of protecting children from undesirable environmental exposures, identified priority areas and made a set of recommendations for countries to take effective action to ensure that people enjoy the human right of growing up and living in a clean and safe environment. The final declaration included several points specifically addressing children's health and the environment (WHO, 1999a):

'We recognize the special vulnerability of children and commit to develop policies and actions to achieve a safe environment in which children can develop to their highest attainable level of health. To this end, we adopt the 1997 Declaration of the Environmental Leaders of the Eight on Children's Environmental Health as a framework to follow in developing policies and actions for our countries.'

'We recognize that exposure prevention is the most effective means of protecting children from environmental threats to health and we will develop prevention-oriented policies and actions. We will facilitate and promote public access to environmental and health information and education as well as actively encourage the participation of children as interested stakeholders.'

'We commit to pursue the recommendations to:

a) develop preventive and management strategies for asthma, evaluate the actual incidence and prevalence of asthma in European countries, identify research needs and orient research directions

b) promote the exchange of information and experiences in implementing public health interventions on childhood injuries, and environmental tobacco smoke

c) develop and implement public health interventions to prevent asthma, accidents and injuries, as well as smoking and the effects of environmental tobacco smoke

d) promote and encourage public health measures into areas of emerging concern to children's health on the basis of the precautionary principle'

'We request WHO to convene an international platform to support, promote and coordinate the actions recommended above, and to act as a secretariat for this

platform. We ask the EC, EEA, OECD, UNDP, UNEP, UNICEF and other international organizations and NGOs to share in the responsibilities of this platform to promote research, provide education, training and technical assistance to countries and ensure public participation. We commit to cooperate in the efforts to exchange information and experiences through the platform, and to help one another in developing policies and public health interventions. We will support the establishment of this platform and work together with national and international organizations in implementing the recommended actions.'

In November 2001, the European Environment and Health Committee (EEHC) discussed the working title "The Future for our Children" within the broader context of sustainable development as the overall theme for the Fourth Ministerial Conference on Environment and Health to be held in Budapest in 2004. Within this framework areas to be addressed and further specifications will be defined in the process of the Conference preparation, which has now initiated (EEHC, 2001).

All these declarations and policy statements show that the commitment to a healthier and safer environment continues at the highest level. The awareness that children lie at the very heart of sustainable development makes the protection of their health and the promotion of their wellbeing a highly strategic issue. Europe has been at the forefront in recognising the fundamental rights of children and in establishing principles such as the right to self-determination, health and sustainable environment, and will continue to play a leading role in the further development and application of these principles. European institutions and the governments of the European Region are called — also as a contribution to the whole international community — to provide appropriate answers to the challenge of protecting children's health and the promotion of their wellbeing.

References

Environment Leaders' Summit of the Eight, 1997. *Declaration of the Environment Leaders of the Eight on Children's Environmental Health*, Miami FL, 5-6 May 1997. http://www.g7.utoronto.ca/g7/environment/1997miami/children.html

European Environment and Health Committee, Minutes of the 5th meeting, 19–21 November 2001, Istanbul. http://www.eehc.dk/

OECD, 1996. *Resolution of OECD the Council Concerning the Declaration on Risk Reduction for Lead*, OECD Document No C(96)42/FINAL, adopted by the Council on its 869th Session of 20 February 1996 [C/M(96)4/PROV].

The World Bank, 1993. *World Development Report 1993 : Investing in health*, Oxford University Press, New York, 1993.

UN Conference on Environment and Development, 1992, UNCED 'Earth Summit', 1992. Rio de Janiero, 3–4 June

UN General Assembly, 1989. Convention on the Rights of the Child, 20 November 1989.UN General Assembly resolution 44/25 http://www.unicef.org/crc/crc.htm

UNECE, Environment and Human Settlements Division, 1998. *Convention on access to information, public participation in decision-making and access to justice in environmental matters*, Aarhus, Denmark, June 1998.

UNICEF, 1994. *The state of the world's children 1994*, Oxford University Press, New York.

UNDP, 1999. *Human development report 1999*, Oxford University Press, New York.

UNEP, 1999. *Global environment outlook GEO2000,* Earthscan Publications, Nairobi, Kenya.

WHO, 1999a. *Declaration of the Third Ministerial Conference on Environment and Health (*London, 16-18 June 1999), WHO Regional Office for Europe, Copenhagen.

WHO, 1999b. *Children's health and the environment,* document EUR/ICP/EHCO 02 02 05/16, WHO Regional Office for Europe, Copenhagen.

WHO, 2001. *Report of the WHO Commission on Macroeconomics and Health*, 2001, World Health Organization, Geneva. http://www. who.int

WHO, 1999c. *Health21: The health for all policy framework for the WHO European Region, European Health for All Series No 6*, WHO Regional Office for Europe, Copenhagen.

PART I:
An overview

Alina Shovsh (age 6), Ukraine

1. Children's special vulnerability to environmental health hazards: an overview

Giorgio Tamburlini
Contributing authors: Kristie Ebi, Bettina Menne

Summary of existing knowledge
- Developing organisms are more vulnerable to environmental toxicants for a variety of reasons including greater and longer exposure and particular susceptibility windows
- Exposure during the various developmental stages from conception to adolescence is also strongly influenced by social and psychosocial factors

Main challenges
- To know more about susceptibility to environmental contaminants during specific developmental stages and about the effects on children of global environmental changes
- To adopt a multi-factorial approach to causation of environment-related diseases in children

Action points
- To establish child-focused protective policies based on better knowledge of biological susceptibility, of socio-economic and psychosocial determinants of environmental exposure and global changes

1.1. Introduction

Children are particularly vulnerable to many environmental threats, including a contaminated and unsafe physical environment. This heightened susceptibility derives primarily from the unique biological features that characterise the various stages of development from conception to adolescence. But it is not just the biology of growth and development that leads to the special impact of environmental threats on children: fetuses, infants, children and adolescents are also special in the way a variety of social and psychosocial factors influence their exposure as well as the consequent health effects.

This chapter offers an overview of the various biological and social factors that influence children's vulnerability to environmental health hazards, as well as of their interactions in the different developmental stages, thus providing the basis for better understanding the need for environmental and health policies specifically aimed at protecting children.

1.2. Biological factors

Increased vulnerability during growth and development

From conception to adolescence, rapid growth and development processes occur that can easily be disrupted by exposures to toxicants. Cell growth is particularly rapid in the embryo, providing more opportunity for toxicants to cause mutations and congenital anomalies. During this period, too, structures are developed and vital connections are established. For example, during the first years of life, most of the development of the nervous system takes place. Since the nervous system has a limited capacity to repair any structural damage, if cells in the developing brain are destroyed by chemicals such as lead or mercury, or if vital connections between nerve cells fail to form during critical periods of vulnerability, there is a high risk that the resulting dysfunction will be permanent and irreversible (Rice and Barone, 2000). The consequences can be loss of intelligence and alteration to normal behaviour. Thus the fetus and infant have different vulnerabilities to damage than do adults and are in general more likely to suffer damage. This aspect of toxicology has tended historically to receive relatively low priority in the setting of environmental standards.

Metabolism

Children's metabolic pathways, especially in the first months after birth, are immature. As a consequence of this biochemical immaturity, children's ability to detoxify and excrete chemicals differs from that of adults. Although in a few instances children are actually better able than adults to deal with environmental toxins, more commonly they are less able than adults to deal with toxic chemicals and are thus more vulnerable to them. This is well known in paediatric pharmacology: lower per kilogram doses and longer intervals are recommended for most drugs during the first weeks and months of life (Chemtob, 1991).

Greater exposure

Children are in proportion more heavily exposed, per unit of body weight, to

environmental toxins than adults. This is well recognised in radiation biology, where the risk of radiation-induced cancer is greater for children than for adults: it is 16 times greater for a three-month-old; eight times greater for a one-year-old; four times greater for a five-year-old and two times as great for a 10-year-old (ICRP, 1991). Children drink more water, eat more food and breathe more air than adults in relation to their body weight. For example, the air intake of a resting infant is twice that of an adult (Snodgrass, 1992) and an infant in the first six months of life drinks several times as much water per kilogram of body weight as the average adult does. Children aged one to five years eat three to four times more food per unit body weight than the average adult (Bearer, 1995). Children also have unique food preferences, due to dietary choices and higher energy requirements. For example, consumption of soft drinks by preschool and school children is several times that of adults while preschool children's consumption of milk and dairy products is much higher than that of school children and adults. Absorption rates may also be greater in the child: for example infants absorb as much as 50 % of the lead present in food while adults have an uptake of only 10 % (Rye, 1983).

Longer time at risk

Children have more years of life ahead of them than adults, so they have more time to develop chronic diseases that take several decades to appear and which may be triggered by early environmental exposure or be determined by continuous exposure. Diseases with long latency periods include benzene-induced leukaemia and sunlight-induced skin cancer.

Long-term and inter-generational effects of bio-accumulation

Every member of human society, whether adult or child, carries body burdens of an estimated 300 or more chemical residues that could not have been present in their grandparents. The fact that a compound bio-accumulates tells us that the body has difficulties in metabolising and eliminating it. This is essentially because for many novel compounds we simply do not possess enzymes to break down their molecular structures. Therefore such chemicals tend to build up in the body with increasing age. They can then be passed on to the next generation across the placenta and in the breast milk, often at high concentrations. In the case of dioxins and polychlorinated biphenyls (PCBs) it is known that current body burdens in a proportion of the population may be sufficient to cause measurable deficits in their offspring (Sauer *et al.*, 1994; Jacobson and Jacobson, 1996; Vreugdenhil *et al.*, 2002).

1.3. Age-specific susceptibility

A child's exposure and susceptibility to environmental hazards varies with each developmental stage: preconception, embryonic and fetal period, neonatal period, first three years of life, preschool and school age, and adolescence. There are special aspects of susceptibility deriving from the biological and psychosocial characteristics of the various developmental stages that need to be understood to better assess risks and target protective policies (Gitterman and Bearer, 2001).

Preconception

Preconceptional parental exposure to toxicants can have a major impact on pregnancy outcome. This kind of exposure threatens the health of the future human being in two ways: toxicants can directly affect the maternal or paternal reproductive organs, as in the case of ionising radiation, or they can be stored in the mother's body and later mobilised during pregnancy to affect the developing fetus and the offspring, as is the case with PCBs (Jacobson and Jacobson, 1996).

Paternal exposure to toxicants might affects the offspring as well. It is known that the short life span of sperm limits the period of their vulnerability to toxicants, while the rapid differentiation of sperm increases their susceptibility to harm from exposure. For example, sperm abnormalities are associated with male cigarette-smoking, which may induce mutagenesis and, hence, an increased cancer risk in the man's offspring (Ji *et al.*, 1997). Associations have been found between paternal exposure to a variety of occupational toxicants and increased risk for spontaneous abortion, stillbirth and congenital anomalies (Savitz, 1989; Brender, 1990).

The embryonic and fetal period

Embryo's tissue is particularly susceptible to damage from environmental toxicants due to rapid cell growth. The more the cell divisions occur, the greater the risk that toxicants may cause cell damage, which can lead to

congenital anomalies and to later development of cancers.

The placenta in some cases acts as a barrier and in other cases (compounds of small molecular weight, such as carbon monoxide or lipophylic compounds, such as polycyclic aromatic hydrocarbons or ethanol) allows toxicants to pass through to the fetus. Lead is thought to displace calcium, iron or other nutrient metals, and thus be transported across the placenta. Many toxicants reach the fetus independently of the placenta, including ionising radiation, electromagnetic fields, heat and noise.

There are several notable examples of toxicants crossing the placenta and causing harm to the fetus, environmental tobacco smoke being the most widespread and well known.

The neonatal period

In the newborn baby, organs and tissues, including the nervous system, lung, blood, somatic cells and epithelium, continue to undergo rapid growth or have rapid turnover, thus increasing their vulnerability to toxicants. The neonatal stage is also characterised by a highly permeable gastrointestinal tract. Toxicants are ingested mainly through packaged formula or breast milk, or absorbed through dermal contact. Formula-fed infants have an average daily consumption of over 150 ml/kg/per day, which explains why elevated blood lead levels caused by tap water have been found in infants (Gittermann and Bearer, 2001). Parental occupational exposures transported to the home environment on clothes, shoes and body can also affect the neonate., as demonstrated by documented case reports of lead poisoning resulting from exposure to dust carried home on the father's clothing (Gerson,1996).

Phthalates, a family of chemicals used to make polyvinyl chloride (PVC) plastic, solid and flexible, can produce adverse effects on the developing male reproductive tract and in the long run have a carcinogenetic effect. Phthalates are widely used in objects to which newborn babies, and particularly premature and sick babies, may get exposed for long periods, such as pacifiers, intravenous catheters and tracheal tubes (Muehlberger and Rossi, 2000).

Particular attention should be paid to substances that come into contact with the baby's skin, because skin is highly permeable during the newborn period. For the surface area of skin covered with a chemical, a newborn baby may absorb up to three times the amount absorbed by an adult (Plunkett *et al.*, 1992). At birth, the respiratory tract also becomes a potential route for the absorption of toxicants. Fetal lung fluid is rapidly cleared by the newborn's pulmonary lymphatic system, demonstrating the integrity of this clearance pathway. This lymphatic route then becomes the primary route for absorption of airborne pollutants, including environmental tobacco smoke.

The first three years

Children in this developmental stage have higher rates of respiration and calorie consumption per kilogram of body weight than adults because of their higher metabolic rate. This factor makes infants and toddlers more vulnerable to inhaled and oral environmental exposure. Children's hands-to-mouth behaviour, shorter stature and their play close to the ground increase their exposure via inhalation and ingestion to toxins in dust, soil and carpets. It also increases exposure to toxicants from the lower layers of the air, such as certain pesticide vapours. Lead poisoning, for example, frequently occurs by this mechanism. Other sources of toxicants include the area around the house, which may be contaminated with pesticides.

Diet can also become a source of exposure. Legal levels of food additives are calculated on the basis of a lifetime exposure for an adult. The infant's higher rate of calorie consumption per kilogram body weight means that any food additive will constitute a higher dose for an infant. Furthermore, by virtue of their processing, infant foods tend to have higher concentrations of additives and residues such as pesticides.

There is also a qualitative difference in the infant and toddler's diet. It is higher in fruit, vegetables and milk products, and tends to be less varied than the average adult diet. These factors affect the relative ingestion of toxicants in the infant.

The preschool and school-age child

In this developmental stage, children explore new environments and are consequently exposed to new sources of contamination.

The school itself may be a source of contamination due, for example, to the

presence of friable asbestos in many buildings. Schools may be situated near old industrial sites with unknown emissions and waste. In rural areas schools often use small private wells that may be contaminated with lead and pesticides. Exposure at school may include poor indoor air quality, high allergen burdens and infectious organisms. Children may also use toxic arts-and-crafts products, while 'non-toxic' art products may cause health problems if ingested or used improperly. Exposure to outdoor air pollution may be particularly important depending on place of residence and periods spent in highly contaminated environments.

Additional hazards derive from transport, such as air pollution (outdoor and inside vehicles) noise, traffic injuries, and reduced opportunities for physical exercise and autonomous travel.

The adolescent

The biology of adolescence provides opportunities for unique effects of toxicants both in terms of disruption of functions and disruption of maturation: maturation of a number of organs and systems occur during this period. Target tissues may differ in adolescents as a result of the changes brought about by puberty. Growing, dividing, differentiating tissues are those that are most sensitive to environmental influences. During puberty, rapid growth occurs in the viscera, skeleton and muscles. There is also development and differentiation of the reproductive system. Adolescence is a time of increased risk of infectious disease and accidental injuries. Exposure can also change. Increased food intake associated with rapid adolescent growth alters exposure to food contaminants. The typical adolescent exploratory and risk-taking behaviour also plays a role in increasing exposure, and we know that health-related behaviour is typically influenced by peers and by the media. Voluntary drug consumption increases, including drinking, smoking and substance abuse, and the use of over-the-counter, prescription and performance-enhancing drugs.

Finally, adolescents may be employed in jobs that expose them to occupational hazards and involved in illegal activities such as the sex market. Employment can expose them to contaminants as well as to risk of accidents due to unsafe working environments and dangerous equipment (Parker *et al.*, 1994; Woolf, 2000). The exploitation of children and adolescents in the sex market is a new and growing hazard, with dramatic consequences for those involved.

1.4. Economic, social and psychosocial factors

Children's special susceptibility to environmental threats is not confined to the biology of growth and development. A variety of external factors, at macro as well as micro level, influence the exposure of fetuses, infants, children and adolescents to various environmental threats and consequently affect their health. These factors include primarily the economic and social status: environmental problems in all countries tend to be borne more heavily by poorer people (see Chapter 3.1). The interaction of these and other factors such as the educational background, place of residence, gender, ethnicity and the knowledge, attitudes and behaviour of parents, teachers and peers determines multiple exposures and risks and as a consequence different and possibly cumulative health effects (Spencer, 2000). This depends not only on genetic susceptibility but also on different exposure patterns deriving from factors such as awareness of risk, concomitant exposures such as alcohol consumption or smoking, access to information, access to preventive as well as diagnostic and curative care and the role of protective factors. For example, the same concentration of a specific pollutant can be markedly more harmful to one child than to another depending on the protective effect of the home environment during the first years of life (Walkowiak *et al.*, 2001).

The importance of specific environments and driving forces in shaping behaviour and lifestyle

The way social factors influence exposure and risk differ in many aspects from the case of adults. There are specific environments that characterise child life and represent the framework within which social and biological determinants play their role. These are primarily the family and the school. There are driving forces at the macro level, such as the state, the market, the media and the communication system, that influence children's lives in a particular way by establishing rules and regulations and by offering information as well as by influencing income distribution, educational opportunities, place of residence, consumerism, lifestyles and, ultimately, health-related behaviour and exposure to health hazards. For example, many

adolescents are involved in working activities that expose them to toxicants and injuries without being able to protect themselves because they are unaware of the dangers and because there is neither legislation nor sufficiently active and informed caretakers to protect them. Child labour laws are often modified to adapt to social needs, such as those of a family farm. In other circumstances, laws are violated outright or disregarded in hiring teenagers (ILO, 1996).

In conclusion, if we want to establish effective policies, we must understand how these various and changing environments and forces contribute to shape the lifestyles of children and adolescents and can ultimately influence exposures and risks and determine health outcomes as well as the success of health policies.

The changing role of the family and the school

The family has historically been the most important institution for children. The concept of family is difficult to define and children grow up under very different conditions: an increasing number of children grow up in single-parent families or in reconstructed family formations and consequently see their parents separately. The social networks of the child include a bigger vertical network than in the immediately preceding historical era, with multiple sets of parents and in addition grandparents who still are alive and active. On the other hand, there are fewer siblings in families and, because of separations and increasing mobility, the networks are geographically more spread out (Rutter, 1996).

The function of the family has also changed. A single important factor is the double employment of the parents as women have increasingly joined the workforce. Child rearing and nurturing is pushed into other institutions. Even in functional families, parents could be working in different cities, and children are reared by public or private providers and the family members only come together at holidays or extended weekends.

The consequence is that even within similar communities and social groups there may be many different family backgrounds influencing children's lives and behaviour.

The growing child develops specific types of behaviour and lifestyle depending on values, relationships and emotions at least as much as on knowledge. Thus, it may happen that the kind of general influence that the young receive at school through teachers and peers (the so-called hidden curriculum) may largely outweigh the possible effect of messages related to health and health education channelled by the school itself, through its formal curriculum. School relationships, with adults as well as with peers, are potent determinants of child behaviour although the school itself seems to be rather unaware of this hidden curriculum and of the shaping environment that it provides.

The increasing role of the media and the communication industry and the changing role of science

The media are increasingly pervasive. They are potent vehicles of market forces through overt and hidden advertising. They appeal to children and adolescents, particularly the film-making industry, radio and television. Music is a medium itself, at least for youth. Media can be powerful vectors of conformist as well as of marginal, non-conformist behaviour. They can help or hinder the acquisition of knowledge. As a consequence, they play an important role in influencing exposure to environmental risks.

In spite of its spectacular advances, the legitimacy of science is thrown into question in the eyes of the people and sometimes of the young. Other forces and explanations (such as the market or 'new age' ideology) compete for the command of mind. Youth are increasingly exposed to science as well as to new paradigms and models that relegate science to a marginal role. The way these various paradigms influence families and young people must be understood if we want to disseminate information based on scientific rationality.

There is, therefore, a need to identify the driving forces that shape types of behaviour by influencing the learning experience in each specific setting. Learning is no longer bound to the traditional education system or the family. The building of competence is obtained to various degrees from the school system, from peers, from technological communication systems and from realities beyond traditional institutions.

The shift of power from the state to market forces

The state regulates and represents the legal rights of its citizens including cultures and traditions. In contemporary Europe most

European states are in a process of delegating their responsibilities: more decision-making is left to local communities. This is thought to increase democratisation and the possibilities for individuals to influence and participate in the decision-making process. At the same time, a significant proportion of economic and political power is shifted outside the state to big multinational corporations, and there is a tendency towards fewer regulations so that market forces become increasingly strong in determining policies and opportunities, sometimes at odds with the public interest and specifically with public health interests. Short-term economic profits may then easily become more important than the sustainable development of the environment and the health of the population (Wagner, 1996), particularly when the specific needs of subgroups of the population are not fully recognised and are politically underrepresented, as is the case with children and disadvantaged communities.

The impact of urbanization

The proportion of the world's population living in large towns or cities has grown from around 5 to 50 % over the past two centuries. Due to an earlier start and a far smaller demographic pressure, cities have expanded less rapidly in the European Region than in most developing countries. Nevertheless, the impact of urbanisation has been quite important (McMichael, 1999). There are three main pathways through which the urban environment affects human health (McMichael, 2000): the social changes that accompany urbanism and the consequent changes in behaviour-based risks to health; the microbiological and toxicity risks deriving from the physical urban environment; and the large scale impact of urbanisation on the biosphere.

Depending on how cities are structured, on the quality of housing, transport and social services, and in general on the quality of communty life, the ultimate balance of risks and benefits of urban life can be quite variable. Certainly, in children's everyday life, risk and exposure are strongly influenced by the quality of the urban environment. The urban poor may be among the most heavily exposed to environmental hazards, while the more affluent can fully enjoy the opportunities given by easy access to information and by enriching social relationships.

1.5. Vulnerability to global environmental changes

Since the 1980s, the worldwide multidimensional integration of world economy, politics and culture has changed environmental and health dynamics. International assessments have shown that the global commons, such as the climate system, the ozone layer and biodiversity, are changing and that natural resource degradation is an ongoing process. The vulnerability of children to these changes depends on: the extent to which health, or the natural or social systems affecting health outcomes, are influenced by changes in weather and climate (i.e., exposure-response relationship); the exposure to these changes; and the ability of institutions, systems and individuals to handle change.

Climate variability and change

The IPCC Third Assessment Report (IPCC, 2001) estimates that the global average land and sea surface temperatures have increased by 0.6 ±0.2 °C since the mid-19th century, with most changes occurring since 1976. Most of Europe experienced an increase of about 0.8°C in surface air temperatures during the 20th century. Patterns of precipitation also changed with arid and semi-arid regions becoming drier, while other areas, especially mid-to-high latitudes, becoming wetter. Projections of regional changes over the next 100 years suggest that temperature and precipitation changes are likely to exceed those experienced during the 19th century.

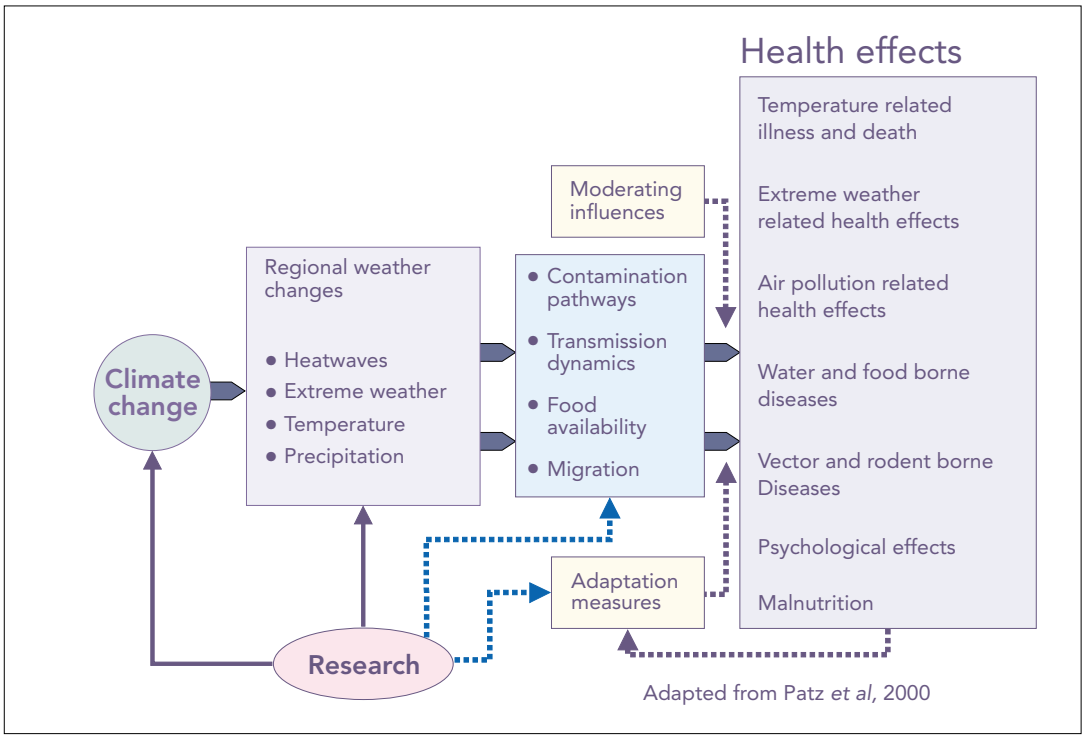
The effects of climate variability and change on human health may be direct or indirect. Figure 1 gives an overview of the major pathways between climate change and health (Patz *et al.*, 2000). For example:

- Climate change may indirectly affect exposures to air pollutants by inducing alterations in weather patterns that could increase or decrease local concentrations of air pollutants, particularly ozone. Exposure to elevated ozone concentrations can lead to decreased lung function, increased airway reactivity, lung inflammation and increased respiratory symptoms (Bernard *et al.* 2001).

- Although risks from flooding in Europe have been greatly reduced by technical and infrastructural measures, the experience of the Central European floods of 1997, when more than 100 people died, shows that floods can have a major impact on health and welfare even in industrialised countries. Flood risk may increase with climate change.

Figure 1.1. **Pathways by which climate change affects health**

Source: Patz *et al.*, 2000



Desertification

Desertification and droughts affect food production, which can result in malnutrition, hunger, and famine. Malnutrition affects all age groups across the entire life span, with a profound influence on growth and development in infancy childhood and adolescence. Climate change may affect the yields of major food crops. The global food trade system may be able to absorb these changes at the global level, but poverty and inequality may result in distributional issues at the local level. In the European Region, vulnerable areas include the Central Asian republics.

Stratospheric ozone depletion

The stratospheric ozone layer is essential in absorbing UV radiation, in particular UVC and UVB. A 10 % decrease in stratospheric ozone is projected to cause an additional 300 000 non-melanoma skin cancers and 4 500 melanoma cases per year, worldwide (WHO, 1994). For each 1 % decrease in stratospheric ozone, the average annual percent increases in the incidence of nonmelanoma skin cancer range from 1 % to 6 %, and for squamous cell carcinoma and basal cell carcinoma from 2.0 ±0.5 % (WHO, to be published in 2002). Over the last two decades it has become clear that UVB exposure can impair specific and non specific immune responses (WHO, 1994). Children are particularly vulnerable to the adverse health effects of stratospheric ozone depletion because of the long time period of exposure, and the length of time available for an adverse health effect to appear.

The vulnerability of children to the effects of global and local environmental changes and the ways in which underlying factors, such as economic and social conditions, welfare and health systems, can influence these effects are well illustrated by the case study in Box 1.1.

Box 1.1.

Case study: A vicious environmental cycle-the case of the autonomous Republic of Karakhalpakastan: can children's health cope with additional environmental pressures

In 2000 drought and water shortages affected northwest Uzbekistan, in particular the autonomous Respublika Karakalpakistan. 45000 people faced severe food shortages, and required international food assistance. These climatic extremes struck an area already severely affected, childhood mortality rates being four times higher than in EC countries. The leading causes of infant mortality are diseases of the respiratory system (ca. 50 % of all deaths). Exposure to high levels of dusts, exacerbated by frequent dust storms, with daily average concentration of total suspended particles (TSP) in the range of 300 µg/m3, has lead to high incidence of bronchial asthma (178 per 100,000 population). 70 % of the drinking water samples taken do not meet chemical and microbiological standards. 40 % of the population does not have access to drinking water.

The incidence of acute intestinal diseases in children is still between 100-400/100.000 (UN, 2002). The average daily calorie consumption per capita was 2,590 kcal in 1998, one of the lowest in the WHO European Region. Chronic malnutrition is present among the poorest households, resulting in protein-energy malnutrition and several micronutrient deficiencies, such as Vitamin A and C deficiencies and Iron deficiencies. (WHO, 1999a)

Climate predictions for the region show that droughts and desertification will increase, with a decrease in crops availability and a reduction in flow of the Syrdarya and Amudarya rivers of 28 % and 21 %, respectively (Uzbekistan National Communication, UNFCCC, 2000). These predictions will add even more pressure on the present health situation amongst children in the Karakhalpakastan Republic. Therefore there is an urgent need to promptly start sustainable preventive measures.

1.6. The complex nature of the causal mechanisms of disease and the need for a multifactorial approach

This publication deals with hazards to the health of children deriving from a variety of toxicants in the physical environment. But the causal link is never a linear link, nor a purely biological one, as pathways of causality are typically complex and multifactorial. Ill-health is always multifactorial, even when causes may appear entirely biological, as in genetic disease. The examples given of how different factors, environments and driving forces shape children's lives and consequently influence the way they are directly or indirectly exposed to environmental threats should make it clear why a purely deterministic and monofactorial 'toxicological' approach to a safe environment for children cannot be sufficient and why a broader approach is needed (EEA, 1999).

Identifying the determinants of ill-health in populations and in specific groups and communities is a difficult task, but an essential one to any public health strategy (WHO, 1999b). Adverse health outcomes are the result of variable combinations of host genetics, host state (including social and 'lifestyle' factors) and exposure to other environmental stresses, both indoors and outdoors. All these factors can operate at different times, influencing each other in various ways, and causing changes in cells, tissues and functions that may ultimately lead to quite variable health effects. A theory of multifactorial etiology, including biological as well as socio-economic and psychosocial factors, that is to say a bio-psychosocial approach, is essential to establish sound and effective public health policies.

Table 1.1. provides a synoptic view of susceptibility to environmental hazards at different ages and, at the same time, offers examples of which multisectoral approches are needed to carry out the appropriate preventive interventions.

Table 1.1. **Environmental exposure, vulnerability and preventive interventions according to developmental stages from preconception to adolescence**

Source: Modified from Bearer, 1995

Developmental stage	Developmental characteristics	Exposure	Vulnerability	Preventive interventions
Preconception	Lack of awareness of gonadal exposure	All environmental exposures	Potential for genotoxicity	Regulations and control on possible sources (waste sites) Information for adolescents and the general public
Pregnancy	High calorie intake Permeable placenta	All environmental exposures Ad hoc diagnostic investigations	Potential for teratogenicity due to embryonic development of various organs and apparatuses	Regulations on occupational and other environmental exposures (environmental tobacco smoke) during pregnancy Health information for couples
First three years	Oral exploration Beginning to walk Stereotyped diet	Food (milk and baby foods) Air (indoor) Tap/well water Mattress/ carpets/floor	Potential for damage to brain (synapses) and lungs (developing alveoli) Allergic sensitisation Injuries	Regulations and control on air pollution (environmental tobacco smoke and others) road traffic, lead, radon Provision of safe water and adequate sanitation Anticipatory advice for injury prevention
Preschool and school-age child	Growing independence Playground activities	Food (milk, fruit, vegetables) Air (indoor and outdoor)	Potential for damage to brain (specific synapse formation, dendritic trimming) and lungs (volume expansion) Injuries	Regulations and control on outdoor (road traffic) and indoor pollutants (air quality standards, tobacco smoke, building and play materials, noise) and food (pesticides) Information for parents, school teachers and children
Adolescence	Puberty Growth spurt Risk-taking behaviour Youth employment	Food (any) Air (outdoor and indoor) Water Occupational exposure	Potential for damage to brain (continued synapse formation) lung (volume expansion) and pubertal development Injuries	Regulations on child labour, injury prevention, tobacco smoke Health information and regulations in recreational areas (ex. Clubs) for young people

Summary

Children are particularly vulnerable to all environmental threats, including a contaminated physical environment. This susceptibility has above all specific biological causes: children breathe, eat and drink more than an adult with respect to their body weight; they can be exposed for a longer time and during highly sensitive periods such as the embryo-fetal period, the first years of life and adolescence, when organs and functions are developed. Their metabolism is different as well as their awareness of risk.

Children's exposure to environmental hazards varies with each developmental stage: preconception, embryonic and fetal period, neonatal period, first three years of life, preschool and school age, and adolescence. There are special aspects of susceptibility deriving from the biological and social characteristics of the various developmental stages that need to be understood to better assess risks and target protective policies.

The reasons for children's particular susceptibility to environmental threats is not confined to biology of growth and development. Fetuses, infants, children and adolescents are also special in that their exposure to various environmental contaminants is influenced by a variety of social factors at macro as well as micro level, and the way these factors influence exposure and their health consequences is also peculiar in many respects. It is important to understand the driving forces that shape children's lives and behaviour if we want to promote health at the individual as well as at the group, family or community level.

The impact of global environmental changes on human health and the specific vulnerability of children represents is a growing concern for the future.

A bio-psychosocial approach based on a multifactorial etiologic framework is essential to establish sound and effective environmental protective policies.

References

Bearer, C.F., 1995. How are children different from adults? *Environmental Health Perspectives*, Vol 103 (suppl 6), pp. 7–12.

Bernard, S.M. and Ebi, K.L., 2001. Comments on the Process and Product of the Health Impacts Assessment Component of the National Assessment of the Potential Consequences of Climate Variability and Change for the United States, *Environmental Health Perspectives*, Vol 109 (suppl 2), pp. 177–84.

Brender, J.D., 1990. Paternal occupation and anencephaly, *Am J Public Health*, Vol 131, pp. 17–24.

Chemtob, S. 1991. Basic pharmacological principles, in *Fetal and neonatal physiology* (edited by R.A. Polin and W.W.Fox), W.B. Saunders, Philadelphia, p 109.

Dahlgren, G., 1995. *European Health Policy Conference:opportunities for the future. Volume II — Intersectoral action for health.* WHO Regional Office for Europe, Copenhagen.

EEA, 1999. *Children in their environment: Vulnerable, valuable and at risk*, WHO Ministerial Conference on Environment and Health, London, 16–18 June 1999, European Environment Agency. http://reports.eea.eu.int:80/CITE01/index_html (in 2001)

Gerson, M.,Van Der Eeden, S.K.and Gahagan, P.,1996. Take-home lead poisoning in a child from his father's occupational exposure, *Am J Int Med*, Vol 29, pp. 507–8.

Gitterman, B.A., and Bearer, C.F., 2001. A developmental approach to pediatric environmental health. *Pediatr Clin N Am*, Vol 48, pp.1071–84.

ICRP, 1991. *1990 Recommendations*, International Commission on Radiological Protection Publications, Pergamon Press, Oxford.

ILO, 1996. *Child Labour: Targeting the intolerable*, International Labour Office Publications, Geneva.

International Panel on Climate Change, IPCC, 2001. *Climate Change 2001: Impacts, Adaptation and Vulnerability. Contribution of Working Group II to the Third assessment Report*, Cambridge University Press, Cambridge.

Jacobson, J.L. and Jacobson, S.W., 1996. Intellectual impairment in children exposed to polychlorinated biphenyls in utero, *N Engl J Med*, Vol 335, pp. 783–9.

Ji, B., Shu, X., Linet, S.M. *et al.*, 1997. Paternal cigarette smoking and the risk of childhood cancer among offspring of nonsmoking mothers, *J Natl Cancer Inst*, Vol 89, pp. 238–44.

McMichael, A.J., 1999. Urbanisation and urbanism in industrialised nations: 1850-present implications for human health, in *Urbanism, health and human biology in industrialised countries* (edited by L.Schell and S.Ulijasek), Cambridge Univ. Press, Cambridge.

McMichael, A.J., 2000. The urban environment and health in a world of increasing globalization: issues for developing countries, *Bull WHO*, Vol 78 (9), pp. 1117–26.

Muehlberger, M. and Rossi, M., 2000. *Neonatal exposure to DEHP (di-2-ethylhexil phthalate) and opportunities for prevention in Europe*, Health Care without Harm, CNEED, Paris.

Murray, C.J.L. and Lopez, A.D., eds., 1996. *The Global Burden of Disease*, The World Bank, Harvard School of Public Health and World Health Organisation, Harvard University Press, Boston MA.

Parker, D.L., Carl, W.R., French L.R., *et al, 1994*. Characteristics of adolescent work injuries reported to the mnnesota Department of labour and Industry, *Am J Public Health,* Vol.84, pp. 606–11.

Patz, J. A., McGeehin, M. A., Bernard, S. M. *et al.*, 2000. The potential health impacts of climate variability and change for the United States: Executive summary of the report of the health sector of the US National Assessment, *Environmental Health Perspectives*, Vol 108, pp. 367–76.

Plunkett, L.M., Turnbull, D. and Rodricks J.V., 1992. Differences between adults and children affecting exposure assessment, in *Similarities and differences between children and adults: Implications for risk assessment* (edited by

P.S. Guzelian, C.J. Henry and S.S. Olin), ILSI Press, Washington, DC, pp. 79–94.

Rice, D. and Barone, S., 2000. Critical periods of vulnerability for the developing nervous system: Evidence from humans and animal models, *Environmental Health Perspectives*, Vol 108 (suppl 3), pp. 511–33.

Rutter, M., 1996. Family trends and children's futures, in *The child in the world of tomorrow* (edited by S. Nakou and S. Pantelakis), Elsevier Science Ltd., Oxford.

Ryu, J.E, Ziegler E.E., Nelson, S.E. and Fomon, S.J., 1983. Dietary intake of lead and blood lead concentration in early infancy. *Am J Dis Child*, Vol 137, pp. 886.

Sauer, P.J.J., Huisman, M., Koopman-Eseeboom, C. *et al.*, 1994. Effects of polychlorinated biphenyls (PCBs) and dioxins on growth and development, *Hum Exp Toxicol*, Vol 13, pp. 900–6.

Savitz, D.A., 1989. Effect of parents' occupational exposures on risk of stillbirth, preterm delivery and small-for-gestationl age infants, *Am J Epidemiol*, Vol 129, pp. 1201–10.

Snodgrass, W.R., 1992. Physiological and biochemical differences between children and adults as determinants of toxic exposure to environmental pollutants, in *Similarities and differences between children and adults: Implications for risk assessment* (edited by P.S. Guzelian, C.J. Henry and S.S. Olin), ILSI Press, Washington, DC, pp. 35–42.

Spencer, N., 2000. *Poverty and child health*, Radcliffe Medical Press, Oxon.

UN, 2002. 'The Environmental Performance Review: Uzbekistan' in *The Environment and Health Situation in Uzbekistan* (Edited by F. Racioppi and B. Menne), Chapter 12, United Nations, New York.

UNDP, 1999. *Initial Communication of the Republic of Uzbekistan to the United Nations Framework Convention of Climate Change*, Administration of Hydrometeorology at the Cabinet of Ministers of the Republic of Uzbekistan.
URL: http://www.unfccc.de (in 2001)

Vreugdenhil, H.J., Lanting, C.I., Mulder, P.G., Boersma E.R. and Weisglas-Kuperus, N., 2002. Effects of prenatal PCB and dioxin background exposure on cognitive and motor abilities in Dutch children at school age, *J Pediatr*, Vol 140, pp. 48–56.

Walkowiak, J., Wiener, J.A., Fastabend, A. *et al.*, 2001. Environmental exposure to polychlorinated byphenils and quality of the home environment: effects on psychodevelopment in early childhood. *Lancet*, Vol 358, pp. 1602–7.

Wagner, M., 1996. The impact of political and economic change on children, in *The child in the world of tomorrow* (edited by S. Nakou and S. Pantelakis), Elsevier Science Ltd., Oxford.

WHO, 1994. *Ultraviolet radiation,* Environmental health criteria,No.160, World Health Organization, Geneva.

WHO, 1999a. *The World Health Report 1999. Making a difference*, World Health Organization, Geneva. [document WHO/HQ/Ser.II/1999]

WHO, 1999b. *Health21: The health for all policy framework for the WHO European Region, European Health for All Series No. 6,* WHO Regional Office for Europe, Copenhagen.

WHO, to be published in 2002. *The combined effects on human health of stratospheric ozone depletion and climate change*, Meeting report Orvieto, 5–6 October 2001, WHO Regional Office for Europe, Copenhagen.

Woolf, A.D., Flynn, E., 2000. Workplace toxic exposures involving adolescents aged 14–19 years, *Arch Ped Adolesc Med*, Vol 154, pp. 234–39.

2. Environmental hazards in specific settings and media: an overview

Giorgio Tamburlini
Contributing author: Francesca Racioppi

Summary of existing knowledge
- A variety of environmental hazards, including poor air quality, poor building standards, noise, contamination of water and food are present in settings where children live, learn and play
- Children are also put at high risk of injury, disease and death by their exploitation in workplaces and in a variety of illegal activities

Main challenges
- To know more about the hazards relating to the various settings where children live and grow
- To adopt a setting approach as a basis for child-focused environmental protection policies

Action points
- To establish and enforce laws and regulations to protect children and adolescents in their various life settings
- To improve environmental control and monitoring, and to provide better information to professionals, families and children themselves

2.1. Introduction

This chapter offers an overview of the hazards to the health of children and adolescents that may be present in environmental settings where children live, learn, play or are be involved in a variety of legal and illegal activities. The main health hazards in environments where children spend most of their time, such as houses, day-care centres, schools and playgrounds are described, as well as those deriving from transport and from contaminantion of air, water and food. Information on health hazards deriving from the exploitation of children and adolescents in workplaces and in illegal activities is provided. Since taking a setting approach helps to fix clear objectives and boundaries of action and identify potential partners for action, suggestions are given on general preventive actions in these settings and media.

2.2. Overview of health hazards in the everyday micro-environment: houses, day-care centres, playgrounds and schools

From birth to adolescence, children spend most of their time in houses, day-care centres, playgrounds and schools. In these settings, environmental health hazards may vary greatly, depending on factors such as climate, socio-economic level, cultural aspects, building materials and legislation.

The main ones are:

- poor indoor air quality;
- hazardous building materials and unsafe building standards;
- chemical or biological contamination of furniture, arts-and-crafts material and playgrounds;
- radiation (ultraviolet, ionising, electromagnetic fields);
- noise.

Poor indoor air quality

Many public and private buildings are old and poorly maintained even in the most developed nations, and poor air quality is common particularly in school buildings. Indoor air pollution may be caused, for example, by the use of biomass for heating purposes, or by improper functioning of stoves and inadequate ventilation. People in the poorest countries, in rural areas, in urban slums and urban fringe areas, still rely on biomass fuel (mainly wood and coal) for the purpose of cooking and heating. This leads to very high levels of indoor air pollution and to an increased risk of lower respiratory infection among children (WHO/EEA 1997). Levels of inhalable particles are the highest in homes with wood-burning stoves, depending on the frequency of cooking and heating and on the adequacy of ventilation. Improperly ventilated wood stoves and fireplaces also generate carbon monoxide (CO), which can cause possibly lethal acute poisoning, and nitrogen dioxide (NO_2) (Lambert and Samet, 1995). Very high indoor levels of NO_2 have been measured in houses where ovens were used as space heaters. Exposure to high levels of SO_2 and NO_2 may cause mucocutaneous irritation and respiratory effects resulting in rhinitis, cough and exacerbation of asthma.

Last but not least, exposure to environmental tobacco smoke is widespread in private houses as well as in public buildings when adults do not refrain from smoking indoors and smoking is not prohibited. The health effects on children of exposure to

environmental tobacco smoke are pervasive and are described in detail in Chapter 10.

The term 'sick building syndrome' has been used to describe a variety of symptoms, ranging from headache and nausea to upper respiratory infection and eye irritation, associated with a person's presence in a building and which typically disappear when the person is not in the building (AAP, 1999). Symptoms are mainly due to inadequate ventilation but low levels of specific pollutants may also contribute.

Hazardous building materials and unsafe building standards

Housing in poor suburban or rural areas may not offer adequate shelter from heat or cold due to inadequate building materials and fuel scarcity. In many countries of the European Region a significant proportion of the population still faces the problem of inadequate housing, and this problem is also present in very poor neighbourhoods and shanty towns in the most industrialised part of Europe. When buildings are apparently adequate, there are still many potential health hazards for dwellers, and particularly for children who spend most of their time inside and are exposed for long periods. Over the last few decades the health hazards deriving from the presence of dangerous substances in building materials, particularly of lead and asbestos, have been extensively studied.

Asbestos has been used for a wide range of building materials, mainly for insulation purposes, including roofing shingles, ceiling and floor tiles, and asbestos cement,. Inhalation of microscopic airborne asbestos fibres is the major route of exposure. Asbestos becomes a health hazard when the asbestos-containing materials deteriorate and fibres are released in the air and can be inhaled. Millions of school students as well as school personnel are exposed to deteriorated asbestos. Field studies have found that at least 10 % of the asbestos which is incorporated in school buildings is deteriorating and accessible to children and thus poses a threat to health (US EPA, 1987). Use of asbestos varies greatly across countries. It was used extensively in public building materials until the 1970s, since when it has been banned or limited as a building material in many countries.

Leaded materials have been extensively used in paints, walls, woodwork and window casings. Lead in paint is usually the most important threat for children in countries where lead paint was extensively used, in spite of the fact that lead was eliminated from paint intended for use in buildings many years ago (AAP Committee on Environmental Health, 1993). Lead can also accumulate in water due to contamination of water sources and water pipes. In addition, lead can be inhaled as fumes or as respirable particles.

Dampness favours the development of moulds and represents a risk factor for asthma and respiratory diseases.

Unsafe building standards and materials may lead to poisoning and injuries. Poisoning may result from inappropriate storing of hazardous substances, or incorrect administration or exposure to medications, chemicals, petroleum products and crafts materials. Injuries are common as a consequence of unsafe building and play materials, unsafe biomass burning (burns, kerosene ingestion), unsafe electrical wiring, etc. Injuries are extensively dealt with in Chapter 9 of this monograph.

Chemical or biological contamination of furniture, arts-and-crafts material and playgrounds

Chemical contamination may originate inside, as well as outside, buildings.

Furniture and household products may contain volatile organic compounds (VOCs). These include chemicals such as aliphatic and aromatic hydrocarbons (formaldehyde, benzene, perchloroethylene). VOCs are released as gases or vapours in case of above-normal room temperatures and tend to be higher in recently constructed or renovated buildings. VOCs are also emitted by office equipment (copiers), graphic and craft materials, paints, cleaning products, etc., and therefore higher concentrations of VOCs can be found indoors. Chronic exposure to VOCs may cause cancer.

The floor is an important micro-environment for infants and toddlers, who typically spend a good deal of time in a playground or lying, crawling and walking on the floor. Both the floor surface and the layer of air closest to the floor are major sources of chemical and biological contaminants. Carpets, rugs and mattresses host a variety of allergens, house dust mite being the most important indoor allergen. Some of the surface contaminants

described in the literature include pesticide residues and formaldehyde from new synthetic carpeting. Formaldehyde is used in hundreds of products as a carrier for solvents, and stiffeners and water repellents in floor coverings such as carpets and linoleums. Exposure to airborne formaldehyde may result in conjunctival and respiratory tract inflammation and precipitate asthma. Contaminants that tend to be found in higher concentrations just above the floor include mercury vapour, from old formulations of latex paint, and radon, which is found in highest concentrations in the lowest elevations of the house. The heavier particles in environmental tobacco smoke also tend to settle near the floor.

Schools may be situated near old industrial sites with unknown emissions and wastes. In rural areas schools often use small private wells that may be contaminated with lead and pesticides. Outside the building, playground soil may be contaminated by lead, with higher concentrations found closest to areas with high traffic loads.

Children may also use toxic arts-and-crafts products, while 'non-toxic' art products can cause health problems if ingested or used improperly. Play areas may contain environmental toxicants. Toys may contain phthalates. Wooden playground equipment is often treated with preservative-containing substances such as arsenic, pentachlorophenol and chromium, which are toxic if ingested.

Biological contamination is common in any group, small or large, of people living in a limited space. Schools and day-care centres are at particularly high risk due to crowding and to the high incidence of infectious diseases among toddlers and children. Biological contamination may be encouraged by high relative humidity and by poorly maintained air conditioners. Moulds (the most common are *Cladosporium*, *Aspergillus*, *Penicillium* and *Alternaria*) proliferate in environments containing excessive moisture such as from leaks in roofs and walls, and can enter the home through heating and conditioning systems. Children may become infected by a variety of microrganisms through contaminated drinking-water (see chapter on biological contamination of water).

Radiation and electromagnetic fields

Exposure to ionising radiation and ultraviolet light is another health hazard. While significant exposure to ionising radiation from radioactive fallout and medical diagnostic equipment (x-ray and radioisotopes) is limited to specific settings and circumstances, exposure to radon is quite common in private and public buildings and represents most of the background radiation. Radon gas is formed from the radioactive decay of radium, and enters homes through cracks in the foundations or in the absence of foundations. Exposure to radiation is obviously higher in basements and first-floor flats. Until recently there were insufficient data to detect an increased risk of lung cancer after lifelong residential radon exposure. A meta-analysis of eight epidemiological studies (Lubin and Boice, 1997) shows the existence of a linear dose-response relationship detectable down to 4 picocuries per litre (pCi/L), the level at which remedial action should be taken, according to the United States Environmental Protection Agency (US EPA) and the US Department of Health and Human Services.

Exposure to ultraviolet light is widespread, although strongly dependent on latitude and sun protection behaviour.

Sources of exposure to electromagnetic fields are ubiquitous in houses and public buildings, and common outdoors. They can be high-voltage, long-distance transmission lines, distribution lines that bring electricity to homes, and electric appliances of all sorts including television monitors, computer games, radios and other electrical equipment.

The health consequences of exposure to ultraviolet radiation and to electromagnetic fields and are dealt with extensively in Chapters 12 and 13.

Noise

Noise contamination exceeding safety thresholds is widespread in neighbourhoods, schools and day-care centres, particularly in urban and suburban areas. It includes exposure to noise originating inside the buildings, such as from children themselves, toys, equipment, etc., or outside such as from heavy road traffic, industrial activities or building and road construction or renovation and nearby railways, highways or airports. Noise levels inside rooms depend on the design, insulation and acoustics of the room and on environmental noise outside.

Table 2.1. **Decibel ranges and effects of common sounds**

Source: Modified from AAP, 1999

Example	dB(A)	Effect
Quiet suburb, quiet conversation	50	No significant effect
Conversation in busy place, background music, background traffic noise	60	Intrusive
Freeway traffic at 15 metres	70	Annoying
Average factory, train at 15 metres	80	Possible hearing damage
Busy urban street, diesel truck	90	Chronic hearing damage (>8-hour exposure), speech interference
Jet take-off (300 metres), power lawn mower	100	As above, more likely and more severe
Stereo held close to ear	110	As above, more likely and more severe
Live rock music, jet take-off (160 metres)	120	As above, more likely and more severe (human pain threshold)
Earphones at loud level	130	As above, more severe
Toy cap pistol, firecracker (very close to ears)	150	Acute hearing damage (eardrum rupture)

Note: dB(A) is an international sound pressure level unit meaning 'decibel with an A frequency weighting' which reflects the sensitivity of the human ear.

Children may be more prone to the adverse effects of noise, because they may be more frequently exposed to noise — due to the lack of ability to control the environment. In addition, they are more susceptible to the impact of noise. Little is known about exposure in very young infants, although it has been shown that pre-term babies in intensive care units are exposed to many sources of noise. Exposure in preschool and school children has been more extensively investigated. School-age children may be routinely exposed to more noise than the 24-hour equivalent (LAeq24) of 70 dB(A) while the WHO Guidelines for Community Noise (WHO, 1999) recommend that during lessons the noise measured in classroom should not exceed 35 Laeq.

The health effects of noise include hearing damage from impulse noise at high levels which may damage inner hair cells and from prolonged exposure to sounds louder than 85 dB(A). Hearing loss may be transient or permanent. Table 2.1. provides an overview of the potential effects of the most common sounds.

However, in children the most important and common effects of noise are interference with speech, communication and learning. For example, speech is normally 100 % intelligible in background noise levels of about 35 dB(A) and can be understood fairly well in background levels of 50–55 dB(A). Problems arise when the ambient noise is 60 dB(A) or more (corresponding to traffic noise through slightly open windows). The ultimate effects are represented by impaired language development and acquisition of reading skills, both in early childhood and at primary school. These effects are more likely to occur in children who have a hearing impairment or who are not familiar with the spoken language.

Background noise may also interfere with concentration and sleep, cause psychological stress, contribute to a reduction in cooperative behaviour and trigger aggressive behaviour (AAP, 1999).

2.3. Overview of health hazards from transport

Children spend considerable amounts of time travelling. The exposure of children to present transport patterns, especially in the urban environment, is an example of the complexity of a situation where they are exposed simultaneously to a large number of health hazards, to which their vulnerability is higher than that of the adult population.

Health effects include those resulting from exposure to air pollution (outdoor and inside vehicles) and noise and from traffic injuries, as well as from reduced opportunities for physical exercise and autonomous travel.

Contrary to the common belief that driving children by car can reduce their exposure to outside air pollution, several studies have shown that in fact the occupants of vehicles can be exposed to internal air which is more polluted than that outside. For example, a study conducted in Amsterdam in 1990 showed in-vehicle CO concentrations of 3–7 ppm for various routes and conditions,

with individual concentrations never being higher than 13 ppm (Wijnen, 1995). Exposure of cyclists travelling the same routes was always lower than that of the the vehicle occupants. Pollutants other than CO have also been measured: mean NO_2 concentrations varied between 44 and 277 µg/m^3, PM10 levels between 71 and 194 µg/m^3.

Several studies, which have been summarized in a review carried out by the WHO (WHO, 2000a), indicate that children living in the proximity of busy roads have an increased risk of around 50 % of suffering from respiratory diseases and suggest increased risk of childhood leukaemia from exposure to vehicle exhaust, where benzene may be the responsible agent.

In addition, results of national case studies carried out in France, Switzerland and Austria to estimate the health impacts and costs of transport-related air pollution showed that in these three countries the number of cases of bronchitis and asthma attacks in children younger than 15 years of age in 1996 was in the order of 300 000 and 162 500, respectively (Künzli, 2000). In countries where leaded petrol is still used, children exposed to lead from fuel are at higher risk of suffering negative impacts on neuro-cognitive functions.

Their limited perception of and reaction to road traffic dangers puts children at higher risk of being involved in road accidents. In the WHO European Region approximately 9 000 children (younger than 18 years) die and 355 000 are injured in traffic accidents every year, accounting respectively for approximately 10 % of the total number of deaths and 15 % of the injuries (WHO, 2000a).

Parents react to the fear of traffic accidents by restricting their children's freedom to walk and cycle. Not only does this contribute to unhealthy levels of inactivity in children, but also hinders the development of their independence, reduces their opportunities for social contact and establishes attitudes towards car use which continue into adulthood.

Levels of overweight and obesity are greatly increasing amongst schoolchildren and the lack of physical activity is, together with diet, one of the main risk factors for obesity (Chinn, 2001). There are also indications that a general increase in physical activity in children, such as that attainable by traveling on foot or by bike and playing, can be more effective than formally structured physical activity or competitive sports (Dietrich, 1993). In addition, the adoption of sedentary lifestyles in childhood increases the risk of developing cardiovascular diseases, diabetes and hypertension in adulthood.

2.4. Overview of health hazards in workplaces

Currently several million adolescents are legally employed in Europe. Many others, including children as young as seven or eight, are employed in a variety of activities such as farm work, commerce and industry, in violation of international codes as well as of national legislation on age limits or safety regulations (ILO, 1996). Migrant children are increasingly used for illegal activities, some of which are extremely dangerous or immediately harmful to children and adolescents. Thousands of female and male adolescents are illegally smuggled into many European countries and forced to work in the sex market (ECPAT, 2000).

Every year many hundreds of children die working on jobsites and many more are poisoned or injured, sometimes irreversibly, from work activities (Parker *et al.* 1994; Dunn *et al.*, 1998). Hazards at workplaces (examples of job-related exposure are listed in Table 2.2) do not differ from those to which adult workers are exposed, with the difference that young people are less experienced and aware of risks, less apt to ask for and be compliant with safety regulations, and less likely to receive technical training (Woolf and Flynn, 2000). Injuries, for example, are four times as frequent in adolescents than in adult workers. Adverse health effects, too, are both more frequent and more severe due to the enhanced sensitivity of developing organisms to toxicants and to injuries, including chronic musculo-skeletal trauma and stress (Runyan and Zakocs, 2000).

By far, those most heavily exposed to physical and psychological trauma and to disease are children and adolescents forced to work in the sex and pornography market, most of whom are actually kidnapped and reduced to slavery.

Table 2.2. **Examples of occupational hazards for children and adolescents**

Agriculture:	pesticides, fertlizers, tetanus and other infectious agents, injuries
Building, masonry:	asbestos, silica dust, injuries
Auto repair:	isocyanates, lead
Restaurants:	cleaning agents, tobacco smoke
Petrol stations:	benzene, lead
Carpentry:	solvents, formaldehyde, wood dusts, injuries
Textiles, dye works and cleaners:	benzene, aniline, methanol
Leather:	chromium
Welding:	fumes and eye injury
Ceramics and glass:	lead, silica dust
Mining:	coal dust, asbestos, phosphorus, injuries
Indoor jobs:	dust, noise and injuries
Outdoor jobs:	cold and heat stress, noise and injuries
Sex market:	sexual abuse, injuries, sexually transmitted diseases, homicideos

2.5. Overview of health hazards in waste sites

Uncontrolled hazardous waste sites are prevalent throughout the world. Although accurate worldwide data are lacking, the US EPA in 1995 listed approximately 15 000 waste sites in the United States of which 1 371 were listed or proposed for listing on the national priority list, on the basis of a hazard ranking system (US EPA, 1996).

Uncontrolled hazardous waste sites include waste storage and treatment facilities including landfills, former industrial sites, waste recycling facilities and unsanctioned discharges of wastewater. Some of the substances found in uncontrolled waste sites are heavy metals such as lead, chromium and arsenic, and organic solvents such as trichloroethylene and benzene. An additional group of hazardous waste sites are military facilities including nuclear energy complexes. Children may be exposed through groundwater, surface water, drinking-water, surface soil, sediments, consumable plants or animals. Children in particular often find waste sites interesting and spend their playtime in them.

Adverse health effects have been reported in investigations into communities near hazardous waste sites. These effects have ranged from non-specific symptoms, such as headache, fatigue and irritative symptoms, to specific conditions such as low birth weight, congenital defects and a constellation of neurobehavioural deficits (Savitz *et al.*, 1997). Most investigations have included some children in the study population but only a few have focused primarily on the health effects on infants and children. A multicenter collaborative study on the risk of congenital anomalies near hazardous waste sites in Europe showed a 33 % increase in risk of non-chromosomal anomalies (Dolk, 1998). The study could not provide conclusive evidence of an association but was considered by a panel of experts convened by WHO sufficient to initiate action to limit exposure and risk to health. A recently published study suggests an increase in risk of chromosomal anomalies similar to that found for non-chromosomal anomalies (Vrijheid, 2002).

2.6. Overview of health hazards in outdoor air, water, and soil

Health hazards related to outdoor air pollution

Air pollution is typically due to a variety of different pollutants, and children may be exposed to various mixtures of contaminants, depending on factors such as proximity to polluting industries, power plants, areas of high traffic load, etc.

Usually air quality measurements and standards are based on four classic main air contaminants (particulate matter, ozone, NO_2, SO_2). Lead and VOCs are other important outdoor air contaminants. Table 2.3. shows the 35 pollutants included in the WHO *Air quality guidelines for Europe* (WHO, 2000b).

Pollutants included in the WHO *Air quality guidelines for Europe* [1] Table 2.3.

Source: WHO, 2000 b

Organic air pollutants	**Inorganic air pollutants**
Acrylonitrile [2]	Arsenic
Benzene	Asbestos [2]
Butadiene	Cadmium
Carbon disulphide [2]	Chromium
Carbon monoxide	Fluoride
1,2-Dichloroethane [2]	Hydrogen sulphide [2]
Dichloromethane	Lead
Formaldehyde	Manganese
Polycyclic aromatic hydrocarbons (PAHs)	Mercury
Polychlorinated biphenyls (PCBs)	Nickel
Polychlorinated dibenzodioxins and dibenzofurans (PCDDs/PCDFs)	Platinum
Styrene	Vanadium [2]
Tetrachloroethylene	
Toluene	**Classic air pollutants**
Trichloroethylene	Nitrogen dioxide
Vinyl chloride [2]	Ozone and other photochemical oxidants
	Particulate matter
Indoor air pollutants	Sulphur dioxide
Environmental tobacco smoke	
Man-made vitreous fibres	
Radon	

[1] Inclusion was based on WHO environmental health criteria.
[2] 1987 evaluation retained, not re-evaluated.

Particulate matter includes solid particulates resulting from combustion of organic matter and dust, originating from the mechanical breakdown of solid matter.. Particulate air pollution is a mixture of suspended solid and liquid particles that vary in size. The particle size is the primary determinant of the level at which they are deposited in the respiratory apparatus. Particles smaller than 10 micrometres (μm) diameter (PM_{10}), such as those produced by motor vehicle exhaust, remain suspended for longer periods and are more likely to be inhaled and to penetrate into and damage the lungs. Respiratory diseases, both acute and chronic, have been clearly associated with temporarily high concentrations of particulate matter, in children as well as in adults.

In addition to fine particles, motor vehicle exhaust also produces CO and NO_2, although higher levels of both these pollutants are more likely to be generated and found indoors.

The primary sources of SO_2 are coal-based power plants, smelters and paper mills. Other sulphur compounds such as sulphuric acid (H_2S0_4) and hydrogen sulphide (H_2S) may be emitted by a variety of industrial processes, for example oil refining. Lead is an important air contaminant particularly where lead has not been phased out from gasoline.

VOCs can be emitted by a variety of industrial sources and benzene is a product of petrol combustion. A chemical reaction between VOCs and NO_2 in the presence of sunlight produces ground ozone, one of the most pervasive and harmful air contaminants. Levels of ozone are generally higher in the afternoon hours of sunny days.

Most air contaminants produce acute damage to the respiratory system, but a variety of chronic health effects, mainly respiratory and cardiovascular, can be consequence of long-term exposure.

Several air pollutants which have been observed to have a strong relationship with adverse health outcomes in childhood are considered in various chapters of this publication: lead, environmental tobacco smoke, ozone, particulate matter,

formaldehyde, sulphur dioxide, nitrogen dioxide.

Health hazards in water, food and soil

Air pollutants also contaminate water and soil and can be ingested though water and food. Water may be polluted from point or non-point sources. Point sources are wastewater and industrial or sewage discharges. Non-point sources include agricultural and urban run-off. In industrialised countries, there are more than 15 000 high volume chemicals, which are produced and dispersed in the environment. The main water contaminants included in the WHO *Guidelines for drinking-water quality* (WHO, 1998) are listed in Table 2.4.

Table 2.4. **Potentially hazardous chemical contaminants of drinking-water and WHO guideline values**

Source: WHO, 1998

Chemical	No of chemicals with WHO guideline value	WHO guideline value (milligrams/litre) [1]
Inorganic constituents	19	Lead 0.01 Fluoride 1.5 Arsenic 0.01 Nitrate (as NO_3) 50
Organic constituents	30	1,1,1-trichloroethane 2 000 Toluene 700
Pesticides	37	Aldrin/dieldrin 0.03 Bentazone 30
Disinfectants	4	Monochloroamine 3 Iodine — no adequate data
Disinfectant by-products	18	Bromoform 100 Chlorite 200 (provisional)

[1] No priority intended by these examples.

The health effects of microbiological contamination of water and food are described in Chapters 7 and 8.

The health risk associated with toxic chemicals in drinking water differs from that of microbiological contamination.. Chemical contaminants are usually not associated with acute effects. The problems often arise after prolonged periods of exposure, and of particular concern are those which have cumulative toxic effects. Symptoms may not therefore be apparent during childhood but may manifest themselves later in life. The delayed effects mean there are large gaps in the knowledge and the cause-effect relationship is difficult to prove.

Chemical contamination may be due to a variety of compounds.

Arsenic is one of the most ubiquitous water and food contaminants. It is produced by a variety of activities, such as smelting and coal-burning, most of which are more frequently encountered in countries with an intermediate level of development, since the use of arsenic is decreasing in many modern industries with the exception of electronics. Arsenic is naturally occuring in the earths crust and may be introduced into water through the dissolution of minerals, from industrial effluents and via atmospheric deposition. Toxicity is highest for inorganic trivalent arsenic

Drinking water represents the greatest hazard, since arsenic in groundwater is predominantly inorganic and of higher toxicity. Diseases associated with arsenic include cancers of the bladder, kidney, lung and skin, neurological effects, cardiovascular and pulmonary disease and diabetes. Since the diseases may develop slowly over many years — generally after a minimum exposure of approximately five years — children who have been exposed to arsenic contaminated drinking waters may show symptoms later in life.

The WHO guideline value of 0.01 mg/L is provisional because of the lack of suitable testing methods.

The health effects of lead are discussed elsewhere (Chapter 4) Lead piping is still an important source of water contamination. Soft water and water below a neutral pH is more likely to cause lead to leak from lead pipes and joints.

The WHO guideline level for lead is set at 0.01 mg/litre. This is derived from the assumption of a 50 % allocation to drinking water for a 5 Kg bottle-fed infant consuming 0.75 litres of drinking water per day. As

infants are considered to be the most sensitive age group to lead, this guideline level will be protective for other age groups.

High concentrations of nitrate in drinking water are of concern because nitrate can be reduced to nitrite, causing methaemglobinaemia. The haemoglobin of young children is particularly susceptible to methaemglobinaemia and this together with the increased ratio of water consumption to bodyweight makes infants particularly vulnerable to this disease. Those affected by bacterial infection, such as gastroenteritis, are more likely to suffer when exposed to high levels of nitrate than a healthy child (WHO/EEA, in press). The vulnerability of infants receiving drinking water from shallow groundwater sources is emphasised by data from Hungary, where between 9 and 41 cases of methaemoglobinemia associated with drinking water are reported annually. All cases are related to individual private wells and almost the whole country is affected, apart from the south-eastern part where deep well water is used. A similar number of water-related incidents are recorded annually in Slovakia and, as in Hungary, the majority of these are associated with drinking water (WHO/EEA, in press). In both Slovakia and Hungary more than 80 per cent of the recorded cases of methamoglobinaemia are reported to be linked to drinking water. In Albania, all 43 reported cases in 1996 were linked to nitrate in drinking water (Bardhoshi, cited in WHO/EEA, in press).

Mercury originates from combustion sources such as coal power plants and municipal waste incinerators, then it is deposited into lakes and rivers and converted into methyl mercury by sediment bacteria. Methyl mercury is then accumulated in fish and can be introduced into the food chain. Health effects are described in Chapter 4.

Other water, food and soil contaminants which are often encountered are organic chemicals such as PCBs, polychlorinated dibenzodioxins (PCDDs), methyl tertiary butyl ether (MTBE) and various pesticides. Effects of PCBs and dioxins, which are very resistant to biological degradation and remain in the environment for decades, have been extensively investigated and are described in Chapter 4. MTBE is increasingly used as a petrol additive and may leak into groundwater from gasoline tanks. Pesticides include insecticides, herbicides and fungicides. Some of the older pesticides have been designed to be persistent and for this reasons they can be found distributed worldwide in water and soil. Newer pesticides degrade more quickly but they still contaminate water and soil and consequently food. Health effects of pesticides are described in Chapter 11.

2.7. Overview of preventive actions to reduce environmental hazards to children in various settings and media

Methodological issues concerning risk assessment and guiding principles for policy development are discussed in detail in the last chapter of the monograph. Control measures to reduce the risk of specific health effects are discussed in specific chapters in the second chapter. Specific preventive actions aimed at reducing risk in particular settings will be briefly discussed in the following paragraphs.

Preventive action to make everyday micro-environments healthier and safer

Current regulations make removal of asbestos mandatory especially when deteriorating asbestos is readily accessible to children or when renovation of buildings is about to occur. Other strategies are containment or 'enveloping' of asbestos behind other materials such as dry walls or drop ceilings. Lead is increasingly being phased out from use in building materials, especially from paint and water pipes. Radon exposure can be reduced by increasing ventilation and by sealing cracks, creating negative pressure under the basement floor. Repairs should be made when levels of radon higher than 4 pCi/L are found.

Building standards have been published by a variety of national and international agencies. Measures that may help to minimise exposure to combustion products include periodic maintenance of furnaces and ventilation directly outdoors. Ventilation also decreases exposure to VOCs. Charcoal should never be burned indoors. WHO is currently developing and testing a range of approaches including the development of better stoves, substitution of cleaner fuels for biomass fuels, and education. Although the causal association between poor indoor air quality and lower respiratory infection in children is well established, there is a need to quantify the exposure-response relationship so that it is possible to judge whether the reductions in exposure obtained by

improved stoves, fuels and household interventions will lead to any useful health improvement. While legislation is necessary to establish building standards, safety standards for heating and cooking equipment, air quality and safety standards for schools, day-care centres, toys, materials and playgrounds, adequate information to families and to professionals involved in the daily care of children remains essential. Improved housing of course is the mainstream intervention, but better information about the adverse effects may lead to better indoor air quality even without major structural interventions. WHO recently updated air quality standards (Table 2.5.).

Table 2.5. **Guideline values for selected air pollutants**

Source: WHO, 2000b

Substance	Time-weighted average	Averaging time
Lead	0.5 microgram/cubic metre	Annual
Nitrogen dioxide	200 micrograms/cubic metre 40 micrograms/cubic metre	1 hour annual
Ozone	120 micrograms/cubic metre	8 hours
Particulate matter [1]	Dose-response	
Hydrogen sulphide [2]	150 micrograms/cubic metre	24 hours
Formaldehyde	0.1 milligram/cubic metre	30 minutes

[1] The available information for short- and long-term exposure to PM_{10} and $PM_{2.5}$ does not allow a judgment to be made regarding concentrations below which no effects would be expected. For this reason no guideline values have been recommended, but instead risk estimates have been provided (see Part II, Chapter 2.1).
[2] Not re-evaluated in the second edition of the Guidelines.

Biological contamination can be reduced by providing adequate ventilation and maintaining air humidity below 50 %, which is also effective in controlling dust mite infestation. Appropriate maintenance of conditioners and dehumidifiers is very important. Chemical contamination must be reduced by removing sources, by avoiding the storage of opened containers of unused paints and similar materials inside schools and by increasing ventilation particularly when using products that emit VOCs.

Improved building regulations and acoustic control in at-risk buildings are essential, as is the careful location or relocation of day-care institutions and schools. Buildings for educational activities should be located outside high traffic areas, whether aircraft, trains or motorised vehicles.

Preventive action to prevent the health effects of transport

Effective prevention of the negative and enhancement of the positive health effects of transport requires a mix of integrated measures and the full involvement of the transport, environment and health sectors, at all levels of the decision-making process. In particular, initiatives promoting traffic calming measures to reduce vehicle speed to beow 30km/h in residential areas and in the proximity of schools, playgrounds and sports and recreational infrastructures attracting children should be broadly implemented.

The provision of safe conditions for walking and cycling (e.g. through the development of cycling paths, the provision of parking places for bicycles, etc.), in combination with the development of flexible and efficient public transport which also takes into account the mobility needs of the youngest are also an essential prerequisite to influence the modal share towards healthier transport patterns. Much can be done at community level, where a number of successful experiences, such as the 'Safe routes to school', and the 'Walking bus', have been tested (The Transport 2000 Trust, 2001). Other relevant measures include the introduction of cleaner vehicles and fuels, the reduction of noise emissions, economic measures and other policies to manage the demand for transport (parking policies, information raising campaigns, etc.).

Among existing policy instruments at international level, the adoption of the 'Charter on Transport, Environment and Health' (WHO, 1999b) and of the final Declaration of the Third Ministerial Conference on Environment and Health (London, 16-18 June 1999) (WHO, 1999c) acted as catalyst for action and political commitment towards placing children-related issues very high in the agenda of the European environment and health ministries. In particular, the Charter identifies children as a specially vulnerable group, commits member States to develop,

implement and monitor specific policies and measures to protect vulnerable groups from the adverse impacts of transport, and calls on the WHO, in co-operation with other international organisations, to develop methods for assessing and monitoring health effects in groups at higher risk, as well as to provide information and develop guidance on transport-related health targets, threshold values and measures regarding vulnerable groups of the population. Areas relevant to transport and children's health also include the exchange of information and experience on prevention and research on asthma and allergies, the implementation of public health interventions on accidents and injuries and a very close collaboration between relevant organizations and actors, such as the WHO, the EC, EEA, UNECE, ECMT, UNEP, OECD, and non-governmental organisations.

Preventive actions to make youth employment safer, eliminate the worst forms of child labour and the sexual exploitation of children and youth

Prevention of occupational risks includes establishing and enforcing laws and regulations on youth employment, engineering controls on equipment and materials and providing information on exposures and health risks.

Establishing labour laws and regulations and enforcing the existing regulations on employment and safety standards are of the utmost importance: they represent by far the most effective way of preventing occupational injuries and negative health effects. The European Union (EU) has approved a directive on youth employment (EU, 1994) and national legislation is improving the coverage of this important issue. Laws and regulations include generic age limits for employment (currently 16 years of age in most of western Europe), special restrictions for working hours and hazardous jobs and safety standards. Illegal child labour is widespread and often coincides with the most dangerous and unsafe work settings. Parents should be put in the condition to know when their child's work situation violates existing standards. Schools should also offer adequate information. Physicians may play a role when requested to issue or sign a work permit as this offers an opportunity to exercise some control and provide anticipatory guidance.

Employers should be informed about health hazards, be made to implement safety standards and be effectively prosecuted when existing laws and regulations are violated. Of course prevention is to be preferred and efforts to build awareness in employers about health hazards and existing safety regulations may be effective in the long run. A structured, multi-layered response to the public health implications of child labour, including the development of new governmental policies, the allocation of resources to address the health implications and the encouragement of the role for non-governmental organisations, is necessary (Forastieri, 1997). Surveillance and monitoring are required to understand how best to approach child labour issues as they vary among nations.

The establishment and enforcement of laws, as well as international cooperation, are essential to prevent the exploitation of children and adolescents in the sex market. A number of countries have recently introduced a new legislation which establishes more severe penalties for whoever is involved, even indirectly (e.g. the tourism industry), in this kind of criminal activity. It also supports international co-operation among national police officers to fight the international networks that are usually involved in the illegal smuggling of minors for the sex market. Improving the competence and skills of health professionals to help them recognise the signs and symptoms of sexual abuse, providing information to the general public and carrying put prevention work among 'at-risk' communities are also important to fight this escalating problem. Legislation on pornographic Internet sites which use children and telematic investigation, are also necessary.

The ILO's Convention 'Concerning the Prohibition and Immediate Action for the Elimination of the Worst Forms of Child Labor' was adopted on June 17, 1999 and ratified by 37 countries by November, 2000. It proscribed the following child labor practices: a) all forms of slavery, debt bondage, child trafficking and sale, or similar practices; b) the use, procuring or offering of a child for prostitution, for pornography, or for pornographic performances; c) the use, procuring or offering of a child for illicit activities, such as drug production and trafficking; d) work which is likely to harm a child's health, safety, or morals.

Preventive actions to reduce the health risks of waste sites

Prevention measures include engineering controls on incinerators, administrative controls and measures, and providing information on community or individual preventive actions. More and better focused scientific data are needed to help governments and the waste management industry to improve their practices, to ensure that the present approaches and standards take into account the specific exposure and risk of children and to effectively improve risk communication The public must be made aware about what is actually known and what is still uncertain concerning the possible health consequences of waste sites for the health of neighbouring communities and particularly of children and women of childbearing age. Public administrators should be made aware of health hazards of waste sites and should be involved in the better planning of waste disposal, particularly when hazardous substances are involved.

Synoptic view of actions to prevent environmental hazards

Taking a setting approach helps to establish clear objectives and boundaries of action and identify potential partners for action. A synoptic view of the main preventive actions to minimise environmental hazards to children and adolescents in the various settings and media is provided in Table 2.6.

Table 2.6. **Main preventive actions to reduce environmental hazards to children in various settings and media**

Public and private buildings
Enforcement of existing laws and regulations for building materials (e.g. for lead and asbestos), safety standards and periodic maintenance (e.g. heating systems, electric wiring, fire prevention requirements) particularly when building renovation or construction is foreseen. Enforcement of indoor air standards in school buildings. Periodic safety checks of schools and day-care centres. Information to households, child carers and children about the potential hazards of heating and cooking equipment, electric equipment and chemicals.
Transport
Promotion of public transport Development of mobility plans to reduce reliance on private motorized transportation Traffic calming measures to increase safety and reduce average speeds Provision of safe conditions for walking and cycling Advice to parents and professionals on opportunities for children independent mobility and raising awareness on effects of individual travel behaviours
Workplaces
Enforcement of existing laws and regulations for youth employment (generic age limits, safety standards, specific hours and hazards limits). Control and anticipatory advice by health professionals through work permits. Information to and involvement of employers about safety standards and youth employment Information and education of parents and youth.
Sex market
Establishment and enforcement of laws on sexual exploitation of children and adolescents. Control by police officers on involvement of minors in the sex markets, including pornography and telepornography. Improvement of competence and skills of health professionals about the signs of sexual abuse. Information and prevention among 'at-risk' communities.
Waste sites
Extraction or removal of contaminants. Disruption of the exposure pathway (water supply or dust control). Relocation of residence. Restrictions on land use for residential purposes.
Air
Establishment and enforcement of safety standards for the most common air pollutants (including additional safety standards for children). Re-engineering or relocating of industrial activities and power plants. Continuous monitoring of air pollution. Policies to reduce traffic load and exposure to traffic pollution. Advice to parents and children to reduce exposure in at-risk areas and times of day. Public warnings to reduce exposure

Main preventive actions to reduce environmental hazards to children in various settings and media, cont. Table 2.6.

Water, food and soil
Enforcement of safety standards for contaminants in food and water (including additional margins of safety for children). Policies to reduce water and soil non-point contamination by the most common contaminants. Policies to reduce point contamination. Control and monitoring of biological and chemical contaminants in water and food. Labelling of foods. Information to parents about possible water and food contaminants and safe dietary principles. Public warnings about use of possibly contaminated water or food
Radiation, electromagnetic fields, ultraviolet light and noise
Establishment and enforcement of standards (distance of power lines from private and public housing). Monitoring of electromagnetic fields and noise in at-risk areas . Advice to parents about appropriate sunscreen. Public warnings about exposure to ultraviolet light Noise insulation of at-risk buildings, particularly schools. Siting of schools and residential areas away from major sources of electromagnetic fields and noise or removal of sources.

Summary

Many hazards to the health of children are present in environmental settings such as houses, day-care centres, playgrounds and schools, where children live, learn and play. The main ones are: poor indoor air quality, hazardous building materials and unsafe building standards; chemical or biological contamination of furniture; hazardous arts-and-crafts material and playgrounds; radiation, ultraviolet and electromagnetic fields; and noise. Residence near hazardous waste landfill sites may expose to increased risk of congenital anomalies. Additional hazards derive from transport, such as ar pollution (outdoor and inside vehicles), noise, traffic injuries and reduced opportunities for physical exercise and autonomous travel.

There are other settings, such as workplaces, which may pose severe threats to the health of children and adolescents. The exploitation of children and adolescents in the sex market is a new and growing hazard, with dramatic consequences for those involved.

The consequences for the health of children and adolescents include acute and chronic respiratory diseases, infectious diseases, neurodevelopmental disorders, cancer, impaired growth and development, reproductive damage, psychological trauma, injuries and death.

Preventive actions are based on new legislation, enforcement of existing laws and regulations, information to and involvement of children, youth, families, school professionals and employers in environmental control and monitoring. Anticipatory advice by health professionals is also important. Taking a setting approach helps to establish clear objectives and boundaries for prevention and identify potential partners for action.

References

American Academy of Pediatrics, 1999. *Handbook on children's environmental health,* American Academy of Pediatrics.

American Academy of Pediatrics, Committee on Environmental Health, 1993. Lead poisoning: from screening to primary prevention, American Academy of Pediatrics Committee on Environmental Health, *Pediatrics*, Vol 92, pp. 176–83.

Chinn, S. Rona, RJ, 2001. Prevalence and trends in overweight and obesity in three cross sectional studies in British children, 1974–94. *British Medical Journal,* Vol 322, pp. 24–26.

Dietrich, K.N., 1993. Lead exposure and the motor developmental staus of urban 6-year-old children in the Cincinnati prospective study. *Pediatrics,* Vol 91, pp. 301–307.

Dolk, H. Vrijheid, M. Armstrong, B. *et al.*, 1998. Risk of congenital anomalies near hazardous waste landfill sites in Europe: the EUROHAZCON study. *Lancet,* Vol 352, pp 423–27.

Dunn, K.A., Runyan, C.W. and Cohen, L.R., 1998. Teens at work: statewide study of jobs, hazards and injuries, *J Adolescent Health*, Vol 22, pp. 19–25.

ECPAT, 2000. End child prostitution, pornography and trafficking for commercial purposes, ECPAT, Rome. http://www.ecpat.it/home.html (in 2001)

EU, 1994. Directive 1994/33 of the European Union regarding protection of young workers, European Union.

Forastieri, V.,1997. Children at work: Health and safety risks. International Labour Office (ILO), Geneva

ILO, 1996. *Child Labour: targeting the intolerable*, International Labour Office Publications, Geneva.

Kunzli, N., Kaiser, R., Medina, S. *et al.*, 2000. Public health impact of outdoor and traffic related air pollution: a European assessment, *Lancet*, Vol 356, pp. 795–801.

Lambert, W.E. and Samet, J.M., 1995. Indoor air pollution, in *Occupational and environmental respiratory diseases* (edited by P. Harber, M.B. Schenker and J.R. Balmes), Mosby, St Louis.

Lubin, J.H. and Boice, J.D., 1997. Lung cancer risk from residential radon: meta-analysis of eight epidemiological studies, *J Natl Cancer Inst*, Vol 89, pp. 49–57.

Parker,D.L., Carl, W.R., French L.R., *et al,* 1994. Characteristics of adolescent work injuries reported to the Minnesota Department of Labour and Industry,. *Am J Public Health,* Vol.84, pp. 606–11.

Runyan, C.W. and Zakocs, R.C., 2000. Epidemiology and prevention of injuries among adolescent workers in the USA, *Ann Rev Public Health*, Vol 21, pp. 247–69.

Savitz, D.A., Bornschein, R.L., Amler, R.W. *et al.*, 1997. Assessment of reproductive disorders and birth defects in communities near hazardous chemical sites, *Reprod Toxicol*, Vol 11, pp. 223–30.

The Transport 2000 Trust, *Safe Routes to School* Sustrans http://www.sustarns.org.uk (in 2001)

US EPA, 1987. Asbestos containing materials in schools, Environmental Protection Agency, *Federal Register*, No 52, pp. 41826–903.

US EPA, 1996. National priorities list for uncontrolled hazardous waste sites, Final rule, Environmental Protection Agency, *Federal Register*, No 61, pp. 67655–77.

Vrijheid, M. Dolk, H Armstrong, B *et al.*, 2002. Chromosomal congenital anomalies and residence near hazardous waste landfill sites. *Lancet*, Vol 359, pp. 320–22.

WHO, 1998, *Guidelines for drinking-water quality,* 2nd edition, Vol 2, Health criteria and other supporting information, Addendum to Vol 2, 1996, World Health Organization, Geneva.

WHO/EEA, 1997. *Air and health,* WHO Regional Office for Europe and European Environmental Agency, Copenhagen.

WHO, 1999a. *Guidelines for community noise,* World Health Organization, Geneva

WHO, 1999b. *Charter on transport, environment and health* , WHO Regional Office for Europe, Copenhagen.

WHO, 1999c. *Declaration of the Third Ministerial Conference on Environment and Health*, WHO Regional Office for Europe, Copenhagen.

WHO, 2000a. *Transport, environment and health,* WHO Regional Publications, European Series, No. 89, WHO Regional Office for Europe, Copenhagen.

WHO, 2000b. *Air quality guidelines for Europe*, 2nd edition, WHO Regional Publications, European Series, No 91, WHO Regional Office for Europe, Copenhagen.

WHO/EEA, in press. *Water and health.* WHO Regional Office for Europe, Copenhagen.

Wijnen, J.H. van, Verhoef, A.P., Jans H.W.A., Bruggen, M. van, 1995. The exposure of cyclists, car drivers and pedestrians to traffic-related air pollutants, *Int Arch Occup Environ Health,* Vol 67, pp. 187–193.

Woolf, A.D. and Flynn,E., 2000. Workplace toxic exposures involving adolescents aged 14–19 years, *Arch Ped Adolesc Med*, Vol 154, pp. 234–39.

PART II:
Health effects and associated environmental factors

Natalia Herta (age 13), Repubic of Moldova

3. Asthma, allergies and respiratory health

Ondine S. von Ehrenstein

Summary of existing knowledge
- Asthma and allergic disorders are a leading cause of chronic illness in childhood.
- An increasing trend was observed in many industrialised countries.
- Early life exposure appear to play an important role for the risk of developing asthma or hay fever in childhood.
- Factors associated with the development of asthma and/or hay fever include the microbial and infectious burden, environmental tobacco smoke, maternal smoking in pregnancy and allergens.

Main challenges
- To understand the role and mechanism of environmental exposure in early life on the maturation of immune responses.
- To improve understanding of the fraction of asthma and other respiratory diseases attributable to indoor and outdoor air pollution.
- To improve understanding of protective environments and the opportunity for the development of preventive measures.

Action points
- Implement measures to reduce exposure of children to environmental tobacco smoke and indoor air pollution, beginning from earliest fetal development.
- Specify and characterise protective environmental factors that may have the potential to prevent asthma and allergies.
- Set safe standards for all children to reduce exposure to outdoor and indoor air pollution.

3.1. Introduction and definitions

Childhood asthma and allergic disorders constitute an important public health concern with high prevalence rates, and substantial morbidity, resulting in extensive use of drugs and medical services in many European countries. There is convincing evidence that the prevalence of asthma is on the rise in industrialised countries. Asthma and allergies are considered to be a leading cause of chronic illness in childhood. Although there is no doubt that a strong genetic component is responsible for the development of asthma and atopic disorders, environmental factors operating early in life are also likely to be important.

This chapter describes the epidemiology of asthma and atopic diseases in childhood. The focus is on the European Region. Also discussed in detail are environmental risk factors that may play a role in the development of asthma and allergy, or that have importance for respiratory health. Conclusions are drawn for future activities aimed at preventive actions.

Atopy, in general, refers to the presence of allergen-specific immunoglobulin E (IgE) antibodies. Atopic diseases are associated with the production of allergen-specific IgE antibodies, including allergic rhinitis ('hay fever'), atopic eczema or dermatitis, and asthma, although only a variable fraction of asthma is atopic. Although these disorders have immunological mediators and reactions in common, they are associated with very different genetic and environmental determinants and risk factors (see section below). Clinically, their impact varies widely, ranging from a small spot of eczema to a lethal anaphylactic shock. Allergic rhinitis is an allergen ([1])-dependent inflammation of the lining of the nose associated with conjunctivitis. It may be chronic, recurrent or seasonal ('hay fever'). Atopic eczema is an inflammatory skin disorder characterised by severe itching, a chronic or chronically relapsing course, and a particular distribution of lesions that changes with age.

There is no widely accepted definition of asthma, which makes it difficult to draw conclusions from epidemiological studies; conclusions depend on the definitions used. In clinical practice, asthma is considered an obstructive lung disease with hyperreactivity of the airways to a variety of stimuli and with a high degree of reversibility of the obstructive process either spontaneously or as result of treatment. The disease has various clinical aspects such as exercise-induced wheeze, attacks of shortness of breath, or persistent nocturnal cough with varying expression throughout infancy and childhood, and is related to different physiological, cellular and biochemical characteristics, which may also vary with age (Behrman *et al.*, 2000). The World Health Organization (WHO) together with the United States National Heart Lung and

(1) By the word allergen we usually mean a protein that at extremely low concentration can cause an IgE-mediated sensitisation or a low molecular weight chemical that, after binding to serum albumin, can cause a lymphocyte-mediated sensitisation.

Blood Institute developed the following definition: 'Asthma is a chronic inflammatory disorder of the airways in which many cells play a role, in particular mast cells, eosinophils and T-lymphocytes. In susceptible individuals this inflammation causes recurrent episodes of wheezing, breathlessness, chest tightness, and cough particularly at night and/or in the early morning. These symptoms are usually associated with widespread but variable airflow limitation that is at least partly reversible either spontaneously or with treatment. This inflammation also causes an associated increase in airway responsiveness to a variety of stimuli' (WHO and International Association of Allergology and Clinical Immunology, IAACI, 1999).

3.2. Epidemiology

Asthma and allergies

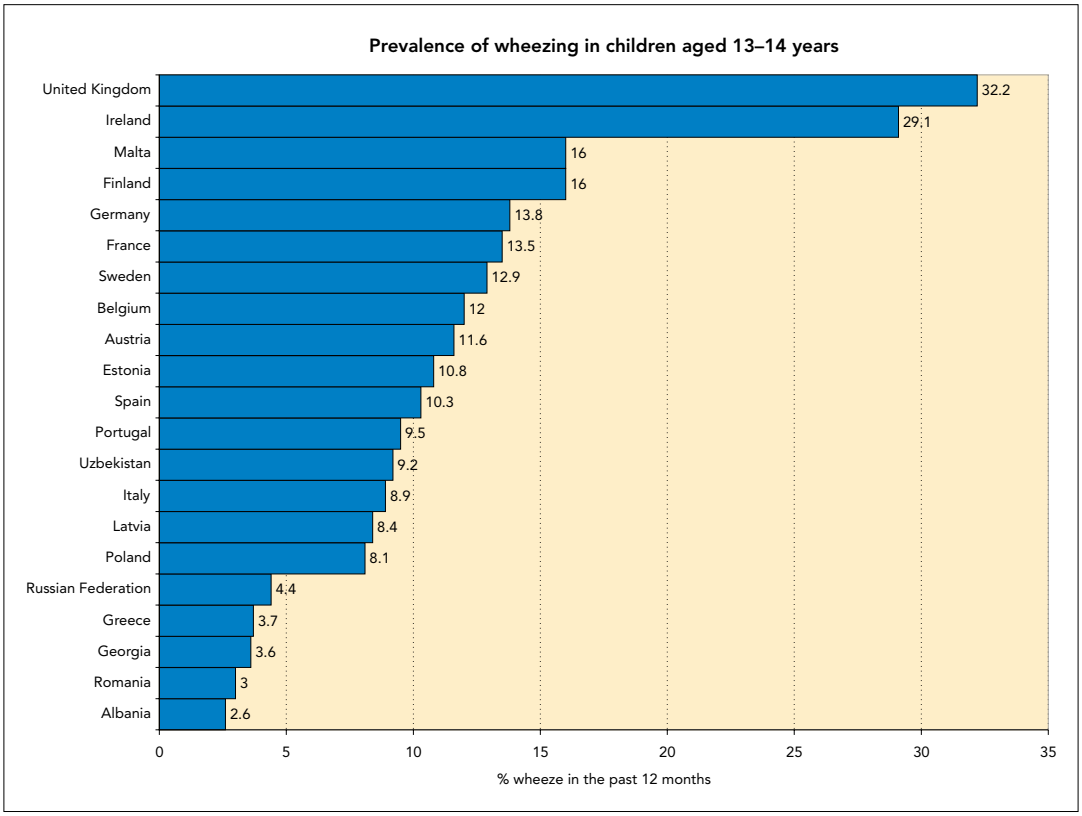
The International Study of Asthma and Allergies in Childhood (ISAAC) collected epidemiological data on the prevalence of childhood asthma, allergic rhinitis and atopic eczema worldwide, based on standardised diagnostic criteria and representative population samples (Pearce *et al.*, 1993; Asher *et al.*, 1995). The ISAAC study involved children in two age groups (6–7 years and 13–14 years), from 155 collaborating centres in 56 countries. Identical video and written questionnaires were used to assess the 12-month period prevalence of symptoms of asthma, allergic rhinitis and eczema (ISAAC Steering Committee, 1998a and 1998b). Comparisons of the prevalence of asthma symptoms among European countries are shown in Figure 3.1. (ISAAC Steering Committee, 1998a).

Globally, the ISAAC study demonstrated a wide range in rates for symptoms of asthma, allergic rhinitis and eczema. For asthma symptoms (wheeze) in the previous 12 months in 13 to 14 year old children, up to 15-fold differences were found between countries, with a range from 2.1 to 4.4 % in Albania, China, Greece, Indonesia, Romania and the Russian Federation, to a range from 29.1 to 32.2 % in Australia, New Zealand, Ireland and the United Kingdom. In the younger age group, the prevalence of wheeze ranged from 4.1 to 32.1 %. For both age groups, the prevalence of wheeze was particularly high in English speaking countries. Countries with a relatively lower prevalence (under 10 %) were mainly found in Asia, Northern Africa, eastern Europe and eastern Mediterranean regions. Notably, within Europe similar variations were found in the range of the prevalence of wheeze, with the lowest rates in Albania, Romania and Georgia and the highest rates in Malta, Ireland and the United Kingdom (Figure 3.1.). Similar gradients were observed for hay fever and atopic dermatitis. Overall, the between-country variation was greater than the within-country variation, both in Europe and worldwide (ISAAC Steering Committee, 1998a). The results of the questionnaire-based ISAAC study were supported by results from ISAAC phase II surveys, which included objective markers of atopy such as skin prick test reactivity, and measures known to be strongly associated with asthma, such as bronchial hyperreactivity (Annus *et al.*, 2001; Weiland *et al.*, 1999). Further ISAAC phase II studies are under way.

Recently, the prevalence of skin test reactivity and exercise-induced bronchial reactivity were compared in the United Kingdom and Albania, in order to further investigate the large geographical difference in reported asthma symptoms found between these two countries (Priftanji *et al.*, 2001). While a large difference in the proportion of exercise induced bronchial reactivity (0.8 % vs. 5.4 %) was found, the frequency of atopic sensitisation was similar in both countries (15.0 % vs. 17.8 %), suggesting that large geographical differences in asthma prevalence can be found without differences in atopy (Priftanji *et al.*, 2001). A comparison between the prevalence of bronchial hyperresponsiveness and skin prick test reactivity between Estonian and Swedish schoolchildren, however, supported the notion of a lower prevalence of asthmatic and allergic disorders in eastern Europe (Annus *et al.*, 2001; Matricardi, 2001).

Figure 3.1. **Twelve-month prevalence of self-reported asthma symptoms in children (age group 13–14) from written questionnaires in the ISAAC study 1995–96**

Source: ISAAC Steering Committee, 1998a



Increasing trends

The change in prevalence of wheeze and asthma over time in Europe was addressed in a number of investigations using identical methodology, repeated after a period of time, recently summarised by von Mutius (von Mutius, 1998a). Most surveys found a significant increase in childhood asthma in 'western affluent' countries over the last few decades, with a trend ranging from only a slight increase up to a three-fold increase (Nystad *et al.*, 1998; Anderson *et al.*, 1994; Rona *et al.*, 1995; Ninan and Russel, 1992; Burney *et al.*, 1990). Increases in awareness and changes in the clinical practice of doctors labeling children with wheezy disorders as 'asthmatic' may have contributed, at least in part, to the rising time trends (Hill *et al.*, 1989). However, studies including measurements of bronchial hyperreactivity indicated that changes in diagnostic practice and labeling of children as asthmatic, did not entirely explain the recent increases in asthma prevalence (Burr *et al.*, 1989; Peat *et al.*, 1994). Objective measures of changes over time in atopic sensitisation are rare. In Japan, for example, specific serum IgE antibodies in schoolgirls aged 13–14 increased significantly from 21.4 % in 1978 to 39.4 % in 1991 (Nakagomi *et al.*, 1994). A recent systematic search and review of articles studying trends over time based on more objective measurements of asthma and allergies between 1966 and 2000 resulted in only 16 published articles reporting on those kind of measures. In six studies, a significant increase in at least one objective measurement was reported (review in Wieringa *et al.*, 2001). The reported increasing trend over time appears to reflect a real increase in atopic disorders in childhood.

Overall, the epidemiological research indicated relatively high rates and increasing trends mostly in 'western', industrialised and affluent countries. In eastern European countries and in developing countries, the rates were generally lower (review in Matricardi, 2001; ISAAC Steering Committee, 1998a; von Mutius *et al.*, 1992; von Mutius *et al.*, 1994). It was suggested that a 'western lifestyle' is associated with factors determining the manifestation of atopic diseases in childhood. In a unique situation, immediately after the German reunification, significantly lower rates of atopic disorders were found in the eastern than in the western part, while physician-diagnosed bronchitis was more prevalent in the eastern than in the western study area (von Mutius *et al.*, 1992). Since then tremendous changes have

occurred leading to a 'western lifestyle' in the former German Democratic Republic. At the same time, significant increases in the prevalence of hay fever (5.1 % vs. 2.3 %) and atopic sensitisation (26.7 % vs. 19.3 %) were found, whereas the prevalence of asthma and bronchial hyperreactivity remained virtually unchanged (von Mutius *et al.*, 1998b). The authors concluded that important differences in the development of atopic disorders may exist, with factors operating very early in life particularly relevant for the acquisition of childhood asthma, while the development of atopic sensitisation and hay fever may also be affected by environmental factors occurring beyond infancy. Further evidence comes from an Estonian cross-sectional study that showed that a change in living conditions was not reflected in changed rates of asthma (2.5 % vs. 3.2 %) or atopic sensitisation (14.3 %) in 10-year-old children between successive four-year periods, indicating that either the time period of observation was too short, or that exposures earlier in life determine the risk of asthma and atopy in childhood (Riikjarv *et al.*, 2000).

A possible change in severity of wheezing illnesses was investigated by a number of researchers. Overall, it has been concluded that although significant increases were seen in the frequency of asthma and in the number of children visiting specialists, there were concurrent declines in the frequency of hospital admissions, intensive care visits, emergency room visits and multiple physician contacts, and in the mean duration of hospital stay. One suggested explanation for these findings was an improvement in treatment and disease management (overview in von Mutius, 1998a; Erzen *et al.*, 1995; Anderson *et al.*, 1994; Weitzman *et al.*, 1992).

Many researchers have aimed to explain the geographical heterogeneity and the increase in the prevalence of asthma and allergies in a number of industrialised countries. In addition to a strong genetic component, several factors were related to the prevalence of asthma and atopic diseases in many studies. These included infections early in life, microbial exposure, allergen exposure, family size, air pollution and environmental tobacco smoke, and nutrition.

Box 3.1. Natural history of atopic diseases

The spectrum of symptoms of atopic disorders changes with age. During early infancy, IgE antibodies are produced predominantly against cow's milk and chicken egg proteins, and are accompanied by clinical manifestations such as atopic dermatitis, gastrointestinal symptoms and, occasionally, by respiratory symptoms. Sensitisation to house dust mites, cat dander and other indoor allergens becomes more frequent during preschool and school age. Seasonal allergic rhinitis (hay fever) and sensitisation to pollen increases during school age and reaches a peak in adolescence.

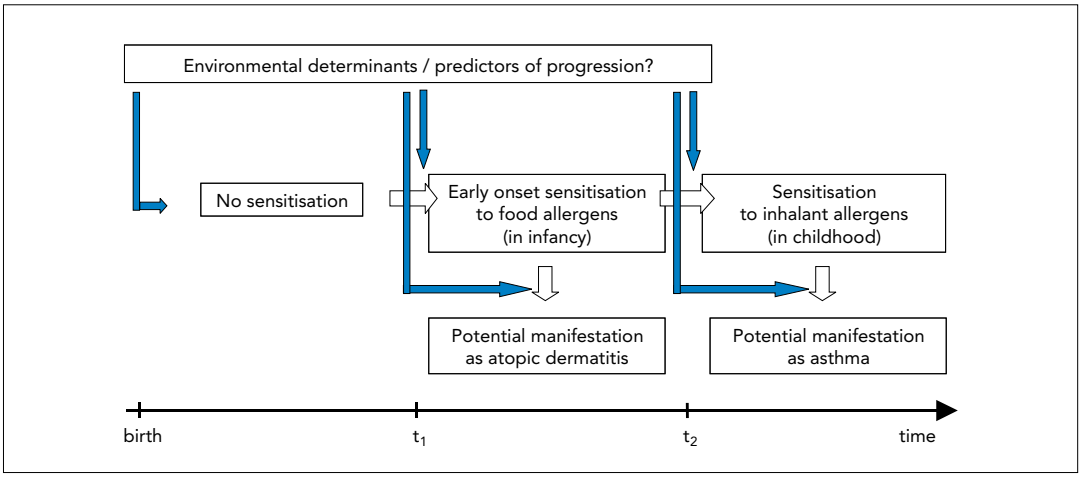
It is clear that atopy is a strong risk factor for asthma. However, it is also clear that additional factors are required for the development of asthma: while most asthmatics are allergic to at least one inhalant allergen, only a subgroup of allergic children develops persistent airway disease (Woolcock *et al.*, 1995; Holt *et al.*, 1999). The current understanding of this 'atopic march' is that early onset of sensitisation to food allergens in infancy potentially manifests itself as atopic dermatitis, and may progress to sensitisation to inhalant allergens that may manifest as asthma in a subset of the sensitised children.

Obstructive airway diseases and wheezing are frequent among young children. However, in a large birth cohort study in the United States, it was shown that the majority of wheezy infants had transient conditions associated with diminished airway function at birth and did not have an increased risk for asthma or allergies later in life. The authors further concluded that in a substantial minority of children, wheezy episodes were probably related to a predisposition to asthma (Martinez *et al.*, 1995). Children with atopic parents were particularly at risk for developing atopic disorders, as confirmed in many studies (Sears, 1997).

The important questions for public health are what are the determinants and predictors of the 'atopic march', and which factors may prevent the development and progression of atopic diseases in childhood (Figure 3.2.).

Figure 3.2. **Environmental factors may modulate the development and progression of atopic diseases in childhood**

Source: Adapted from Illi, 2001

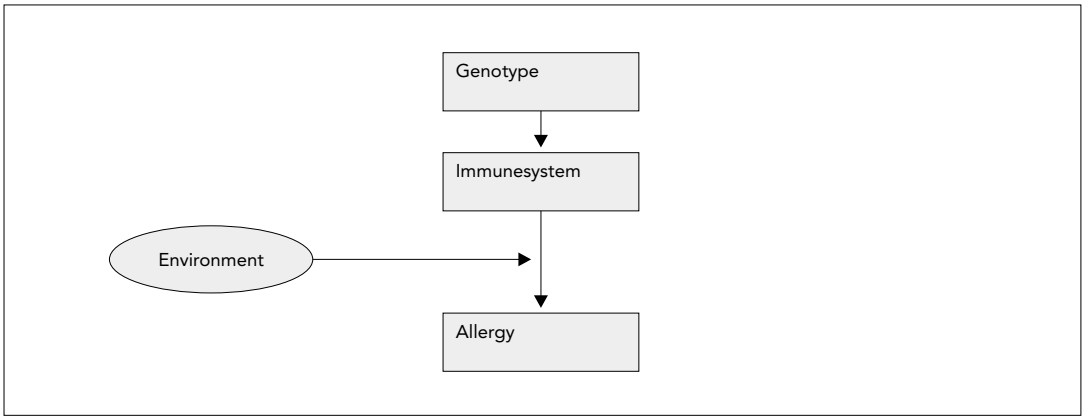


3.3. Environmental determinants

While genetic factors are considered important and may predispose children to develop asthma (Koeppen-Schomerus *et al.*, 2001; Duffy *et al.*, 1998; Sears, 1997; ECRHS Group, 1997; Crane *et al.*, 1989), convincing evidence demonstrates the important role of environmental factors in the manifestation of atopic disorders, pointing towards a gene-environmental interaction (Martinez, 2001). Earlier twin studies suggested that genetic predisposition might account for 20–75 % of asthma cases, leaving a substantial number unexplained (Edfors-Lubs, 1971). Genetic studies confirmed a polygenic inheritance pattern, and further studies are under way searching for genetic variations relevant for the response to environmental exposures (Martinez, 2001). Several observations underline the relevance of environmental factors in the 'multifactorial' nature of atopic disorders, including: differences in asthma rates between a genetically homogenous population (von Mutius *et al.*, 1992); differences related to specific differences in living conditions within same geographical regions (Riedler *et al.*, 2001; Kilpelainen *et al.*, 2000; Riedler *et al.*, 2000; von Ehrenstein, *et al.*, 2000); variations between social groups (Lewis and Britton, 1998a); changes in prevalences in migrating populations (Leung 1996); increasing trends over time in relatively short periods of time as described in the previous section of this chapter. The development of asthma and allergic disease is understood as a complex interaction between environmental influences, genotype and the immune system, with the early life environment modulating immune responses (Figure 3.3).

Figure 3.3. **Interaction between environment, genotype and immune system in the expression of the allergenic phenotype**

Source: Source: Renz, 1999



Indoor air pollution

European children generally spend more time indoors than outdoors, putting them near sources of indoor air pollutants, such as tobacco smoke, cooking stoves, vehicle exhausts (inside the car), etc. These exposures may contribute to the risk of

adverse respiratory and allergic health outcomes.

Environmental tobacco smoke

Environmental tobacco smoke is an important indoor pollutant and detrimental to children's respiratory health, particularly during lung growth and development. It is associated with lower respiratory illness, onset and worsening of asthma, and reduced lung growth and function, summarised by von Ehrenstein and von Mutius (in press), and described in further detail in Chapter 10. The developing fetus can be involuntarily exposed to tobacco smoke through an actively smoking mother or by the mother's exposure to environmental tobacco smoke during pregnancy. Exposure may continue throughout childhood. These early exposures may have persistent adverse effects throughout life.

Exacerbation of asthma, an increase in wheezing and airway responsiveness, and the need for treatment of symptoms have been observed in children exposed to passive smoking (Chilmonczyk *et al.*, 1993; Halken *et al.*, 1995; Oliveti *et al.*, 1996; Lewis *et al.*, 1995). A 14 % increase in childhood wheezy bronchitis was observed among children when the mother smoked more than four cigarettes per day, and a 49 % increase when the mother smoked 14 cigarettes daily (Neuspiel *et al.*, 1989). Children with wheezing who were exposed to environmental tobacco smoke through childhood showed progressive impairment of lung function between ages 9 and 15, whereas lung function was almost normal in wheezing children who were not exposed (Sherryl *et al.*, 1992). Murray and Morrison (1990) found that children with atopic dermatitis were more at risk for asthma if exposed to environmental tobacco smoke than children without dermatitis. In the United States, 380 000 excess cases of childhood asthma and wheezing (Stoddard and Miller, 1995) — or 7.5 % of all symptomatic children — have been attributed to maternal smoking. Most studies report adverse effects of parental smoking on asthma in infancy and early childhood, while the effects of past and current exposure to environmental tobacco smoke on the incidence and persistence of wheeze and asthma in adolescence are less clear. This, however, may be partially explained by parents changing their smoking behaviour due to their children having asthma, reporting bias and other methodological limitations, and to the natural history of asthma overlapping the effects of passive smoking.

Evidence is conflicting on the association between exposure to environmental tobacco smoke and atopic sensitisation in childhood. In two studies, increased allergic sensitisation (Ronchetti *et al.*, 1992) and an enhanced prevalence of eosinophilia (Ronchetti *et al.*, 1990) were found in relation to parental smoking, while other investigators did not confirm these findings (Henderson *et al.*, 1995; Kuehr *et al.*, 1992; Arshad *et al.*, 1993).

Consistent evidence suggests that small but significant decrements in pulmonary function are associated with passive smoke exposure before and after birth, and throughout childhood (review in Cook *et al.*, 1998). Maternal smoking during pregnancy was related to impaired lung-function in newborn infants (Stick *et al.*, 1996). Decrements in childhood lung function may be associated with reductions in pulmonary function throughout life, because childhood and adult lung function are known to 'track' (Weiss and Ware, 1996). Permanent effects of parental smoking on lung function were found in adults of 30–59 years of age (Upton *et al.*, 1998). In addition, reduced pulmonary lung function was shown to be a risk factor for morbidity and mortality for several non-respiratory and respiratory diseases, by contributing to various pathogenic mechanisms in different organ systems (Beaty *et al.*, 1982). A pronounced but asymptomatic loss in lung function relating to moderate passive smoke or traffic exposure in susceptible children (levels of alpha-1-antitrypsin $\leq$fifth percentile) was suggested to be an intermediate phenotype in a causal pathway eventually leading to COPD in adulthood (von Ehrenstein *et al.*, in press).

Adverse effects of maternal smoking have been reported more frequently than those of paternal smoking, suggesting either higher exposure through the mother than the father or persistent effects of *in utero* exposure. However, it is difficult to disentangle the long-term effects of exposure to maternal smoking during different time windows of susceptibility (prenatal or postnatal) because mothers who smoke during pregnancy are likely to continue afterwards. (Other respiratory effects, such as the increased risk for lower respiratory infections in children of smokers and non-respiratory health effects of

environmental tobacco smoke are described in Chapter 10.).

Indoor biomass combustion
Smoke from household fuel burning is a complex mixture of many potentially toxic components that varies with source, materials burned, etc. The association of the indoor use of biomass fuels with acute lower respiratory infection was predominantly shown in developing countries (reviews in Smith *et al.*, 2000; Bruce *et al.*, 2000; editorial in McMichael and Smith, 1999). Respiratory diseases, particularly pneumonia in childhood, have been causally linked to exposure to particulate matter from combustion of biofuels (wood, charcoal, agricultural residues, dung) in developing countries (de Francisco *et al.*, 1993; Ellegard, 1996; Bruce *et al.*, 2000; review by Smith *et al.*, 2000). Smith and co-workers reported that the 'studies of indoor air pollution from household biomass fuels were reasonably consistent and, as a group, showed a strong significant increase in risk for exposed young children compared with those living in households using cleaner fuels or being otherwise less exposed'. They further noted that most studies found a strong and significant risk after adjustment for confounders. Indoor air pollution may be considered as an important environmental risk factor for childhood respiratory morbidity and mortality in countries where indoor cooking and heating with biomass is common (Smith *et al.*, 2000). In the European Region this was reported to be the case in some areas, for example, in Central Asia.

The relationship between exposure and adverse respiratory health effects is difficult to quantify (Ezzati and Kammen, 2001). Although the attributable fraction of acute respiratory mortality (including pneumonia) is not yet certain, it is likely that acute respiratory infections (ARI) represent the largest class of health impacts from air pollution worldwide. This is due to the fact that it is predominantly infants and young children who are affected, and to the three following factors: the relatively high odds ratio; the frequency of exposure particularly in developing countries; and the high base rate of the disease in these countries (Smith *et al.*, 2000).

Formaldehyde and nitrogen dioxide
Indoor air concentrations of formaldehyde are several magnitudes higher than outdoor levels. There are various indoor sources of formaldehyde (e.g. glue for carpets and furniture, chipboards). Smoking is also a major source. Formaldehyde's predominant route of exposure is inhalation, and its main absorption is in the upper airways. Exposure to formaldehyde may cause irritation to the mucous membranes of the upper airways, and may also lead to non-specific symptoms of the eyes, nose and throat.

Nitrogen dioxide (NO_2) concentrations are related to the use of cooking stoves and space heaters. High levels may lead to acute mucocutaneous irritation and respiratory effects. Adverse pulmonary effects were found in adult subjects with mild asthma after exposure to high levels of NO_2 (650 parts per billion) in exposure chamber studies (Beckett *et al.*, 1995). Epidemiological effects of NO_2 on children are discussed in a recent review by Ackermann-Liebrich and Rap (1999).

Outdoor air pollution
The role of common outdoor pollutants (sulphur dioxide, nitrogen oxide, particulate matter (PM), ozone) in allergic illnesses is uncertain (Braun-Fahrländer *et al.*, 1997; Riedel *et al.*, 1988). It was shown in several studies from the United States and Europe that adverse respiratory health effects in children were related to short-term increases in exposure levels (Braun-Fahrländer *et al.*, 1992, 1994 and 1997; Pope and Dockery, 1992; Dockery *et al.*, 1989; Neas *et al.*, 1995; Gilliland *et al.*, 2001) as well as to long-term exposure to levels of air pollutants as they occur in Europe and the United States (Dockery *et al.*, 1989; Schwartz and Neas, 2000; Ware *et al.*, 1986; von Mutius *et al.*, 1995). Particularly fine particles with a diameter less than 2.5 micrometres (μm) ($PM_{2.5}$) (Schwartz and Neas, 2000) and ultra fine particles ($PM_{0.1}$) are of increasing interest.

Because average concentrations of ambient air pollutants are highly correlated in most studies, it is difficult to disentangle the relative impact of a single pollutant in epidemiological studies. The most consistent relationships have been found for PM and ozone. Comparisons between geographical regions in cross-sectional studies provide consistent evidence of an association between long-term exposure to particulate air pollution and children's respiratory health in the United States (Dockery *et al.*, 1989; Schwartz and Neas, 2000; Ware *et al.*, 1986)

and in Europe (Braun-Fahrländer *et al.*, 1997). Furthermore, children with bronchial hyperresponsiveness and increased levels of IgE were reported to be prone to develop acute lower respiratory symptoms and decreases in peak expiratory flow if they were exposed to elevated concentrations of PM_{10} (particulate matter with a diameter smaller than 10 µm) or black smoke (Boezen *et al.*, 1999).

A case-control study conducted in the Czech Republic provides evidence of an association between ambient levels of particulate pollution in Europe and infant mortality from respiratory causes (Bobak and Leon, 1999). During the study period, exposures were relatively high. The Czech study supports the findings of other studies from Mexico City (Loomis *et al.*, 1999) and Sao Paulo (Saldiva *et al.*, 1994) showing that air pollution was related to increased mortality from respiratory diseases in children, particularly in infants, and suggesting that this effect may not be confined exclusively to less affluent societies.

Table 3.1. gives risk estimates for annual health effects in children due to long-term exposure to a $PM_{2.5}$ concentration of 10 or 20 µg/m^3 above a background level of 10 µg/m^3, as calculated in the framework of the *Air quality guidelines for Europe* by WHO (2000a).

Risk estimates for respiratory health effects in children due to long-term exposure to $PM_{2.5}$ Table 3.1.

Source: WHO, 2000a

Estimated number of children (out of 200 000 in a population of 1 million) experiencing health effects per year due to long-term exposure to a $PM_{2.5}$ concentration of 10 or 20 µg/m^3 above a background level of 10 µg/m^3		
Health effect indicator	**Number of children affected per year at $PM_{2.5}$ concentrations above background of**	
	10 µg/m^3	20 µg/m^3
Number of additional children with bronchitis symptoms	3 350	6 700
Number of additional children with lung function (FVC* or FEV_1**) below 85 % of predicted	4 000	8 000

* Forced vital capacity; ** Forced expiratory volume in 1 second.

Moderate increases in ambient NO_2 concentration were associated with lower respiratory symptoms in children with bronchial hyperresponsiveness and relatively high levels of total serum IgE (Boezen *et al.*, 1999). Upper respiratory symptoms were increased in children after long-term exposure to moderate and high levels of ambient NO_2, SO_2, and PM (von Mutius *et al.*, 1995). Many studies reported an effect of NO_2 on respiratory symptoms, while the evidence on the impact of ambient levels of NO_2 on asthma is considered as conflicting (see review by Ackermann-Liebrich and Rap, 1999).

The American Thoracic Society (ATS) concluded that ozone may lead to decreases in pulmonary function, increased airway reactivity, lung inflammation, increased respiratory symptoms and decreased exercise capacity in healthy adults and children (ATS, 1995). Recent studies in children give further support to these findings. For example, asthma aggravation and symptoms were related to exposure to particles and O_3 in African-American children (8–13 years) (Ostro *et al.*, 2001) and to particles and carbon monoxide in a random sample of children aged 5–12 years in Seattle (Yu *et al.*, 2000). Elevated O_3 concentrations were associated with school absenteeism due to respiratory illnesses in a population sample of school children (Gilliland *et al.*, 2001). A very recent cohort study from Southern California reported an increased relative risk (3.3; 95 % CI: 1.9-5.8) of developing asthma in children who played at least three sports outdoors compared with children playing no sports (Mc Connell *et al.*, 2002). Increased levels of ambient ozone (O_3) were also related to transient exacerbation of asthma in children (Gielen *et al.*, 1997). Decreases of ambient ozone during the Olympic games in Atlanta, United States, due to restricted road traffic, resulted in a significantly reduced risk of asthma events (OR: 0.48; 95 % CI: 0.44–0.86) (Friedman *et al.*, 2001). In addition, some people might be particular susceptibility to develop decrements in pulmonary function and respiratory symptoms in response to ozone exposure (ATS, 1995).

Exposure to high levels of road traffic was linked in several cross-sectional studies to increased prevalence of respiratory

symptoms (Osterlee *et al.*, 1996; Wijst *et al.*, 1993), non-specific airway responsiveness (NG'anga, 1996) and impairments of lung function (Wijst *et al.*, 1993; Brunekreef *et al.*, 1995; Brunekreef *et al.*, 1997) in children in Africa (NG'anga, 1996) and Europe (Brunekreef *et al.*, 1997). Hospital admission of children 4–48 months of age due to obstructive bronchitis (Pershagen *et al.*, 1995) and children up to five years of age due to asthma (Nitta *et al.*, 1993) were associated with increased traffic density. In a cross-sectional study in Munich, impairments of pulmonary function were slightly but significantly related to numbers of vehicles on the main street in the school district (PEF – 0.71 % (95 % CI: 1.08–0.33 %); MEF_{25} – 0.68 % (95 % CI: 1.11–0.25 %) per 25 000 vehicles daily) (Wijst *et al.*, 1993). However, bronchial hyperresponsiveness and diagnosis of asthma were not related to road traffic although a positive association for recurrent asthmatic symptoms was found (OR: 1.08; 95 % CI: 1.01–1.16). Similar reductions in lung function were found in a Netherlands study in children living close to a busy highway, in which road traffic exposure was measured on the basis of vehicle counts and PM_{10} concentrations (Brunekreef *et al.*, 1997). Two studies from the United Kingdom found no association between the frequency of treatment for asthma or symptoms of asthma and living close to a main road (Livingstone *et al.*, 1996; Waldron *et al.*, 1995). Epidemiological evidence suggests that lorry (diesel) traffic might be particularly harmful, which may be due to high particulate emissions (Brunekreef *et al.*, 1997). Several experimental studies have shown that diesel exhaust may stimulate and increase airway inflammation (Salvi *et al.*, 1999; Ohtoshi *et al.*, 1998; Takano *et al.*, 1997) and IgE responses (Takenaka *et al.*, 1995).

Overall, exposure to ambient air pollution in concentrations that occur in western Europe is unlikely to explain the observed increase in asthma prevalence over the last few decades (Nicolai and von Mutius, 1996). This is further supported by a number of studies that found allergic diseases to be relatively less frequent in eastern parts of Europe, although levels of many air pollutants were found to be — in many areas — higher than in the western Europe (Dotterud *et al.*, 2001; von Mutius *et al.*, 1992). A pronounced adverse impact of outdoor pollutants on respiratory health in asthmatic and non-asthmatic children has been found in many studies from different countries. The attributable risk of outdoor air pollution remains to be established, and the extent to which reduction of air pollution levels would reduce morbidity and mortality of asthmatic and non-asthmatic infants and children remains unknown. Although the individual risk may be small, the public health impact is considerably higher due to the large number of affected individuals (Künzli *et al.*, 2000).

Allergens

Exposure to allergens is thought to play an important role in asthma, based on evidence from many studies in different climatic areas in which sensitisation of asthmatic children was associated with measured allergens (Peat *et al.*, 1996; Wahn *et al.*, 1997a and 1997b; Sporik *et al.*, 1990). The majority of children and adolescents with asthma show allergic sensitisation to inhalant allergens. The evidence is conclusive for a dose-response relationship between house dust mite allergen exposure and both asthma and atopic sensitisation (Peat *et al.*, 1996; Sporik *et al.*, 1990; Wahn *et al.*, 1997a). A two-fold increase in exposure to the dust mite allergen in early childhood was associated with a significantly increased rate of specific sensitisation (Wahn *et al.*, 1997a; Munir *et al.*, 1997), doubling of the risk that sensitised children would develop asthma (Peat, 1997), and with an increase in asthma symptoms in children with asthma (Custovic *et al.*, 1995). The age at first wheezing episode was found to be inversely related to the level of exposure at age one year, especially in atopic children (Sporik *et al.*, 1990). In urban areas in the United States, sensitisation to cockroach allergens is very common, particularly in poor hygienic conditions (review in Liccardi *et al.*, 2001).

In contrast, the evidence is conflicting on the connection between exposure to pet allergen and allergic disorders. Recent population-based studies indicated a decreased risk for atopic sensitisation and asthma in children with a cat in the house (Roost *et al.*, 1999; Hesselmar *et al.*, 1999) and measured high exposure to cat allergen (Platts-Mills *et al.*, 2001). Platts-Mills *et al.* (2001) suggested that exposure to cat allergen can produce an antibody response without sensitisation or risk for asthma, which may be regarded as a form of tolerance.

Carpeting, upholstered furniture, mattresses, humidifiers and central air conditioning or heating make it easier for dust mites, moulds

and other potent allergens to thrive, and the increasing airtightness of homes concentrates indoor allergens. Damp houses were shown to be a risk factor for the development and persistence of asthma (Nicolai *et al.*, 1998). Increased indoor humidity has led to mounting infestation of houses with dust mites and cockroaches.

The nature and concentration of outdoor allergens varies according to location and time. Pollen allergens may account for 10–20 % of allergic disease in Europe, particularly allergic rhinoconjunctivitis (D'Amato *et al.*, 1998). The main allergies are to grasses and birch pollens in northern Europe. The mild winters and hot, dry summers of southern Europe favour species such as cypresses. The importing of plants is leading to the emergence of new allergies that were previously unknown in Europe, for example to the ragweed, *Ambrosia*. Cross-reactivity has been demonstrated between allergens from trees. In addition, partial cross-reactivities have been observed between allergens carried by inhaled pollen grains and ingested fruit or vegetables (Bauer *et al.*, 1996; Leitner *et al.*, 1998). These trends may be exacerbated by global climate change as changing temperature and precipitation result in plant species altering their range (Gitay *et al.*, 2001).

Early exposure to infections or sibship size

Many epidemiological studies have shown associations between changing patterns of childhood infections and atopic disorders, even when considering the reduced total burden of infections in early infancy, as well as the decline of certain infections, in many affluent countries. A protective effect of infections on atopy was suggested by Strachan (1989), who described an inverse association between the number of older siblings and hay fever. This observation was confirmed by a number of studies reporting on different markers of infectious burden, such as attendance at day-care facilities (Kraemer *et al.*, 1998), number of older siblings (Matricardi *et al.*, 1997 and 1998; von Mutius *et al.*, 1994; von Mutius, 1998c) and positive serology to orofaecal infections (Matricardi *et al.*, 2000).

It has been hypothesised that the lack of immunological challenge during early infancy in many industrialised countries may result in an increased propensity to develop atopy, the so-called 'hygiene hypothesis' (Strachan, 1989; Martinez and Holt, 1999). Several investigators reported an inverse relation between allergic sensitisation and a tuberculin response to BCG (Aaby *et al.*, 2000) while others did not (Omenaas *et al.*, 2000). An inverse association was observed between early measles infection or vaccination and the development of atopic disorders in childhood (Shaheen *et al.*, 1996; Lewis and Britton, 1998). It appears that exposure to infections early in life promotes the T-helper (Th) 1 associated immunological response in favour of the Th2 response, the latter being associated with IgE-related atopic diseases (review in Holt and Jones, 2000).

The association between asthma and infections in early life is less clear (von Mutius, 1998c). Based on the ecological analyses of standardised data from 85 study centres involved in the ISAAC study, children's (13–14 years) lifetime prevalence of wheeze and the 12-month period prevalence of wheeze at rest were significantly inversely associated with the prevalence of tuberculosis (notification rates provided by WHO) (von Mutius *et al.*, 2000a). However, several other studies reported an increased risk for asthma in relation to childhood infections, particularly with respiratory syncytial virus (Sigurs *et al.*, 1995; Stein *et al.*, 1999). In line with these observations, results of a recent prospective birth cohort study suggested that repeated lower respiratory tract infections may be positively associated with subsequent development of asthma, wheeze and bronchial hyperreactivity (Illi *et al.*, 2001). Interestingly, early episodes of other infections, particularly runny nose and viral infections of the herpes type, were inversely related to the development of asthma and respiratory symptoms (Illi *et al.*, 2001).

The limited evidence regarding a direct effect of vaccinations on the development of atopic manifestations suggested no major effect of some types of vaccination (overview in Pershagen, 2000). The implementation of European vaccination programmes in the last decade is not thought to have had a direct effect on the development of allergy.

Rural, farming environments

The evidence is conflicting about a lower risk for atopic diseases in rural as compared with urban areas. It was suggested that asthma and allergic disorders tend to be less common in rural, traditional areas than in urban regions of Africa (Addo Yoba *et al.*, 1997;

Yemaneberhan *et al.*, 1997). However, in a large study in North America, for example, no trend for the distribution of allergic rhinitis was evident with regard to urban or rural location (Nathan *et al.*, 1997). On the other hand, recent studies from Europe independently found that children who lived on a farm during childhood had a substantial reduction in risk for hay fever and asthma compared with their peers in non-farming families in the same rural regions (Kilpelainen *et al.*, 2000; Riedler *et al.*, 2000; von Ehrenstein *et al.*, 2000). Increased exposure to livestock was related to a decreased risk for atopic diseases (Riedler *et al.*, 2000; von Ehrenstein, *et al.*, 2000). Findings from a recent study from Austria, Switzerland and Germany suggest that exposure to stables and farm milk starting very early in life has a strong protective effect against the development of asthma, hay fever and atopic sensitisation (Riedler *et al.*, 2001). Certain components (lipopolysaccharides) of the cell wall of Gram-negative bacteria, which were found to be more prevalent in farming environments, were suggested to be involved in the modulation of the immune response, possibly protecting against the development of atopy (von Mutius *et al.*, 2000b). These reports that exposure to environmental bacterial products that do not directly cause specific diseases may influence the pattern of immune responses in humans provide a new framework for understanding the 'hygiene hypotheses' (Martinez, 2001).

Nutrition

Various studies suggested that factors such as changes in nutrition may be linked to the increased prevalence of allergy in 'westernised' countries. The balance of dietary unsaturated and saturated fatty acids has changed due to the raised awareness of a potential increase in the risk of heart disease in relation to high intake of animal fats. There is some indication that a high intake of omega-3 fatty acids from fish may protect against the development of bronchial hyperreactivity and impairments in lung function (Peat *et al.*, 1995; Schwartz and Weiss, 1994; Black and Sharpe, 1997; Schwartz, 2000). In males, the severity of asthma has been related to high salt consumption (Carey *et al.*, 1993).

The pattern of bacterial colonisation of the intestine in early life may be important. For example, a recent study reported an inverse association between high exposure to orofaecal and foodborne diseases as they are usually acquired early in life and the prevalence of respiratory allergy (Matricardi *et al.*, 2000). However, the influence of childhood nutrition on the development of allergic disorders and the potential for prevention needs further investigation, in order to determine dietary recommendations. From a global perspective, malnutrition is a major risk factor for respiratory mortality (Rice *et al.*, 2000).

Although a protective effect of breastfeeding on the development of asthma has been the subject of debate, there is no doubt about the protective effect on respiratory infections (Wright *et al.*, 1989). Saarinen and Kajosaari found in a 17-year follow-up study a lower risk for atopic disorders throughout childhood and adolescence associated with breastfeeding (1995). A number of prospective studies reported that breastfeeding has a transient protective effect on the development of eczema, food allergy and early wheezy illness in the first one to three years of life (Chandra, 1979; Fergusson *et al.*, 1981). In a recent meta-analysis based on 12 prospective studies a protective effect of breastfeeding on the risk for asthma of 0.70 (95 % CI: 0.60-0.81) was found with a pronounced effect on children with a family history of atopy (Gdalevich *et al.*, 2001). It is however unclear whether the protective effect on asthma persists into later childhood, particularly in atopic children with asthmatic mothers (Wright *et al.*, 2001).

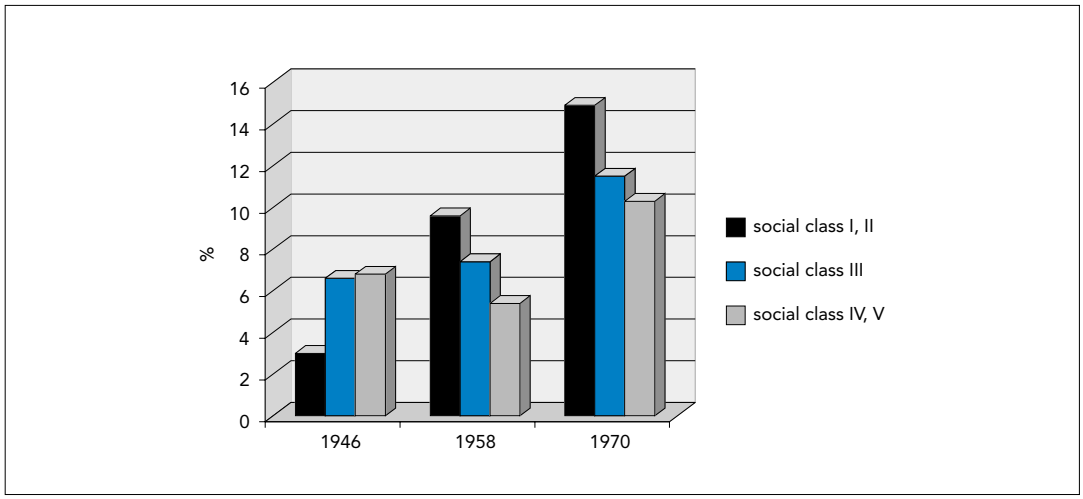
3.4. Socio-economic factors

The role of socio-economic status in association with atopic diseases has been widely debated. High prevalences of atopic disorders have been found in affluent countries, as discussed previously. A gradient between wealthier and poorer districts has been reported within countries. In Harare, the capital of Zimbabwe, the prevalence of airway hyperresponsiveness as assessed by a free-running test was significantly higher in the more affluent areas than in its poorer districts (Keeley *et al.*, 1991). In Italian military students a striking inverse relationship between parental socio-economic status and skin test reactivity to a panel of aeroallergens was found (Matricardi *et al.*, 1998). One potential explanation for the increased risk of atopy associated with high socio-economic status may relate to the size of families with lower and higher living

standards and the association with early infections as reported in the previous section.

Changing patterns of prevalence of atopic eczema were found in three United Kingdom cohorts. While in the 1946 cohort a higher social class was associated with a lower risk for eczema, the pattern changed in the 1958 and the 1970 cohorts towards a relatively decreased risk in children with a lower social class (Figure 3.4.) (Taylor *et al.*, 1984). However, an increasing rate of eczema was found in all social classes. These results may reflect a changing pattern of environmental (risk) factors associated with the living conditions of different social classes. They may also reflect changes in the diagnostic criteria and disease reporting.

Association between social class and atopic eczema in three national cohorts in the United Kingdom Figure 3.4.



Source: Taylor *et al.*, 1984

In the United States, children from poorer families may have a higher prevalence of wheezing, but children from better-off families are more likely to be diagnosed as asthmatic and to receive treatment for asthma, possibly reflecting different levels of access to health care in the United States (Sears, 1997). Studies in the United States reported increased mortality due to asthma in the inner city (Carr *et al.*, 1992). Hospitalisation rates for asthma showed a similar pattern, with indications that poverty was a more significant factor than ethnicity in explaining inequalities in asthma hospitalisation rates (Wissow *et al.*, 1988). Differences in prevalence rates among ethnic groups may, however, also be associated with differences in genetic background. For example, in a comparison between Turkish and German children living in the same area in Germany, Turkish children had lower prevalences of asthma and skin test reactivity, adjusted for social status, than their German peers (Kabesch *et al.*, 1999). A study from New York City showed an association between asthma hospitalisation rates in different neighbourhoods and a low family income, percentage of minorities in the population and percentage of children under the age of 18 (Claudio *et al.*, 1999). The authors suggested that — in addition to genetic factors — lack of access to preventive health care, poor housing conditions and environmental exposure contributed to the high rate of hospital admissions in poorer neighbourhoods. A study from the United Kingdom supported this, suggesting that higher rates of children's hospital admission due to asthma attacks were related to social deprivation; these increased admission rates were not explained by asthma prevalence rates but could be attributable to the aggravation of symptoms by active or passive smoking and poor disease management (Burr *et al.*, 1997). Parental smoking, which is more frequent in lower income groups in many countries, may explain variations in prevalence rates of childhood wheezing by socio-economic class (Sears, 1997). Increases in asthma rates in low socio-economic status groups in the United States were also associated with dampness in houses (Sears, 1990; Infante-Rivard, 1993; Platts-Mills and De Wech, 1989; Woolcock, 1994) which promotes the growth of moulds and house dust mites (Platts-Mill and De Wech, 1989); use of certain fuels for home heating (Infante-Rivard, 1993); and cooking with unvented gas appliances (Infante-Rivard, 1993; Holt and Sly, 1997; Weiss, 1994).

3.5. Public health impact

Pediatric asthma is a major public health concern in Europe and represents an enormous burden on family and society. It places a drain on healthcare resources related to medication use, emergency and hospitalisation care, and physicians' consultations (direct costs). Childhood asthma may also deprive children of academic achievement and social interaction (von Mutius 2000); such 'indirect costs' are associated, e.g., with days lost from school, care-giver costs, and environmental adaptation costs. Worldwide, the economic costs associated with asthma are estimated to exceed those of HIV and tuberculosis (WHO, 2000b). The early onset of atopic diseases may make people chronically ill for long time periods, with the frequent need of continuous medical treatment.

The prevalence of asthma varies worldwide. Although factors have been identified that appear to predispose children to develop asthma, the preventable part of the causes for the high and increasing prevalence in many countries is only poorly understood. On the other hand, indoor (particularly second hand smoke, bio fuel combustion) and outdoor air pollution has been shown to be associated with exacerbation of asthma, respiratory illnesses, and reductions in lung function. Childhood pulmonary function is known to track with adult lung function (Weiss and Ware, 1996). Reductions in lung function and respiratory illnesses early in life may thereby increase the risk for adult lung disease (review in von Mutius, 2001; Weiss and Ware, 1996; Upton *et al.*, 1998), and contribute to various pathogenic mechanisms in different organ systems (Beatty *et al.*, 1982), possibly leading to life-long chronic morbidity.

Smith *et al.* (2000) concluded that ARI represent one of the major health consequences of air pollution globally, although research on air pollution and acute respiratory infections in developed countries is limited. Even if the effect attributable to air pollution (indoor and outdoor) might be relatively small, this will result in an important health impact due to the ubiquitous exposure and the prevalence of the related health outcomes. Increasing joint efforts between research and policy-making are needed in order to reduce air pollution-related health impacts.

3.6. Control measures

The following measures are currently advocated to prevent sensitisation, particularly of infants at risk of developing allergic diseases (i.e. those with a strong family history of atopy):

- prenatal and postnatal avoidance of environmental tobacco smoke;
- exclusive breastfeeding for four to six months combined with avoidance of solid foods (Businco *et al.*, 1993);
- promotion of a healthy indoor environment, including design and construction of well-ventilated, low-allergen housing;
- measures to prevent indoor air pollution;
- avoidance of allergens such as animal dander, house dust mites and moulds (Hide *et al.*, 1996), substances that cause irritation on contact with the skin and metals used in ear-piercing, etc.;
- measures to control (avoid) outdoor air pollution.

Secondary prevention in children who already have asthma should include education on how to avoid environmental factors that have the potential to trigger asthma attacks and symptoms. WHO advocates to 'educate the public about the potentially fatal risks of allergy (anaphylaxis) and asthma, especially in children, and to encourage greater dialogue with their physicians. Better education and increased dialogue could avoid approximately 25 000 childhood deaths due to asthma each year' (WHO, 2000b).

Respiratory health in children would benefit in a long-term of a substantial reduction of air pollution exposure from traffic (Künzli *et al.*, 2000) and other indoor and outdoor sources. Passive smoke is known to track tobacco consumption. Therefore, measures are needed to control the use of tobacco.

These goals may be achieved by:

- technical improvements in vehicles and fuels;
- measures of transport regulation at local level (see Chapter 2);
- measures to prevent indoor air pollution (e.g. indoor biomass combustion);
- interventions aimed at the prevention of children's exposures to second-hand smoke.

Although several of these recommendations rest on extensive epidemiological and clinical evidence, the benefits of their implementation are, for the most part, not yet evaluated. Operational research is required to investigate the impact of measures aimed at the reduction of air pollution on children's respiratory health. A systematic approach to the development and evaluation of interventions is required, including the consideration of social deprivation and the risk for multiple exposures (e.g. traffic and tobacco smoke) (Bruce *et al.*, 2000). It is necessary to assess how policies might affect children, the population group at risk for high exposures and who are susceptible to the adverse effects of indoor and outdoor air pollution (Smith *et al.*, 2000).

Suggestions for research and public health investigations lie mainly in two areas:

- Investigation of environmental factors that may have the potential to prevent the manifestation of asthma and atopy, by modulating the immune response towards a Th1 profile. Promising results were recently derived from epidemiological studies on the role of the microbial burden early in life and reduced risk for asthma and allergic sensitisation.
- Operational research aiming at evaluation of the effectiveness of measures aimed at reducing indoor and outdoor air pollution, including the assessment of the fraction of childhood asthmatic, allergic and respiratory disorders attributable to air pollution.

Summary

Over the last three decades allergic diseases and asthma have become increasingly prevalent throughout Europe. There are, however, large inter-country differences, with more than 10-fold higher asthma symptom rates in western than in eastern countries. A yet unknown proportion of the difference is likely to be attributable to environmental factors.

Allergies and asthma are 'multifactorial', i.e. they result from complex interactions of genes and environment. Exposure to indoor (environmental tobacco smoke, biomass combustion) pollutants can increase the severity or frequency of asthmatic symptoms, the risk for respiratory illness, and was associated with decrements in lung function. Tobacco smoke is known to increase the risk of the manifestation of asthma and respiratory infections, and to impair pulmonary function. Outdoor air pollution (e.g. ozone, particulate matter) was shown to increase the risk for asthma attacks and to have an adverse impact on respiratory health. Factors related to a 'westernised' lifestyle (infections, sibship size, nutrition), which may reflect a lack of specific influences on the developing immune system, may increase the risk of development of atopic diseases. The microbial burden early in life may play a role in the risk for asthma by modulating immune responses. However, the influence of many environmental factors on the natural history of asthma and allergies are not clear, and pathways for potential prevention need to be identified.

The burden of disease due to asthma and allergic diseases in Europe is important. The impact of the environment on asthma and atopic diseases needs to be further addressed. In order to reduce the prevalence and severity of these conditions in childhood, operational research on the implementation of protective measures is needed in the field of indoor and outdoor air pollution reduction. Research on protective environmental factors may further help understanding of the role of environmental factors for asthma and atopy, and may contribute to the development of preventive measures.

References

Aaby, P., Shaheen, S.O., Heyes, C.B. *et al.*, 2000. Early BCG vaccination and reduction in atopy in Guinea-Bissau, *Clin Exp Allergy*, Vol 30, pp. 644–50.

AAP, 1999. *Handbook of pediatric environmental health* (edited by R. Etzel and S.J. Balk), American Academy of Pediatrics, Elk Grove Village, IL.

Ackermann-Liebrich, U. and Rapp, R., 1999. Epidemiological effects of oxides of nitrogen, especially NO_2, in *Air pollution and health* (edited by S.T. Holgate, J.M. Samet, H.S. Koren *et al.*), Academic Press, San Diego.

Addo Yoba, E.O.D., Custovic, A., Taggarart, S.C.O. *et al.*, 1997. Exercise induced bronchospasm in Ghana: Differences in prevalence between urban and rural schoolchildren, *Thorax*, Vol 52, pp. 161–5.

Anderson, H.R., Butland, B.K. and Strachan, D.P., 1994. Trends in prevalence and severity of childhood asthma, *Br Med J*, Vol 308, pp. 1600–4.

Annus, T., Bjorksten, B., Mai, X.M., *et al.*, 2001. Wheezing in relation to atopy and environmental factors in Estonian and Swedish school children, *Clin Exp Allergy*, Vol 31, pp. 1846–53.

Arshad, S.H., Stevens, M. and Hide, D.W., 1993. The effect of genetic and environmental factors on the prevalence of allergic disorders at the age of two years, *Clin Exp Allergy*, Vol 23, pp. 504–11.

Asher, I.M., Keil, U., Anderson, H.R. *et al.*, 1995. International study of asthma and allergies in childhood (ISAAC): Rationale and methods, *Eur Respir J*, Vol 8, pp. 483–91.

ATS, 1995. American Thoracic Society, Health effects of outdoor air pollution, *Am J Respir Crit Care Med*, Vol 153, pp. 3–50.

Bauer, L., Ebner, C., Hirschwehr, R. *et al.*, 1996. IgE cross-reactivity between birch pollen, mugwort pollen and celery is due to at least three distinct cross-reacting allergens: immunoblot investigation of the birch-mugwort-celery syndrome, *Clin Exp Allergy*, Vol 26, pp. 1161–70.

Beaty, T.H., Cohen, B.H., Newill, C.A. *et al.*, 1982. Impaired pulmonary function as a risk factor for mortality, *Am J Epidemiol*, Vol 116, pp. 102–13.

Beckett, W.S., Russi, M.B., Haber, A.D. *et al.*, 1995. Effect of nitrous acid on lung function in asthmatics: A chamber study, *Environ Health Perspect*, Vol 103, No 4, pp. 372–5.

Nelson textbook of pediatrics, 2000, 16th ed. (edited by Behrman R.E., Kliegman R.M., Jenson H.B.), W.B. Saunders Company, Philadelphia.

Black, P.N. and Sharpe, S., 1997. Dietary fat and asthma — is there a connection? *Eur Respir J*, Vol 10, pp. 6–12.

Bobak, M. and Leon, D.A., 1999. The effect of air pollution on infant mortality appears specific for respiratory diseases in the postneonatal period, *Epidemiology*, Vol 10, pp. 665–9.

Boezen, H.M., van der Zee, S.C., Postma, D.S. *et al.*, 1999. Effects of ambient air pollution on upper and lower respiratory symptoms and peak expiratory flow in children, *Lancet*, Vol 353, pp. 874–8.

Braun-Fahrländer, C., Ackermann-Liebrich, U., Schwartz, J. *et al.*, 1992. Air pollution and respiratory symptoms in preschool children, *Am Rev Respir Dis*, Vol 145, No 1, pp. 42–7.

Braun-Fahrländer, C., Kunzli, N., Domenighetti, G. *et al.*, 1994. Acute effects of ambient ozone on respiratory function of Swiss schoolchildren after a 10-minute heavy exercise, *Pediatric Pulmonology*, Vol 17, pp. 169–77.

Braun-Fahrländer, C.H., Vuille, J.C., Sennhauser, F.H. *et al.*, 1997. Respiratory health and long-term exposure to air pollutants in Swiss schoolchildren, *Am J Respir Crit Care Med*, Vol 155, pp. 1042–9.

Bruce, N., Perez-Padilla, R., Albalak, R., 2000. Indoor air pollution in developing countries: A major environmental and public health challenge, *Bull World Health Organization*, Vol 78, pp. 1078–92.

Brunekreef, B., Dockery, D.W. and Kryzanowski, M., 1995. Epidemiologic studies on short-term effects of low levels of major ambient air pollution components, *Environ Health Perspect*, Vol 103, pp. 3–13.

Brunekreef, B., Janssen, N.A.H., de Hartog, J. *et al.*, 1997. Air pollution from truck traffic and lung function in children living near motorways, *Epidemiology*, Vol 8, pp. 298–303.

Burney, P.G.J., Chinn, S. and Rona, R.J., 1990. Has the prevalence of asthma increased in children? Evidence from the national study of health and growth 1973–86, *Br Med J*, Vol 300, pp. 1306–10.

Burr, M.L., Butland, B.K., King, S. *et al.*, 1989. Changes in asthma prevalence; two surveys 15 years apart, *Arch Dis Child*, Vol 64, pp. 1452–6.

Burr, M.L., Verrall, C. and Kaur, B., 1997. Social deprivation and asthma, *Respir Med*, Vol 91, pp. 603–8.

Businco, L., Dreborg, S., Einarsson, R. *et al.*, 1993. An ESPACI position paper. Hydrolysed cow's milk formulae. Allergenicity and use in treatment and prevention, *Pediatr Allergy Immunol*, Vol 4, pp. 101–11.

Carey, O.J., Locke, C., Cookson, J.B., 1993. Effect of alterations of dietary sodium on the severity of asthma in men, *Thorax*, Vol 48, pp. 714–8.

Carr, W., Zeitel, L. and Weiss, K.B., 1992. Variations in asthma hospitalisation and death in New York City, *Am J Public Health*, Vol 82, pp. 59–65.

Chandra, R.K., 1979. Prospective studies of the effect of breast feeding on incidence of infection and allergy, *Acta Paedriatr Scand*, Vol 68, pp. 691–4.

Chilmonczyk, B.A., Salmun, L.M., Megathlin, K.N. *et al.*, 1993. Associations between exposure to environmental tobacco smoke and exacerbations of asthma in children, *N Engl J Med*, Vol 328, pp. 1665–9.

Claudio, L., Tulton, L., Doucette, J. *et al.*, 1999. Socioeconomic factors and asthma hospitalization rates in New York City, *J Asthma*, Vol 36, No 4, pp. 343–50.

Cook, D.G., Strachan, D.P. and Carey, I.M., 1998. Parental smoking and spirometric indices in children, *Thorax*, Vol 53, pp. 884–93.

Crane, J., O'Donell, T.V., Prior, I.A.M. *et al.*, 1989. Symptoms of asthma, methacholine airway responsiveness and atopy in migrant Tokelauan children, *NZ Med J*, Vol 102, pp. 36–8.

Custovic, A., Taggart, S.C.O., Francis, H.C. *et al.*, 1995. Exposure to house dust mite allergens and the clinical activity of asthma, *J Allergy Clin Immunol*, Vol 98, pp. 64–72.

D'Amato, G., Spieksma, F., Liccardi, G. *et al.*, 1998. Pollen-related allergy in Europe, *Allergy*, Vol 53, pp. 567–78.

de Francisco, A., Morris, J., Hall, A.J. *et al.*, 1993. Risk factors for LRI in young Gambian children, *Int J Epidemiol*, No 22, pp. 1174–82.

Dockery, D.W., Speizer, F.E., Stram, O. *et al.*, 1989. Effects of inhalable particles on respiratory health of children, *Am Rev Respir Dis*, Vol 139, pp. 587–94.

Dotterud, L.K., Odland, J.O. and Falk, E.S., 2001. Atopic diseases among schoolchildren in Nikel, Russia, an Arctic area with heavy air pollution, *Acta Derm Venereol*, Vol 81, No 3, pp. 198–201.

Duffy, D.L., Mitchell, C.A. and Martin, N.G., 1998. Genetic and environmental risk factors for asthma, a cotwin-control study, *Am J Respir Crit Care Med*, Vol 157, pp. 840–5.

ECRHS Group, 1997. Genes for asthma? An analysis of the European Community Respiratory Health Survey (ECRHS), *Am J Respir Crit Care Med*, No 156, pp.1773–80.

Edfors-Lubs, M.L., 1971. Allergy in 7,000 twin pairs, *Acta Allergologica*, Vol 26, pp. 249–85.

Ellegard, A., 1996. Cooking fuel smoke and respiratory symptoms among women in low income areas in Maputo, *Environ Health Perspect*, Vol 104, pp. 980–5.

Erzen, D., Roos, L.L., Manfreda, J. *et al.*, 1995. Changes in asthma severity in Manitoba, *Chest*, Vol 108, pp. 16–23.

Ezzati, M. and Kammen, D.M., 2001. Quantifying the effects of exposure to indoor air pollution from biomass combustion on ARI in developing countries, *Environ Health Perspect*, Vol 109, pp. 481–8.

Fergusson, D.M., Horwood, J.L., Shannon, F.T. *et al.*, 1981. Breast feeding, gastrointestinal and lower respiratory illness in the first two years, *Aust Paediatr J*, Vol 17, pp. 191–5.

Friedman, M.S., Powell, K.E., Hutwanger, L. *et al.*, 2001. Impact of changes in transportation and commuting behaviors during the 1996 summer Olympic games in Atlanta on air quality and childhood asthma, *JAMA*, Vol 285, pp. 897–905.

Gdalevich M., Mimouni D., Mimouni M., 2001. Brestfeeding and the risk of bronchial asthma in childhood — a systematic review with meta-analysis of prospective studies, *J Pediatr*, Vol 139, pp. 261–6.

Gielen, M.H., van der Zee, S.C., van Wijnen, J.H. *et al.*, 1997. Acute effects of summer air pollution on respiratory health of asthmatic children, *Am J Respir Crit Care Med*, Vol 155, pp. 2105–8.

Gilliland, F.D., Berhane, K., Rappaport, E.B. *et al.*, 2001. The effects of ambient air pollution on school absenteeism due to respiratory illnesses, *Epidemiology*, Vol 12, pp. 43–54.

Gitay, H., Brown, S., Easterling, W. *et al.*, 2001. Ecosystems and their goods and services, in *Climate change 2001: Impacts, adaption, and vulnerability* (Intergovernmental Panel on Climate Change, edited by J.J. McCarthy, O.F. Canziani, N.A. Leary *et al.*), Cambridge University Press.

Halken, S., Hst, A., Nilsson, L. *et al.*, 1995. Passive smoking as a risk factor for development of obstructive respiratory disease and allergic sensitisation, *Allergy*, Vol 50, pp. 97–107.

Henderson, F.W., Henry, M.M., Ivins, S.S. *et al.*, 1995. Correlates of recurrent wheezing in school-age children, *Am J Respir Crit Care Med*, Vol 151, pp. 1786–93.

Hesselmar, B., Aberg, B., Eriksson, B. *et al.*, 1999. Does early exposure to cat or dog protect against later allergy development? *Clin Exp Allergy*, Vol 29, pp. 611–7.

Hide, D.W., Matthews, S., Tariq, S. *et al.*, 1996. Allergen avoidance in infancy and allergy at 4 years of age, *Allergy*, Vol 51, pp. 89–93.

Hill, R., Williams, J., Tattersfield, A. *et al.*, 1989. Changes in use of asthma as a diagnostic label for wheezing illness in schoolchildren, *Br Med J*, Vol 299, p. 898.

Holt, P.G. and Sly, P.D., 1997. Allergic respiratory disease: Strategic targets for primary prevention during childhood, *Thorax*, Vol 52, pp. 1–4.

Holt, P.G., Macaubas, C., Stumbles, P.A. *et al.*, 1999. The role of allergy in the development of asthma, *Nature*, Vol 402, pp. B12–6.

Holt, P.G. and Jones, C.A., 2000. The development of the immune system during pregnancy and early life, *Allergy*, Vol 55, pp. 688–97.

Illi, S., von Mutius, E., Lau, S. *et al.*, 2001. Early childhood infectious diseases and the development of asthma up to school age: A birth cohort study, *Br Med J*, Vol 322, pp. 390–5.

Illi, S., 2001. Presented at the 20th Congress of the European Academy of Allergology and Clinical Immunology, Berlin, Germany.

Infante-Rivard, C., 1993. Childhood asthma and indoor environmental risk factors, *Am J Epidemiol*, Vol 137, pp. 834–44.

ISAAC Steering Committee, 1998a. Worldwide variations in the prevalence of asthma symptoms: The International Study of Asthma and Allergies in Childhood (ISAAC), *Eur Resp J*, Vol 12, pp. 315–35.

ISAAC Steering Committee, 1998b. Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema: ISAAC, *Lancet*, Vol 351, pp.1225–32.

Kabesch, M., Schaal, W., Nicolai, T. *et al.*, 1999. Lower prevalence of asthma and atopy in Turkish children living in Germany, *Eur Respir J*, Vol 13, pp. 1–6.

Keeley, D.J., Neill, P. and Gallivan, S., 1991. Comparison of the prevalence of reversible airways obstruction in rural and urban Zimbabwean children, *Thorax*, Vol 46, pp. 549–53.

Kilpelainen, M., Terho, O., Helenius, H. *et al.*, 2000. Farm environment prevents the development of allergies, *Clin Exp Allergy*, Vol 30, pp. 201–8.

Koeppen-Schomerus, G., Stevenson, J. and Plomin, R., 2001. Genes and environment in asthma: A study of 4 year old twins, *Arch Dis Child*, Vol 85, pp. 398–400.

Kraemer, U., Heinrich, J., Wijst, M. *et al.*, 1998. Age of entry to day nursery and allergy in later childhood, *Lancet*, Vol 352, pp. 450–5.

Kuehr, J., Frischer, T., Karmaus, W. *et al.*, 1992. Early childhood risk factors for sensitization at school age, *J Allergy Clin Immunol*, Vol 90, pp. 358–63.

Künzli, N., Kaiser, R., Medina, S. *et al.*, 2000. Public-health impact of outdoor and traffic-related air pollution: A European assessment, *Lancet*, Vol 356, p. 795–801.

Leung R., 1996. Asthma and migration, *Respirology*, Vol 1, pp. 123–6.

Leitner, A., Jensen-Jarolim, E., Grimm, R. *et al.*, 1998. Allergens in pepper and paprika. Immunologic investigation of the celery-birch-mugwort-spice syndrome, *Allergy*, Vol 53, pp. 36–41.

Lewis, S.A. and Britton, J.R., 1998a. Consistent effects of high socioeconomic status and low birth order, and the modifying effect of maternal smoking on the risk of allergic disease during childhood, *Respir Med,* Vol 92, pp. 1237–1244.

Lewis, S.A. and Britton, J.R., 1998b. Measles infection, measles vaccination and the effect of birth order in the aetiology of hay fever, *Clin Exp Allergy*, Vol 28, pp. 1493–500.

Lewis, S., Richards, D., Bynner, J. *et al.*, 1995. Prospective study of risk factors for early and persistent wheezing in childhood, *Eur Respir J*, Vol 8, pp. 349–56.

Liccardi, G., Cazzola, M., Russo, M. *et al.*, 2001. Mechanisms and characteristics of airway sensitization to indoor allergens, *Monaldi Arch Chest Dis*, Vol 5, No 1, pp. 55–63.

Livingstone, A.E., Shaddick, G., Grundy, C. *et al.*, 1996. Do people living near inner city main roads have more asthma needing treatment? Case-control study, *Br Med J*, Vol 312, pp. 676–7.

Loomis, D., Castillejos, M., Gold, D.R. *et al.*, 1999. Air pollution and infant mortality in Mexico City, *Epidemiology*, Vol 10, pp.118–23.

Martinez, F., 2001. The coming-of-age of the hygiene hypotheses, *Respir Res,* Vol 2, pp. 129–32.

Martinez, F.D. and Holt, P.G., 1999. Role of microbial burden in aetiology of allergy and asthma, *Lancet*, Vol 354 (suppl II), pp. SII 12–5.

Martinez, F.D., Wright, A.L., Taussig, L.M. *et al.*, 1995. Asthma and wheeze in the first six years of life, *N Engl J Med*, Vol 332, pp.133–8.

Matricardi, P.M., 2001. Prevalence of atopy and asthma in eastern versus western Europe: Why the difference? *Ann Allergy Asthma Immunol*, Vol 87, pp. 24–7.

Matricardi, P.M., Rosmini, F., Ferrigno, I. *et al.*, 1997. Cross-sectional retrospective study of prevalence of atopy among Italian military students with antibodies against hepatitis A virus, *Br Med J*, Vol 314, pp. 999–1003.

Matricardi, P.M., Franzinelli, F., Franco, A. *et al.*, 1998. Sibship size, birth order, and atopy in 11,371 Italian young men, *J Allergy Clin Immunol*, Vol 101, pp. 439–44.

Matricardi, P.M., Rosmini, F., Riondino, S. *et al.*, 2000. Exposure to foodborne microbes versus airborne viruses in relation to atopy and allergic asthma: Epidemiological study, *Br Med J*, Vol 320, pp. 412–7.

McConnell R., Berhane K., Gilliland F., *et al.*, 2002. Asthma in children exposed to ozone: a cohort study, *Lancet*, Vol 359, pp. 386–91.

McMichael, A.J. and Smith, K.R., 1999. Air pollution and health: Seeking a global perspective (editorial), *Epidemiology*, Vol 10, pp. 1–4.

Munir, A.K.M., Kjellman, N.M. and Bjorksten, B., 1997. Exposure to indoor allergens in early infancy and sensitisation, *J Allergy Clin Immunol*, Vol 100, pp. 177–81.

Murray, A.B. and Morrison, B.J., 1990. It is children with atopic dermatitis who develop asthma more frequently if the mother smokes, *J Allergy Clin Immunol*, Vol 6, pp. 732–3.

Nakagomi, T., Itaya, H., Tominaga, T. *et al.*, 1994. Is atopy increasing? *Lancet*, Vol 343, pp. 121–2.

Nathan, R.A., Meitzer, E.O., Seiner, J.C. *et al.*, 1997. Prevalence of allergic rhinitis in the United States, *J Allergy Clin Immunol*, Vol 99, pp. S808–14.

Neas, L.M., Dockery, D.W., Koutrakis, P. *et al.*, 1995. The association of ambient air pollution with twice daily peak expiratory flow rate measurements in children, *Am J Epidemiol*, Vol 141, No 2, pp. 111–22.

Neuspiel, D.R., Rush, D., Butler, N.R. *et al.*, 1989. Parental smoking and post-infancy wheezing in children: A prospective cohort study, *Am J Public Health*, Vol 79, pp. 168–71.

NG'anga, L.N., 1996. The epidemiology of childhood asthma in Kenya (PhD dissertation, McGill University, Montreal). http://www.epi.mcgill.ca/grads95.html (in 2001)

Nicolai, T. and von Mutius, E., 1996. Respiratory hypersensitivity and environmental factors: East and West Germany, *Toxicol Lett*, Vol 86, pp. 105–13.

Nicolai, T., Illi, S. and von Mutius, E., 1998. Effect of dampness at home in childhood on bronchial hyperreactivity in adolescence, *Thorax*, Vol 53, No 12, pp. 1035–40.

Ninan, T.K. and Russel, G., 1992. Respiratory symptoms and atopy in Aberdeen schoolchildren: Evidence from two surveys 25 years apart, *Br Med J*, Vol 304, pp. 873–5.

Nitta, H., Sato, T., Nakai, S. *et al.*, 1993. Respiratory health associated with exposure to automobile exhaust, I. Results of cross-sectional studies in 1979, 1982, and 1983, *Arch Environm Health*, Vol 48, pp. 53–8.

Nystad, W., Magnus, P. and Gulsvik, A., 1998. Increasing risk of asthma without other atopic diseases in school children: A repeated cross-sectional study after 13 years, *Eur J Epidemiol*, Vol 14, pp. 247–52.

Ohtoshi, T., Takizawa, H., Okazaki, H. *et al.*, 1998. Diesel exhaust particles stimulate human airway epithelial cells to produce cytokines relevant to airway inflammation in vitro, *J Allergy Clin Immunol*, Vol 101, pp. 778–85.

Oliveti, J.F., Kercsmar, C.M. and Redline, S., 1996. Pre-and perinatal risk factors for asthma in inner city African-American children, *Am J Epidemiol*, Vol 143, pp. 570–7.

Omenaas, E., Jentoft, H.F., Vollmer, W.M. *et al.*, 2000. Absence of relationship between tuberculin reactivity and atopy in BCG vaccinated young adults, *Thorax*, Vol 55, pp. 454–8.

Osterlee, A., Drijver, M., Lebret, E. *et al.*, 1996. Chronic respiratory symptoms in children and adults living along streets with high traffic density, *Occup Environ Med*, Vol 53, pp. 241–7.

Ostro, B., Lipsett, M., Mann, J., *et al.*, 2001. Air pollution and exacerbation of asthma in African-American children in Los Angeles, *Epidemiology*, Vol 12, pp. 200–8.

Pearce, N., Weiland, S., Keil, U. *et al.*, 1993. Self reported prevalence of asthma symptoms in children in Australia, England, Germany and New Zealand: An international comparison using the ISAAC protocol, *Eur Respir J*, Vol 6, pp. 1455–61.

Peat, J.K., 1997. Can asthma be prevented? Evidence from epidemiological studies of children in Australia and New Zealand in the last decade, *Clin Exp Allergy*, Vol 28, pp. 261–5.

Peat, J.K., van den Berg, R.H., Green, W.F., *et al.*, 1994. Changing prevalence of asthma in Australian children, *Br Med J*, Vol 308, pp. 1591–6.

Peat, J.K., Hodge, L., Salome, C.M. *et al.*, 1995. Dietary fish intake and asthma in children, *Am J Respir Crit Care Med*, Vol 151(suppl A), p. 469.

Peat, J.K., Tovey, E., Toelle, B.G. *et al.*, 1996. House dust mite allergens: A major risk factor for childhood asthma in Australia, *Am J Respir Crit Care Med*, Vol 153, pp. 141–6.

Pershagen, G., 2000. Can immunization affect the development of allergy? *Pediatr Allergy Immunol,* Vol 11 (suppl 13), pp. 26–8.

Pershagen, G., Rylander, E., Norberg, S. *et al.*, 1995. Air pollution involving nitrogen dioxide exposure and wheezing bronchitis in children, *Int J Epidemiol*, Vol 24, pp. 1147–53.

Platts-Mills, T.A.E. and De Wech, A.L., 1989. Dust mite allergens and asthma; a world wide problem, *J Allergy Clin Immunol*, Vol 83, pp. 416–27.

Platts-Mills, T., Vaughan, J., Squillace, S. *et al.*, 2001. Sensitisation, asthma, and a modified Th2 response to cat allergen: A population-based cross-sectional study, *Lancet*, Vol 357, pp. 752–6.

Pope, A.C. and Dockery, D.W., 1992. Acute health effects of PM_{10} pollution on symptomatic and asymptomatic children, *Am Rev Respir Dis*, Vol 145, pp. 1123–8.

Priftanji, A., Strachan, D., Burr, M. *et al.*, 2001. Asthma and allergy in Albania and the UK, *Lancet*, Vol 358, pp. 1426–7.

Renz, H., 1999. Immunologische Grundlagen allergischer Erkrankungen, in *Pdiatrische Allergologie und Immunologie* (edited by Wahn U, Seher R, Wahn V) 3rd ed., Urban & Fischer, München.

Rice, A.L., Sacco L., Hyder A., *et al.*, Malnutrition as an underlying cause of childhood deaths associated with infectious diseases in developing countries. *Bull World Health Organ,* Vol 78, pp. 1207-21.

Riedel, F., Kraemer, M., Scheibenbogen, C. *et al.*, 1988. Effects of SO_2 exposure on allergic sensitization in the guinea pig, *J Allergy Clin Immunol*, Vol 82, pp. 527–34.

Riedler, J., Eder, W., Oberfeld, G. *et al.*, 2000. Austrian children living on a farm have less hay fever, asthma and allergic sensitisation, *Clin Exp Allergy*, Vol 30, pp. 194–200.

Riedler J., Braun-Fahrländer, C., Eder, W. *et al.*, 2001. Exposure to farming in early life and development of asthma and allergy: A cross-sectional survey, *Lancet*, Vol 358, pp. 1129–33.

Riikjarv, M.A., Annus, T., Braback, L. *et al.*, 2000. Similar prevalence of respiratory symptoms and atopy in Estonian schoolchildren with changing lifestyle over 4 years, *Eur Respir J*, No 16, pp. 85–90.

Rona, R.J., Chinn, S. and Burney, P.G., 1995. Trends in the prevalence of asthma in Scottish and English primary school children 1982–92, *Thorax,* Vol 50, pp. 992–3.

Ronchetti, R., Macri, F., Ciofetta, G. *et al.*, 1990. Increased serum IgE and increased prevalence of eosinophilia in 9-year-old children of smoking parents, *J Allergy Clin Immunol*, Vol 86, pp. 400–7.

Ronchetti, R., Bonci, E., Cutrera, R. *et al.*, 1992. Enhanced allergic sensitisation related to parental smoking, *Arch Dis Child*, Vol 67, pp. 496–500.

Roost, H.P., Kuenzli, N., Schindler, C. *et al.*, 1999. Role of current and childhood exposure to cat and stopic sensitization, *J Allergy Clin Immunol*, Vol 104, pp. 941–7.

Saldiva, P.H.N., Lichtenfels, A.J.F.C., Paiva, P.S.O. *et al.*, 1994. Association between air pollution and mortality due to respiratory diseases in children in Sao Paulo, *Environ Res*, Vol 65, pp. 218–25.

Salvi, S., Blomberg, A., Rodell, B. *et al.*, 1999. Acute inflammatory responses in the airway and peripheral blood after short term exposure to diesel exhaust in healthy human volunteers, *Am J Respir Crit Care Med*, Vol 159, pp. 702–9.

Saarinen U.M., Kajosaari M., 1995. Breastfeeding as prophylaxis against atopic disease: prospective follow-up studyuntil 17 years old, Lancet, Vol. 346, pp. 1065-9.

Schwartz, J., 2000. Role of polyunsaturated fatty acids in lung disease, *Am J Clin Nutr*, Vol 71 (suppl 1), pp. S393–9.

Schwartz, J. and Neas, L.M., 2000. Fine particles are more strongly associated than coarse particles with acute respiratory health effects in schoolchildren, *Epidemiology*, Vol 11, No 1, pp. 6–10.

Schwartz, J. and Weiss, S.T., 1994. The relationship of dietary fish intake to level of pulmonary function in the first National Health and Nutrition Survey (NHANES I), *Eur Respir J*, Vol 7, pp. 1821–4.

Sears, M.R., 1990. The epidemiology of asthma, in *Asthma as an inflammatory disease* (edited by P.M. O'Byrne), Marcel Dekker, New York, pp. 15–48.

Sears, M.R., 1997. Descriptive epidemiology of asthma, *Lancet*, Vol 350 (suppl II), pp. 1–4.

Shaheen, S.O., Aaby, P., Hall, A.J. *et al.*, 1996. Measles and atopy in Guinea-Bissau, *Lancet*, Vol 347, pp. 1792–6.

Sherryl, D.L., Martinez, F.D., Lebowitz, M.D. *et al.*, 1992. Longitudinal effects of passive smoking on pulmonary function in New Zealand children, *Am Rev Respir Dis*, Vol 145, pp. 1136–41.

Sigurs, N., Bjarnason, R., Sigurbergsson, F. *et al.*, 1995. Asthma and immunoglobulin E antibodies after respiratory syncytial virus bronchiolitis: A prospective cohort study with matched controls, *Pediatrics*, Vol 95, pp. 500–5.

Smith, K.R., Samet, J.M., Romieu, I. *et al.*, 2000. Indoor air pollution in developing countries and acute LRI in children, *Thorax*, Vol 55, pp. 518–32.

Sporik, R., Holgate, S.T., Platts-Mills, T.A.E. *et al.*, 1990. Exposure to house-dust mite allergen (Der p I) and the development of asthma in childhood. A prospective study, *N Engl J Med*, Vol 323, pp. 502–7.

Stein, R.T., Sherrill, D., Morgan, W.J. *et al.*, 1999. Respiratory syncytial virus in early life and risk of wheeze and allergy by age 13 years, *Lancet*, Vol 354, pp. 541–5.

Stick, S.M., Burton, P.R., Gurrin, L. *et al.*, 1996. Effects of maternal smoking during pregnancy and a family history of asthma on respiratory function in newborn infants, *Lancet*, Vol 348, pp. 1060–4.

Stoddard, J.J. and Miller, I., 1995. Impact of parental smoking on the prevalence of wheezing respiratory illness in children, *Am J Epidemiol*, Vol 141, pp. 96–102.

Strachan, D.P., 1989. Hay fever, hygiene, and household size, *Br Med J*, Vol 299, pp. 1259–60.

Takano, H., Yoshikawa, T., Ichinose, T. *et al.*, 1997. Diesel exhaust particles enhance antigen-induced airway inflammation and local cytokine expression in mice, *Am J Respir Crit Care Med*, Vol 156, pp. 36–42.

Takenaka, H., Zhang, K., Diaz-Sanchez, D. *et al.*, 1995. Enhanced human IgE production results from exposure to the aromatic hydrocarbons from diesel exhaust: Direct effects of B-cell IgE production, *J Allergy Clin Immunol*, Vol 95, pp. 103–15.

Taylor, B., Wadsworth, M., Wadsworth, J. *et al.*, 1984. Changes in the reported prevalence of childhood eczema since the 1939–45 war, *Lancet*, Vol 2, No 8414, pp. 1255–7.

Upton, M.N., Watt, G.C.M., Davey Smith, G. *et al.*, 1998. Permanent effects of maternal smoking on offsprings' lung function, *Lancet*, Vol 352, p. 453.

von Ehrenstein, O.S. and von Mutius, E., in press. Smoking and the lung, *Eur Respir Monograph*.

von Ehrenstein, O.S., von Mutius, E., Illi, S. *et al.*, 2000. Reduced risk of hay fever and asthma among children of farmers, *Clin Exp Allergy*, Vol 30, pp. 187–93.

von Ehrenstein, O.S., von Mutius, E., Maier, E. *et al.*, in press. Lung function of school children with low levels of alpha1-antitrypsin and tobacco smoke exposure, *Eur Respir J*.

von Mutius, E., Fritzsch, C., Weiland, S.K. *et al.*, 1992. Prevalence of asthma and allergic disorders among children in united Germany: A descriptive comparison, *Br Med J*, No 305, pp. 1395–9.

von Mutius, E., Martinez, F.D., Fritzsch, C. *et al.*, 1994. Skin test reactivity and number of siblings, *Br Med J*, Vol 308, pp. 692–5.

von Mutius, E., Sherill, D.L., Fritzsch C., *et al.*, 1995. Air pollution and upper respiratory symptoms in children from East Germany, *Eur Respir J*, Vol 8, pp. 723–8.

von Mutius, E., 1998a. The rising trends in asthma and allergic disease, *Clin Exp Allergy*, Vol 28 (suppl 5), pp. 45–9, discussion pp. 50–1.

von Mutius, E., Weiland, S.K., Fritzsch, C. *et al.*, 1998b. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany, *Lancet*, Vol 351, pp. 862–6.

von Mutius, E., 1998c. The influence of birth order on the expression of atopy in families: A gene-environment interaction? *Clin Exp Allergy*, Vol 28, pp. 1454–6.

von Mutius, E., 2000. The burden of childhood asthma, Arch Dis Child, Vol 82 (suppl2), pp. ii2-ii5.

von Mutius, E., Pearce, N., Beasley, R. *et al.*, 2000a. International patterns of tuberculosis and the prevalence of symptoms of asthma, rhinitis, and eczema, *Thorax*, Vol 55, pp. 449–53.

von Mutius, E., Braun-Fahrländer, C., Schierl, R. *et al.*, 2000b. Exposure to endotoxin or other bacterial components might protect against the development of atopy, *Clin Exp Allergy*, Vol 30, pp. 1230–4.

Von Mutius, E., 2001. Peadiatric origins of adult lung disease. *Thorax*, Vol 56, pp. 153-7.

Wahn, U., Lau, S., Bergmann, R. *et al.*, 1997a. Indoor allergen exposure is a risk factor for early sensitisation during the first three years of life, *J Allergy Clin Immunol*, Vol 99, pp. 763–9.

Wahn, U., Bergmann R., Kulig M., *et al.*, 1997b. The natural course of sensitisation and atopic diseases in infancy and childhood, *Pediatr Allergy Immunol*, Vol 8 (suppl 10), pp. 16–20.

Waldron, G., Pottle, B. and Dod, J., 1995. Asthma and the motorways — one district's experience, *J Publ Health Med*, Vol 17, pp. 85–9.

Ware, J.H., Ferris, B.G., Dockery, D.W. *et al.*, 1986. Effects of ambient sulfur oxides and suspended particles on respiratory health of preadolescent children, *Am Rev Respir Dis*, Vol 133, pp. 824–42.

Weiland, S.K., von Mutius, E., Hirsch, T. *et al.*, 1999. Prevalence and atopic disorders among children in the East and West of Germany five years after the unification, *Eur Respir J*, Vol 14, pp. 862–70.

Weiss, S.T., 1994. The origins of childhood asthma, *Monaldi Arch Chest Dis*, Vol 49, pp. 154–8.

Weiss, S.T and Ware, J.H., 1996. Overview of issues in the longitudinal analysis of respiratory data, *Am J Respir Crit Care Med*, Vol 154, pp. S208–11.

Weitzman, M., Gortmaker, S.L., Sobol, A.M. *et al.*, 1992. Recent trends in the prevalence and severity of childhood asthma, *JAMA*, Vol 268, pp. 2673–7.

Wieringa, M.H., Vermeire, P.A., Brunekreef, B. *et al.*, 2001. Increased occurrence of asthma and allergy: Critical appraisal of studies using allergic sensitization, bronchial hyperresponsiveness and lung function measurements, *Clin Exp Allergy*, Vol 31, pp. 1553–63.

Wijst, M., Reitmeir, P., Dold, S. *et al.*, 1993. Road traffic and adverse effects on respiratory health in children, *Br Med J*, Vol 307, pp. 596–600.

Wissow, L., Gittelsohn, A., Szklo, M. *et al.*, 1988. Poverty, race and hospitalisation for childhood asthma, *Am J Public Health*, Vol 78, pp. 777–82.

Woolcock, A.J., 1994. Asthma, in *Textbook of respiratory medicine* (edited by J.F. Murray and J.A. Nadel) 2nd edition, W.B. Saunders, Philadelphia, pp. 1288–330.

Woolcock, A.J., Peat, J.K. and Trevillion, L.M., 1995. Is the increase in asthma prevalence linked to increase in allergen load? *Allergy*, Vol 50, pp. 935–40.

WHO/IAACI, 1999. Prevention of allergy and asthma interim report, Geneva, Switzerland, WHO/NMH/MNC/CRA/00.2.

WHO, 2000a. *Air quality guidelines for Europe,* 2nd ed., WHO Regional Publications, European Series, No. 91, WHO Regional Office for Europe, Copenhagen.

WHO, 2000b. Fact sheet No 206, on line at: http://www.who.int/inf-fs/en/fact206.html

Wright, A.L., Holberg, C.J., Martinez, F.D. *et al.*, 1989. Breast feeding and lower respiratory tract illness in the first year of life, *Br Med J*, Vol 299, pp. 946–9.

Wright, A.L., Holberg, C.J. and Martinez, F.D., 2001. Factors influencing the relation of infant breast feeding to asthma and recurrent wheeze in childhood, *Thorax*, Vol 56, pp. 192–7.

Yemaneberhan, H., Bekele, Z., Venn, A. *et al.*, 1997. Prevalence of wheeze and asthma and relation to atopy in urban and rural Ethiopia, *Lancet*, Vol 350, pp. 83–90.

Yu, O., Sheppard, L., Lumley, T. *et al.*, 2000. Effects of air pollution on symptoms of asthma in Seattle-area children enrolled in the CAMP study, *Environ Health Perspect*, Vol 108, pp. 1209–14.

4. Neurodevelopmental disorders

Philippe Grandjean and Roberta White

Summary of existing knowledge
- The central nervous system is particularly vulnerable to toxic effects during early development.
- Nervous system damage, once incurred during a developmental stage, is likely to be irreversible and may change the affected individual's quality of life and economic and social success.
- The extent to which current environmental pollution causes adverse effects on brain development is unknown. The contaminants that have been studied in the greatest detail, i.e. lead, methylmercury and polychlorinated biphenyls (PCBs), are likely to cause adverse health effects in subgroups of European populations with increased exposures.

Main challenge
- To improve our understanding of the attributable portion of developmental disabilities due to neurotoxicants.

Action points
- Set up exposure monitoring in at-risk areas.
- Reduce exposure through setting safe standards for children.
- Reduce exposure through healthy behaviour.

4.1. Introduction and definitions

Environmental exposure to a large number of substances have been associated with developmental disabilities, many of which involve the nervous system. Neurotoxic substances usually cause adverse effects on the nervous system through direct toxic actions on the nervous system cells. Current knowledge in this field is limited because the implications of hazardous exposures may not be immediately apparent, and because evaluation of developmental neurotoxicity is not required in the routine testing of chemicals. Also, the biochemical intricacies of brain development are only now being unravelled, and our understanding of neurotoxic substances and their mechanisms of action is still rather limited.

Health statistics suggest that these effects may be important in regard to public health. Developmental disabilities constitute a group of physical, cognitive, sensory and speech impairments that occur during childhood up to the age of 18 years. They include specific learning disabilities, intellectual retardation and attention deficit hyperactivity disorder (ADHD). Prevalence rates of specific developmental disabilities range up to about 10 % in certain populations, but differences in diagnostic criteria and in the degree of assessment may affect the apparent regional differences. Although rates in Europe seem to be lower than in the United States, for example, the occurrence is certainly large enough to constitute a significant public health problem.

An increasing number of environmental factors have been implicated as causes of developmental disabilities, in addition to the genetic components of the disorders. Even in the absence of developmental disabilities, neurotoxic effects on attention span, concentration, motor speed, memory and language functions would be expected to affect cognitive skills, education, social abilities and career. When incurred early in life, such developmental effects are likely to be permanent and may therefore affect an individual's lifetime prospects with regard to quality of life and social success.

Box 4.1. Risks to early brain development

'For much of the history of toxicology, the sensitivity of the developing organism to chemical perturbation attracted limited attention. Several tragic episodes and new insights finally taught us that the course of early brain development incurs unique risks. Although the process is exquisitely controlled, its lability renders it highly susceptible to damage from environmental chemicals. Such disturbances, as recognised by current testing protocols and legislation such as the Food Quality Protection Act, can result in outcomes ranging from death to malformations to functional impairment. The latter are the most difficult to determine. First, they require a variety of measures to assay their extent. Second, adult responses may prove an inadequate guide to the response of the developing brain, which is part of the reason for proposing additional safety factors for children. Third, neuropsychological tests are deployed in complex circumstances in which many factors, including economic status, combine to produce a particular effect such as lowered intelligence quotient score. Fourth, the magnitude of the effect, for most environmental exposure levels, may be relatively small but extremely significant for public health. Fifth, changes in brain function occur throughout life, and some consequences of early damage may not even emerge until advanced age. Such factors need to be addressed in estimating the influence of a particular agent or group of agents on brain development and its functional expression. It is especially important to consider ways of dealing with multiple risks and their combinations in addition to the prevailing practice of estimating risks in isolation.' (Weiss, 2000)

4.2. Vulnerability to neurotoxicants during brain development

Children's susceptibility to environmental toxicants (see Part I) also relates to the central nervous system. During fetal development, the placenta offers limited protection against unwanted compounds, but it is not an effective barrier against environmental neurotoxicants (Andersen *et al.*, 2000). For example, methylmercury easily crosses the placenta, and the concentration in the cord blood is considerably higher than in maternal blood (Hansen *et al.*, 1990). Further, the mobilisation of nutrients from maternal storage depots during pregnancy may transfer toxicants, such as lead hitherto stored in the maternal skeleton, to the fetus (Symanski and Hertz-Picciotto, 1995). More specifically, the blood brain barrier, which protects the adult brain from many toxic agents, is not completely formed until about six months after birth (Adinolfi, 1985) and therefore provides no protection during sensitive developmental stages.

Postnatally, infants continue to be at risk because of increased exposure and augmented absorption rates, e.g. for lead and methylmercury. A child may absorb as much as 50 % of the lead present in food, while adults seem to have an uptake of only 10 % (US EPA, 1986). Methylmercury excretion from the body is increased by bacterial demethylation in the gut, but such bacteria do not colonise the gut until the child has been weaned. The lack of this process during the breastfeeding period therefore results in an increased retention of methylmercury in the infant (Rowland *et al.*, 1984). Further, immaturity of liver and kidneys can hamper the detoxification and elimination of other neurotoxicants.

In addition to these toxicokinetic factors, the developing central nervous system is much more vulnerable to injury from toxic agents than is the adult's (Dobbing, 1968). The susceptibility of the central nervous system originates from the combination of immaturity and ongoing development (Dobbing, 1968; Rodier, 1994; Court *et al.*, 1996; Rice and Barone, 2000). For optimal central nervous system development to occur, a number of processes must take place within a rigidly controlled time frame. Because each developmental stage must be reached according to a carefully designed schedule and in a certain sequence, windows of susceptibility to toxic interference occur that would not appear in the mature brain. If a developmental process in the brain is halted or inhibited, there is little chance for repair, and a small change may have substantial consequences if the time schedule is disturbed. On a relative scale, the weight of the neonatal brain, and its blood supply, are much greater than in adults. The brain continues to develop well after birth, and the period of increased vulnerability extends to some degree until the central nervous system is completely developed.

A brief review of brain development will illustrate the multitude of processes that may be affected. The first nerve cells (neurons) are formed by the middle of the first trimester of pregnancy, and these cells continue to be generated into the first year after birth. Neuronal production exceeds the number of cells needed, and proliferation is therefore followed by cell death (apoptosis) that establishes the final number of neurons at each location. No further proliferation of neurons occurs after that time, and any subsequent loss of neurons is therefore permanent. In addition to the proliferation and differentiation of neurons, the detailed architecture of the brain also has to develop. Thus, shortly after their formation, the neurons begin to move toward their final location within the cerebral hemispheres, and this process is complete shortly after birth. When cell migration is disturbed, the neurons may not reach their correct position and are therefore kept from making the proper connections with the neurons that should have been their neighbours, thus potentially affecting normal function.

Having reached their final location, the nerve cells start to develop contact points with other cells by synaptogenesis. The generation of nervous connections (synapses) continues until about two years of age in humans. At this stage and during the preceding cell migration, neurotrophic signals are needed for guidance, and these chemical substances include some that are also used for communication purposes (neurotransmitters) (Lauder, 1988). One such substance is acetylcholine. It is therefore possible that substances such as insecticides that inhibit the enzyme cholinesterase, may interfere with these processes and perhaps lead to permanent damage (Ahlbom *et al.*, 1995). Such interference might be likely to be temporary in the adult, but the disturbance could cause permanent

abnormalities if it occurs during a sensitive stage of development.

During the second trimester of pregnancy, the glial cells also increase in number and eventually provide support and coating for neurons and the neuronal projections, thereby allowing more rapid transmission of nerve impulses. The growth of glial cells and the coating (myelinisation) of nerve cell projections continue for several years; the weight of the brain therefore increases somewhat up to the age of 20. Thus, at age six years, the brain has reached 80 % of its final weight, although at this age the body of the child corresponds to only about 30 % of the adult weight.

In summary, the correct 'wiring' of the growing brain depends upon an intricate and interconnected scaffolding of neurons and other cells laid down in the prenatal period which provides essential cues for the later development of nerve connections. This creates 'windows of susceptibility' to hazardous agents at doses that might be totally innocuous to the mature brain. Any damage to this 'wiring' process can lead to brain damage, behavioural disorders and effects on intelligence. If one of these processes is delayed or inhibited, there is little chance to catch up. Many of these processes continue until well after birth and some degree of vulnerability therefore continues until the central nervous system is completely formed.

Box 4.2. The vulnerable brain and multiple risks

Although many processes in brain development have been reasonably well characterised, much remains to be understood about the adverse effects that may occur as a result of neurotoxicant exposures. Thus, environmental exposures can potentially affect brain development in a variety of ways, but the mechanisms of individual neurotoxicants are still only poorly known. (Court *et al.*, 1996; Rice and Barone, 2000)

4.3. Neurotoxicants

Most neurotoxic chemicals belong to three main groups: metals and metal compounds, solvents and other simple organic compounds, and pesticides, especially the organophosphates and carbamates. These compounds are not the only neurotoxic chemicals currently in use. However, they represent three different classes of chemicals and act through different mechanisms, rendering them useful to illustrate the sensitivity of the developing brain to environmental exposures.

Based on the physiology and biochemistry of the brain, it might be suspected that a large number of chemicals would be classified as neurotoxic. In fact, the majority of the approximately 250 industrial chemicals that have caused clinical intoxications also cause effects on the nervous system, and this organ system therefore seemed the one most vulnerable (Kimbrough *et al.*, 1989; Grandjean *et al.*, 1991). However, the total number of industrial chemicals with a neurotoxic effect must be much higher than those for which detailed human evidence is available. Neurotoxicity testing is not part of the current requirements for classification of new chemicals, except for organophosphate pesticides. Also, subtle forms of neurotoxicity are difficult to examine in experimental models, and the extrapolation to humans is complicated.

With regard to effects in early life, the evidence of neurotoxicity is even more meagre. Only three environmental chemicals have been documented as definite causes of brain dysfunction following exposure before birth or during early childhood. Those three are lead, methylmercury and the polychlorinated biphenyls (PCBs) (see below). Some evidence, though much less definitive, is available on mercury vapour, certain solvents and pesticides. The experimental evidence on developmental neurotoxicity is also limited. One complication is that prenatal brain damage may not necessarily be apparent until the animal has reached a critical age when the neurobehavioural abnormalities can be detected (Spyker *et al.*, 1972). Recent research in this area has shown that prenatal exposure to, for example, pyrethroids, organophosphates, DDT and PCBs may cause lasting adverse effects on brain development (Eriksson, 1997). Also, neurotoxic effects may be 'unmasked' or precipitated by challenging the affected animal with another chemical or drug after the original toxic insult. Tests to detect such effects are not routinely conducted as part of test protocols for industrial chemicals.

Box 4.3. Prenatal exposure leads to adult deficits

'... these results indicate that low-dose exposure to environmental agents during the rapid development of the neonatal brain ('brain growth spurt') can lead to irreversible changes in adult brain function. The induction of these disturbances occurs at doses that apparently have no permanent effects when administered to the adult animal. Our studies have also indicated that there is a critical period in neonatal development of the mouse brain when these persistent effects are induced. Furthermore, the increased susceptibility to toxic agents at adult age in animals exposed during neonatal life indicates that neonatal exposure to toxic agents can potentiate and/ or modify the reaction to adult exposures to xenobiotics.' (Eriksson, 1997)

Lead

The majority of lead released into the environment originates from industrial activities. Children may be exposed to lead from car emissions through leaded petrol, water contaminated by lead pipes, paint, emissions from factories, contaminated soil, and improperly glazed ceramic ware for cooking and food storage. The relative importance of these sources varies regionally.

Air pollution is the main contributor to lead in the environment, and deposited lead particles cause contamination of soil, waterways and food. House dust is an important exposure source for small children, and lead-containing paints may add to this hazard. Children may also be exposed to lead that has leached into beverages and food from pipes and other materials that contain this metal or its compounds.

The elimination of lead additives in petrol has resulted in substantial decreases in blood lead levels in European Union populations (IEH, 1998). However, organolead compounds are still used for this purpose in many countries. Local sources of air pollution, including lead smelters and lead-manufacturing industries, continue to emit substantial amounts of this toxic metal, thus placing susceptible populations at risk. Because a child's total exposure may originate from several sources, it is difficult to predict. Monitoring of blood lead concentrations in populations at risk therefore deserves continued attention.

Lead is probably the best-known example of a neurotoxicant to which children are more susceptible than are adults. In healthy male workers, blood-lead concentrations below about 300 micrograms per litre (µg/l) (1.5–2.0 micromoles per litre (µmol/l)) are thought to be relatively innocuous. However, recognising that there is no known threshold for developmental neurotoxicity of this metal, the Centers for Disease Control (CDC, 1991) recommend that the blood-lead concentration be kept below 100 µg/l (0.5 µmol/l) in children.

The susceptibility of children is due to several factors that put them at a disadvantage in comparison with adults. First, there is the special susceptibility of the developing central nervous system, as outlined above. Lead exposure may begin prenatally, when lead is transported across the placenta, perhaps originating from occupational exposure or from release of maternal lead stores in the skeleton (US EPA, 1986). Once absorbed, lead is much more mobile in children, and retention in a skeleton system during rapid growth is not likely to provide safe and lasting storage.

Increased exposure potential in children derives from their behavioural and activity patterns, which are likely to place them in close proximity to different types of lead, with the subsequent risk of ingesting or inhaling it. From birth to about six months of age, infant exposure typically occurs through human milk and/or water and formula (Rye *et al.*, 1983). While human milk is generally low in lead (Jensen and Slovach, 1991), the use of lead-contaminated tap-water in preparing infant formula can result in elevated exposure levels. Infants may continue to be exposed from lead-contaminated air and dust from many sources, including their parents' work clothes (Grandjean and Bach, 1986).

As children become more mobile, their behavioural patterns (particularly their hands-to-mouth behaviour) is a significant risk factor. Thus, the average child aged three to five years is said to suck his or her fingers 1.5 times per hour. At the same time, the child's breathing zone may be close to the height of exhaust pipes from cars running on leaded petrol. Children also have relatively greater intakes of many foods and beverages, especially when adjustment is made for differences in body weight. For example, poisoning cases have occurred in the past due to release of lead from lead-glazed ceramics that were used for storage of fruit juices, a beverage favoured by many children.

The levels of lead within the body which result from exposure to a given concentration of lead are also higher for children than for adults (US EPA, 1986). Thus, children absorb and retain relatively greater amounts of the lead to which they are exposed. Lead is normally deposited in the skeleton, but the active bone remodelling occurring during childhood renders this storage depot much less protective than it is in adults. Once absorbed into the body, excretion of lead is relatively lower for children than for adults.

Most of the early studies on developmental lead neurotoxicity described the adverse effects in terms of IQ results (Needleman and Gatsonis, 1990). A systematic review has been carried out on 26 epidemiological studies from Europe, New Zealand and Australia regarding the lead-IQ association. The geometric mean for blood-lead concentrations in children aged 6–14 years ranged from 74 µg/l to 189 µg/l. The evidence strongly supports an inverse association between body lead burden and the IQ of the child. A typical doubling of body-lead burden was associated with a mean deficit in full-scale IQ of about 1–2 points. While small in individual terms, an average fall in population IQ of one point would certainly be regarded as unacceptable.

The neurotoxic effects of lead depend on the exposure level and the stage of central nervous system development at the time of insult. The heterogeneity of outcomes associated with exposures at different stages of development and in different population groups has resulted in inconsistencies regarding the type and severity of behavioural effects, especially when comparing cross-sectional and retrospective studies. Prospective studies (Bellinger *et al.*, 1992; Dietrich *et al.*, 1993) have documented beyond doubt that developmental exposure to lead adversely affects several specific brain functions, in particular attention, motor coordination, visuospatial function and language. Average blood-lead concentrations in these studies were 100 µg/l (0.5 µmol/l) and below.

Mild lead-related deficits in behavioural and cognitive functions in infants tend to persist, but may become undetectable, or masked by other factors, as the child grows older. However, some follow-up studies of teenage children have shown that cognitive dysfunctions were lasting and affected functional skills and academic abilities (Damm *et al.*, 1993). Also, examination of adults 50 years after they had recovered from lead poisoning in childhood revealed deficits in the domains known to be susceptible to childhood lead exposure, and the exposed subjects had less economic success in life than a matched comparison group (White *et al.*, 1993). It is possible that the consequences of early lead exposure increase with time because the individual would be less able to benefit from experience and education.

Although the majority of children in European Union countries are expected to have lead concentrations below the safe limit, much higher concentrations are still common in countries using leaded petrol and in the vicinity of lead-emitting sources such as smelters (Osman *et al.*, 1998; Wasserman *et al.*, 1997). In 1998, the ministers of health of the European countries expressed their commitment to eliminate the use of lead additives in petrol. This effort will result in a substantial decrease in lead pollution, lead exposure and blood-lead levels. However, monitoring of blood-lead concentrations will still be necessary, as lead accumulated in the environment will not disappear, and other sources of lead releases will continue to play a role.

A downward trend in European blood-lead concentrations has been observed since the late 1970s, especially while petrol lead additives were phased out (IEH, 1998). Between 1978 and 1988 decreases of 25–45 % in average blood-lead levels in children were reported in countries such as Germany, Sweden and the United Kingdom, but it is not clear how much of this fall was due to the changes in petrol constitution. During the same period, old technology using lead for soldering tin cans was replaced by other methods that decreased the likelihood of lead leaching into the contents. However, the relative impact of other known sources, such as food from contaminated soil, water contaminated by lead pipes and use of improperly glazed ceramicware for cooking and food storage, has increased.

Limited evidence suggests that individual susceptibility can modify the risk of adverse effects of lead. Thus, populations living under sub-optimal economic conditions may be at greater risk of lead poisoning. Populations with low socio-economic status may endure greater exposures to pollution than affluent populations, as shown most

clearly by studies in the United States. Children from such populations may also have a decreased capacity to compensate for these effects (Needleman and Gatsonis, 1990), for example because of the lack of access to educational tutoring to overcome learning difficulties. In addition, such children may suffer from inadequate nutrition, which may increase the fractional lead absorption and the toxicity. Thus, lead tends to be absorbed in inverse relationship to the availability of iron, calcium, phosphorus, zinc and copper in the diet (Mahaffey, 1990); this may place children with deficiencies in these minerals at a greater risk of developing lead toxicity. Other important factors in children's diets, including milk, can also affect lead absorption (US EPA, 1986). Nutritional deficiencies and lead exposure may therefore aggravate the overall risks of lasting health impairment among poor populations. Efforts to implement nutritional supplementation programmes may be a low-cost strategy for a partial mitigation of toxic exposures to lead and should always be thought of as an adjunct to, rather than a substitute for, primary prevention of lead exposures.

Methylmercury

Environmental methylmercury derives from methylation of inorganic mercury, some of which originates from natural degassing from the earth's crust. Industrial sources of mercury pollution include coal-burning, incinerators for municipal waste and hospital waste, and industrial effluents (US EPA, 1997).

Methylated mercury in the marine or freshwater environment is absorbed by fish and shellfish, and some biomagnification occurs in the food chain. The highest concentrations are therefore found in predatory fish with longer lifespans, including freshwater trout, pike, bass and, in marine species, particularly tuna and swordfish, as well as shark, seals and cetaceans (US EPA, 1997). Increased exposures most often occur in fishing communities and in societies relying on subsistence whaling. In this case, the exposure to methylmercury during a vulnerable period occurs mainly during the fetal stage, i.e. caused by the maternal seafood diet during pregnancy.

Methylmercury is a well-established neurotoxicant that can cause serious adverse effects on the development and functioning of the human central nervous system, especially when exposure occurs prenatally (Harada, 1995). At high exposure levels, seizures and spasticity (cerebral palsy) occur. In less severe poisoning, methylmercury produces blindness, deafness and mental retardation. A dose-response relationship has been established at high exposure levels between maternal hair-mercury levels during pregnancy and the prevalence of severe psychomotor retardation in the children (Marsh *et al.*, 1990). In some cases, the mother seemed unaffected by the toxic exposure that she had unwittingly passed on to her child. Postnatal exposures include mercury from human milk: in a fishing community, the child's hair-mercury concentration has been found to increase with the duration of the breastfeeding period (Grandjean *et al.*, 1994).

At intake levels widely encountered in fish-eating populations, new evidence of developmental effects at low exposure levels is emerging. In a cohort of 1 000 births on the Faroe Islands, methylmercury exposure was determined from the mercury concentration in the umbilical cord blood. Most of the dietary mercury intake there comes from pilot whalemeat, which has been a traditional food item for centuries. More than 90 % of these children were examined at the age of seven years. While clinical examination did not reveal any clear-cut mercury-related abnormalities, mercury-related neuropsychological deficits were particularly pronounced in language, attention and memory, and to a lesser extent in visuospatial and motor functions. The associations could not be explained by other possible causes, and they remained after exclusion of highly exposed children with maternal hair-mercury concentrations above 10 µg/g (Grandjean *et al.*, 1997).

In a study carried out in a fishing community in Madeira, current mercury exposures were even higher than in the Faroe Islands, as judged from maternal hair-mercury concentrations (Murata *et al.*, 1999). In this community, the increased exposure level probably results from eating black scabbard, a predatory deep-sea fish. Examination of 149 children from first grade of local schools showed mercury-related delays in the electrical signals of the brain, as recorded by the evoked potentials technique. A similar pattern was seen in the Faroes.

By comparing exposure biomarkers at different points of time during development, the study in the Faroes clearly showed that prenatal exposure, i.e. passage of methylmercury through the placenta, entails far the greatest risk. However, the child's visuospatial performance at age seven years was also affected by postnatal exposure (Grandjean *et al.*, 1999a).

More studies are being carried out in other populations with increased exposure to methylmercury. A large prospective study in the Seychelles has not revealed any clear adverse effects related to maternal hair-mercury concentrations, but results beyond five years of age are not yet available (Davidson *et al.*, 1998). In Brazil, cross-sectional studies of Amazonian children aged 7–12 years showed mercury-associated effects in agreement with the Faroese findings (Grandjean *et al.*, 1999b). Similar findings have been recorded in French Guyana (Cordier *et al*, 1999). In both of the latter locations, freshwater fish constitute a staple food and are contaminated by mercury released during gold-mining operations.

The important question is to what degree these findings relate to fish-consuming populations in general. Although this question cannot be answered with any confidence at this time, it looks as if the recommended one to two fish meals per week during pregnancy would be very unlikely to cause any risk to the fetus, unless the seafood were severely contaminated. A recent report from the United States National Academy of Sciences recommended that a limit of about 0.1 µg/kg body weight per day should not be exceeded by pregnant women (NRC, 2000). If a contaminated fish contains a mercury concentration of 0.5 µg/g — a limit used by many countries — then a woman weighing 60 kg should not eat more than 12 g of that fish per day (and no other source of methylmercury). It is therefore likely that regulatory agencies will develop more detailed guidelines in future regarding avoidance of certain species and sizes of fish that are likely to contain high mercury concentrations. However, such efforts should in no way detract from the need to increase the efforts against continued mercury releases to the environment.

Polychlorinated biphenyls (PCBs) and related compounds

Among the persistent organochlorine compounds, most attention has focused on the polychlorinated biphenyls (PCBs). These industrial chemicals have been widely used in electrical equipment, but their use is now banned in most of Europe. However, PCBs may still leak into the environment, e.g. from discarded transformers. The PCB congeners with a high degree of chlorination are especially lipophilic and are very persistent in the environment. They biomagnify in food chains and often occur along with some chlorinated pesticides and related industrial compounds such as dioxins (Kimbrough and Jensen, 1989).

The earliest evidence on PCB-related neurotoxicity in children originates from two poisoning episodes in Asia. However, in both cases, the PCBs had been thermally degraded, and the exposure included polychlorinated dibenzofurans, terphenyls and quaterphenyls. As the PCB congener mixtures were also different from those occurring in seafood, the evidence is difficult to use for risk assessment for general environmental exposure to PCBs.

Studies were then initiated in the United States to examine populations with an increased dietary PCB exposure. In Michigan and North Carolina, results tended to show mild deficits in children with increased prenatal exposures to PCBs (Gladen *et al.*, 1988; Jacobson *et al.*, 1990). Although PCBs are also transferred to the child via human milk (Jensen and Slovach, 1991), no adverse effect could be determined in relation to postnatal exposure. However, adverse neurologic and intellectual effects were still apparent at the age of 11 years in the most highly exposed children (Jacobson and Jacobson, 1996). *In utero* exposure to PCBs in this group of children was associated with an average IQ score 6.2 points below that of children with lower exposure levels. Further, eight of the 12 children in the highest exposure group were at least one year behind their peers in word or reading comprehension, and all but one lagged behind by at least six months.

More recently a European cohort of 418 healthy infants and their mothers was generated in Rotterdam and Gröningen, in the Netherlands; half of the babies were bottle-fed, the other half breastfed (Sauer *et al.*, 1994). Slight decrements on the neonatal neurological examination and subsequent developmental tests were related to increased PCB exposure. The researchers concluded that 'prenatal exposure to background PCB

levels as found in the Netherlands is negatively associated with cognitive abilities in preschool children and may have long-term implications for cognitive functioning'. However, continued follow-up of this cohort suggested that the effects may be modified or masked, with associations at seven years of age being much weaker (Vreugdenhil *et al.*, 2000).

Preliminary results from the Faroes (Steuerwald *et al.*, 2000) suggest that PCB-related effects may differ between populations, perhaps because PCB exposure is associated with different amounts of other persistent pollutants as well as methylmercury. None of the studies has been able to document any adverse effect due to breastfeeding. Perhaps, with the expansion of the fat compartment of the body, the nursing infant may be able to dilute somewhat the lipid-soluble contaminants, such as the PCBs absorbed from human milk. Thus, despite the occurrence of these contaminants in human milk, the advantages of breastfeeding for four to six months apparently override any limited neurotoxic damage due to the contaminants. Thus, the main problem is the prenatal exposure.

Although the evidence supports the notion that PCBs may have neurotoxic effects, crucial questions remain concerning the specific identity of the causal factors and the detailed dose-response relationship. Overall, the evidence suggests that PCBs and perhaps other organochlorine compounds may cause neurobehavioral deficits in children who have been exposed prenatally. The Netherlands study particularly (Sauer *et al.*, 1994) suggests that these effects may occur in European populations with background exposures from animal fats, including dairy products.

Although environmental PCB exposure in western Europe may have decreased somewhat following the banning of PCBs, those groups who frequently eat contaminated fatty fish or who reside in contaminated areas may still be exposed at levels that have been associated with adverse effects. Old electrical equipment still abounds, and the contamination of chicken in Belgium in 1999 showed that these neurotoxic substances are not just a problem of the past. This experience calls for continued surveillance and strict rules for handling any discarded materials containing these substances.

Other neurotoxicants

The evidence on other suspect neurotoxicants is much less extensive. In general, only case reports or small epidemiological studies are available on the neurotoxic potential in children exposed to solvents, other pesticides and other compounds. One of the reasons for the uncertainty in this field is that the exposure may not be 'pure', and the specific causation may therefore be difficult to disentangle.

Neurotoxic risks to the fetus or infant include a variety of chemicals that may not normally be considered associated with 'environmental pollution'. Among these is maternal smoking. Nicotine targets specific neurotransmitter receptors in the developing brain, thereby possibly affecting nervous cell proliferation and differentiation as well as the programming of synaptic competence (Slotkin, 1998). While experimental evidence is convincing, epidemiological studies have suffered from confounding by other factors, and conclusions have tended to be tentative. Similarly, studies on exposure to environmental tobacco smoke have so far not provided convincing evidence of a neurotoxic risk to the small child.

Concomitant exposures have often included alcohol and illicit drugs. Consumption of more than two drinks per day, or at least one occasion of ingestion of five drinks, during pregnancy, appears to be associated with cognitive deficits in the child (Streissguth *et al.*, 1990). Data on adverse effects related to maternal cocaine use are less certain, although available evidence strongly suggests possible neurotoxic effects in the child (Martin *et al.*, 1996).

Several environmental pollutants and food contaminants have been implicated in a variety of studies. Most attention has been paid to solvents (Eskenazi *et al.*, 1988; Pearson *et al.*, 1994).

Another important matter deserves particular attention. Endocrine disruption has attracted much interest, and recent research suggests that this mechanism may also affect brain development. For example, the thyroid hormone is of major importance for the development of the central nervous system, and the consequences of iodine deficiency amply demonstrate the dramatic significance of this single hormone. New research has suggested that a variety of environmental chemicals may interfere with

thyroid function and thereby produce neurotoxicity (Porterfield, 1994). This potential may be generalised to a larger group of endocrine disrupters which due to their interference with hormone systems may generate brain damage (Tilson, 1998).

Box 4.4. Different research approaches

Two groups of young children, one of them exposed to pesticides from agricultural practices, were asked to draw a person. The random undifferentiated lines drawn by exposed children averaged only 1.6 body parts per figure, whereas non-exposed children produced reasonably lifelike figures averaging 4.4 body parts each. These results were part of a battery of developmental end-points considered in a study of indigenous children living in the Yaqui Valley of north-western Mexico (Guillette *et al.*, 1998).

However, the exposure classifications were not documented by corresponding tissue or environmental pesticide concentrations, but were instead assumed based on residential proximity to farms that used high quantities of organophosphate, organochlorine and pyrethroid compounds. Furthermore, to identify developmental problems, the researchers used an anthropological technique known as rapid assessment, which is a broad approach designed to look for problems in a community and identify areas for future research, rather than to diagnose specific indicators of neurobehavioral dysfunction. Nonetheless, this study suggests that current evidence may have identified only a small fraction of the true scope of the prenatal neurotoxicity problem.

While these studies have rendered suggestive evidence only, this lack of proof is by no means an indication that prenatal neurotoxicity does not occur. Research in this field faces daunting problems that lead to exposure misclassification and problems in dissociating the outcome effects from those of other origin. For this reason, only the tip of the iceberg is within view, and we are looking at it through a haze.

4.4. Public health impact

Neurotoxicity is difficult to document from available health statistics, as specific diagnoses would not represent the true extent of the problem. Available epidemiological evidence suffers from a variety of weaknesses, as such research is unusually complex and expensive (Dietrich and Bellinger, 1994). However, effects reported on attention span, concentration, motor speed, memory and language functions would be expected to affect cognitive development, education, social functions and career. Indeed, a study of subjects who had suffered excess lead exposure as children clearly revealed that they were less successful in life than a control group (White *et al.*, 1993). Antisocial and criminal behaviour has also been linked with a history of developmental lead exposure (Needleman *et al.*, 1996). Although documentation of such environmentally induced effects is very limited, the implications are nonetheless rather dramatic.

Studies of lead-exposed children have also revealed that small differences in the average performance of children may have little consequence for children with average functions. The most impressive differences occur at the extremes of the distributions (Needleman *et al.*, 1982). Thus, among highly exposed children in this study, virtually nobody had superior function. On the other hand, the number of children with obvious deficits increased considerably. The latter group of children would be more likely to require special education in school, and they would be less likely to benefit from career options in society. Social implications may be substantial if lead exposures cause an increasing prevalence of children with severe intelligence deficits while decreasing the frequency of children scoring in superior IQ categories.

The particular vulnerability of the nervous system and the added susceptibility during development would therefore suggest that exposure limits and other means of prevention should emphasise these effects as critical when setting standards.

4.5. What we do not know

The developing brain is more vulnerable to chemical damage because of a combination of immaturity and ongoing development. An exposure that is virtually harmless to a pregnant woman or a young mother may seriously impact on the brain development of her child. What follows therefore is that protection of the adult is far from sufficient to ensure that exposure does not cause developmental neurotoxicity. However, while this pattern is well documented for a small number of substances, only suggestive evidence or none at all is available for other chemicals that are known to or suspected to cause neurotoxic effects.

The main challenge of neurobehavioural toxicology is to refine the tests of cognitive and developmental skills in exposed children, to identify causative pollutants and

their mechanisms for adverse behavioural effects, to characterise other factors that may render a subject more vulnerable, and to improve dose-response measures in a way that facilitates effective risk assessment. Epidemiological studies must integrate the results of neuropsychological and toxicological testing with population-level impact. These areas should be linked more closely to the burgeoning neuroscience field, and renewed emphasis on environmental health and prevention is needed. Research directions of additional interest include the possible links between chemical exposure and autism, attention deficit hyperactivity disorder and learning disabilities, thus expanding the focus of toxicity testing to include clinical neurodevelopmental end-points.

While developmental neurotoxicity testing is not required for classification of chemicals and chemical products, experimental models are being evaluated, and various *in vitro* test systems have shown promising results. The long-term goal of prevention in this field should be avoidance of environmental exposure to chemicals that have not been cleared of developmental toxicity potential.

Box 4.5. The reductionist problem

Neurodevelopmental disabilities are widespread, and chemical exposure is an important and preventable contributor to these conditions. Reductionist analyses that separately address environmental and genetic factors may illuminate important details but fail to acknowledge the complexities of multiple, interacting factors that ultimately influence neurological development. Both genetic factors and environmental factors must be simultaneously considered to properly understand these disabilities.
(Schettler *et al.*, 2000)

4.6. Control measures

High priority must be placed upon:

- Monitoring of exposure in at-risk areas. Lead concentrations in air, water and in biological material (hair or blood) should be part of routine environmental health surveillance and monitoring systems at national and regional levels. Methylmercury and PCBs must be monitored in areas with contaminated fish.
- Setting standards and enforcing measures to reduce environmental pollution by neurotoxicants; substituting lead additives in petrol and limiting solvent concentrations in paints and construction materials.
- Disseminating information to the public and health professionals to promote healthy lifestyles to decrease risks of exposure.
- Preventing nutrient deficiencies, alcohol and drug exposure as contributory factors.

The Declaration of the Environmental Leaders of the Eight on Children's Environmental Health in 1997 agreed an upper limit for blood-lead in children of 100 µg/l. However existing epidemiological studies do not provide definitive evidence of a threshold for onset of adverse effects in relation to blood-lead levels, and there is evidence of an association between blood-lead levels and adverse effects below this limit. With lead and other neurotoxicants, exposures should be reduced as much as reasonably achievable.

Summary

The central nervous system is particularly vulnerable to toxic effects during early development.

Nervous system damage, once incurred during a developmental stage, is likely to be irreversible and may change the affected individual's quality of life and economic and social success.

Neurotoxic effects may be particularly serious as a result of exposure during the development of the nervous system. For PCBs, effects seem to be related to prenatal exposure only. Methylmercury may cause neurotoxicity both prenatally and during early childhood. With lead, most of the existing evidence relates to increased exposure occurring during the toddler age. These different patterns may, to some extent, be related to the particular properties of the chemicals, but the age at which peak exposures are most likely to occur certainly also plays an important role.

Although the prenatal exposure via the mother is lower than postnatal exposure from breast milk, it appears that prenatal doses are more toxic because they affect critical growth periods in brain development.

The extent to which current environmental pollution causes adverse effects on brain development is unknown. The contaminants that have been studied in the greatest detail, i.e., lead, methylmercury and PCBs, are likely to cause adverse health effects in subgroups of European populations with increased exposure. Solvents and pesticides and possibly other industrial chemicals may have adverse effects as well, but only limited documentation is available in this regard at present.

Given the irreversibility of such effects and their adverse implications for child development, education and productive life, these issues deserve increased attention.

Control measures are based on establishing safety standards for children of the known neurotoxicants, on policies aimed at reducing contaminants in air, water and other media, and on information to the public and health professionals.

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References

Adinolfi, M., 1985. The development of the human blood-CSF-brain barrier, *Dev Med Child Neurol*, Vol 27, pp. 532–7.

Ahlbom, J., Fredriksson, A. and Eriksson, P., 1995. Exposure to an organophosphate (DFP) during a defined period in neonatal life induces permanent changes in brain muscarinic receptors and behaviour in adult mice, *Brain Res*, Vol 677, pp. 13–9.

Andersen, H.R., Nielsen, J.B. and Grandjean, P., 2000. Toxicologic evidence of developmental neurotoxicity of environmental chemicals, *Toxicology*, Vol 144, pp. 121–7.

Bellinger D.C., Stiles, K.M. and Needleman, H.L., 1992. Low-level lead exposure, intelligence and academic achievement: a long-term follow-up study, *Pediatrics*, Vol 90, pp. 855–61

CDC, 1991. *Preventing lead poisoning in young children. A statement by the Centers for Disease Control,* US Department of Health and Human Services.

Cordier, S., Garel, M., Amiel-Tison, C. *et al.*, 1999. Neurologic and neurodevelopmental investigations of methylmercury exposed children in French Guiana, [abstract], *Epidemiology*, Vol 10 (4) Suppl, p. S102.

Court, J., Cuomo, V., Eriksson, P. *et al.*, 1996. *Perinatal developmental neurotoxicity,* Report R4, Institute for Environment and Health (IEH), Leicester.

Damm, D., Grandjean, P., Lyngbye, T. *et al.*, 1993. Early lead exposure and neonatal jaundice: Relation to neurobehavioral performance at 15 years of age, *Neurotoxicol Teratol*, Vol 15, pp. 173–81.

Davidson, P.W., Myers, G.J., Cox, C. *et al.*, 1998. Effects of prenatal and postnatal methylmercury exposure from fish consumption on neurodevelopment, *JAMA*, Vol 280, pp. 701–7.

Dietrich, K.N. and Bellinger, D., 1994. The assessment of neurobehavioral development in studies of the effects of prenatal exposure to toxicants, in *Prenatal exposure to toxicants: Developmental consequences* (edited by H.L. Needleman and D. Bellinger), Johns Hopkins University Press, Baltimore, pp. 57–85.

Dietrich, K.N., Berger, O.G. and Succop, P.A., 1993. Lead exposure and the motor developmental status of urban 6 year-old children in the Cincinnati prospective study, *Pediatrics*, Vol 91, pp. 301–7.

Dobbing, J., 1968. Vulnerable periods in developing brain, in *Applied Neurochemistry*, (Edited by A.N. Davison and J. Dobbing), Davis, Philadelphia, pp. 287–316.

'Environment leaders' Summit of the Eight, 1997. *Declaration of the Environment Leaders of the Eight on Children's Environmental Health,* Miami FL, 5–6 May 1997.

Eriksson, P., 1997. Developmental neurotoxicity of environmental agents in the neonate, *Neurotoxicology*, Vol 18, pp. 719–26.

Eskenazi, B., Gaylord, L., Bracken, M.B. *et al.*, 1988. In utero exposure to organic solvents and human neurodevelopment, *Dev Med Child Neurol*, Vol 30, pp. 492–501.

Gladen, B.C., Rogan, W.J., Hardy, P. *et al.*, 1988. Development after exposure to polychlorinated biphenyls and dichlorodiphenyl dichloroethene transplacentally and through human milk, *J Pediatr*, Vol 113, pp. 991–5.

Grandjean, P. and Bach, E., 1986. Indirect exposures: The significance of bystanders at work and at home, *Am Ind Hyg Assoc J*, Vol 47, pp. 819–24.

Grandjean, P., Sandoe, S.H. and Kimbrough, R.D., 1991. Nonspecificity of clinical signs and symptoms caused by environmental chemicals, *Hum Exp Toxicol*, Vol 10, pp. 167–73.

Grandjean, P., Jørgensen, P.J. and Weihe, P., 1994. Human milk as a source of methylmercury exposure in infants, *Environmental Health Perspectives*, Vol 102, pp. 74–7.

Grandjean, P., Weihe, P., White, R.F. *et al.*, 1997. Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury, *Neurotoxicol Teratol*, Vol 19, pp. 417–28.

Grandjean, P., Budtz-Jørgensen, E., White, R.F. *et al.*, 1999a. Methylmercury exposure biomarkers as indicators of neurotoxicity in 7-year-old children, *Am J Epidemiol*, Vol 150, pp. 301–5.

Grandjean, P., White, R.F., Nielsen, A. *et al.*, 1999b. Mercury neurotoxicity in Amazonian children downstream from gold mining, *Environmental Health Perspectives*, Vol 107, pp. 587–91.

Guillette, E.A., Meza, M.M., Aquilar, M.G. *et al.*, 1998. An anthropological approach to the evaluation of preschool children exposed to pesticides in Mexico, *Environmental Health Perspectives*, Vol 106, pp. 347–53.

Hansen, J.C., Tarp, U. and Bohn, J., 1990. Prenatal exposure to methylmercury among Greenlandic Polar Inuits, *Arch Environ Health*, Vol 45, pp. 355–8.

Harada, M., 1995. Minamata disease: Methylmercury poisoning in Japan caused by environmental pollution, *Crit Rev Toxicol*, Vol 25, pp. 1–24.

IEH, 1998. *Recent UK blood lead surveys*, Report R9, Institute for Environment and Health, Leicester.

Jacobson, J.L. and Jacobson, S.W., 1996. Intellectual impairment in children exposed to polychlorinated biphenyls *in utero*, *N Engl J Med*, Vol 335, pp. 783–9.

Jacobson, J.L., Jacobson, S.W. and Humphrey, H.E.B., 1990. Effect of *in utero* exposure to polychlorinated biphenyls and related contaminants on cognitive functioning in young children, *J Pediatr*, Vol 116, pp. 38–45.

Jensen, A.A. and Slovach, S., eds, 1991. *Chemical contaminants in human milk*, CRC, Boca Raton, FL.

Kimbrough, R.D. and Jensen, A.A., 1989. *Halogenated biphenyls, terphenyls, naphthalenes, dibenzodioxins and related products*, 2nd edition, Elsevier, Amsterdam.

Kimbrough, R.D., Mahaffey, K.R., Grandjean, P. *et al.*, 1989. *Clinical effects of environmental chemicals: A software approach to etiologic diagnosis*, Hemisphere, New York.

Lauder, J.M., 1988. Neurotransmitters as morphogens, *Prog Brain Res*, Vol 73, pp. 365–87.

Mahaffey, K.R., 1990. Environmental lead toxicity: Nutrition as a component of intervention, *Environmental Health Perspectives*, Vol 89, p.75.

Marsh, D.O., Myers, G.J., Clarkson, T.W. *et al.*, 1990. Fetal methylmercury poisoning: Clinical and pathological features, *Ann Neurol*, Vol 7, pp. 348–53.

Martin, J.C., Barr, H.M., Martin, D.C. *et al.*, 1996. Neonatal neurobehavioral outcome following prenatal exposure to cocaine, *Neurotoxicol Teratol*, Vol 18, pp. 617–25.

Murata, K., Weihe, P., Renzoni, A. *et al.*, 1999. Delayed evoked potentials in Madeiran children exposed to methylmercury from seafood, *Neurotoxicol Teratol*, Vol 21, pp. 343–8.

NRC, 2000. *Toxicological effects of methylmercury*, National Research Council, National Academy Press, Washington, DC.

Needleman, H.L. and Gatsonis, C., 1990. Low level lead exposure and the IQ of children, *JAMA*, Vol 263, pp. 673–8.

Needleman, H.L., Leviton, A. and Bellinger, D., 1982. Lead-associated intellectual deficit (letter), *N Engl J Med*, Vol 306, p. 367.

Needleman, H.L., Riess, J.A., Tobin, M.J. *et al.*, 1996. Bone lead levels and delinquent behavior, *JAMA*, Vol 275, pp. 363–9.

Osman, K., Zejda, J.E., Schütz, A. *et al.*, 1998. Exposure to lead and other metals in children from Katowice district, Poland, *Int Arch Occup Environ Health*, Vol 71, pp. 180–6.

Pearson, M.A., Hoyme, H.E., Seaver, L.H. *et al.*, 1994. Toluene embryopathy: Delineation of the phenotype and comparison with fetal alcohol syndrome, *Pediatrics*, Vol 93, pp. 211–5.

Porterfield, S., 1994. Vulnerability of the developing brain to thyroid abnormalities: Environmental insults to the thyroid system, *Environmental Health Perspectives*, Vol 102 (suppl 2), pp. 125–30.

Rice, D. and Barone, S. Jr., 2000. Critical periods of vulnerability for the developing nervous system: Evidence from humans and animal models, *Environmental Health Perspectives*, Vol 108 (suppl 3), pp. 511–33.

Rodier, P.M., 1994. Vulnerable periods and processes during central nervous system development, *Environmental Health Perspectives*, Vol 102 (suppl 2), pp. 121–4.

Rowland, I.R., Robinson, R.D. and Doherty, R.A., 1984. Effects of diet on mercury metabolism and excretion in mice given methylmercury: Role of gut flora, *Arch Environ Health*, Vol 39, pp. 401–8.

Rye, J.E., Ziegler, E.E., Nelson, S.E. *et al.*, 1983. Dietary intake of lead and blood lead concentration in early infancy, *Am J Dis Child*, Vol 137, pp. 886–91.

Sauer, P.J.J., Huisman, M., Koopman-Eseeboom, C. *et al.*, 1994. Effects of polychlorinated biphenyls (PCBs) and dioxins on growth and development, *Hum Exp Toxicol*, Vol 13, pp. 900–6.

Schettler T, Stein J, Reich F, *et al.*, 2000. In harm's way: Toxic threats to child development. Boston: Greater Boston Physicians for Social Responsibility, 2000. URL: http://www.igc.org/psr/ihw-report_dwnld.htm#ihwRptDwnld

Slotkin, T.A., 1998. Fetal nicotine or cocaine exposure: Which one is worse? *J Pharmacol Exp Therap*, Vol 285, pp. 931–45.

Steuerwald, U., Weihe, P., Jørgensen, P.J. *et al.*, 2000. Maternal seafood diet, methylmercury exposure, and neonatal neurological function, *J Pediatr*, Vol 136, pp. 599–605.

Streissguth, A.P., Barr, H.M. and Sampson, P.D., 1990. Moderate prenatal alcohol exposure: Effects on child IQ and learning problems at age 7½ years, *Alcohol Clin Exp Res*, Vol 14, pp. 662–9. [what is this?]

Symanski, E. and Hertz-Picciotto, I., 1995. Blood lead levels in relation to menopause, smoking, and pregnancy history, *Am J Epidemiol*, Vol 141, pp. 1047–58.

Spyker, J.M., Sparber, S.R. and Goldberg, A.M., 1972. Subtle consequences of methylmercury exposure: Behavioral deviations in offspring of treated mothers, *Science*, No 177, pp. 621–3.

Tilson, H.A., 1998. Developmental neurotoxicology of endocrine disruptors and pesticides: Identification of information gaps and research needs, *Environmental Health Perspectives*, Vol 106 (suppl 3), pp. 807–11.

US EPA, 1986. *Air quality criteria for lead*, Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, EPA Report, EPA-600/8-83-028aF-dF, US Environmental Protection Agency, Research Triangle Park, NC.

US EPA, 1997. *Mercury study report to Congress*, US Environmental Protection Agency, Washington, DC.

Vreugdenhil, H., Duivenvoorden, H.J. and Weisglas-Kuperus, N., 2000. The relative importance of prenatal PCB exposure, feeding type, and parental characteristics for cognitive and motor development in healthy children studied 3 to 84 months of age, *Organohalogen Compounds*, Vol 48, pp. 139–42.

Wasserman, G.A., Liu, X., Lolacono, N.J. *et al.*, 1997. Lead exposure and intelligence in 7-year-old children: The Yugoslavia Prospective Study, *Environmental Health Perspectives*, Vol 105, pp. 956–62.

Weiss, B., 2000. Vulnerability of children and the developing brain to neurotoxic hazards, *Environmental Health Perspectives*, Vol 108 (suppl 3), pp. 375–81.

White, R.F., Diamond, R., Proctor, S. *et al.*, 1993. Residual cognitive deficits 50 years after lead poisoning during childhood, *Br J Ind Med*, Vol 50, pp. 613–22.

5. Cancer

Benedetto Terracini

Contributing authors: Maria Jose Carroquino, Irva Hertz-Picciotto

Summary of existing knowledge

- Geographical differences in incidence are less marked for childhood than for adult cancer, thus suggesting a relatively limited role of environmental exposures in childhood cancer.
- The role of hereditary factors in the etiology of childhood cancer is proven for a minority of cancer types.
- Some childhood cancers, notably acute lymphoblastic leukaemia, tend to aggregate in geographical clusters. Neither are the reasons for this phenomenon understood, nor are the causes of individual clusters easy to interpret.
- Exposure to ionising radiation has the potential to cause childhood cancer, and excessive exposure to sunlight during childhood causes skin cancer (and probably melanoma) later in life. A number of other chemical, physical and biological agents are suspected but not proven to cause childhood cancer (e.g. extremely low frequency electromagnetic fields, parental tobacco smoke, parental occupational exposure to solvents).
- Children are likely to be more prone than adults to events related to carcinogenesis.

Main challenges

- To assess robustness of current etiological hypotheses regarding 'suspected' environmental carcinogens.
- To identify hitherto unrecognised environmental agents causally associated to childhood cancer.
- To improve understanding of the susceptibility of children to environmental carcinogens.
- To improve estimates of the attributable portion of childhood cancer due to preventable environmental factors.

Action points

- Reduce diagnostic x-ray exposure during pregnancy to a minimum.
- Control exposure to sunlight during childhood without having recourse to sunscreens.
- Monitor exposure to proven environmental carcinogens.
- Carry out epidemiological surveillance of clusters of childhood cancers.
- Inform the public about ways of reducing exposure to agents suspected to cause cancer.

5.1. Introduction

Childhood cancers are rare diseases with potentially dramatic outcome. In countries delivering good medical care, advances in treatment have increased survival rates up to 70 % for leukaemia and some other cancers over the last 30 years. The suggestion, in some countries, of an increase over time in the incidence of childhood cancer has raised concern among clinicians, policy-makers and public interest groups about the potential role of environmental causes of childhood cancer.

Cancer in all ages is a result of the interaction between genetic and environmental factors (including exposure to exogenous agents as a result of behavioural traits such as sedentariness, excessive exposure to sun, smoking, alcohol consumption, etc.). For cancer in adults, different opportunities for environmental exposure have commonly been considered a major (albeit not exclusive) reason for the geographical distribution of cancer. Worldwide, with the exception of lymphomas, the ratio between highest and lowest incidence rates in children does not exceed five, i.e. orders of magnitude smaller than the corresponding ratio for many adult cancers. Genetic factors and ethnic variation account for a limited part of these differences.

Although cancer is considered to be a disease of adulthood and old age, children may be more prone to biological events potentially related to the carcinogenesis. Compared with adults, absorption and retention of environmental chemicals is greater in early life: metabolic pathways responsible for detoxification may differ with age so that fetuses and children may have a lower ability to detoxify exogenous agents and to repair damage. Cell proliferation in tissues of children is higher whereas immunological surveillance is less efficient. Finally, the point has been made that cancers initiated in the womb and in the early years have the opportunity to develop over many decades (Perera, 1997).

The first part of the present chapter provides some data on the descriptive epidemiology of the major types of childhood cancer in Europe. Attention is then addressed to indirect clues that exogenous factors might interact with genetic susceptibility. This is followed by a review of environmental exposures which have either been shown (e.g. ionising radiation, ultraviolet light) or are suspected (e.g. some parental occupational exposures) to cause some types of childhood cancer. The final paragraphs provide some suggestions for a public health approach to the issue of childhood cancer.

5.2. Epidemiology

All cancers

A recent World Health Organization (WHO) publication has reported incidence rates of childhood cancer from population-based cancer registries in Africa (seven countries), Asia (11 countries), Europe (21 countries), Latin America (eight countries), Australia, Canada, New Zealand and the United States (Parkin *et al.*, 1998). Diagnoses were registered according to an agreed protocol and coded to a histology-based scheme developed specifically for childhood tumours (Birch and Marsden, 1987). Worldwide, in the early 1990s, age-standardised annual incidence rates per million children ranged between a minimum of 46 in Namibia and 164 in non-Hispanic whites in Los Angeles. Differences among European countries were less marked (Table 5.1.) and are partly attributable to differences in case ascertainment and diagnosis. In all registries, the male:female ratio is above unity and ranges between 1.1 and 1.2. Also the distribution of different childhood cancer types is similar across European countries. As an example, Table 5.2. shows, separately for boys and girls, age-standardised and cumulative cancer-specific rates from the Swiss registries around 1990, when six cancer registries served approximately 45 % of the Swiss population (Parkin *et al.*, 1998). The cumulative rate is an approximation to the risk for an individual of developing the cancer in question before age 15, if no other causes of death were in operation. Cumulative rates in the order of 2 000 per million, such as estimated in European countries, mean that cancer is diagnosed during childhood in one child out of 500.

The descriptive epidemiology of the major childhood cancer types is summarised in the following paragraphs, with particular regard to those aspects which might be related to environmental exposure. Most information reported below has been retrieved from an excellent review of the descriptive epidemiology of childhood cancer (Little, 1999; Sharp *et al.*, 1999).

Table 5.1. **Age-standardised incidence rates (annual per million children) of all cancers in children aged 0–14 in European cancer registries around 1990**

Source: Parkin *et al.*, 1998

	Rate boys	Rate girls		Rate boys	Rate girls
Czech Republic 1980–89	137.0	113.1	Italy others 1980–91	152.5	133.8
Denmark 1983–91	168.1	148.9	Netherlands 1989–92	149.9	119.9
Estonia 1980–89	134.4	117.1	Norway 1980–89	163.5	139.8
Finland 1980–89	163.5	143.1	Slovakia 1980–89	139.9	118.0
France, Lorraine 1983–92	148.6	128.4	Slovenia 1981–90	138.2	98.4
France PACA* and Corsica 1984–92	142.6	128.7	Spain Valencia 1983–90	158.6	131.9
France others 1983–92	141.2	128.1	Spain others 1982–91	154.7	127.0
Germany former GDR1981–89	137.3	117.9	Sweden 1980–89	157.4	151.2
Germany former FRG 1985–90	144.1	119.3	Switzerland 1980–92	155.4	132.7
Germany 1991–95	145.8	118.6	England and Wales 1981–90	130.8	113.1
Iceland 1960–89	120.6	100.4	Scotland 1981–90	137.0	112.1
Italy Piedmont 1982–89	151.8	139.0			

*Provence-Alpes-Côte d'Azur

Note: Registries where underreporting was considered to be possible and/or where there may have been difficulties in establishing the correct population at risk are excluded.

Leukaemias

Throughout Europe, leukaemias represent between a quarter and a third of all childhood cancers and acute lymphoblastic leukaemias (ALL) account for three-quarters of all childhood leukaemias. There are several immunophenotypic variants of ALL (B-cell precursor of the common (cALL) and null (nALL) types and T-cell precursor ALL): geographical and ethnic differences in their relative frequencies have been reported but their relevance to environmental etiological agents is not known. Around 1990, among European registries, with the exception of Estonia, annual rates per million children ranged between 28.5 in Slovakia and 47.0 in Denmark in males and between 27.7 in Iceland and 42.8 in Denmark in girls (in Estonia, corresponding rates were around 22.3 and 17.4 in boys and girls, respectively). The sex ratio ranged between 1.1 and 1.3.

Childhood cancers reported to the Swiss registries during 1980–92: absolute number, age-standardised incidence rate (ASR, annual per million) and cumulative rate (in children aged 0–14) per million

Table 5.2.

	Boys			Girls		
	N	ASR	Cum	N	ASR	Cum
Leukaemia	161	50.4	713	131	43.4	612
Lymphomas	88	24.4	381	43	12.3	194
Brain and spinal cord	93	27.2	409	88	27.2	406
Sympathetic nervous system	47	15.9	210	34	12.0	160
Retinoblastoma	15	5.2	67	12	4.4	56
Renal tumours	14	4.7	62	29	9.9	136
Hepatic tumours	5	1.6	22	4	1.3	18
Malignant bone tumours	28	7.5	120	16	4.5	71
Soft tissue sarcomas	43	12.8	188	27	8.6	124
Germ cell and gonadal neoplasms	8	2.4	34	11	3.1	49
Carcinomas and epithelial neoplasms	12	3.3	51	22	6.1	99
Other and unspecified neoplasms	0	0.0	0	0	0.0	0
Total	**514**	**155.4**	**2 263**	**417**	**132.7**	**1 929**

Source: Parkin *et al.*, 1998

Incidence rates in western Europe are similar to rates in the white populations in North America, the latter being twice as high as the corresponding incidence in black children. Comparisons of incidence by ethnic origin in Europe have been limited, because of the sample size and the lack of adequate population denominators. In two relatively large series in the United Kingdom, the relative frequency of ALL over other childhood cancers was similar in white, 'West Indian' and 'Asian' children and the same applied to the distribution of the immunophenotypes (Stiller *et al.*, 1991; Powell *et al.*, 1994).

Currently, in western European countries, the distribution of age-specific incidence rates of ALL shows a peak at ages two to three years, which declines progressively in older children. Typically, annual rates per million are in the order of 80 at age three years *vs.* less than 20 both at ages birth to one and at 10. Around 1990, a striking difference between western and eastern Europe was seen in that in the latter the peak was much less pronounced and corresponded to age five years (Parkin *et al.*, 1996). This is much more likely to reflect a difference in environmental exposure than in genetically determined susceptibility. The peak was evident from mortality data in United Kingdom and United States whites around 1930–40 but not before. In general, the peak is particularly obvious in populations with the highest incidence rates of ALL. In United States blacks, as well as in countries such as Israel, Japan and Kuwait, the peak appeared as late as after the Second World War. As yet, no peak has been observed in the African series. In the United Kingdom, an exaggerated peak has been noticed in communities isolated from urban centres and of high socio-economic status: this contributed to the hypothesis that ALL risks may be related to patterns of exposure to common infectious agents (Kinlen, 1995).

Several studies in Australia, the United Kingdom and the United States (see, for instance, McWhirter, 1982) have investigated the role of socio-economic factors (assessed through a variety of proxies) in the risk of ALL. In spite of some discrepancies, these studies indicate a somewhat higher risk for the highest socio-economic status. The relative risk was lower than 2 in most studies, but the ecological nature of most of these studies may have underestimated risks. In addition, the possibility of confounding exposures cannot be ruled out.

Time trends in childhood leukaemia, if any, are likely to reflect changes in environmental exposure, rather than in susceptibility. Most studies in Europe suggest a positive trend in incidence rates: a part of which is likely to be real, given that in most studies the slope is steeper in ages one to four years, whereas artefacts due to improved ascertainment of cases over a long period of time ought to reflect also on more grown-up children. Changes over the period 1980–91 were analysed after pooling data from 36 registries in 23 European countries. Average annual increases of 0.6 and 0.4 % were estimated in 1980–86 and 1987–91 respectively (thus, unrelated to the Chernobyl accident)

(Parkin *et al.*, 1996). Annual increases up to 2 % were estimated in analyses of registered cases in England and Wales in 1953–91 (Draper *et al.*, 1994), in New Zealand (Dockerty *et al.*, 1996) and from data in the United States during 1974–91 (Gurney *et al.*, 1996), but not in Germany up to 1992 (Kaatsch *et al.*, 1995). Differences in the degree of case ascertainment and in sophistication of the statistical methods used in each study might explain part of the discrepancy in the findings. In addition, environmental influences (including exposure to infectious agents) are not uniformly distributed, so that different patterns are not surprising. Even recently, the use of adequate statistical analyses suggested a statistically significant temporal increase in the incidence of ALL, particularly the precursor B-cell subtype in ages one to four years (annual increase in the order of 3 %) in north-west England (McNally *et al.*, 2000) but not in Yorkshire (Feltbower *et al.*, 2000).

Childhood leukaemia, particularly ALL, exhibits a tendency to aggregate in space-time clusters to a greater extent than most other childhood and adult cancers (although clusters account for a relatively small proportion of childhood leukaemias). Over the last 30 years, several methods intended to identify and quantify the phenomenon of clustering have been developed. Spatial clustering of childhood leukaemia has been observed (particularly in children under five years of age) in the United Kingdom, Greece and Hong Kong, but not in Sweden or in metropolitan areas in the United States. The units of space considered in the studies in the United States were larger than those in the other countries, which may have diluted the effects of clustering at a smaller scale. In the United Kingdom, the evidence of clustering was confined to sparsely populated areas.

Assessment of the phenomenon of clustering of a given disease in a given population should not be confused with the interpretation of individual clusters. Indeed, distinguishing between individual clusters reflecting chance and those reflecting excess exposure to a risk factor is problematic. Usually, identification of a cluster implies a comparison between the occurrence of a disease in a small population with the corresponding occurrence in a larger population, used as reference. Differences in criteria of case ascertainment might lead to apparent but spurious aggregation of cases, and the use of rate denominators from different sources might lead to non-comparable indicators of incidence or mortality. These sources of bias ought to be considered when facing any apparent cluster, particularly if based on a small number of cases.

Time and space clusters, if real, might be the consequence of infection, chemical or physical exposure (they may also reflect a particular socio-economic status or, more unlikely, peculiar genetic traits of the population of interest). The most obvious hypothesis that comes to mind in order to interpret a cluster is the presence of a chemical or physical contaminant in the general environment, whose nature may remain undetermined. This was the case with the well-known cluster of childhood leukaemia in Woburn, Massachusetts, United States, where between 1966 and 1986 more than 20 children developed leukaemia (a four-fold increase over expected figures from the national average): residents may have been exposed to levels of arsenic, chromium and organic solvents in the drinking-water in excess of standards. The epidemics subsided after closure of two wells, but it is not demonstrated that the events were associated (Cutler *et al.*, 1986; Durant *et al.*, 1995). The excess of childhood leukaemia around the Sellafield nuclear reprocessing plant in the United Kingdom (Gardner *et al.*, 1990) may be interpreted as reflecting physical influences directly attributable to the plant. An alternative interpretation is implied in the Kinlen hypothesis (Kinlen *et al.*, 1990). The latter states that childhood leukaemia excesses in some areas (including, possibly, Sellafield) might reflect a rare response to some unidentified mild or sub-clinical infection, the transmission of which is facilitated by contacts between large numbers of people. An influx of a population of diverse origin into a previously isolated area would particularly facilitate transmission, whereas mild or moderate exposure would be immunising.

Whether or not the Kinlen hypothesis explains the findings in Sellafield falls beyond the purpose of the present review. The fact remains that it proved correct when tested in other populations living in isolated areas into which there had been substantial immigration and in which there was no nuclear installation, and in 'rural new towns' (Kinlen *et al.*, 1990).

Lymphomas

Whereas in most of Africa lymphomas are the most frequent type of childhood cancer, in European countries they rank third, following leukaemias and tumours of the central nervous system. The most common types of lymphoma are Hodgkin's disease (HDL), non-Hodgkin lymphoma (NHD) and Burkitt disease. Table 5.3. indicates the range of rates in European countries. Some of the differences between countries may be related to diagnostic practices in different countries and periods.

As the table indicates, rates are higher in boys than in girls, particularly for NHD. For HDL, in Finland, Norway, Sweden, Switzerland and some French and Italian registries, the sex ratio is lower than 1.5, whereas for NDH all male:female ratios are above 1.5, up to 4 and above in Estonia, Slovenia, Sweden and Switzerland. Although some geographical pattern is evident, its interpretation in terms of exposure to risk factors is extremely uncertain.

Age-standardised incidence rates (annual per million children) of the three major types of lymphoma in children aged 0–14 years in European cancer registries reporting highest and lowest rates around 1990 (dates in which rates were estimated are those given in Table 5.1.)

Table 5.3.

Source: Parkin *et al.*, 1998

	European countries with highest rates	European countries with lowest rates
HDL boys	13.5 Slovenia 12.0 Estonia 10.0 Slovakia	3.9 Norway 4.1 Finland 4.3 Scotland
HDL girls	6.9 Slovakia 6.4 Switzerland 5.9 Lorraine	0.8 Valencia 0.9 Iceland 1.7 France PACA and Corsica
NHD boys	12.1 Germany 11.3 Spain others 11.3 Slovakia	2.9 Iceland 3.6 France PACA and Corsica 5.3 France others
NHD girls	6.0 Spain others 5.9 Netherlands 5.5 Germany	1.3 France PACA and Corsica 1.5 Denmark 2.2 Switzerland
Burkitt boys	9.9 France PACA and Corsica 8.3 Spain Valencia 7.3 France others	0.0 Estonia 0.0 Iceland 0.0 Norway
Burkitt girls	2.5 Spain Valencia 2.5 Spain others 2.1 France Lorraine	0.0 Scotland 0.0 Sweden 0.0 Iceland

Note: Registries where underreporting was considered to be possible and/or where there may have been difficulties in establishing the correct population at risk are excluded.

A number of epidemiological studies have addressed the association between HDL and indicators of socio-economic status and infection with Epstein-Barr virus, but very little is known about environmental influences. Some interest has been raised by the recent observation (Mandelli *et al.*, 2001) of an increased incidence of HDL among Italian soldiers returning from the ex-Yugoslavia, possibly exposed to depleted uranium (11 observed cases vs. 3.7 expected on the basis of the rates of Italian cancer registries). However, this finding requires confirmation and potential biases need to be examined in detail.

Determinants of childhood NHD are difficult to unravel from incidence rates. The high sex ratio has long been known and can hardly be explained in terms of environmental exposure. In the United Kingdom, a non-statistically significant two-fold excess in children of Asian origin compared with white children has been reported (Powell *et al.*, 1994). Ecological analyses in the same country failed to identify any pattern related to socio-economic variables, at least up to the mid-1980s (Draper *et al.*, 1991; Rodrigues *et al.*, 1991). Whereas in European adults there has been an obvious increase in incidence over time, as a consequence of the AIDS epidemics, corresponding observations in children are much less clear, at least up to the early 1990s, i.e. the most recent times for which reports from cancer registries are available. More recent epidemiological studies on other databases, in Italy and in the United Kingdom, have clearly established the association between HIV transplacental infection and NHD (and other sarcomas) (Evans *et al.*, 1997; Caselli *et al.*, 2000).

The incidence of Burkitt lymphoma is very high in tropical Africa, but low in Europe. It can be seen from Table 5.3. that in both sexes, around 1990, the incidence of Burkitt

lymphoma was highest in Mediterranean countries and negligible in Scandinavian countries. The extent to which this pattern is real or reflects diagnostic practices remains to be established on larger databases.

Results of studies addressing the issue of clustering of lymphomas in space and time are much less clear-cut than findings for leukaemias (Alexander *et al.*, 1991).

Tumours of the central nervous system

In European countries, around 1990, annual age-standardised incidence rates for all brain and spinal neoplasms ranged between 20 and 40 per million in boys and slightly less in girls (sex ratio around 1.2 in most populations). Consistency between registries in criteria for recording benign glial tumours has been limited. In addition, relative frequencies of the different histological types are influenced by diagnostic attitudes. In most cancer registries, astrocytomas and medulloblastomas account, respectively, for a little less than half and for about one-third of all cases, whereas ependymomas represent 10 %. A worldwide trend in time towards an increased incidence has long been known (Breslow and Langholz, 1983), but it is largely attributable to diagnostic refinement. Ependymomas are known to have a propensity to occur in younger children.

Limited studies comparing ethnic groups in the United Kingdom have suggested a non-statistically significant slightly lower risk for children of Asian origin (Stiller *et al.*, 1991; Powell *et al.*, 1994), which is consistent with the low rates typical of countries of southern Asia. Incidence in the United States is about 20 % higher in white than in black children (Parkin *et al.*, 1998). Evidence for an association with socio-economic status is scanty and contradictory (Sharp *et al.*, 1999).

Little's review (Little, 1999) tabulates the factors which have been reported to be associated with tumours of the central nervous system (CNS) in children, distinguishing between those for which the association is generally accepted and those for which the association shows 'some degree' of consistency across studies. The former, in addition to a number of congenital conditions (one of which is neurofibromatosis), includes the occurrence of a cancer in a sibling and intrauterine exposure to diagnostic x-rays (at doses used decades ago). The latter include maternal consumption of cured meats and maternal use of vitamin supplements during the index pregnancy. The association with the consumption of cured meats (Preston-Martin *et al.*, 1982) is interesting: the underlying hypothesis is that curing meat leads to the formation of N-nitroso compounds from amines and sodium nitrite. N-nitroso compounds are known to produce brain cancer in the rat. Were this the case also in humans, its relevance to public health would extend to exposures to N-nitroso compounds in the workplace.

Other childhood cancers

With minor exceptions, the Swiss rates reported in Table 5.2. are representative of the European situation.

Most tumours of the sympathetic system are neuroblastomas. It is known that this type of cancer is rare in sub-Saharan Africa, and that in the United States it is somewhat rarer in black than in white children (Parkin *et al.*, 1998). Time-related increases in incidence have been reported but it is unclear whether they are entirely attributable to improved diagnosis. In the United States, an average annual percentage increase in incidence of 3.1 % was recorded between 1974 and 1991 (Gurney *et al.*, 1996). However, the increase was limited to children in their first year of life, which would suggest a role for early detection. Studies in Denmark and in the United States have suggested that risk of developing a neuroblastoma is higher in children of lower socio-economic status.

The incidence of retinoblastoma recorded in European countries is similar to that estimated in other white populations and lower than in Africa (whereas in the United States rates do not consistently differ between black and white children). In the United Kingdom, Asian children exhibited a non-statistically significant doubled risk compared with white children (Powell *et al.*, 1994).

In European populations, as well as in white North Americans, renal tumours (95 % of which are nephroblastomas) represent 5–6 % of all cancers, a relative frequency lower than the 10 % recorded in US black children (Parkin *et al.*, 1988; Parkin *et al.*, 1998). In contrast, the risk for children of Asian origin in the United Kingdom is about a half that of white children (Stiller *et al.*, 1991): the difference is statistically significant and suggests that environmental factors are of little relevance in the etiology of renal cancer.

Also socio-economic factors do not seem to influence rates.

Other childhood cancers are uncommon in European children and their descriptive epidemiology does not provide any clue which might be of interest with regard to their etiology. In Europe and in contrast to Australian white children (McWhirter *et al.*, 1996), as yet no clear-cut and significant increase of cutaneous melanoma in childhood has been reported from cancer registries. Such an increase is to be expected, given the well-known and clear association of melanoma in all ages with sunburn and excessive exposure to ultraviolet light (see review in Whiteman *et al.*, 2001), as well as the tendency to increase the leisure time during which European children are exposed to the sun. This is a situation which allows for effective preventive measures.

In Europe and in white North-American children osteosarcomas and Ewing's sarcomas are equally represented in the group of malignant bone tumours. This contrasts strikingly with the fact that Ewing's sarcoma accounts for less than 10 % of bone cancers in black children in the United States, and is almost unknown in sub-Saharan Africa (Fraumeni and Glass, 1970; Parkin *et al.*, 1988; Parkin *et al.,* 1998).

In white populations, differences in the order of 20–30 % have been recorded in incidence rates of soft tissue sarcomas in childhood and approximately 60 % of these are rhabdomyosarcomas. Time-related increases have been recorded in Italy (Mosso *et al.*, 1992), Japan (Ajiki *et al.*, 1994) and the United Kingdom (Draper *et al.*, 1994). In Europe and North America, as yet, in children, there is no evidence of any dramatic increase in the occurrence of Kaposi sarcomas, attributable to the AIDS epidemics (Parkin *et al.*, 1998).

5.3. Genetic susceptibility

Cancer is considered to be a truly genetic disease because malignancy is the result of multiple mutations of cellular DNA. Cellular genetic changes do not necessarily imply heredity, i.e. transmission from the parent to the child of genetic changes, including new mutations occurring in the oocyte or sperm before fertilisation. Indeed, the proportion of paediatric cancers exhibiting a clearly hereditary component or associated to hereditary predisposition, even if higher than the corresponding proportion for adult cancers, is low, in the order of 4 % (Narod *et al.*, 1991). For leukaemias and neoplasms of the central nervous system, i.e. the most common cancer types in childhood, estimates of the proportion of cases associated to familial aggregation and hereditary predisposition (e.g. Down syndrome) amount respectively to less than 5 % and less than 3 %. Corresponding proportions are higher for rarer tumours, such as retinoblastoma, optic glioma and pheochromocytoma (Plon and Peterson, 1997).

An increased cancer risk results from a number of inheritable disorders, including autosomal dominant conditions (such as retinoblastoma, familial colon cancer, Li Fraumeni syndrome, neurofibromatosis) and autosomal recessive disorders. Among the latter, xeroderma pigmentosum and ataxia teleangectasia magnify the mutagenic effects of environmental exposure that all individuals experience. Cancers in early life associated with these congenital conditions are unlikely to represent more than 5 % of all childhood cancers. Familial bilateral retinoblastoma occurs in about five out of 100 000 children born in the United States. It is not clear whether, for a given environmental exposure, the individuals who develop malignancy represent the general population or, alternatively, a small percentage of the population with a genetic predisposition to cancer. As the genes that predispose to malignancy are identified, this question can be answered at the molecular level (Plon and Peterson, 1997).

About 30 years ago, based on epidemiological observations on the age distribution of monolateral and bilateral retinoblastoma, Knudson and Strong developed the two-mutation hypothesis (Knudson, 1971). This states that a cell must undergo at least two mutations in order to become malignant. In non-hereditary retinoblastoma, all mutations occur after conception, whereas in the hereditary form the first mutation occurs before conception (Knudson, 1971). This model could also explain the distribution of Wilms' tumours (Knudson, 1978) and possibly other childhood cancers. The two-stage hypothesis leaves room for the possibility of a role for environmental influences after conception, either before or after birth.

Much research has been addressed in the last decade or two to genetic polymorphisms influencing detoxification or metabolic activation to intermediates reacting with DNA of chemical carcinogens. In contrast to genes such as xeroderma pigmentosum implicated in rare and cancer-inducing conditions (which affect a DNA-repair enzyme), metabolic polymorphisms are caused by mutations in genes that are not directly involved in the cancer process. They are common, low penetrant conditions governing the function of an enzyme that metabolises toxic chemicals. The relevance of metabolic polymorphisms in some circumstances of chemical carcinogenesis in adult humans is known (e.g. NAT-2, the metabolism of aromatic amines and bladder cancer), whereas as yet no circumstance has been reported suggesting that they may be implicated in the origin of childhood cancer. This may simply reflect the fact that with the exception of ionising radiation, stilbestrol and directly acting alkylating agents used for cancer treatment, no environmental cause of childhood cancer has been identified beyond any doubt.

Davies *et al.* (2000) reported an increased risk for acute myeloid leukaemia (AML) and myelodysplasia in children associated with the GSTM1 null genotype (OR = 2.0, 95 % CI 1.3–3.1). The GSTM1 genes are responsible for detoxification of epoxides and alkylating agents, potentially increasing internal concentrations of specific carcinogens in these chemical classes. Even higher odds ratios were found in connection with specific subtypes of AML. Results were less clear in a Canadian case-control study of childhood leukaemia investigating parental smoking and the potential interaction with CYP1A1 polymorphisms (Infante-Rivard *et al.*, 2000). These associations are interesting but require confirmation.

5.4. Exogenous agents

By and large the environmental determinants of childhood cancer — as with most rare diseases — have been investigated through the case-control approach, which implies the collection of large series of cases and a retrospective assessment of exposures, usually through interviews with the children's parents. The psychological conditions often differ between case and control parents, which creates a potential for recall bias. A detailed account of findings of studies on physical, chemical and biological risk factors for childhood cancer can be found in the IARC monograph published in 1999 (Little, 1999). Only major findings in areas investigated in depth and risk factors that have caused or cause concern will be reported here.

Ionising radiation

The potential of ionising radiation to induce childhood cancer can be estimated from studies carried out under a variety of exposure circumstances and populations, such as in Hiroshima and Nagasaki survivors, populations affected by accidents at nuclear plants, those exposed to fallout from weapon tests or residents near nuclear installations, as well as in investigations on the long-term effects of indoor radon and on the consequences of exposure to x-ray for diagnostic or therapeutic reasons. Studies started in the 1950s in children exposed *in utero* to diagnostic x-rays have great historical interest and have contributed to the quantitative risk assessment (Stewart *et al.*, 1958; Monson and McMahon, 1984). Current diagnostic practices have greatly reduced the risk and have led to a more rational approach to risk *vs.* benefit evaluation. Similarly, the occurrence of cancer following therapeutic administration of x-rays for non-neoplastic conditions (such as thymus enlargement or tinea capitis) has a historical interest. Nevertheless, whether awareness of the consequences of unnecessary medical procedures is uniform throughout countries remains to be determined.

Plon and Peterson (Plon and Peterson, 1997) have adapted previous estimates in order to compare projected lifetime risks of cancer incidence among persons exposed at 10 cSv (centisieverts) at age 10 as compared with non-exposed persons. They estimated the proportion of cases attributable to the exposure among the exposed: around 20–30 % of all leukaemias (50 % for ALL) and 13 % of breast cancer in women. For all cancers excluding leukaemia the estimated proportion was 4 % in men and 9 % in women. The authors point out that the fact that in Hiroshima and Nagasaki no excess genetic effects were seen in children of parents receiving less than 10 cSv does not rule out the possibility that effects may occur at higher doses. Their conclusion is that 'there are many questions that remain unanswered, and additional study is needed'.

Hiroshima and Nagasaki survivors

Of the 1 630 survivors who had been exposed to the bombing *in utero* and were included in the follow-up starting in 1950, 16 developed cancer in childhood and 16 in adulthood (i.e. before and after 1960) (Yoshimoto *et al.*, 1988), with no particular organ being affected. The figures indicate a five-fold increased risk per 10 000 person-year-gray. The cancer experience of the 15 584 survivors aged under 10 at the time of the explosions was compared to that of about 5 000 controls (living in Nagasaki and Hiroshima but not present at the time of the explosions, which might have led to a difference in socio-economic conditions between the two groups and thus reduce comparability). Between 1955 and 1969, i.e. up to age 24, statistically significant excesses were observed, limited to those who had been exposed to more than 1 gray: the observed/expected ratios were 19.1 for leukaemia and 7.3 for other cancers (both based on eight cases observed) (Jablon and Kato, 1970). Findings may have been obscured by the five-year (1945–50) delay in starting the follow-up and estimates may have been influenced by effect modifications brought about by other health problems created by the explosions, such as malnutrition and infectious diseases.

Accidents at nuclear plants

The ecological studies launched after the Three Mile Island accident (March 1979), which released ^{131}I and ^{133}XE, did not detect any childhood cancer excess in the area around the plant in the period up to 1985 (Hatch *et al.*, 1990; Hatch and Susser, 1990). Indeed, the number of leukaemia cases was well below expected figures from national data, which might reflect an underascertainment of cases.

Studies on the possible excesses of cancer in children consequent to the Chernobyl accident (April 1986) were focused on leukaemias and thyroid cancer. Up to 1991 there were no appreciable changes in the incidence of acute leukemia in children living in Belarus as a whole or in the most contaminated areas of Gomel and Mogilev (Ivanov *et al.*, 1993). An international study coordinated by the International Agency for Research on Cancer provided no evidence of a change in incidence rates of childhood leukaemia estimated by cancer registries, either in Belarus or in other European countries (Parkin *et al.*, 1996). Indeed, the number of expected excess cases on the basis of previous studies was small, even in Belarus, where exposure was highest. Additional analyses in a number of European countries, such as Greece, Sweden, Finland and Germany failed to detect a clear-cut increase in childhood leukaemias for several years after the accident.

Information on childhood thyroid cancer is more substantial, but contradictory. A very high incidence of childhood thyroid cancer has been reported in Belarus (Kazakov *et al.*, 1992). In 1991–92 the annual rate per million approached 80 vs. 1 per million in most areas covered by a cancer registry. Morphologically, most thyroid tumours in the contaminated areas were aggressive papillary carcinoma (Nikiforov and Gnepp, 1994). The extent to which the excess in incidence was real is difficult to establish. Part (not necessarily all) of the excess may have been caused by the intense screening offered to children living in those areas. In addition, it has been noted that an increase of thyroid cancer within five years after the accident is inconsistent with previous findings that thyroid cancers consequent to the fallout from nuclear tests in the Marshall Islands had a much longer latent period (Ron *et al.*, 1995) and that there is no evidence of a dose-response relationship (Boice and Linet, 1994).

Fallout from weapons tests

Over the last 50 years, the effects of fallout have been investigated in Utah and Nevada, in the United Kingdom, in the Nordic countries and in Kazakhstan. A detailed account of these studies is given by Little (Little, 1999). In a case-control study of children dying of leukaemia in Utah between 1952 and 1981, cases were more likely to have been exposed than controls: the odds ratio (an approximation to the relative risk) for leukaemia among children whose marrow dose was estimated to range between 0.6 and 3 cSv was 1.7, of borderline statistical significance (Stevens *et al.*, 1990). A cohort study including non-exposed children in Arizona and children in Nevada and Utah exposed at the Nevada Test Site showed a 16 % excess death rate from thyroid cancer among persons who had been exposed at 2 cSv or more (Kerber *et al.*, 1993). Findings in studies carried out in other areas have been less clear-cut, with the possible exception of those carried out in Kazakhstan (Zaridze *et al.*, 1994), which estimated a statistically significant double risk for acute leukemia for children living within 200 km of the air or underground testing sites

compared to those living 400 km away. Nevertheless, completeness of ascertainment of cases may have been different in the different areas.

Proximity to nuclear installations
A number of ecological studies in several countries did not demonstrate a tendency for childhood cancers to aggregate in the vicinity of nuclear installations (Little, 1999). Some European plants, such as those mentioned below, have been investigated through analytical studies. Overall, findings are not unequivocal.

The most relevant studies are those carried out in the area of the Sellafield nuclear reprocessing facility in the United Kingdom by the late Martin Gardner and his colleagues in Southampton. These studies did not detect a significant association between childhood leukemia and maternal exposures but did estimate a two-fold increased risk for children whose fathers worked in the nuclear reprocessing facility. The relative risk was 8 for children whose fathers had received a career dose greater than 10 cSv or a dose greater than 1 cSv within six months before the birth of the index child (Gardner *et al.*, 1990). This was based on four out of 46 cases compared to three out of 276 controls. The authors interpreted their findings as suggesting the possibility of an effect of preconceptional ionising radiation in the fathers that may be leukaemogenic in their offspring. An effect of population inflow has been suggested as an alternative hypothesis by Kinlen (Kinlen, 1995, see under Childhood infections, below).

Another European population living in the proximity of a nuclear reprocessing plant which has been recently investigated in much detail for the incidence of leukaemia in young people is located in La Hague in Normandy (Viel *et al.*, 1993; Viel, 1997). Some studies have estimated statistically significant increased risks for residence close to the plant and for other sources of exposure in the general environment. With regard to these findings, the possibility of an effect of selection bias, recall bias and chance has been debated (Little, 1999).

Indoor radon
Ecological and analytical studies carried out in several countries have not provided firm evidence or suggestion of an association between indoor radon and childhood cancer risk (Little, 1999).

In utero exposure to diagnostic x-ray
An excess cancer risk among children exposed prenatally to diagnostic x-ray was reported in the 1950s from the Oxford Survey of Childhood Cancer (Stewart *et al.*, 1958). Similar results were provided by a follow-up study of 1.5 million children born in New England and the mid-Atlantic states in the United States (Monson and McMahon, 1984). Exposure during the third trimester of pregnancy is more associated with leukaemia whereas earlier exposure is more associated with solid cancers. These studies have a great historical interest and have contributed to the quantitative risk assessment. Current diagnostic practices have reduced the risk. However, as late as in the 1980s, risk excesses attributable to the practice of submitting pregnant women to diagnostic x-rays were estimated in different countries (McKinney *et al.*, 1987; Ji *et al.*, 1997).

Other iatrogenic exposures
Excesses of cancers in children who had undergone x-ray treatment for scalp ringworm (tinea capitis), enlarged thymus glands and enlarged tonsils, which have been described decades ago, are likely to have exclusively historical interest. The risk for thyroid cancers in children irradiated for thymic enlargement was increased 100-fold, with a clear-cut dose-response relationship (Hempelman *et al.*, 1975). The thyroid was also the main target organ in persons given radiation therapy for tinea capitis (Ron and Modan, 1980). An apparent association of brain tumours with five or more full-mouth dental x-rays (Preston-Martin *et al.*, 1982) was interpreted to be non-causal by the authors and was not confirmed in a subsequent case-control study (McCredie *et al.*, 1994a; McCredie *et al.*, 1994b).

Ultraviolet (UV) radiation
Sun exposure is known to be a risk factor for the development of skin cancer later in life, although the evidence for squamous cell carcinoma is stronger than for basal cell carcinoma and skin melanoma. The occurrence of sunburn is an indicator of risk (Whiteman *et al.*; 2001; English *et al.*, 1997). Given the tendency to increase the leisure time during which European children are exposed to the sun, this topic allows for preventive measures. In recent years, the possibility of photoprotection by sunscreens has been debated. In April 2000, the International Agency for Research on Cancer convened a working group of experts to evaluate the cancer-preventive activity of

sunscreens. It was concluded that the topical use of sunscreens reduces the risk of sunburn and that sunscreens probably prevent squamous-cell carcinoma of the skin when used mainly during unintentional sun exposure. On the contrary, no conclusion was drawn about the cancer preventive activity of topical use of sunscreens against basal-cell carcinoma and cutaneous melanoma. It has also been pointed out that the use of sunscreens can extend the duration of intentional sun exposure, such as sunbathing: such an extension can increase the risk for cutaneous melanoma. The working group warned against relying solely on sunscreens for protection from ultraviolet radiation (Vainio *et al.*, 2000). (See Chapter 12 in this publication for further information.)

Electromagnetic fields

Power-frequency electromagnetic fields (EMF) are generated by power lines, electrical appliances, large electrical machinery, etc. Risks for children exposed to EMF are covered in Chapter 13. The association of exposure to these fields with childhood cancer, particularly leukaemia, has been investigated in multiple countries using cohort and case-control study designs. Two recent meta-analyses (Ahlbom *et al.* 2000, Greenland *et al.* 2000) of case control studies addressed to the association between extremely low fields and childhood leukaemia estimated significantly increased risks (relative risks between between 1.7 and 2.0) for children with measured or estimated exposures higher than 0.3-0.4 μT. IARC recently concluded that the scientific evidence, in particular the evidence as it relates to childhood leukaemia, suggests that power-frequency EMF is possibly carcinogenic to humans (category 2B) (WHO, 2001). The decision was based on the evaluation that there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. Among children up to 14 years of age, about 430 cases of leukaemia (all types) are registered each year in England and Wales. The United Kingdom Childhood Cancer Study Investigators (2000) found that 0.4 % of children are exposed to $\geq$ 0.4 μT. Although the corersponding proportion may be slightly higher in other European countries, assuming that the association is causal, the number of cases in excess would be in the order of 1 % (i.e. 4-5 cases annually in a country of the size of England and Wales. In addition, if a relative risk of 1.5 were operating for children exposed to between 0.2 and 0.4 μT, then the annual number of attributable cases in England and Wales might be 6-7.Whether or not this is to be considered acceptable (keeping in mind that the association is not proven) is an ethical matter, requiring a thorough and transparent discussion among different stakeholders.

The possible adverse health effects in children associated with exposure to radiofrequency fields have not been fully investigated. Although the research on radiofrequency fields is extensive, the epidemiological studies are individually weak and inconsistent.

Childhood infections

There is concern about the association between the hepatitis B virus (HBV) and the hepatitis C virus (HCV) and hepatocarcinoma (IARC, 1994) and the association between Epstein-Barr virus (EBV) and Burkitt lymphoma and HDL (Weiss *et al.*, 1989; Herbst *et al.*, 1990). HBV viral DNA has been found to be integrated in the DNA of liver cancer cells. A corresponding finding applies to Burkitt lymphoma: however, viral DNA integration is much more common in Africa (up to 90 %) than in 'sporadic' Burkitt lymphoma in other parts of the world (down to 20 %). Thus, it is not clear whether or not EBV infection is a sufficient condition for the appearance of Burkitt lymphoma. The infectious origin of HDL was originally hypothesised following the occurrence of a time-space cluster in a school, in which, however, no agent was identified. Nevertheless, excess antibodies against infectious mononucleosis and viral DNA of EBV were detected in some Reed Sternberg cells.

As mentioned above, the typical tendency of ALL to cluster is suggestive of an infectious origin. Two different etiological hypotheses have been forwarded. According to Greaves (1988), at a critical time for the development of the immunological system of the child, exposure to non-specific infectious agents may trigger a proliferation of clones of cells which had undergone mutation before birth and so determine the appearance of leukaemia. This may also explain the incidence peak at two to three years of age typical of industrialised societies, at a time when the child comes into contact with infectious agents. On the contrary, according to Kinlen, the concentration of cases in small

communities undergoing massive immigration suggests a role of an agent as yet unidentified which induces the disease in a small proportion of exposed children (Kinlen, 1995).

Tobacco smoke

Tobacco smoke contains many carcinogenic polycyclic aromatic hydrocarbons, which are known to be able to cross the placenta and accumulate in fetal blood. Nevertheless, the abundant literature regarding maternal or paternal tobacco smoke and childhood cancer does not provide consistent results and clear-cut evidence of an association: this is supported by large studies such as the Inter-regional Epidemiology Study of Childhood Cancer in England (McKinney and Stiller, 1986) and the Children's Cancer Study Group in the United States (Buckley *et al.*, 1989; Severson *et al.*, 1993). The probable lack (or very limited) evidence of a causal role of tobacco smoke in childhood cancer contrasts with the very strong association with, and high relative risks for, many cancers in the adult. Results are unlikely to be caused by recall bias (Little, 1992).

Nevertheless, occasionally, interesting findings have been reported which require confirmation from independent studies. An association between paternal smoke and the risk for rhabdomyosarcoma (Grufferman *et al.*, 1982), if confirmed, would suggest an increased susceptibility of the child deriving from a mutation in the paternal sperm. A study carried out in China a few years ago suggested an effect of paternal smoke on their children's risk for cancer. Statistically significant relative risks among children of heavy smokers compared with children born from non-smoking fathers between 2.8 and 4.5 were estimated for ALL during the first year and a half of life, and for lymphomas and brain cancer (Ji *et al.*, 1997).

Diet and alcohol

Maternal diet during pregnancy has been investigated, with two goals. One was the assessment of whether there is a risk associated with the consumption of nitrates, thus possibly leading to endogenous formation. The other was testing the hypothesis of a protective effect of vitamin supplements. Studies investigating the association of brain cancer with maternal exposure to nitrosamines in the United States (Preston-Martin *et al.*, 1982) and in New Zealand (McCredie *et al.*, 1994a,b) showed a statistically significant association with relative risks between 2.0 and 2.5 and a dose-response relationship. However, no association was found in another study on neuroblastomas (Michalek *et al.*, 1996).

There is a general consensus on the protective role of vitamin supplements and of a diet rich in fruit and vegetables during pregnancy against childhood cancer. However, only a few formal epidemiological studies have produced quantitative estimates, which nevertheless are consistent, with relative risks in the order of 0.5 for brain cancer or neuroblastoma (Bunin *et al.*, 1994; Michalek *et al.*, 1996).

Ethyl alcohol and its metabolites cross the placenta and are teratogenic in the human species producing a condition known as fetal-alcohol syndrome. They are also well known carcinogens for the upper aerodigestive tract and for the liver (IARC, 1988). Some case reports describing the occurrence of cancers in children with the syndrome can hardly be interpreted in terms of causality. An association between maternal alcohol consumption during pregnancy and non-lymphoblastic leukaemias, with relative risks in the order of 2–3 has been reported in at least three studies (Severson *et al.*, 1993; Van Duijin *et al.*, 1994; Shu *et al.*, 1996).

Air pollution and road traffic

Air pollutants affect children more than adults, because of their narrow airways, more rapid rate of respiration, and because they inhale more pollutants per kilogram of body weight (AAP, 1993). Indoor and outdoor air pollutants include agents which have been shown or are suspected of being carcinogenic, such as benzene, radon, environmental tobacco smoke, asbestos, formaldehyde and particulate matter. Given the mixture of exposures, agent-specific effects are difficult to investigate both in adults and in children. Benzene is well known for its ability to induce leukaemia (particularly of the acute myeloblastic type) in occupationally exposed workers, but whether this effect also occurs in children exposed to the lower concentrations typical of the general environment is not known.

Road traffic is a major source of children's exposure to air pollutants. Several proxies of exposure to atmospheric contaminants caused by vehicle traffic have been used in epidemiological studies on childhood leukaemia. Some are highly debatable, such as number of cars per family or in the

neighbourhood. Estimates of traffic density, such as counting the number of cars passing in the area where the children reside, are more reliable. A population-based study in Denver which compared 328 children with cancer (almost all leukaemias) and 262 controls, estimated a relative risk for leukaemia of 2.7 (95 % CI 1.3–5.9) for children living in areas with more than 5 000 cars passing per day, compared with children living in areas where the corresponding number was less than 500. The risk was unlikely to be influenced by potential confounders (Savitz and Feingold, 1989). In another case-control study in Sweden, annual exposure to nitrogen dioxide (NO_2) was estimated in a model, which included monitoring data, traffic characteristics and residential history of each child. The risk for cancer (any type) for children falling in the upper quartile of exposure (NO_2 above 50 micrograms per cubic metre ($\mu g/m^3$)), relative to children whose exposure was lower than the median (39 $\mu g/m^3$) was 2.7 (95 % CI 0.9–8.5). Similar estimates were obtained for leukaemias, but statistical significance was less satisfactory (Feychting *et al.*, 1998).

In the United Kingdom, the residence of children diagnosed with cancer between 1990 and 1994 was characterised in terms of proximity to main road and petrol stations. Comparisons between children with leukaemia and children with solid cancer led to estimates of relative risks of 1.61 (95 % CI 0.90–2.87) and 1.99 (0.73–5.43) for children living within 100 metres of a main road or petrol station, respectively. Corresponding incidence ratios estimated as compared with the general population were 1.16 (0.74–1.72) and 1.48 (0.65–2.93). Results were not explicable on the basis of impact of deprivation index of the area of residence (Harrison *et al.*, 1999).

A recent, register-based, study compared the residential history since conception of 1 989 Danish children diagnosed with leukaemia, lymphoma or tumour of the central nervous system between 1968 and 1991 with the corresponding data of 5 506 control children. For each of the 18 440 addresses, concentrations of benzene and NO_2 were calculated for the relevant period and exposures were calculated separately for the intra-uterine period and life after birth. A statistically significant association was found only for Hodgkin's disease, with risks increased by 25 % and 50 % for a doubling of the concentration of benzene and nitrogen dioxide respectively (Raaschou-Nielsen *et al.*, 2001).

The association between air pollution from traffic at the residence and childhood cancer cannot be considered to be proved and current information may well be influenced by publication bias. Nevertheless, it deserves attention, given other well-known consequences on children's health of this hazard (e.g. bronchitis, pneumonia, decreased lung function and others — see Chapters 2 and 3).

Waste sites

Incinerators and landfill sites are commonly considered a source of carcinogenic chemicals (particularly dioxins and related compounds) but a quantification of the association between distance from suspect sources and cancer risks has been attempted only in a very few studies, a minority of which address childhood cancer. A recent ecological study in the United Kingdom could not distinguish clearly between effects of municipal incinerators and those of adjacent industrial sources of combustion effluents. An association seemed to exist for both, but not for landfill waste sites (Knox, 2000).

Exposure to pesticides and other chemicals

Children's exposure to environmental chemicals is difficult to quantify, with the possible exception of exposure which is characterised by parental activities or which is linked to the geographical position of the residence or to activities related to it. In the last few decades, a number of studies have considered the possibility of an etiological role for parental occupation in the cancers appearing in their offspring: these studies have been the object of a number of reviews (Savitz and Chen, 1990; O'Leary *et al.*, 1991; Colt and Blair, 1998; Zahm and Ward, 1998). Sources of exposure can be materials carried into the home from the workplace, breastfeeding of contaminated milk or the placenta. Nevertheless, the interpretation of the available epidemiological evidence requires much caution: occupational titles are often grouped in very broad categories and the methods for converting occupational titles into exposure are usually crude. Most often a given occupation includes exposure to several chemicals, and actual exposure may vary according to specific activities within the job. Further, many investigations were based on multiple comparisons, thus implying a relatively high probability of

chance findings. Finally, the statistical power of most studies is low, so that they can hardly confute any hypothesis raised by previous studies.

Nevertheless, the huge literature has provided some clues. Colt and Blair (1998) reviewed 48 published epidemiological studies and provided relative risk estimates for over 1 000 specific cancer/occupation or cancer/exposure combinations. The strongest evidence for an association between father's occupation and the risk of childhood cancer was found to be for exposure to solvents and paints and the risk of leukaemias and cancer of the nervous system in the offspring. A number of suspected parental occupations entail exposure to benzene, whose ability to induce leukaemia in adults is well known (IARC, 1987). Parental exposure to hydrocarbons in the workplace was found to be associated with brain cancer in more than one study (Fabia and Thuy, 1974; Hemminki *et al.*, 1981; Peters *et al.*, 1981; Johnson and Spitz, 1989; Wilkins and Sinks, 1990) and the same can be said for Wilms' tumours (Kantor *et al.*, 1979; Kwa and Fine, 1980; Bunin *et al.*, 1989; Olshan *et al.*, 1993).

Concern about pesticides (i.e. insecticides, herbicides, fungicides, nematocides and rodenticides) derives from the fact that by definition their production and use are related to their biological activities. At least in developed countries, increased awareness of acute pesticide poisoning has led to a decrease in acute episodes of toxicity, and public health concern has moved to the long-term effects of low-level chronic pesticide exposure. In addition, conditions with a long latent period, such as cancer, are more likely to appear when the relevant exposure occurs early in life. Some biological effects of pesticides may interfere with the physiological processes of the child, including the immune, respiratory and neurological systems as well as the endocrine imbalance (NRC, 1993).

The association with exposure to pesticides has been suggested by case reports of cancer in children who had been exposed to chlordane, heptachlor or organophosphorus insecticides (Zahm and Devesa, 1995). Subsequently, a number of formal epidemiological studies reported statistically significant associations between parental occupational exposure to pesticides and ALL, childhood non-lymphoblastic leukaemia, Wilms' tumours and Ewing's sarcoma (Shu *et al.*, 1988; Buckley *et al.*, 1989; Holly *et al.*, 1992; Sharpe *et al.*, 1995). Associations have been reported also for domestic exposure to pesticides (Buckley *et al.*, 1989; Lowengart *et al.*, 1987; Olshan *et al.*, 1993). None of the reported associations satisfies the criteria commonly used to recognise causality.

5.5. Conclusions and implications for public health

Childhood cancers are rare diseases, but the burden they put on affected patients, on families and on the health system is heavy. Treatments are becoming increasingly complex, and a significant proportion of children have to undergo bone marrow transplantation to increase their chances of survival. Long-term consequences on health in survivors may be heavy, including the development of second primary neoplasms caused by the treatment for the first tumour. Further, exposures to carcinogens during childhood will reflect on cancer occurrence later in life. Thus, the need for primary prevention is obvious. Additionally, with the possible exception of neuroblastomas, there is no effective approach to secondary prevention (i.e. improvement of the natural history of the disease through diagnosis before symptoms appear) for any childhood cancer.

For some exposures, the scientific background required for primary prevention is clear-cut. Historically, the first circumstance open to preventive action was offered by the finding that diagnostic x-rays during pregnancy are strongly (and causally) associated with cancer in children. The evidence was collected about half a century ago. Unjustified maternal exposure is nowadays much less common and exposure per diagnostic examination is sharply reduced. Nevertheless, it is not known whether current practices are uniformly rational throughout European countries and some form of monitoring is needed.

Another convincing epidemiological finding open to prevention regards exposure to ultraviolet rays, following the model which in Australia has proved to be effective (Lower *et al.*, 1998). Whether or not children are as susceptible as adults to the carcinogenicity of ultraviolet radiation (Pfahlberg *et al.*, 2001) is irrelevant. In European countries, it has been found that sun protection of children is less than optimum and parents and children are

unaware of the long-term risks of over-exposure to the sun (MacGregor and White, 2001). Information and education seem to be crucial in this respect, as the use of sunscreens — as mentioned above — is not proven to provide full protection and may create a falsely reassuring attitude inducing undue extension of heavy exposure to ultraviolet light.

For other environmental agents considered in the present review, knowledge as to their ability to induce cancer in children (or later in life, following exposure during childhood) ranges between limited evidence (e.g. vehicle exhausts) and suspicion (e.g. radiofrequency and microwaves, pesticides). These uncertainties reflect the insufficient number of relevant studies as well as unavoidable shortcomings in the epidemiological studies that have been carried out.

During recent years, much debate has taken place on the amount and type of evidence of the hazardous nature of an agent that is required in order to take action aimed at protecting those who are exposed to it. As for children, a policy of prudent avoidance seems appropriate, i.e. a strategy aiming at protecting them from unnecessary exposures to suspected carcinogens, such as those which have been reviewed in the present chapter. A feature of most of these agents is that they are also associated with other conditions and that the evidence of association with non-neoplastic conditions during childhood is stronger (e.g. respiratory conditions for vehicle exhausts and tobacco smoke; liver toxicity for some pesticides). Thus, lack of full proof of carcinogenicity should not prevent the implementation of measures intended to reduce to a minimum children's exposure. The extent to which this can be achieved through legislative measures (e.g. electromagnetic fields), training of physicians (e.g. diagnostic x-ray during pregnancy) and risk communication (most agents described above) falls beyond the purpose of the present chapter.

Summary

Childhood cancers are rare diseases with potentially dramatic outcome. Children are more prone to biological events potentially related to carcinogenesis, due to greater exposures, immature detoxification mechanisms and higher cell proliferation. In addition, exposure to carcinogens during childhood can reflect on cancer occurrence later in life.

For some exposures, the scientific evidence for causality is clear-cut. Exposure to ionising radiation has the potential to cause childhood cancer and excessive exposure to sun-light during childhood causes skin cancer and probably melanoma later in life. For a number of other chemicals, physical and biological agents, knowledge as to their ability to induce cancer in children or later in life ranges between limited evidence (e.g. vehicle exhausts) and suspicion (pesticides, extremely low frequency electromagnetic fields, environmental tobacco smoke, parental occupational exposures). These uncertainties reflect the insufficient number of relevant studies as well as unavoidable shortcomings in the studies that have been carried out. But lack of full proof of carcinogenicity should not prevent the implementation of measures intended to reduce to a minimum childhood exposures, through legislative measures and risk communication.

References

AAP, 1993. Ambient air pollution: Respiratory hazards in children, *American Association of Pediatrics News.*

Ahlbom, A., Day, N., Feychting, M. *et al.*, 2000. A pooled analysis of magnetic fields and childhood leukaemia, *Br J Cancer,* Vol 83, pp. 692–8.

Ajiki, W., Hanai, A., Tsukuma, H. *et al.*, 1994. Incidence of childhood cancer in Osaka, Japan, 1971–88. Reclassification of registered cases by Birch's scheme using information on clinical diagnosis, histology and primary site, *Jpn J Cancer Res,* Vol 85, pp. 139–46.

Alexander, F.E., Ricketts, T.J., Williams, J. *et al.*, 1991. Methods of mapping and identifying small clusters of rare diseases with application to geographical epidemiology, *Geog Analysis,* Vol 23, pp. 156–73.

Birch, J.M. and Marsden, H.B., 1987. A classification scheme for childhood cancer, *Int J Cancer,* Vol 40, pp. 620–4.

Boice, J. and Linet, M., 1994. Fallout from Chernobyl — Editorial authors' response, *British Medical Journal,* Vol 309, p. 1300.

Breslow, N. and Langholz, B., 1983. Childhood cancer incidence: Geographical and temporal variations, *Int J Cancer*, Vol 32, pp. 703–16.

Buckley, J.D., Robison, L.L., Swotinsky, R. *et al.*, 1989. Occupational exposures of parents of children with acute nonlymphocytic leukemia: A report from the Children's Cancer Study Group, *Cancer Res*, Vol 49, pp. 4030–7.

Bunin, G.R., Nass, C.C., Kramer, S. *et al.*, 1989. Parental occupation and Wilms' tumor: Results of a case-control study, *Cancer Res*, Vol 49, pp. 725–9.

Bunin, G.R., Kuitjen, R.R., Boesel, C.P. *et al.*, 1994. Maternal diet and risk of astrocytic glioma in children: A report from the Children's Cancer Group (United States and Canada), *Cancer Causes Control*, Vol 5, pp. 177–87.

Caselli, D., Klersy, C., De Martino, M. *et al.*, 2000. Human immunodeficiency virus-related cancer in children: Incidence and treatment outcome — report of the Italian Register, *J Clin Oncol*, Vol 18, pp. 3854–61.

Colt, J.S. and Blair, A., 1998. Parental occupational exposures and risk of childhood cancer, *Environmental Health Perspectives*, Vol 106 (suppl 3), pp. 909–25.

Cutler, J.J., Parker, G.S., Rosen, S. *et al.*, 1986. Childhood leukemia in Woburn, Massachusetts, *Public Health Report*, Vol 101, pp. 201–5.

Davies, S.M., Robison, L.L., Buckley, J.D. *et al.*, 2000. Glutathione S-transferase polymorphisms in children with myeloid leukemia: A Children's Cancer Group study, *Cancer Epidemiol Biomarkers Prev*, Vol 9, pp. 563–6.

Dockerty, J.D., Cox, B. and Cockburn, M.G., 1996. Childhood leukaemia in New Zealand: Time trends and ethnic differences, *Br J Cancer*, Vol 73, pp. 1141–7.

Draper, G.J., Vincent, T.J., O'Connor, C.M. *et al.*, 1991. Socio-economic factors and variations in incidence rates between county districts, in *The geographical epidemiology of childhood leukaemia and non-Hodgkin lymphoma in Great Britain, 1966–83* (edited by G.J. Draper), Studies on Medical and Population Subjects No. 53, HMSO, London, pp. 37–45.

Draper, G.J., Kroll, M.E. and Stiller, C.A., 1994. Childhood cancer, in *Trends in cancer incidence and mortality* (edited by R. Doll, J.F. Fraumeni Jr. and C.S. Muir), Cancer Surveys 19/20, Cold Spring Harbor Laboratory Press, New York, pp. 493–517.

Durant, J.L., Chen, J., Hemond, H.F. *et al.*, 1995. Elevated incidence of childhood leukemia in Woburn, Massachusetts: NIEHS Superfund Basic Research Program searches for cause, *Environmental Health Perspectives*, Vol 103 (suppl 6), pp. 93–8.

English, D.R., Armstrong, B.K., Kricker, A. *et al.*, 1997. Sunlight and cancer, *Cancer Causes Control*, Vol 8, pp. 271–83.

Evans, J.A., Gibb, D.M., Holland, F.J. *et al.*, 1997. Malignancies in UK children with HIV infection acquired from mother to child transmission, *Arch Dis Child*, Vol 76, pp. 330–3.

Fabia, J. and Thuy, T.D., 1974. Occupation of father at time of birth of children dying of malignant diseases, *Br J Prev Soc Med*, Vol 28, pp. 98–100.

Feltbower, R.G., Moorman, A.V., Dovey, G. *et al.*, 2000. Incidence of childhood acute lymphoblastic leukaemia in Yorkshire UK, *Lancet*, Vol 358, pp. 385–7.

Feychting, M., Svensson, D. and Ahlbom, A., 1998. Exposure to motor vehicle exhaust and childhood cancer, *Scand J Work Environ Health*, Vol 24, pp. 8–11.

Fraumeni, J.F. Jr. and Glass, A.G., 1970. Rarity of Ewing's sarcoma among US Negro children, *Lancet*, Vol 1 (7642), pp. 366–7.

Gallagher, R.P., Hill, G.B., Bajdik, C.D. *et al.*, 1995a. Sunlight exposure, pigmentary factors, and risk of non-melanocytic skin cancer II. Squamous cell carcinoma, *Archives of Dermatology*, Vol 131, pp. 164–9.

Gardner, M.J., Snee, M.P., Hall, A.J. *et al.*, 1990. Results of the case-control study of leukaemia and lymphoma among young people near Sellafield nuclear plant in West Cumbria, *British Medical Journal*, Vol 300, pp. 423–9.

Greaves, M.F., 1988. Speculations on the cause of childhood acute lymphoblastic leukemia, *Leukemia*, Vol 2, pp. 120–5.

Greenland, S., Sheppard, A.R., Kaune, W.T. *et al.*, 2000. A pooled analysis of magnetic fields, wire codes, and childhood leukemia, *Epidemiology*, Vol 11, pp. 624–34.

Grufferman, S., Wand, H.H., DeLong, E.R. *et al.*, 1982. Environmental factors in the etiology of rhamdomyosarcoma in childhood, *J Natl Cancer Inst*, Vol 68, pp. 107–13.

Gurney, J.G., Davis, S., Severson, R.K. *et al.*, 1996. Trends in cancer incidence among children in the US, *Cancer*, Vol 78, pp. 532–41.

Harrison, R.M., Leung, P.L., Somervaille, L. *et al.*, 1999. Analysis of incidence of childhood cancer in the West Midlands of the United Kingdom in relation to proximity to main road and petrol stations, *Occup Environ Med*, Vol 56, pp. 1774–80.

Hatch, M. and Susser, M., 1990. Background gamma radiation and childhood cancers within ten miles of a US nuclear plant, *Int J Epidemiol*, Vol 19, pp. 546–52.

Hatch, M., Beyea, J., Nieves, J.W. *et al.*, 1990. Cancer near the Three Mile Island nuclear plant: Radiation emissions, *Am J Epidemiol*, Vol 132, pp. 397–412.

Hemminki, K., Salomeni, I., Salonen, T. *et al.*, 1981. Childhood cancer and prenatal occupation in Finland, *J Epidemiol Comm Health*, Vol 35, pp. 11–5.

Hempelman L.H., Hall, W.J., Phillips, M., *et al.*, 1975. Neoplasm in persons treated with x-rays in infancy: Fourth survey in 20 years, *J Natl Cancer Inst*, Vol 55, pp. 519–30.

Herbst, H., Niedobitek, G., Kneba, M. *et al.*, 1990. High incidence of Epstein-Barr virus genome in Hodgkin's disease, *Am J Pathol*, Vol 137, pp. 13–8.

Holly, E.A., Aston, D.P., Ahn, P.K.A. *et al.*, 1992. Ewing's bone sarcoma, parental occupational exposure, and other factors, *Am J Epidemiol*, Vol 135, pp. 122–9.

IARC, 1987. *Overall evaluations of carcinogenicity: An updating of IARC Monographs Vols 1 to 42* (suppl 7), IARC Monographs on the evaluation of the carcinogenic risk to humans, International Agency for Research on Cancer, Lyon.

IARC, 1988. *Alcohol drinking*, IARC Monographs on the evaluation of the carcinogenic risk to humans, Vol 44, International Agency for Research on Cancer, Lyon.

IARC, 1992. *Solar and ultraviolet radiation*, IARC Monographs on the evaluation of carcinogenic risks to humans, Vol 55, International Agency for Research on Cancer, World Health Organization, Lyon, France.

IARC, 1994. *Hepatitis viruses*, IARC Monographs on the evaluation of the carcinogenic risk to humans, Vol 59, International Agency for Research on Cancer, Lyon.

Infante-Rivard, C., Krajinovic, M., Labuda, D. *et al.*, 2000. Parental smoking, CYP1A1 genetic polymorphisms and childhood leukemia (Quebec, Canada), *Cancer Causes Control*, Vol 11, pp. 547–53.

Ivanov, E.P., Tolochko, G., Lazarev, V.S. *et al.*, 1993. Child leukaemia after Chernobyl, *Nature*, Vol 365, p. 702.

Jablon, S. and Kato, H., 1970. Childhood cancer in relation to prenatal exposures to A-bomb radiation, *Lancet*, Vol 2, pp. 1000–3.

Ji, B.T., Shu, X.O., Linet, M.S. *et al.*, 1997. Paternal cigarette smoking and the risk of childhood cancer among offspring of non smoking mothers, *J Natl Cancer Inst*, Vol 89, pp. 238–44.

Johnson, C.C. and Spitz, M.R., 1989. Childhood nervous system tumor: An assessment of risk associated with paternal occupations involving use, repair, or manufacture of electrical and electronic equipment, *Int J Epidemiol*, Vol 18, pp. 756–62.

Kaatsch, P., Haaf, G. and Michaelis, J., 1995. Childhood Malignancies in Germany — methods and results of a nationwide registry, *Eur J Cancer*, Vol 31, pp. 993–9.

Kantor, A.F., McCrea Curnen, M.G., Wister Meigs, J. *et al.*, 1979. Occupation of fathers of patients with Wilms' tumor, *J Epidemiol Comm Health*, Vol 33, pp. 253–6.

Kazakov, V.S., Demidchik, E.P. and Astakhova, L.N., 1992. Thyroid cancer after Chernobyl, *Nature*, Vol 359, p. 21.

Kerber, R.A., Till, J.E., Simon, S.L. *et al.*, 1993. A cohort study of thyroid disease in relation to fallout from nuclear weapons testing, *JAMA*, Vol 270, pp. 2076–82.

Kinlen, L.J., 1995. Epidemiological evidence for an infective basis in childhood leukaemia, *Br J Cancer*, Vol 71, pp. 1–5.

Kinlen, L.J., Clarke, D. and Hudson, C., 1990. Evidence from population mixing in British New Towns 1946–1985 of an infective basis for childhood leukemia, *Lancet*, 336, pp. 577–82.

Knox, E., 2000. Childhood cancers, birthplaces, incinerators and landfill sites, *Int J Epidemiol*, Vol 29, pp. 391–7.

Knudson, A.G. Jr., 1971. Mutation and cancer: Statistical study of retinoblastoma, *Proc Natl Acad Sci USA*, Vol 68, pp. 820–3.

Knudson, A.G., 1978. Mutation and cancer: A model for Wilms' tumor of the kidney, *J Natl Cancer Inst*, Vol 48, pp. 313–23.

Kwa, S.L. and Fine, L.J., 1980. The association between parental occupation and childhood malignancy, *J Occup Med*, Vol 22, pp. 792–4.

Little, J., 1992. Ascertainment, registration and assessment of exposure, in *Epidemiology and control of neural tube defects* (edited by J.M. Elwood, J. Little and J.H. Elwood), Oxford University Press, Oxford, pp. 37–95.

Little, J., 1999. *Epidemiology of childhood cancer*, IARC Scientific Publications No 149, International Agency for Research on Cancer, World Health Organization, Lyon.

Lowengart, R.A., Peters, J.M., Cicioni, C. *et al.*, 1987. Childhood leukemia and parent's occupational and home exposures, *J Natl Cancer Inst*, Vol 79, pp. 39–46.

Lower, T., Girgis, A., Sanson-Fisher, R., 1998. The prevalence and predictors of solar protection use among adolescents, *Prev Med*, Vol 27, pp. 391–9.

MacGregor, D.M. and White, M.I., 2001. Sunburn in children, the Aberdeen experience, *Clin Exp Dermatol*, Vol 26, pp. 137–40.

Mandelli, F., Biagni, C., Grandolfo, M. *et al.*, 2001. Seconda relazione della Commissione istituita dal Ministro della Difesa sull'incidenza di neoplasie maligne tra I militari impiegati in Bosnia e Kossovo, *Epidemiol Prev*, Vol 25, pp. 105–12.

McCredie, M., Misonneuve, P. and Boyle, P., 1994a. Antenatal risk factors for malignant brain tumors in New South Wales children, *Int J Cancer*, Vol 56, pp. 6–10.

McCredie, M., Misonneuve, P. and Boyle, P., 1994b. Perinatal and early post-natal risk factors for malignant brain tumours in New South Wales children, *Int J Cancer*, Vol 56, pp. 11–5.

McKinney, P.A. and Stiller, C.A., 1986. Re: Maternal smoking during pregnancy and the risk of childhood cancer, *Lancet*, Vol 2, 519.

McKinney, P.A., Cartwright, R.A., Saiu, J.M.T. *et al.*, 1987. The interregional epidemiological study of childhood cancer (IRESCC): A case-control study of aetiological factors in leukaemia and lymphoma, *Arch Dis Child*, Vol 62, pp. 279–87.

McNally, R.J., Birch, J.M., Taylor, G.M. *et al.*, 2000. Incidence of childhood precursor B-cell acute lymphoblastic leukaemia in north-west England, *Lancet*, Vol 356, pp. 485–6.

McWhirter, W.R., 1982. The relationship of incidence of childhood lymphoblastic leukemia to social class, *Br J Cancer*, Vol 46, pp. 640–5.

McWhirter, W.R., Dobson, C. and Ring, I., 1996. Childhood cancer incidence in Australia 1982–1991, *Int J Cancer*, Vol 65, pp. 34–8.

Michalek, A.M., Buck, G.M., Nasca, P.C. *et al.*, 1996. Gravid health status, medication use and risk of neuroblastoma, *Am J Epidemiol*, Vol 143, pp. 996–1001.

Monson, R.R. and McMahon, B., 1984. Prenatal x-ray exposure and cancer in children, in *Radiation carcinogenesis: Epidemiology and biological significance* (edited by J.D. Boice Jr. and J.F. Fraumeni Jr.), Raven Press, New York.

Mosso, M.L., Colombo, R., Giordano, L. *et al.*, 1992. Childhood Cancer Registry of the Province of Torino, Italy, *Cancer*, Vol 69, pp. 1300–6.

Narod, S.A., Stiller, C. and Lenoir, G.M., 1991. An estimate of the heritable fraction of childhood cancer, *Br J Cancer*, Vol 63, pp. 993–9.

Nikiforov, Y. and Gnepp, D.R., 1994. Pediatric thyroid cancer after the Chernobyl disaster, *Cancer*, Vol 74, pp. 748–66.

NRC, 1993. *Pesticides in the diets of infants and children*, National Research Council, National Academic Press, Washington DC.

O'Leary, L.M., Hicks, A.M., Peters, J.M. *et al.*, 1991. Parental occupational exposures and risk of childhood cancer: A review, *Am J Ind Med*, Vol 20, pp. 17–35.

Olshan, A.F., Breslow, N.E., Falletta, J.M. *et al.*, 1993. Risk factors for Wilms tumor. Report from the National Wilms Tumor Study, *Cancer*, Vol 72, pp. 938–44.

Parkin, D.M., Stiller, J.A., Draper, J.G. *et al.*, eds, 1988. *International incidence of childhood cancer*, International Agency for Research on Cancer, IARC Scientific Publications No 87, Lyon.

Parkin, D.M., Clayton, D., Black, R.J. *et al.*, 1996. Childhood leukaemia in Europe after Chernobyl: 5 year follow-up, *Br J Cancer*, Vol 73, pp. 1006–12.

Parkin, D.M., Kramarova, E., Draper, G.J. *et al.*, eds, 1998. *International incidence of childhood cancer*, Vol II, International Agency for Research on Cancer, IARC Scientific Publications, No 144, World Health Organization, International Association of Cancer Registries, Lyon.

Perera, R., 1997. Environment and cancer: Who are susceptible? *Science*, No 278, pp. 1068–73.

Peters, J.M., Preston-Martin, S. and Yu, M.C., 1981. Brain tumors in children and occupational exposure of parents, *Science*, No 213, pp. 235–6.

Pfahlberg, A., Kolml, K.F. and Gefeller, O., 2001. Timing of excessive ultraviolet radiation and melanoma: Epidemiology does not support the existence of a critical period of high susceptibility to solar ultraviolet radiation-induced melanoma, *Br J Dermatol*, Vol 144, pp. 471–5.

Plon, A.E. and Peterson, L.E., 1997. Childhood cancer, heredity and the environment, in *Principles and practice of pediatric oncology* (edited by P.A. Pizzo and D.G. Poplack), 3rd edition, Lippincott-Raven Publishers, Philadelphia and New York, pp. 11–36.

Powell, J.E., Parkes, S.E., Cameron, A.H. *et al.*, 1994. Is the risk of cancer increased in Asians living in the UK? *Arch Dis Child*, Vol 71, pp. 398–403.

Preston-Martin, S., Yu, M.C., Benton, B., *et al.*, 1982. N-Nitroso compounds and childhood brain tumors: A case-control study, *Cancer Res*, Vol 42, pp. 5240–5.

Preston-Martin, S., Pogoda, J.M., Mueller, B.A. *et al.*, 1998. Results from an international case-control study of childhood brain tumors: The role of prenatal vitamin supplementation, *Environmental Health Perspectives*, Vol 106 (suppl 3), pp. 887–92.

Raaschou-Nielsen, O., Hertel, O., Thomsen, B.L. *et al.*, 2001. Air pollution from traffic at the residence of children with cancer, *Am J Epidemiol*, Vol 153, pp. 433–43.

Rodrigues, L., Hills, M., McGale, P. *et al.*, 1991. Socio-economic factors in relation to childhood leukaemia and non-Hodgkin lymphomas; an analysis based on small area statistics for census tracts, in *The geographical epidemiology of childhood leukaemia and non-Hodgkin lymphoma in Great Britain, 1966–83* (edited by G.J. Draper), Studies on Medical and Population Subjects No 53, HMSO, London, pp. 47–56.

Ron, E. and Modan, B., 1980. Benign and malignant thyroid neoplasms after childhood irradiation for tinea capitis, *J Natl Cancer Inst*, Vol 65, pp. 7–11.

Ron, E., Lubin, J.H., Shore, R.E. *et al.*, 1995.Thyroid cancer after exposure to external radiation: A pooled analysis of seven studies, *Radiation Res*, Vol 141, pp. 259–77.

Savitz, D.A. and Chen, J., 1990. Parental occupation and childhood cancer: Review of epidemiologic studies, *Environmental Health Perspectives*, Vol 88, pp. 325–37.

Savitz, D.A. and Feingold, L., 1989. Association of childhood cancer with residential traffic density, *Scan J Work Environ Health*, Vol 15, pp. 360–3.

Severson, R.K., Buckley, J.D., Woods, W.G. *et al.*, 1993. Cigarette smoking and alcohol consumption by parents of children with acute myeloid leukemia: An analysis within morphological subgroups — A report from the Children's Cancer Group, *Cancer Epidemiol Biomarkers Prev,* Vol 2, pp. 433–439.

Sharp, L., Cotton, S. and Little, J., 1999. Descriptive epidemiology, in *Epidemiology of childhood cancer* (edited by J. Little), IARC Scientific Publications No 149, International Agency for Research on Cancer, World Health Organization, Lyon, pp. 10–67.

Sharpe, C.F., Franco, E.L., de Camargo, B. *et al.*, 1995. Parental exposure to pesticides and risk of Wilms' tumor in Brazil, *Am J Epidemiol*, Vol 141, pp. 210–7.

Shu, X.O., Gao, Y.T., Brinton, L.A. *et al.*, 1988. A population-based case-control study of childhood leukemia in Shanghai, *Cancer,* Vol 62, pp. 635–44.

Shu, X.O., Ross, J.A., Pendergrass, T.W. *et al.*, 1996. Parental alcohol consumption, cigarette smoking and risk of infant leukaemia: A Children's Cancer Group study, *J Natl Cancer Inst*, Vol 88, pp. 24–31.

Stevens, W., Thomas, D.C., Lyon, J.L., *et al.* 1990. Leukemia in Utah and radioactive fallout from the Nevada test site: A case-control study, *JAMA*, Vol 264, pp. 585–91.

Stewart, A., Webb, J. and Hewitt, D., 1958. A survey of childhood malignancies, *British Medical Journal*, Vol 1, pp. 1495–508.

Stiller, C.A., McKinney, P.A., Bunch, K.J. *et al.*, 1991. Childhood cancer and ethnic group in Britain: A United Kingdom Children's Cancer Study Group (UKCCSG) study, *Br J Cancer,* Vol 4, pp. 543–8.

UK Childhood Cancer Study Investigators, 2000. Childhood cancer and residential proximity to power lines, *Br J Cancer*, Vol 83, pp. 1573–80.

Vainio, H., Miller, A.B. and Bianchini, F., 2000. An international evaluation of the cancer-preventive potential of sunscreens, *Int J Cancer,* Vol 88, pp. 838–42.

Van Duijin, C.M., van Steensel-Moll, H.A., Coeberg, J.W. *et al.*, 1994. Risk factors for childhood acute non-lymphotic leukemia: An association with maternal alcohol consumption during pregnancy? *Cancer Epidemiol Biomarkers Prev,* Vol 3, pp. 457–60.

Viel, J.F. 1997. Leukaemia near La Hague nuclear plant. Author's reply, *British Medical Journal*, Vol 314, p. 1555.

Viel, J.F., Richardson, S., Danel, P. *et al.*, 1993. Childhood leukemia incidence in the vicinity of La Hague nuclear-waste reprocessing facility (France), *Cancer Causes Control* 1993, Vol 4, pp. 341–3.

Walter, S.D., King, W.D. and Marrett, L.D., 1999. Association of cutaneous malignant melanoma with intermittent exposure to ultraviolet radiation: Results of a case-control study in Ontario, Canada, *Int J Epidemiol*, Vol 28, pp. 418–27.

Weiss, L., Movahed, L.A., Warnke, R.A. *et al.*, 1989. Detection of Epstein-Barr viral genomes in Reed-Sternberg cells of Hodgkin's disease, *N Engl J Med,* Vol 320, pp. 502–6.

Whiteman, D.C., Whiteman, C.A. and Green, A.C., 2001. Childhood sun exposure as a risk factor for melanoma: A systematic review of epidemiologic studies, *Cancer Causes Control,* Vol 12, pp. 69–82.

WHO, 2001. Fact Sheet 263: *Electromagnetic Fields and Public Health: Extremely Low Frequency Fields and Cancer.* http://www.who.int/inf-fs/en/fact263.html.

Wilkins, J.R. and Sinks, T., 1990. Parental occupation and intracranial neoplasms of childhood: Results of a case-control interview study, *Am J Epidemiol,* Vol 132, pp. 275–92.

Yoshimoto, Y., Kato, H. and Schull, W.J., 1988. Risk of cancer among children exposed in utero to A-bomb radiations, 1950–1984, *Lancet*, Vol 2, pp. 665–9.

Zahm, S.H. and Devesa, S.S., 1995. Childhood cancer: Overview of incidence and environmental carcinogens, *Environmental Health Perspectives,* Vol 103 (suppl 6), pp. 177–84.

Zahm, S.H. and Ward, M.H., 1998. Pesticides and childhood cancer, *Environmental Health Perspectives,* Vol 106 (suppl 3), pp. 893–908.

Zaridze, D.G., Li, N., Men, T. *et al.*, 1994. Childhood cancer incidence in relation to distance from the former nuclear testing site in Semipalatinsk, Kazakhstan, *Int J Cancer,* Vol 59, pp. 471–5.

6. Birth defects

Tina Kold Jensen

Summary of existing knowledge
- Birth defects involving death of the infant or severe physical and mental problems recognised at birth occur in 2 % of all births and they account for more than 50 % of children's disabilities.
- Temporal changes occur in the birth prevalence of important birth defects (gastroschisis and neural tube defects). This evidence has helped pinpoint the role of folic acid deficiency as one risk factor for neural tube defects.
- Few environmental exposures have been documented so far as very likely causal factors for birth defects but many others are suspected possible or likely causes. The exposures that are very likely, likely or possible causes of birth defects include pharmaceuticals, maternal diseases and infections, nutritional deficiencies, lifestyle and physical factors, occupational exposures and drinking water contaminants.
- Many obstacles such as multicausality hamper research in this field, and many published studies suffer from limitations in design and bias problems.

Main challenges
- Greater attention to investigating the causes of birth defects, with a multidisciplinary approach involving epidemiologists, geneticists, environmental scientists and clinicians.

Action points
- Educate women of reproductive age and primary health-care professionals about the prudent use of vitamin supplements to prevent birth defects.
- Counsel pregnant women about the importance of a healthy diet and advise about the likely health risk to their unborn baby of intake of medicines, alcohol and caffeine, and smoking.
- Provide routine basic prenatal care to prevent some causes of birth defects by testing for genetic abnormalities and adequate control and treatment of maternal diseases.
- Apply prudent caution and avoid or decrease chemical, physical and infectious exposures by all reasonable means.

6.1. Introduction and definitions

Birth defects are normally defined as macroscopic abnormalities of structure attributable to faulty development or deformation. With a few exceptions, they are recognisable at birth. The wider term 'developmental disorders' is generally used when considering all effects observed on the conceptus from fertilisation to sexual maturity (Scialli, 1992; Wilson, 1973). Developmental disorders therefore include both structural birth defects and functional defects, such as blindness, deafness or neurobehavioral disabilities. In this chapter, only structural birth defects will be discussed and the term birth defects will be used; chromosomal abnormalities and syndromes will not be considered. The birth defects can be categorised by organ or tissue affected; the most important can be seen from Table 6.1.

If one restricts birth defects to those that cause the death of the infant, cause severe physical and mental disabilities, or necessitate medical treatment, an approximate rate of 2 % is found for abnormalities detected in the neonatal period (Källén, 1988). An equal number will be detected later, and if functional defects are added, the total rate is around 5 %. In 1997, birth defects accounted for an estimated 495 000 deaths worldwide (Rosano *et al.*, 2000). The great majority of these defects occur in the first year of life and thus tend to contribute substantially to the infant mortality rate. Birth defects have been the leading cause of infant mortality in the developed world for more than 20 years, with a rate of 173.4 per 100 000 live births in 1994 (Petrini *et al.*, 1997), where one in every five infant deaths was due to birth defects. In addition, birth defects account for more than 50 % of children's disabilities, and economically their cost in terms of public health expenses is considerable.

In industrialised countries, the adverse health impact of some of the environmental exposures involved has been reduced already. For example, vaccination against rubella and food fortification with folic acid has reduced the birth prevalence of certain birth defects. In many countries, certain exposures must be notified to the health authorities because of their very likely adverse effects on human reproduction, and such notification has led to targeted abatement efforts. In addition, other environmental exposures, such as those originating from landfill sites, have been studied because of public concern, but without consistent evidence of possible effects, the exposures continue. Thus, preventive efforts are limited by the lack of documentation.

The term 'very likely cause' for a birth defect will be used here when the exposure has

Table 6.1. **Categorisation of birth defects by organ/tissue affected**

Central nervous system	**Urinary tract**
Anencephaly	Agenesis renis
Encephalocely	
	Limbs
Spina bifida	Reduction deformities
Hydrocephaly	Dislocation of the hip
Microcephaly	Clubfoot
	Polydactyly
Alimentary system	Syndactyly
Cleft lip	
Cleft palate	
	Others
Cleft lip and palate	Cataract
Trachaeo-oesophageal fistula	Hypospadias
Infantile hypertrophic pyloric stenosis	Omphalocele
Anal atresia	Gastroschisis
Heart and vessels	
Heart, septum and valve abnormalities	
Vessel abnormalities	

been widely studied and the evidence for its action is substantial. The term 'likely cause' will be used when the literature is less extensive and not as convincing, while the term 'possible cause' will be used for exposures for which the evidence is insufficient. The literature in this field is extensive and only a short summary can be provided here. Despite the amount of studies undertaken, very few environmental exposures have been established as very likely causes for birth defects. This apparent paradox may be partially due to the fact that birth defects are rare outcomes, and large study populations are therefore required to identify the causes of these defects. In the majority of such studies, no single and very likely cause for the observed birth defect has been found. In addition, more and more birth defects are thought to be due to an interaction between genetic and multiple environmental exposures, which further complicates research in this field.

Environmental causation of structural birth defects will be discussed below. First, seasonal and time trends in birth prevalence are considered as possible clues. A discussion of environmental exposures follows. It distinguishes between environmental exposures that are very likely causes of birth defects and exposures that are likely or possible causes. A summary then follows. Finally, a conclusion is presented with suggestions for action.

6.2. Epidemiology

Prevalence at birth

The incidence of a specific birth defect is the number of affected cases divided by the total number of births including stillbirths. Most birth defects originate in early pregnancy and the fetuses are then miscarried; only a fraction survives long enough to be born. Furthermore, some pregnancies are terminated following prenatal diagnosis. Therefore, only a small proportion of true cases occur in the numerator. Likewise, denominator underestimation occurs because at least 10–15 % of all conceptions are miscarried or aborted. Therefore, the term 'birth prevalence' is often used to indicate the proportion of births including stillbirths affected by the defect. The birth prevalence is lower than the true incidence, which may be difficult to assess.

Temporal, seasonal and spatial variations

Studies examining temporal and spatial variations in birth defects are particularly vulnerable to bias, as they require consistent case definition and compatible reporting levels over time. Variation in prenatal screening policy and coverage between study areas will affect geographical and temporal trends. Some fetuses with birth defects are miscarried without the woman knowing that she was carrying an affected fetus, but with increased early screening these cases will be detected and reported and therefore result

in an increase in birth prevalence. In addition, records are often prepared at the time of birth and as some birth defects are diagnosed after hospital discharge (for example congenital heart disease) these are underreported, whereas others are over-reported (for example congenital dislocation of the hip, which often disappears spontaneously). These defects are therefore particularly vulnerable to regional differences in reporting, and interpretation of trends across and within registries must therefore be carefully evaluated. Changes in classification may also alter the birth prevalence. For example, the international classification of diseases (ICD) 10th edition classification is more defined and includes expanded subtypes and exclusion categories compared with ICD9, which has poor diagnostic specificity for conditions such as neural tube defects and gastroschisis (there is no specific diagnosis for gastroschisis, which is registered under omphalocele) two of the main categories of birth defects. Furthermore, changes in reporting practices in registers are important. For example, many congenital malformation registers changed the case definition of hypospadias during 1985–95 to exclude minor forms. Such changes will inevitably decrease the reported birth prevalence.

Large ethnic variation exists in prevalence of many birth defects, especially neural tube defects and cleft lip. The pattern for cleft lip varies largely between primary racial groups, which may point to a genetic explanation (Leck, 1994). In contrast, neural tube defects vary markedly within as well as between these groups, and both genetic and environmental factors are therefore very likely causes. Genetic factors are not discussed further in this chapter but are reviewed, e.g. by Leck (1994).

Variations in prevalence over time can be important markers of changing exposures to environmental factors. For example an epidemic of cataract led Gregg to discover maternal rubella infection was teratogenic in 1941 (Gregg, 1941), and another epidemic, this time of limb and ear defects, led to the discovery that thalidomide, a pharmaceutical used against morning sickness, was a powerful teratogen (Lenz, 1961). Time trends and seasonal changes in birth prevalence of birth defects can be assessed from various sources, especially the International Clearinghouse for Birth Defects Monitoring Systems (ICBDMS, 2000; ICBDMS, 2001), EUROCAT (EUROCAT Working Group, 1999) and the US National Birth Defects Prevention Network (NBDPN) (Erickson, 2000). The reports from these sources are based on birth defects registry data, and the completeness of the registries used may vary. Significant and real temporal trends likely to be caused by environmental exposures are recognised only for neural tube defects, hypospadias and gastroschisis and only in some parts of the world. An increasing trend of urinary tract anomalies has been observed in the last decade, but has been attributed to improvement in detection by ultrasound, which is usually not followed by termination of the pregnancy. The data on neural tube defects and gastroschisis will be outlined below to illustrate how descriptive data may provide leads regarding causation.

Neural tube defects

In the United Kingdom and several other countries, anencephaly and/or spina bifida fluctuate with high birth prevalence in spring conceptions and low birth prevalence in autumn conceptions (Leck, 1994). In contrast, most studies from the United States find no seasonal variation (Leck, 1994). A high birth prevalence of neural tube defects was recorded in England and the northern part of the United States during the 1920s and again in England in 1954–55. Since the early 1970s, a substantial decline has been observed in many countries. Data from the International Clearinghouse for Birth Defects Monitoring System from 1987–96 showed a significant fall in prevalence rates for all neural tube defects in Atlanta (United States), England and Wales, Hungary and Japan, and a significant rise in Norway and South America (Rosano *et al.*, 1999). EUROCAT data suggested that during the 1980s and early 1990s neural tube defects decreased in Ireland but not in mainland Europe where the birth prevalence was already lower (EUROCAT Working Group, 1991). The Northern England Congenital Abnormality Survey (Rankin *et al.*, 2000) reported an increase in the proportion of neural tube defect pregnancies terminated from 60 % during 1984–90 to 79 % during 1991–96. When all cases of neural tube defects were ascertained, a two-fold reduction in birth prevalence between 1984 and 1996 was observed.

In all Western countries, a decrease in the birth prevalence has partly resulted from an increase in ultrasound detection and termination of neural tube defect-affected

pregnancies. However, studies from the United Kingdom have shown that inclusion of neural tube defect terminations could only account for half of the decline in the birth prevalence (Morris and Wlad, 1999). Other changes must be considered as explanation for this decrease, especially improved maternal nutrition and changed fertility patterns. Neural tube defect rates have not declined further in the United Kingdom since the early 1990s. A number of underlying factors could be involved, including changing frequency of unplanned pregnancies, failure to reach high-risk groups with preconception folate supplementation, and differential access to health services. It is also possible that the birth prevalence of neural tube defects has reached such a low level now that further reduction though supplementation may not be possible.

Four hundred micrograms of folic acid before conception and during early pregnancy is thought to significantly reduce the birth prevalence of neural tube defects (Czeizel and Dudas, 1992; Daly *et al.*, 1995). As many as 70 % of all cases of spina bifida and anencephaly now appear to be preventable by folic acid (and vitamin) supplementation. Therefore, the US Food and Drug Administration authorised addition of folic acid to enriched grain products in March 1996, with compliance mandatory by January 1998. A national study of birth certificate data documented a 19 % reduction in neural tube defect birth prevalence following this folic acid fortification of the food supply (Honein *et al.*, 2001). However, the authors emphasise that factors other than fortification may have contributed to this decline. This caveat was emphasised by a study from the United Kingdom, which found that the birth prevalence of neural tube defects started to decrease before folic acid recommendation was introduced (Abramsky *et al.*, 1999). More recently, other types of malformations were found to be partly preventable by preconception folic acid supplementation, including facial clefts (Shaw *et al.*, 1995a; Tolarova and Harris, 1995), urinary malformations (Li *et al.*, 1995; Czeizel, 1996), and cardiac defects (Botto *et al.*, 1996; Shaw *et al.*, 1995b). Now, several governments in Europe and the United States recommend, with minor variations, the supplementation with 0.4 mg folic acid daily to all women, from one month before to two months after conception. Recommended food fortification would benefit both planned and unplanned pregnancies. The neural tube defect experience illustrates how epidemiological observations have provided documentation which has led to identification of a specific cause, and that this information has even spurred new prevention efforts against other birth defects.

Gastroschisis

Increasing birth prevalence of gastroschisis has been described in several countries. In the northern health region of England (Rankin *et al.*, 1999) the birth prevalence per 10 000 increased from 1.48 in 1986 to 4.72 in 1996. Comparable results were reported from Western Australia during 1980–93 (Nichols *et al.*, 1997). This alteration in birth prevalence was age-specific: a sharp rise in women aged 15–19 years was observed. A larger survey was performed at the International Centre for Birth Defects during 1974–98 and included 29 national and regional registries from Europe, the Americas, Asia, Australia and South Africa, with more than 51 million births monitored (Di Tanna *et al.*, 2001). There was a significant increase over the study period (from 0.29 in 1974 to 1.67 in 1998). Analysing the trend separately for each registry, the authors found nine significant increases in birth prevalence: Ireland, France, Finland, Japan, Mexico, Norway, New Zealand, South America and Australia. A significant decrease in birth prevalence was found in Italy. So far, these trends are largely unexplained.

6.3. Some methodological difficulties in identifying birth defects

Many studies have found that the risk of birth defects is associated with maternal factors such as age, parity or socio-economic status. These maternal characteristics may not represent the ultimate cause of the adverse outcomes, but may act as proxy indicators. Thus, women with higher socio-economic status probably have a different diet, smoke less etc. This chapter will focus on the role of specific environmental exposures in causing birth defects, not factors associated with characteristics of the infant (e.g. sex or birth weight), of the mother (e.g. age, parity, diseases in pregnancy) or her family (e.g. affected family members).

Most of the epidemiological studies on birth defects have been designed as either descriptive studies using registry data or case-control studies. Both of these designs have limitations including data quality and

problems with selection and recall. This limitation should be born in mind when interpreting reports on birth defect causation. Further, studies must consider when the relevant exposure may have occurred. Determining accurate exposure levels around specific windows of critical embryonic development that varies between the different defects remains a severe obstacle. This problem is aggravated in case-control studies where mothers of children with birth defects are questioned about possible exposures in early pregnancy and these are compared with mothers of normal babies. Mothers of babies with birth defects are more likely to remember exposures during pregnancy compared with mothers of non-affected babies (recall bias).

In hospital-based case-control studies, cases are selected from hospital records but the hospital catchment area may change over time, and the collection of specific maternal exposures may be limited. Also, changing staff and criteria for diagnosis and data entry and maintaining the motivation for the data collection among the staff may reduce validity. Hospital controls may not represent the source population from which the cases arise and this may introduce selection bias if associated with the exposure. In addition, controls with other birth defects are often used for comparison, but if the exposures studied are related to other birth defects as well, underestimation of the risk may occur. Some studies use surgical records to identify cases, but this can introduce bias if changes in criteria for surgery occur or if there are differences between surgeons' criteria for operation.

In population-based case-control studies cases are often selected from the general population from multiple sources such as ultrasound departments, cytogenetic laboratories and special baby care units. Controls are randomly selected from the general population. This is generally a less biased study design that may offer more valid results. However, often healthy controls are less willing to participate and a low, non-random participation rate may introduce bias.

6.4. Some very likely environmental causes

Some 20 exposures or maternal diseases have been documented as very likely causes of birth defects in humans (Leck, 1994). These include infections (cytomegalovirus, rubella, herpes simplex, toxoplasmosis, Venezuelan equine encephalitis and varicella zoster), maternal disease (phenylketonuria and insulin dependent diabetes mellitus), pharmaceuticals (androgens and progestins, anticonvulsants, coumarin derivates, lithium, retinoids, thalidomide, folic acid antagonists and diethylstilbestrol), other chemical agents (ethyl alcohol, methyl mercury and cocaine) and miscellaneous influences (hypoxia, iodine deficiency and ionising radiation) Some examples will be discussed in the following section.

Two general points should be noted. Firstly, prenatal exposure to some of the very likely teratogens listed may also cause other diseases (for example vaginal adenocarcinoma after exposure to diethylstilboestrol). Secondly, other likely teratogens are omitted, because the evidence for their teratogenity is less strong than for the exposures listed. Some of these omitted exposures are cigarette smoke (see *Lifestyle factors*, below), assisted conception (Lancaster, 1987), hyperthermia (Milunsky *et al.*, 1991), chorionic villus sampling (Dolk *et al.*, 1992) and solvents and pesticides (see *Occupational exposures*, below). Certain other exposures are omitted because they cause non-structural conditions, such as abnormal colouration of the teeth (tetracycline). On the other hand, lithium, hypoxia and cocaine are only likely causes of birth defects.

Infections

Maternal rubella infection was the first infectious disease to be identified as a very likely teratogen (Gregg, 1941). The infection was shown to cause mental retardation, deafness, cardiovascular malformations, congenital cataracts and glaucoma in offspring. There have been documented rubella epidemics, such as one the United States in 1964, resulting in birth defects in more than 20 000 children. The introduction of a rubella vaccine has greatly reduced the number of birth defects caused by this infection.

In the United States, 3 000 infants each year have been congenitally infected with toxoplasmosis (Krick and Remington, 1978). Affected infants may suffer encephalitis and/or hydrocephalus with calcification within the brain, chorioretinitis with scarring and loss of vision, hepatitis and lymphadenopathy. The probability of transfer of toxoplasmosis infection from

mother to fetus is not known, but studies among offspring of mothers with known infection give congenital infection rates of 20–40 % (Stray-Pedersen, 1980; Foulon *et al.*, 1984; Dunn *et al.*, 1999).

Seroconversion is less common for cytomegalovirus infection (CMV), which is very likely to cause severe neurological complications. Health care professionals are at special risk and prevention includes avoidance of contacts with secretions of patients and young children. Primary maternal infection by CMV results in fetal infection in up to 40 % of the cases and the risk of symptomatic congenital infection in the infant is 15–20 % (Daniel *et al.*, 1995). The intrauterine infection of the fetus may result in microcephaly (Ahlfors *et al.*, 1986; Yow *et al.*, 1988).

Several strategies are available for preventing these infections during pregnancy:

- Women of reproductive age who are at risk, such as physicians, nurses and teachers should have their antibody status tested, and the seronegative ones should be vaccinated against rubella and varicella.
- At the first antenatal examination, women should systematically be tested for rubella, and toxoplasmosis antibody status; the seronegative women should be vaccinated immediately after delivery to prevent infection of future infants.
- Pregnant women should avoid contact with cat excrement.

6.5. Environmental exposure likely to cause birth defects

Lifestyle factors

The fetal alcohol syndrome (Jones *et al.*, 1974) was first described as a very likely cause of mental deficiency or attention deficit disorder with or without facial characteristics among children of alcoholic mothers (Bagheri *et al.*, 1998; Aronson and Hagberg, 1998; Eckardt *et al.*, 1998). In studies with detailed exposure assessment, no consistent threshold dose for damage of the fetal brain has been found (McDonald *et al.*, 1992; Shaw and Lammer, 1999).

Pregnant women are widely exposed to tobacco smoke both actively and passively. Because of the almost ubiquitous exposure in society, even a small increased individual risk would result in a significant risk on a population scale. Maternal smoking during pregnancy has been shown to increase perinatal mortality and the risk of low birth weight, intrauterine growth retardation and sudden infant death (Kullander and Källén, 1971; Wu *et al.*, 1998; Cooke, 1998) (see Chapter 10). Smoking may also be the possible cause of some major birth defects, including orofacial clefts (Ericson *et al.*, 1979; Källén, 1997a), craniosynostosis (Alderman *et al.*, 1994), and limb reduction defects (Czeizel *et al.*, 1994; Källén, 1997b). Smoking and cocaine use are also possible causes of gastroschisis (Torfs *et al.*, 1996), but no studies have linked maternal smoking to neural tube defects in offspring (Källén, 1998).

An interesting new area of research is the investigation of the interaction between smoking and genetic polymorphisms. Recent studies have found interactions with transforming growth factor alpha (TGFα) gene variants, smoking and orofacial clefts (Hwang *et al.*, 1995; Shaw *et al.*, 1996) and smoking, MSX1 variants and risk of limb reduction defects (Hwang *et al.*, 1998).

Caffeine has long been a very likely cause of birth defects when administered in high doses in laboratory animal studies, but this effect has not been confirmed in humans and caffeine can currently only be considered as a possible teratogen. A review by Golding (1995) concludes: 'currently there is little to implicate caffeine consumption with congenital malformation or preterm delivery but there are many associations with subfertility, miscarriage and intrauterine growth retardation. Definitive prospective studies are required.'

Studies of lifestyle factors and birth defects must be cautiously interpreted, as they are often case-control studies where recall bias is likely. Furthermore, alcohol, caffeine and smoking are known to increase the risk of miscarriages; if some of the early-miscarried fetuses are affected this way and not registered, the effect of the lifestyle factor on birth defects may be underestimated. In addition, information on usage of legal and illegal stimulants is not necessarily reliable, and the use of different substances shows a high degree of correlation (e.g. smoking women drink more alcohol), which makes it difficult to separate out the individual effects of the exposures. Nevertheless, since the use of these stimulants is widespread also among

pregnant women, more prospective research into the possible adverse effects is needed. However, the evidence is sufficiently convincing that pregnant women should be informed of the possible health risk to their unborn baby and should be offered help to reduce or eliminate intake/use during pregnancy.

Physical factors

Reproductive risk from exposure to non-ionising electromagnetic fields (EMFs), mainly related to video display terminals and power distribution and appliances, has been investigated. A recent review (Shaw, 2001) summarised the epidemiological evidence of parental exposures to EMFs as a possible cause of adverse reproductive outcomes: 'evidence is lacking for a strong association between a woman's use of a video display terminal (VDT) and adverse reproductive outcomes other than fetal loss, primarily a result of too few available data and the paucity of data on other parental EMF exposures and subsequent adverse outcomes of pregnancy limits drawing a valid scientific conclusion'.

Only a few studies have looked at noise during pregnancy as a possible cause of birth defects and inconsistent findings have been reported (Zhang *et al.*, 1992).

In summary, the literature on physical factors, such as electromagnetic fields and noise, is too sparse to draw valid conclusions, and further research, especially prospectively designed studies with good exposure assessment (see *Occupational exposures*, below) are needed.

Drinking water contaminants and releases from landfills

Several studies of environmental chemicals as possible causal agents have focused on exposures that involve large sections of the population, such as drinking water contaminants and emissions from toxic waste disposal. Although such exposures may not necessarily represent serious hazards, they involve substantial numbers of people potentially exposed and may represent a significant public health risk even where the individual risk may be low.

Chlorination has been the major disinfectant process for domestic drinking water for many years. Chlorination disinfection by-products (DBPs) have been proposed as possible causes of adverse pregnancy outcomes. Relatively few studies have been undertaken (reviewed by Nieuwenhuijsen *et al.* (2000)). The existing evidence suggests that DBPs constitute a likely cause of low birth weight (Kanitz *et al.*, 1996; Källén and Robert, 2000) and a possible cause of spontaneous abortion, stillbirth and birth defects, especially neural tube defects (Klotz and Pyrch, 1999). The main limitations of these studies are the relatively crude methodology, in particular concerning exposure assessment. No exposure models have been developed and the specific teratogenic component is unknown. Therefore, the review (Nieuwenhuijsen *et al.* 2000) suggests: 'Large well designed epidemiological studies focusing on well defined end points taking into account relevant confounders and with particular emphasis on exposure assessment are needed'.

Epidemiological studies suggest that living near hazardous-waste landfill sites is a possible cause of delivering children with low birth weight (Goldberg *et al.*, 1995) and with several categories of birth defects, including neural tube defects, heart, skeleton and abdominal wall defects (Croen *et al.*, 1997; Marshall *et al.*, 1997; Geschwind *et al.*, 1992; Vianna and Polan, 1984) (reviewed in Vrijheid, 2000). This association was confirmed in the EUROHAZCON study (Dolk *et al.*, 1998) of 21 hazardous waste sites from several European countries where excess prevalence existed within 3 kilometres for all birth defects combined, and for cardiac defects, neural tube defects and gastroschisis. This finding led to public concern in the United Kingdom and a study of the population living near the Nant-y-Gwyddon landfill in Wales also reported increased birth prevalence of gastroschisis, but was based on only four cases (Fielder *et al.*, 2000). The increase appeared to have been present even before the opening of the landfill. Therefore, an ecological study of populations living within 2 kilometres of 9 500 landfill sites in the United Kingdom was undertaken (Elliott *et al.*, 2001). Small excess risks of birth defects were found, but again the risks were present before the opening of the sites. This experience suggests that confounding or other exposures than those arising from landfills must be considered as explanation for the findings. Often landfills are opened in industrial areas and exposure to other chemicals emerging from these may already have been present at the time of opening. In addition, populations living close to landfills may be more deprived

and have a different diet and lifestyle, i.e. exposures that may be difficult to fully adjust for in epidemiological studies.

The problems with many of the studies examining the effects of landfills and DBPs are related to their so-called ecological designs with no individual exposure information (ecological fallacy). Thus, exposure status is often defined according to the residential postal code at delivery, not by means of some specific factor assessed on an individual basis. However, some women may spend most of their time away from their home or change their address between the period at risk and the delivery and may thus be misclassified. Furthermore, there is considerable uncertainty as to the extent of any possible exposure to chemicals found in landfills (potentially toxic chemicals in landfill include volatile organic compounds, pesticides, solvents and heavy metals). Human exposure could result from contact with contaminated air or soil, leaching or runoff, or dispersion by animals or birds, but none of the exposures in the reported low doses are very likely causes of the observed birth defects (Elliott *et al.*, 2001).

As no causal mechanism currently explains the findings that women living near landfill sites have a higher risk of adverse pregnancy outcomes, further understanding of the potential toxicity from landfill emissions, and possible routes, pathways and extent of any human exposure, is needed in order to help interpret the epidemiological findings. Likewise, epidemiological studies with individual exposure information and information about relevant potential confounders are needed.

Occupational exposures

Many potentially toxic chemicals are used in workplaces, and occupational exposure of pregnant women is likely, perhaps especially before a female worker has recognised her pregnancy. Studies of occupationally related birth defects may provide causative clues to possible environmental risk factors, although they are often limited by the lack of information about specific chemical exposure levels.

It has long been known that exposure to high concentrations of anaesthetic gases among nurses in operating theatres was a very likely cause of adverse pregnancy outcomes. The concentration of these gases has been considerably reduced by the introduction of improved anaesthetic procedures, so demonstrating the importance of identifying work-related causal factors.

Despite the increasing body of literature about specific occupational exposures and adverse pregnancy outcomes, so far only exposures to organic solvents, antineoplastic pharmaceuticals and pesticides have been found to be likely or possible causes of birth defects. Thus, organic solvents have been reported as a likely cause of growth retardation and facial clefts, neural tube defects, gastroschisis, cardiac defects and multiple anomalies (Torfs *et al.*, 1996; Khattak *et al.*, 1999; Laumon *et al.*, 1996; Cordier *et al.*, 1997; Garcia and Fletcher, 1998; Agnesi *et al.*, 1997; Bianchi *et al.*, 1997; Tikkanen and Heinonen, 1992), but some studies have been unable to confirm these findings. A review of the literature concludes that maternal exposure to organic solvents (especially toluene) is a likely cause of spontaneous abortions but only a possible cause of birth defects (Lindbohm, 1995). Studies have suggested work in agricultural occupations or exposure to specific pesticides as possible causes of birth defects among offspring (Golden *et al.*, 1998; Garcia, 1998).

Many studies have compared the prevalence of birth defects among children where either parent is employed in various occupations and found higher prevalence for example among women employed in the leather industry or as hairdressers and men working as painters, printers or welders (Lorente *et al.*, 2000; Blatter *et al.*, 1996). In their large study of more than 50 000 births in Montreal, male work in food and beverage processing and female work in agriculture, and as telephonists and receptionists was associated with increased prevalence of birth defects (McDonald *et al.*, 1989; McDonald *et al.*, 1988).

These studies lack adequate exposure information. For example, not all parents working in agricultural occupations are necessarily exposed to pesticides, so it is hard to link the observations to specific causal exposure. In addition, when up to 40 different work titles are compared, some are likely to have increased prevalence of birth defects just by chance, and as this is a rare outcome, the number of cases in each occupational group is likely to be small. Some occupational studies are case-control studies where parents of affected children are questioned about potential exposures during

pregnancy and this is compared with information from healthy control parents. Recall bias is likely to occur as parents of affected children search for a cause in their occupation. Some studies have attempted to avoid this bias by having trained occupational hygienists to assess exposure from parental questionnaire information. This task is difficult, as it does not take into account ventilation, use of protective equipment, etc. Therefore, epidemiological studies with good exposure assessment, if possible by measurement of chemicals in air or by the use of biomarkers, are badly needed. As Ahlborg and Heminski conclude (Ahlborg and Heminski, 1995): 'Among the potentially harmful substances are: anaesthetic gases, antineoplastic agents and sterilants. The epidemiological evidence of adverse reproductive outcomes from these compounds is not unequivocal but because of their general toxic potential, exposures should be kept at a minimum among women in reproductive age.'

6.6. Gene environment interaction

The possibility that inherited genetic factors, in combination with environmental exposures, may confer an increased risk of a variety of birth defects is of growing interest. Studies of methylene tetrahydrofolate reductase (MTHFR), TGFα and diet and smoking are recent examples (Van Rooij *et al.*, 2001).

A number of variants or polymorphisms of maternal and fetal genes are known to be involved in the metabolism of relevant toxicants. The evaluation of polymorphisms of phase I enzymes (P450s), phase II enzymes (GSTs, NATs), DNA repair genes, and other genes that metabolise or interact with environmental exposures provide interesting new research avenues, similar to their current application in cancer studies. The rapid identification of genes critical for normal development also generates opportunities to explore the potential role of environmental exposures in altering the structure and function of these major genes. Future molecular epidemiological studies of birth defects should incorporate these genetic factors to determine the importance of gene-environment interaction. In some countries, the availability of routinely collected newborn blood spots provides an efficient source of fetal DNA. Close collaboration with basic scientists is essential in this research. However, even though a majority of cases might be found to be due to genetic factors in conjunction with some environmental exposures, such findings should not deter from identifying and, ultimately, reducing or eliminating adverse environmental exposures as the most efficient course of prevention.

6.7. Conclusions and recommendations for actions

This chapter has reviewed the current state-of-the-art and has emphasised the unfortunate lack of documentation concerning birth defects. Such incomplete information makes targeted primary prevention difficult. Few environmental exposures have been documented as very likely causal factors so far but others have been suggested as likely or possible causes. Exposures that are very likely, likely or possible causes of birth defects include pharmaceuticals, maternal diseases and infections, nutritional deficiencies, lifestyle and physical factors, occupational exposures and drinking water contaminants. Preventive medicine can incorporate recent findings in educating women of reproductive age and primary health care professionals about the use of prenatal vitamins to prevent birth defects and the counselling of pregnant women about the importance of healthy diet. In addition, information about the likely health risk to their unborn baby caused by intake of medicine, alcohol and caffeine and smoking, and help to eliminate intake/use in pregnancy should be provided. Routine basic prenatal care may also prevent some causes of birth defects by means of testing for genetic abnormalities and adequate control and treatment of maternal diseases. Nonetheless, given that nearly 70 % of all birth defects have no known cause, much greater attention needs to be paid in investigating the causes of birth defects, with a multidisciplinary approach, involving epidemiologists, geneticists, environmental scientists and clinicians. Even if there is no established evidence of the exact role of the environment in birth defects, it would be wise to exert caution and to eliminate or decrease all chemical, physical and infectious exposures by all reasonable means given the lifetime costs of birth defects caused by pharmaceuticals and other environmental risk factors (EEA, 2000). The early application of 'precautionary prevention' to potentially hazardous exposures can often lead to less harm and more welfare.

Summary

Birth defects involving death of the infant or severe physical and mental disabilities recognised at birth occur in 2 % of all births, and an equal number will be recognisable later on. Birth defects constitute the leading cause of infant mortality in the developed world, and they account for more than 50 % of children's disabilities.

Descriptive studies have amply documented that temporal changes occur in the birth prevalence of important births defects, and that these changes may vary geographically. While this evidence has helped pinpoint the role of folic acid deficiency as a very likely risk factor for neural tube defects, other data simply document that unknown environmental factors play a role.

Additional leads have been obtained from studies of residents exposed to drinking water contaminants or releases from toxic waste dumps, and from studies of occupational groups. Many obstacles such as multicausality and the lack of exposure data hamper research in this field, thus leading to incomplete documentation. While few environmental exposures have been documented so far as very likely causal factors, many others are suspected possible or likely causes. Exposures that are very likely, likely or possible causes of birth defects include pharmaceuticals, maternal diseases and infections, nutritional deficiencies, lifestyle and physical factors, occupational exposures and drinking water contaminants.

References

Abramsky, L., Botting, B., Chapple, J. *et al.*, 1999. Has advice on periconceptional folate supplementation reduced neural tube defects? *Lancet*, Vol 354, pp. 998–9 Agnesi, R., Valentini, F. and Mastrangelo, G., 1997. Risk of spontaneous abortion and maternal exposure to organic solvents in the shoe industry, *Int Arch Occup Environ HealthOK* , Vol 69, pp. 311–6.

Ahlborg, G. and Heminski, K., 1995. Reproductive effects of chemical exposures in health professions, *J Occup Environ Med*, Vol 37, pp. 957–61.

Ahlfors, K., Ivarsson, S.A. and Bjerre, I., 1986. Microcephaly and congenital cytomegalovirus infection: A combined prospective and retrospective study of a Swedish infant population, *Pediatrics*, Vol 78, pp. 1058–63.

Alderman, B.W., Bradley, C.M., Greene, C. *et al.*, 1994. Increased risk of craniosynostosis with maternal cigarette smoking during pregnancy, *Teratology*, Vol 50, pp. 13–8.

Aronson, M. and Hagberg, B., 1998. Neuropsychological disorders in children exposed to alcohol during pregnancy: A follow-up study of 24 children to alcoholic mothers in Goeteborg, Sweden, *Alcoholism, clinical and experimental research*, Vol 22, pp. 321–4.

Bagheri, M.M., Burd, L., Martsolf, J.T. *et al.*, 1998. Fetal alcohol syndrome: Maternal and neonatal characteristics, *J Perinat Med*, Vol 26, pp. 263–9.

Bianchi, F., Cianciulli, D., Pierini, A. *et al.*, 1997. Congenital malformations and maternal occupation: A registry based case-control study, *Occup Environ Med*, Vol 54, No 4, pp. 223–8.

Blatter, B.M., Roeleveld, N., Zielhuis, G.A. *et al.*, 1996. Spina bifida and parental occupation, *Epidemiology*, Vol 7, pp. 188–93.

Botto, L.D., Khoury, M.J., Mulinare, J. *et al.*, 1996. Periconceptional multivitamin use and the occurrence of conotruncal heart defects, *Pediatrics*, Vol 98, No 5, pp. 911–7.

Cooke, R.W., 1998. Smoking, intrauterine growth retardation and sudden infant death syndrome, *Int J Epidemiol*, Vol 27, pp. 238–41.

Cordier, S., Bergeret, A., Goujard, J. *et al.*, 1997. Congenital malformations and maternal occupational exposure to glycol ethers, *Epidemiology*, Vol 8, pp. 355–63.

Croen, L.A., Shaw, G.M., Sanbonmatsu, L. *et al.*, 1997. Maternal residential proximity to hazardous waste sites and risk for selected congenital malformations, *Epidemiology*, Vol 8, pp. 347–54.

Czeizel, A.E., 1996. Reduction of urinary tract and cardiovascular defects by periconceptional vitamin supplementation, *Am J Hum Genet*, Vol 62, pp. 179–83.

Czeizel, A.E. and Dudas, I., 1992. Prevention of first occurrence of neural-tube defects by periconceptional vitamin supplementation, *N Engl J Med*, Vol 327, pp. 1832–5.

Czeizel, A., Kodaj, I. and Lenz, W., 1994. Smoking during pregnancy and congenital limb deficiency, *British Medical Journal*, Vol 308, pp. 1473–6.

Daly, L.E., Kirke, P.N., Molloy, A.M. *et al.*, 1995. Folate levels and neural tube defects. Implication for prevention, *JAMA*, Vol 274, pp. 1698–702.

Daniel, Y., Gull, I., Peyser, M.R. *et al.*, 1995. Congenital cytomegalovirus infection, *Eur J Obstet Gynecol Reprod Biol*, Vol 63, pp. 7–16.

Di Tanna, G.L., Rosano, A. and Mastroiacovo, P., 2001. Trend in gastroschisis in 29 registries of congenital anomalies worldwide (Abstract), *Frontiers in Fetal Health*, Vol 3, p. 220.

Dolk, H., Bertrand, F. and Lechat, M.F., 1992. Chorionic villus sampling and limb abnormalities, *Lancet*, Vol 339, pp. 876–7.

Dolk, H., Vrijheid, M., Armstrong, B. *et al.*, 1998. Risk of congenital anomalies near hazardous-waste landfill sites in Europe: The EUROHAZCON study, *Lancet*, Vol 352, pp. 423–7.

Dunn, D., Wallon, M., Peyron, F. *et al.*, 1999. Mother-to-child transmission of toxoplasmosis: Risk estimates for clinical counselling, *Lancet*, Vol 353, pp. 1829–33.

Eckardt, M.J., File, S.E., Gessa, G.L. *et al.*, 1998. Effects of moderate alcohol consumption on the central nervous system, *Alcoholism, clinical and experimental research*, Vol 22, pp. 998–1040.

EEA, 2000. *Late lessons from early warnings: The precautionary principle 1896–2000*, European Environment Agency, Copenhagen.

Elliott, P., Briggs, D., Morris, S. *et al.*, 2001. Risk of adverse birth outcomes in populations living near landfill sites, *British Medical Journal*, Vol 323, pp. 363–8.

Erickson, J.D., 2000. Introduction: Birth defect surveillance in the United States, *Teratology*, Vol 61, pp. 1–3.

Ericson, A., Källén, B. and Westerholm, P., 1979. Cigarette smoking as an etiologic factor in cleft lip and palate, *Am J Obstet Gynecol*, Vol 135, pp. 348–51.

EUROCAT Working Group, 1991. *EUROCAT Report 4: Surveillance of congenital anomalies 1980–1988*, EUROCAT Central Registry, Brussels.

EUROCAT Working Group, 1999. *EUROCAT Report 7A: Prevalence of congenital anomalies in Europe 1995–1996* (update to Report 7), EUROCAT Central Registry, Brussels.

Fielder, H.M., Poon-King, C.M., Palmer, S.R. *et al.*, 2000. Assessment of impact on health of residents living near the Nant-y-Gwyddon landfill site: Retrospective analysis, *British Medical Journal*, Vol 320, pp. 19–22.

Foulon, W., Naessens, A., Volckaert, M. *et al.*, 1984. Congenital toxoplasmosis: A prospective survey in Brussels, *Br J Obstet Gynaecol*, Vol 91, pp. 419–23.

Garcia, A.M., 1998. Occupational exposure to pesticides and congenital malformations: A review of mechanisms, methods, and results, *Am J Ind Med*, Vol 33, pp. 232–40.

Garcia, A.M. and Fletcher, T., 1998. Maternal occupation in the leather industry and selected congenital malformations, *Occup Environ Med*, Vol 55, pp. 284–6.

Geschwind, S.A., Stolwijk, J.A.J., Bracken, M. *et al.*, 1992. Risk of congenital malformations associated with proximity to hazardous waste sites, *Am J Epidemiol*, Vol 135, pp. 1197–207.

Goldberg, M.S., Goulet, L., Riberdy, H. *et al.*, 1995. Low birth weight and preterm births among infants born to women living near a municipal solid waste landfill site in Montreal, Québec, *Environ Res*, 1995, Vol 69, pp. 37–50.

Golden, R.J., Noller, K.L., Titus-Ernstoff, L. *et al.*, 1998. Environmental endocrine modulators and human health: An assessment of the biological evidence, *Crit Rev Toxicol*, Vol 28, pp. 109–227.

Golding, J., 1995. Reproduction and caffeine consumption — A literature review, *Early Hum Dev*, Vol 43, pp. 1–14.

Gregg, N.M., 1941. Congenital cataract following German measles in the mother, *Trans Ophthalmol Soc Aust*, Vol 3, pp. 35–46.

Hall, S.M., 1992. Congenital toxoplasmosis, *British Medical Journal*, Vol 305, pp. 291–7.

Honein, M.A., Paulozzi, L.J., Mathews, T.J. *et al.*, 2001. Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects, *JAMA*, Vol 285, pp. 2981–6.

Hwang, S.J., Beaty, T.H., Panny, S.R. *et al.*, 1995. Association study of transforming growth factor alpha (TGF alpha) TaqI polymorphism and oral clefts: Indication of gene-environment interaction in a population-based sample of infants with birth defects, *Am J Epidemiol*, Vol 141, pp. 629–36.

Hwang, S.J., Beaty, T.H., Mcintosh, I. *et al.*, 1998. Association between homeobox-containing gene MSX1 and the occurrence of limb deficiency, *Am J Med Genet*, Vol 75, pp. 419–23.

ICBDMS, 2000. *Annual report*, International Clearinghouse for Birth Defects Monitoring Systems, Rome.

ICBDMS, 2001. *World atlas*, 2nd edition, International Clearinghouse for Birth Defects Monitoring Systems, Rome.

Jacobson, S.L., Jones, K., Johnson, K. *et al.*, 1992. Prospective multi-centre study of pregnancy outcome after lithium exposure during first trimester, *Lancet*, Vol 339, pp. 530–7.

Janz, D., 1982. On major malformations and minor anomalies in the offspring of parents with epilepsia: Review of the literature, in *Epilepsia, pregnancy, and the child* (edited by D. Janz, M. Dam, A. Richens *et al.*), Raven Press, New York.

Jones, K.L., Smith, D.W., Streissguth, A.P. *et al.*, 1974. Outcome in offspring of chronic alcoholic women, *Lancet*, Vol 1, pp. 1076–8.

Källén, B. 1988. *Epidemiology of human reproduction*, CRC Press, Boca Raton, FL.

Källén, K., 1997a. Maternal smoking and orofacial clefts, *Cleft Palate-Craniofacial Journal*, Vol 34, pp. 11–6.

Källén, K., 1997b. Maternal smoking during pregnancy and limb reduction malformations in Sweden, *Am J Pub Health*, Vol 87, pp. 29–32.

Källén, K., 1998. Maternal smoking, body mass index and neural tube defects, *Am J Epidemiol*, Vol 147, pp. 1103–11.

Källén, B. and Robert, E., 2000. Drinking water chlorination and delivery outcome. A registry based study in Sweden, *Reprod Toxicol*, Vol 14, pp. 303–9.

Kanitz, S., Franco, Y., Patrone, V. *et al.*, 1996. Association between drinking water disinfection and somatic parameters at birth, *Environ Health Perspect*, Vol 104, pp. 516–20.

Khattak, S., Moghtader, K., Mcmartin, K. *et al.*, 1999. Pregnancy outcome following gestational exposure to organic solvents: A prospective controlled study, *JAMA*, Vol 281, pp. 1106–9.

Klotz, J.B. and Pyrch, L.A., 1999. Neural tube defects and drinking water disinfection by-products, *Epidemiology*, Vol 10, pp. 383–90.

Krick, J. and Remington, J., 1978. Toxoplasmosis in the adult: An overview, *N Engl J Med*, Vol 298, pp. 550–3.

Kullander, S. and Källén, B., 1971. A prospective study of smoking and pregnancy, *Acta Obstet Gynecol Scand*, Vol 50, pp. 83–94.

Lammer, E.J., Hayes, A.M., Schunior, A. *et al.*, 1998. Unusually high risk for the adverse outcomes of pregnancy following fetal isotretinoin exposure, *Am J Hum Genet*, Vol 43, p. A58.

Lancaster, P., 1987. Congenital malformations after in-vitro-fertilisation, *Lancet*, 2 (8572), pp. 1392–3.

Laumon, B., Martin, J.L., Collet, P. *et al.*, 1996. Exposure to organic solvents during pregnancy and oral clefts: A case-control study, *Reprod Toxicol*, Vol 10, pp. 15–9.

Leck, I., 1983. Fetal malformations, in *Obstetrical epidemiology* (edited by S.L. Barron and A.M. Thomson), Academic Press, London.

Leck, I., 1994. Structural birth defects, in *The epidemiology of childhood disorders* (edited by I.B. Pless), Oxford University Press, Oxford.

Lenz, W., 1961. Kindliche Missbildungen nach medicament-einnahme während der gravidität? *Dtsch Med Wochenschr*, Vol 86, p. 2555.

Li, D.K., Daling, J.R., Mueller, B.A. *et al.*, 1995. Periconceptional multivitamin use in relation to the risk of congenital urinary tract anomalies, *Epidemiology*, Vol 6, pp. 212–8.

Lindbohm, M.L., 1995. Effects of parental exposure to solvents on pregnancy outcome, *J Occup Environ Med*, Vol 37, pp. 908–14.

Lipson, A., Beuhler, B., Bartley, J. *et al.*, 1984. Maternal hyperphenylalaninemia fetal effects, *J Pediatr*, Vol 104, pp. 216–20.

Lorente, C., Cordier, S., Bergeret, A. *et al.*, 2000. Maternal occupational risk factors for oral clefts, Occupational Exposure and Congenital Malformation Working Group, *Scand J Work Environ Health*, Vol 26, pp. 137–45.

Lutiger, B., Graham, K., Einarson, T.R. *et al.*, 1991. Relationship between gestational cocaine use and pregnancy outcome: A meta-analysis, *Teratology*, Vol 44, p.405–14.

Marshall, E.G., Gensburg, L.J., Deres, D.A. *et al.*, 1997. Maternal residential exposure to hazardous wastes and risk of central nervous system and musculoskeletal birth defects, *Arch Environ Health*, Vol 52, pp. 416–25.

McDonald, A.D., McDonald, J.C., Armstrong, B. *et al.*, 1988. Congenital defects and work in pregnancy, *Br J Ind Med*, Vol 45, pp. 581–8.

McDonald, A.D., McDonald, J.C., Armstrong, B. *et al.*, 1989. Fathers' occupation and pregnancy outcome, *Br J Ind Med*, Vol 46, pp. 329–33.

McDonald, A.D., Armstrong, B.G. and Sloan, M., 1992. Cigarette, alcohol and coffee consumption and congenital defects, *Am J Public Health*, Vol 82, pp. 91–3.

Miao, C.Y., Li, W.X., Geng, D. *et al.*, 1988. Effect of high altitude on prevalence of congenital heart disease, *Chinese Med J*, Vol 101, pp. 415–18.

Miller, E., Cradock-Watson, J.E. and Pollock, T.M., 1982. Consequences of confirmed maternal rubella at successive stages of pregnancy, *Lancet*, Vol 2, pp. 781–84.

Milunsky, A., Ulcickas, M.E., Willett, W. *et al.*, 1991. Hyperthermia and neural tube defects, *Pediatr Rev*, Vol 29, p. 71A.

Morris, J.K. and Wlad, N.J., 1999. Quantifying the decline in the birth prevalence of neural tube defects in England and Wales, *J Med Screen*, Vol 6, pp. 182–5.

Nakane, Y., Okuma, T., Takahshi, R. *et al.*, 1980. Multi-institutional study on the teratogenicity and fetal toxicity of antiepileptic drugs: A report of a collaborative study group in Japan, *Epilepsia*, Vol 21, pp. 663–80.

Nichols, C.R., Dickinson, J.E. and Pemberton, P.J., 1997. Rising incidence of gastroschisis in teenage pregnancies, *J Matern Fetal Med*, Vol 6, pp. 225–9.

Nieuwenhuijsen, M.J., Toledano, M.B., Eaton, N.E. *et al.*, 2000. Chlorination disinfection byproducts in water and their association with adverse reproductive outcomes: A review, *Occup Environ Med*, Vol 57, pp. 73–85.

Petrini, J., Damus, K. and Johnston, R.B. Jr., 1997. An overview of infant mortality and birth defects in the United States, *Teratology*, Vol 56, pp. 8–10.

Pharoah, P.O.D., Ellis, S.M., Elkins, R.P. *et al.*, 1976. Maternal thyroid function, iodine deficiency and fetal development, *Clin Endocrinol*, Vol 5, p. 159–66.

Preblud, S.R., Cochi, S.L. and Orenstein, W.A., 1986. Varicella-zoster infections in pregnancy, *N Engl J Med*, Vol 315, pp. 1415–7.

Rankin, J., Dillon, E. and Wright, C., 1999. Congenital anterior abdominal wall defects in the north of England, 1986–1996: Occurrence and outcome, *Prenat Diagn*, Vol 19, pp. 662–8.

Rankin, J., Glinianaia, S., Brown, R. *et al.*, 2000. The changing prevalence of neural tube defects: A population-based study in the north of England, 1984–96, Northern Congenital Abnormality Survey Steering Group, *Paediatr Perinat Epidemiol*, Vol 14, pp. 104–10.

Rosa, F., 1991. Detecting human retenoid embryopathy, *Teratology*, Vol 43, p. 419.

Rosano, A., Botto, L.D., Botting, B. *et al.*, 2000. Infant mortality and congenital anomalies from 1950 to 1994: An international perspective, *J Epidemiol Community Health*, Vol 54, pp. 660–6.

Rosano, A., Smithells, D., Cacciani, L. *et al.*, 1999. Time trends in neural tube defects prevalence in relation to preventive strategies: An international study, *J Epidemiol Comm Health*, Vol 53, pp. 630–5.

Scialli, A.R., 1992. *A clinical guide to reproductive and developmental toxicology*, CRC Press, Boca Raton, FL.

Shaw, G.M., 2001. Adverse human reproductive outcomes and electromagnetic fields: A brief summary of the epidemiologic literature, *Bioelectromagnetics*, (suppl 5), pp. S5–18.

Shaw, G.M. and Lammer, E.J., 1999. Maternal periconceptional alcohol consumption and risk for orofacial clefts, *J Pediatr*, Vol 134, pp. 298–303.

Shaw, G.M., Lammer, E.J., Wasserman, C.R. *et al.*, 1995a. Risks of orofacial clefts in children born to women using multivitamins containing folic acid periconceptionally, *Lancet*, Vol 345, pp. 393–6.

Shaw, G.M., O'Malley, C.D., Wasserman, C.R. *et al.*, 1995b. Maternal periconceptional use of multivitamins and reduced risk for conotruncal heart defects and limb deficiencies among offspring, *Am J Med Genet*, Vol 59, pp. 536–45.

Shaw, G.M., Wasserman, C.R., Lammer, E.J. *et al.*, 1996. Orofacial clefts, parental cigarette smoking, and transforming growth factor-alpha gene variants, *Am J Hum Genet*, Vol 58, pp. 551–61.

Stagno, S., 1990. Cytomegalovirus, in *Infectious diseases of the fetus and newborn infant* (edited by J.S. Remington and J.O. Klein), W.B. Saunders, Philadelphia, p. 241.

Stray-Pedersen, B., 1980. A prospective study of acquired toxoplasmosis among 8048 pregnant women in the Oslo area, *Am J Obstet Gynecol*, Vol 136, pp. 399–406.

Tikkanen, J. and Heinonen, O.P., 1992. Occupational risk factors for congenital heart disease, *Int Arch Occup Environ Health*, Vol 64, pp. 59–64.

Tolarova, M. and Harris, J., 1995. Reduced recurrence of orofacial clefts after periconceptional supplementation with high-dose folic acid and multivitamins, *Teratology*, Vol 51, pp. 71–8.

Torfs, C.P., Katz, E.A., Bateson, T.F. *et al.*, 1996. Maternal medications and environmental exposures as risk factors for gastroschisis, *Teratology*, Vol 54, pp. 84–92.

Van Rooij, I., Wegerif, M., Roelofs, H. *et al.*, 2001. Smoking, genetic polymorphisms in biotransformation enzymes, and nonsyndromic oral clefting: A gene-environment interaction, *Epidemiology*, Vol 12, pp. 502–7.

Vianna, N.J. and Polan, A.K., 1984. Incidence of low birth weight among Love Canal residents, *Science*, Vol 226, pp. 1217–9.

Vrijheid, M., 2000. Health effects of residence near hazardous waste landfill sites: A review of epidemiologic literature, *Environ Health Perspect*, Vol 108, pp. 101–12.

Wilson, J.G., 1973. *Environment and birth defects*, Academic Press, New York.

Wu, T., Buck, G. and Mendola, P., 1998. Maternal cigarette smoking, regular use of multivitamin/mineral supplements, and risk of fetal death: The 1988 National Maternal and Infant Health Survey, *Am J Epidemiol*, Vol 148, pp. 215–21.

Yow, M.D., Williamson, D.W., Leeds, L.J. *et al.*, 1988. Epidemiologic characteristics of cytomegalovirus infection in mothers and their infants, *Am J Obstet Gynecol*, Vol 158, pp. 1189–95.

Zhang, J., Cai, W.W. and Lee, D.J., 1992. Occupational hazards and pregnancy outcomes, *Am J Ind Med*, Vol 21, pp. 397–408.

7. Waterborne gastrointestinal diseases

Kathy Pond

Summary of existing knowledge
- Burden of the health conditions considered: very important.
- Evidence on causal role of environmental factors: strong.
- Fraction of the problem attributable to environmental factors: large.
- Evidence on effectiveness of risk-reduction interventions: strong.

Main challenges
- To improve the surveillance of outbreaks of waterborne infectious diseases in children.
- To identify major deficiencies in providing safe drinking and recreational water.

Action points
- Improve water treatment, sanitation and hygiene education.
- Train public health personnel to detect and investigate waterborne disease outbreaks.
- Promote data collection and analysis to assess specific risks at country level to inform policies and interventions.
- Promote research into improving diagnostic capabilities for known pathogens to determine their endemic importance and their role in outbreaks.

7.1. Introduction

Waterborne diseases include infectious diseases due to biological contamination and acute and chronic poisoning by a variety of chemicals. This chapter deals with waterborne gastrointestinal infections that may affect children. The health effects of chemical contamination of water are dealt with in several other chapters of this monograph.

Biological contamination of water causes a range of water-related diseases and there are many estimates which indicate the scale of the problem. Gastrointestinal diseases account for most waterborne infant and child deaths and a high proportion of illnesses. They are the second (after respiratory diseases) largest single category of communicable diseases contributing to infant mortality worldwide (WHO, 1999; Satterthwaite *et al.,* 1996), accounting for an estimated 90 % of the global burden of disease due to environmental factors (Global Forum for Health Research, 2000).

In the European Region deaths of children from diarrhoeal diseases are much less than in other regions of the world. However, in many countries diarrhoeal diseases still represent an important cause of child mortality and morbidity, particularly in countries where many households do not have home connection to water (Figure 7.1.).

7.2. The particular vulnerability of children to waterborne infectious diseases

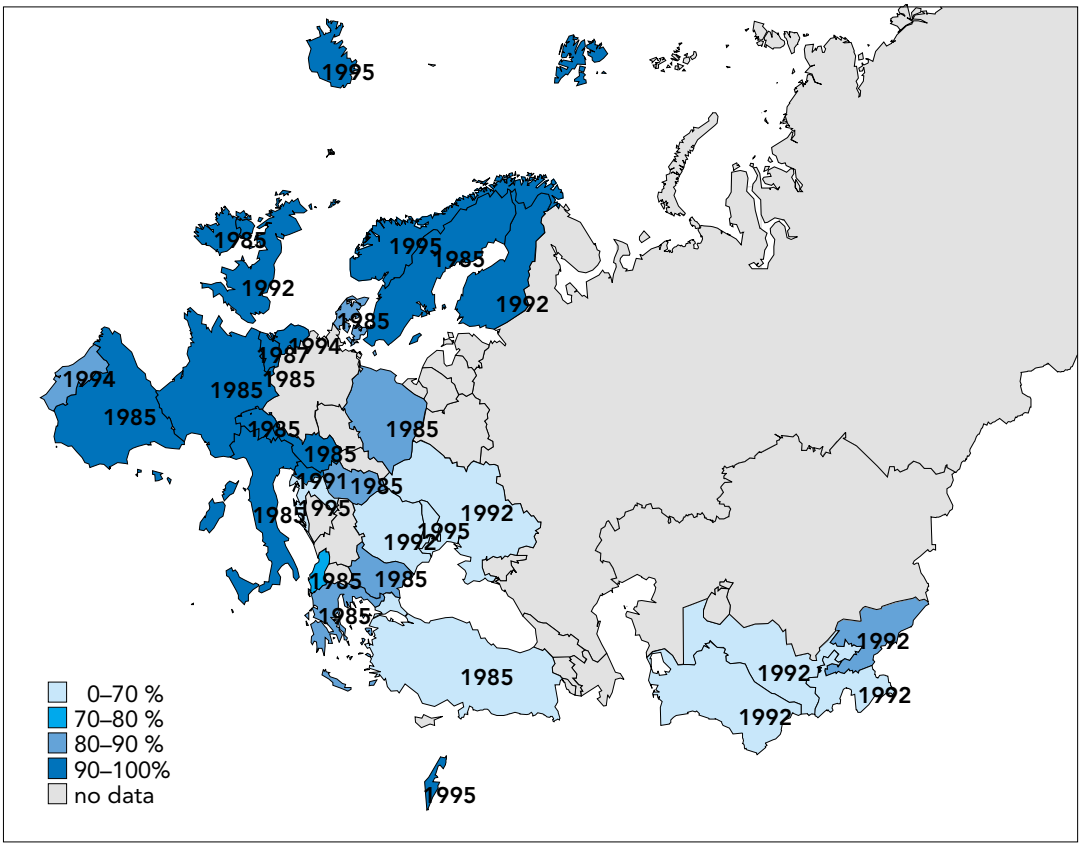
Children are particularly at risk from waterborne diseases compared to other age groups due to weak body defences, susceptibility and inadequate or no understanding of how to avoid hazards. Age is an important risk factor for gastroenteritis. The age of highest risk and therefore of highest incidence of diarrhoeal disease is 6–11 months, when the child is more susceptible and subject to greater exposure to pathogens through the combination of declining maternal antibodies and the introduction of new food (Ho Mei *et al.,* 1988).

Behaviour

As children grow they learn about the importance of washing after defecation, and of personal hygiene in general, and therefore the risk of contracting certain waterborne diseases may diminish. However, children living in houses or communities with poor sanitation and personal hygiene face a greater risk of ingesting faecal pathogens. Children have a natural curiosity and disregard for safety, and thus may play in (or drink) contaminated water. As their mobility increases they expose themselves to more hazards thus increasing risk of infection. Children's vulnerability is also increased by their parents' vulnerability to the same hazards if they face difficulties in caring for the children for economic reasons or because the parent is sick. The close contact children have with each other also increases the risk of infection.

Figure 7.1. **Percentage of total population with home connection to water in the WHO European Region in the time period between 1985–95**

Source: WHO, 1998



Environmental hazards

Some factors which have an impact on children's health are beyond parental control, for example access to safe, sufficient water supplies, provision for the hygienic removal of sewage, and affordable and acceptable health care, including rapid treatment for diarrhoeal diseases. Figure 7.1. shows the proportion of populations in Europe with home connections to drinking water. Because of logistical difficulties, increased cost and political priorities rural populations are less likely to receive piped water and house connections. In less-populated areas of some countries the provision of piped water supplies may not be viable and rural populations may rely on small, private supplies which may not receive adequate treatment due to the capital costs of water treatment. In addition, a number of areas within European countries do not receive a continuous supply of water. Discontinuity in the supply may have implications for human health comparable to those experienced when there is inadequate water (WHO/EEA, in press).

Diarrhoeal disease incidence seems to be inversely proportional to the amounts of water used in a family, even in the same environments. Hygiene interventions (the use of soap, and encouraging hand-washing after defecation and before preparing food) undoubtedly contribute to a reduction in morbidity (Esrey *et al.*, 1991).

Immunodeficiency

Environmental hazards interact with other hazards such as malnutrition, where particular deficiencies in micronutrients such as vitamin A and zinc hamper the immune response. Repeated or prolonged diarrhoea episodes may lead to malnutrition and impaired immune response. Children with congenital or acquired immunodeficiency diseases are at particularly high risk for enteric infection from a wide variety of organisms. In addition, immunosuppressed children may develop persistent infections with common agents, such as rotavirus, resulting in chronic diarrhoea (Pedley *et al.*, 1984).

7.3. Waterborne gastrointestinal diseases

Over the past two decades, paediatric acute gastroenteritis has been the subject of considerable worldwide attention and effort. Particular emphasis has been given to prevention through education, water and sanitation, and to the development and

promotion of inexpensive, easy-to-use oral rehydration solutions for the treatment of dehydration. The most common etiologic agents are listed in Table 7.1.

Etiologic agents for paediatric infectious gastroenteritis Table 7.1.

Viruses	Rotavirus Adenovirus Norwalk Calicivirus Astrovirus Parvovirus
Bacteria	Salmonella Shigella *Escherichia coli* (toxigenic) Campylobacterjejuni Yersinia enterocolitica *Escherichiacoli 0*157:H7(haemorrhagic) *Clostridium difficile* (iatrogenic)
Parasites	Giardia lamblia Cryptosporidium

Source: Northrup and Flanigan, 1994; Hunter, 1997

Viruses are responsible for 70–80 % of infectious diarrhoea cases in the developed world; various bacterial pathogens account for another 10–20 % of cases; and parasitic organisms such as Giardia species cause less than 10 % of cases (Merrick *et al.,* 1996). This distribution is affected by climate and season. Other factors that increase the risk of acute gastroenteritis in children include attendance at day-care centres and impoverished living conditions with poor sanitation (Merrick *et al.,* 1996). Bacterial and protozoal infections are often more severe than viral infections.

Infection occurs either directly from infected humans or indirectly through contaminated food or water. The distribution of viral gastroenteritis agents in the environment reflects the distribution of human faecal contamination.

Rotavirus

Rotavirus is a major cause of gastroenteritis in children worldwide (Szucs *et al.,* 1995). It is responsible for up to 50 % of the gastroenteritis in infants and children admitted to hospital during the cooler months of the year in temperate climates (WHO, 1996). Children aged between five and 24 months are the most severely infected and affected (WHO, 1996). Rotavirus may have multiple routes of transmission, with both contact or droplet and faecal-oral spread occurring in developing countries (Mahmood and Feacham, 1987). Rotavirus diarrhoea is a self-limiting disease of 5–10 days' duration.

Calicivirus

A study in the United Kingdom suggests that approximately 3 % of children hospitalised for diarrhoea excrete calicivirus (Ellis *et al.,* 1984). It is estimated from antibody-prevalence studies of pooled immunoglobulin and serum samples from many parts of the world that most people are infected by the age of 12 and the peak time of acquisition is between three months and six years (Cubitt and McSwiggan, 1987). In addition to contaminated drinking-water, person-to-person transmission, contaminated shellfish and cold foods have been implicated as vehicles. It appears that young adults retain effective immunity from earlier exposures, although this may become less with age as outbreaks have been reported in the elderly.

Hepatitis A

Hepatitis A is common throughout the world. Direct person-to-person contact is the most common transmission route, especially in children. It causes nausea, vomiting, muscle ache and jaundice, and is spread by faecal contamination of food, drinking-water or water used for recreation.

Box 7.1. Case study: Hepatitis A in Hungary

In September 1979, 31 children were hospitalised with Hepatitis A in a small town in north-east Hungary. An epidemiological investigation into potential common sources eliminated food and drink and person-to-person transmission. All of the patients had reported bathing in a summer camp swimming pool. Further investigation showed 25 additional cases. All of the cases were males aged 5–17. The pool was not chlorinated and was half full of water and used by younger children. The pool was generally crowded during the month of August. It was concluded that the overcrowded conditions and poor hygienic behaviour contributed to the outbreak (Solt *et al.,* 1994).

It has been shown that the younger age groups demonstrate increased symptom rates relating to recreational use of water (Pike,

1994; UNEP/WHO, 1991). There is a broad variety of illnesses that have been associated with swimming in marine and fresh recreational waters. *Shigella*, *Escherichia coli* (*E. coli*), *Leptospira*, *Giardia*, *Cryptosporidium*, Norwalk virus and adenovirus 3 are some of the microbes that have been linked to swimming-associated disease outbreaks. A number of outbreaks of *Giardia* and *Cryptosporidium* have been shown to occur in very small, shallow bodies of water which are generally frequented by children. Epidemiological investigations of the outbreaks found that the source was usually the bathers themselves, most likely children (WHO, 1999).

Escherichia coli

The presence of *E. coli* is a well-known indicator of faecal pollution. *E. coli* are capable of causing many diseases and are a major cause of gastroenteritis: enterotoxigenic *E. coli* cause a dehydrating diarrhoea in children; enteroinvasive *E. coli* can cause fever and watery mucoid diarrhoea in infants; enterohaemorrhagic *E. coli* are associated with haemorrhagic colitis, some cases progressing to haemolytic uraemic syndrome, particularly in children. Many waterborne outbreaks of *E. coli* are known — some associated with drinking-water and others with recreational water.

Box 7.2. Case study: Haemolytic uraemic syndrome from *E. coli* 0157 in the United Kingdom

In 1993 *E. coli* 0157 infected six children in south-west London, United Kingdom (Hildebrand *et al.*, 1996). Three children developed haemolytic uraemic syndrome, and one died. Four of the six cases had been to paddling pools within 10 days of becoming ill and three had visited the same pool. Half of the pool waters sampled had no detectable chlorine levels and *E. coli* was isolated from 40 %. The haemolytic uraemic syndrome is the most common cause of acute renal failure in infants and young children, and an important cause of chronic renal failure and shock during youth.

Shigella

Bacillary dysentery is an infectious intestinal disease caused by *Shigella* spp. The disease is spread primarily by person-to-person contact and the infectious dose is low. However, poor quality drinking-water contaminated by sewage has been the cause of disease outbreaks (Gray, 1994) although *Shigella* is readily destroyed by chlorination (WHO, 1996).

Box 7.3. Case study: Shigella in Crete and Israel

An outbreak of *Sh. sonnei* affected 30 % of children under 12 and 4 % of adults in a village on Crete over a one-month period in December 1990. It was thought that the source was a fountain sited in a valley below a sewage outflow. It was also considered that the children under 12 years of age were likely to be the primary cases rather than the secondary ones (Samonis *et al.*, 1994).

Cholera

Cholera can be transmitted through water and food**.** Environmental sources of the causative agent include sewage, sea and surface waters. Direct person-to-person transmission is uncommon. The symptoms of cholera are sudden diarrhoea with watery faeces, accompanied by vomiting, and the resultant dehydration and collapse is fatal in over half of untreated cases.

In 1998 the United Kingdom Public Health Laboratory Service (PHLS) Laboratory of Enteric Pathogens confirmed 24 cases of cholera; all the cases acquired infection outside the United Kingdom. Six of the cases were below the age of 16 years. Table 7.2. shows the number of European cases of cholera and deaths reported to WHO in 2001.

Table 7.2. **Number of European cases of cholera and deaths reported to WHO as of August 6, 2001**

Source: WHO, 2001

Country	Number of cases	Number of deaths	Imported cases
France		0	2
Germany		0	1
Russian Federation	53	0	0

Salmonella typhi

Typhoid fever is a bacterial infection of the intestinal tract and occasionally the bloodstream. Typhoid germs are passed in the faeces and, to some extent, the urine of infected people. The germs are spread by eating or drinking water or foods contaminated by faeces from the infected individual. Sinha *et al.* (1999) reported that typhoid fever is a common and important

cause of morbidity in children aged one to five. They did not observe any case of typhoid fever in children aged less than one year, probably because of passive immunity from their mothers in a population in which typhoid fever is endemic. A sharp contrast in incidence of typhoid fever between age groups in this population (27.3 % aged under 5 years, 11.7 % 5–19 years, and 1.1 % over 19 years) could indicate early exposure to typhoid, and therefore strong immunity in older age groups. In an epidemic in Ankara, Turkey, 24 children with typhoid fever were admitted to Ihsan Dogramaci Children's Hospital during two months. Only two patients were aged less than five years and 14 were aged five to nine years, which might indicate that typhoid fever is not common in children aged less than five years outside endemic areas, even in less-developed countries.

Giardia lamblia

Giardiasis is a common disease throughout the world, affecting all age groups, although the highest incidence is in children (Hunter, 1997). Waterborne outbreaks are particularly common and a few outbreaks have been reported from recreational waters.

Cryptosporidium

Cryptosporidium is a protozoan parasite, which is recognised to be a common cause of diarrhoea throughout the world. Severe diarrhoea is accompanied by weight loss, and malaise and fever are also common. The disease is usually self-limiting but can be fatal in children or the very old or immunosuppressed. The source of environmental contamination can be both human and animal sewage. Oocysts have been regularly isolated from potable water but recreational water use, farm animal contact and old piping have been associated as risk factors (Fewtrell and Delahunty, 1995; Duke *et al.,* 1996). The oocysts are found to be particularly resistant to disinfection.

Box 7.4. Case study: Cryptosporidium in England

Sixty-seven cases of cryptosporidiosis were identified by a hospital in northern England in 1988 and linked to a particular swimming pool. Thirty-one children in local schools were found to have gastroenteritis and a significant association was found between illness and swimming at the implicated pool. Water samples contained oocysts at a concentration of 50 per litre. When the pool was drained 30 centimetres of liquid sewage were found in the deep end (Joce *et al.,* 1991).

Campylobacter

In recent years Campylobacter spp. have been recognised as important agents of enteritis, gastritis and other human diseases (WHO, 1996). Several waterborne outbreaks of campylobacteriosis have been reported in the past decade. The numbers of persons involved ranged from a few to several thousands.

Although Campylobacter and Cryptosporidium have been associated with outbreaks of waterborne disease in England and Wales (Table 7.3.) the infections are transmitted via other routes and the contribution of waterborne transmission to the overall burden of disease caused by these pathogens is not known. While the other pathogens may be associated with waterborne transmission in other parts of the world there is little to suggest that domestic water supplies are associated with transmission of these pathogens in the United Kingdom; indeed some are mainly associated with foreign travel.

Entamoeba histolytica

Ameobic dysentery is caused by the protozoa *Entamoeba histolytica.* It is not a frequent disease in children.

Laboratory isolates of the major bacterial and protozoal causes of gastrointestinal diseases (England and Wales) are reported in Table 7.3.

Laboratory isolates for the major bacterial and protozoal causes of gastrointestinal diseases in England and Wales

Table 7.3.

Age group	*Shigella sonnei* (1997)	*Giardia lamblia* (1997)	*Cryptosporidium* (1998)	*Campylobacter* sp. (1998)	*Entamoeba histolytica* (1997)
0–4 years	168	832	1 506	5 437	9
5–14 years	220	511	1 007	2 411	29
All ages	1 465	5 288	3 745	94 621	637

Source: PHLS Communicable Disease Surveillance Centre

7.4. What we do not know

The bacterial and viral agents responsible for serious infections in children have been largely identified, although children continually face significant and unique threats from a range of environmental hazards. Continued work on identifying the causes of disease and death in children is required. Treatment-resistant microbes in drinking-water will remain an issue for research and development in the future.

Available data on waterborne disease outbreaks are often incomplete and inconsistent. Most countries report fewer cases than actual incidences for a number of reasons. Not all waterborne disease outbreaks may be recognised, investigated or reported, and the availability and utilisation of laboratory services, and the expertise of persons responsible for resources allocated to the surveillance system, may vary among countries. Furthermore, the recognition of waterborne disease outbreaks is dependent on several other characteristics such as the severity of the disease, relative size of the outbreak and the type of water system. Finally, the ratio of cases from waterborne disease outbreaks to 'sporadic' cases of waterborne diseases is unknown and probably varies among countries (WHO/EEA, in press).

7.5. Control measures

The provision of microbiologically safe drinking-water is the most important measure that can be taken to protect the health of children from waterborne diseases.

In western Europe, drinking-water is usually safe in microbiological terms because effective treatment processes have largely eliminated outbreaks of infectious diseases. Although infant mortality is 2.31 and 2.97 times higher, respectively, in the countries of central and eastern Europe and the newly independent states compared with that in the European members of the Organisation for Economic Co-operation and Development (OECD), the contribution of waterborne communicable and diarrhoeal diseases to these figures is unknown. Differences in infant mortality also occur locally according to socio-economic conditions.

Lack of safe water supply can be associated with the occurrence of cholera, typhoid fever, hepatitis A, gastrointestinal disease and a number of parasitic diseases. Incidents of these diseases linked with poor water quality have been recorded in many countries of the region, but especially in the countries of central and eastern Europe and the newly independent states. The most common type of local epidemic would appear to be gastrointestinal disease attributable to bacterial, viral or protozoal agents, but hepatitis A is of particular concern in the newly independent states. The levels of general low-level morbidity are impossible to assess.

Standards exist for both total and faecal coliforms of 0/100 millilitres (ml) in drinking-water in many European countries although some central and eastern European countries permit up to 3/100 ml. Community-managed supplies may not be subject to such strict standards as public supplies and therefore the quality may be compromised. A number of factors affect the bacterial quality of drinking-water — the condition of the pipes and the depth of the aquifer for example — so children in certain areas may be at higher risk of exposure to contaminated water than others.

A number of studies have been conducted, mostly in developing countries, to investigate the incidence of, and contributory factors to, children with diarrhoea. The source of drinking-water (unprotected surface water, for example, resulted in increases in diarrhoea), sanitary conditions, overcrowding, low income, distance of habitation from the water supply (the further the distance the higher the risk of diarrhoea) were found to be possible risk factors for prolonged diarrhoea in children (Moe *et al.,* 1991; Mahalanabis *et al.,* 1991; Gorter *et al.,* 1991).

Breastfeeding is thought to have a major protective effect against waterborne disease (Feacham and Koblinski, 1984; WHO, 2000). Studies indicate that infant mortality rates are five times higher for exclusively bottle-fed infants than for those exclusively breast fed (Grant, 1984). In less developed countries, infant formulas may be diluted with contaminated water, spoilage may occur and proper cleansing of equipment is difficult (Wilmoth and Elder, 1995). It has been shown that the benefits of breastfeeding on diarrhoea occurrence are most pronounced among children living in rural poverty (Forste, 1998).

Prospective surveillance for major pathogens is a priority in order to treat and prevent major pathogens in developing countries. The need for community-level surveillance is of particular importance since many children die before reaching hospital or health care.

Summary

Pathogenic microorganisms (viruses, bacteria and protozoal parasites) remain the most important danger to drinking water and recreational water, and gastrointestinal diseases are still a major cause of child morbidity all over the world and one of the major causes of childhood deaths in countries where a significant proportion of families do not have access to safe water.

The following interventions should be prioritised to decrease the burden of waterborne gastrointestinal diseases in children:

- education aimed at getting communities to take responsibility for improving the sanitary standards in their area;
- education of women about the benefits of breastfeeding;
- provision of an adequate supply of water close to the home;
- improving the quality of the water supply;
- education of the benefits of hand-washing and making soap available;
- provision of excreta disposal facilities and sanitation.

Health personnel must be trained to detect and investigate waterborne disease outbreaks. The data gathered through surveillance systems are useful for identifying major deficiencies in providing safe drinking and recreational water. Surveillance information also influences research priorities and can lead to improved regulations on water quality.

References

Cubitt, W.D. and McSwiggan, D.A. 1987. Seroepidemiological survey of the prevalence of antibodies to a strain of calicivirus, *J Med Virol*, Vol 21, pp. 361–8.

Duke, L.A., Breathnach, A.S., Jenkins, D.R. *et al.*, 1996. A mixed outbreak of cryptosporidium and campylobacter infection associated with a private water supply, *Epidemiol Infect*, Vol 116, pp. 303–8.

Ellis, M.E., Watson, B., Mandal, B.K., *et al.*, 1984. Micro-organisms in gastroenteritis, *Archives of Disease in Childhood*, Vol 59(9), pp. 848–855.

Esrey, S.A., Potash, J.B., Roberts, L. *et al.*, 1991. Effects of improved water supply and sanitation on ascariasis, diarrhoea, dracunculiasis, hookworm infection, schistosomiasis, and trachoma, *Bulletin of the World Health Organisation*, Vol 69, 1991, pp. 609–21.

Feachem, R.G. and Koblinski, M.A., 1984. Interventions for the control of diarrhoeal diseases among young children: promotion of breastfeeding. *Bulletin of the World Health Organisation*, Vol 62, pp. 271–291.

Fewtrell, L. and Delahunty, A., 1995. The incidence of crytosporidiosis in comparison with other gastro-intestinal illnesses in Blackpool, Wyre and Fylde. *Journal of the Chartered Institution of Water and Environmental Management*, Vol 9(6); pp. 598–601.

Forste, R. 1998. Infant feeding practices and child health in Bolivia, *Journal Biosoc Sci*, Vol 30, pp. 107–25.

Global Forum for Health Research 2000. *The 10/90 Report on Health Research 2000*. Global Forum for Health Research, Geneva.

Gorter, A.C., Sandiford, P., Smith, G.D. *et al.*, 1991.Water supply, sanitation and diarrhoeal disease in Nicaragua: results from a case-control study, *International Journal of Epidemiology*, Vol 20, pp. 527–33.

Grant, J. 1984. *State of the World's Children* (UNICEF). Oxford University Press, Oxford.

Gray, N.F., 1994. *Drinking water quality, problems and solutions*, John Wiley and Sons, Chichester.

Hildebrand, J.M., Maguire, H.C., Holliman, R.E., *et al.*, 1996. An outbreak of *Escherichia coli* 0157 infection linked to paddling pools, *Commun Dis Rep CDR Rev*, Vol 6, pp. R33–R36.

Ho Mei, S., Glass, R.I., Pinsky, P.F. *et al.*, 1988. Diarrheal deaths in American children: are they preventable? *JAMA*, Vol 260, pp. 3281–85.

Hunter, P.R., 1997. *Waterborne disease. Epidemiology and ecology*, John Wiley and Sons, Chichester.

Joce, R.E., Bruce, J., Kiely, D., *et al.*, 1991. An outbreak of cryptosporidiosis associated with a swimming pool. *Epidemiology and Infection*, Vol 107, pp. 497–508.

Mahalanabis, D., Alam, A.N., Rahman, N. *et al.*, 1991. Prognostic indicators and risk factors for increased duration of acute diarrhoea and for persistent diarrhoea in children, *Int. J Epidemiol*, Vol 20, pp. 1064–72.

Mahmood, D.A. and Feacham, R.G. 1987. Clinical and epidemiological characteristics of rotavirus- and EPEC-associated hospitalised infantile diarrhoea in Basrah, Iraq, *J Tropical Pediatr*, Vol 33, pp. 319–25.

Merrick N., Davidson, B. and Fox, S. 1996. Treatment of acute gastroenteritis: too much and too little care, *Clin Pediatr* [Phila], Vol 35, pp. 429–35.

Moe, C.L., Sobsey, M.D., Samsa, G.P. *et al.* 1991 Bacterial indicators of risk of diarrhoeal disease from drinking water in the Philippines, *Bulletin World Health Organization*, Vol 69, pp. 305–17.

Northrup, R.S. and Flanigan, T.P. 1994. Gastroenteritis, *Pediatr Rev*, Vol 15, pp. 461–72.

Pedley, S., Hundley, F., Chrystie, I. *et al.*, 1984. The genomes of rotavirus isolated from chronically infected immunodeficient children, *J Gen Virol*, Vol 65, pp. 1141–50.

Pike, E.B. 1994. *Health effects of sea bathing* (WMI 9021) — Phase III: Final report to the Department of the Environment. Report No. DoE 3412/2. Water Research Centre plc, Medmenham, United Kingdom, pp. 1–38.

Samonis, G., Elting, L., Skoulika, E. *et al.*, 1994. An outbreak of diarrhoeal disease attributed to *Shigella sonnei*, *Epidemiol Infect*, Vol 112, pp. 235–45.

Satterthwaite, D., Hart, R., Levy, C. *et al.*, eds., *The Environment for Children*, UNICEF, New York, 1996, pp. 284.

Sinha, A., Sazawal, S., Kumar, R. *et al.* 1999. Typhoid fever in children aged less than 5 years, *Lancet*, Vol 354, pp. 734–37.

Solt, K., Nagy, T., Csohan, A., *et al.,* 1994. An outbreak of hepatitis A due to a thermal spa. *Budapesti Kozegeszsegugy*, Vol 26, pp. 8–12. In Hungarian.

Szucs, G., Matson, D.O., Uj, M. *et al.,* 1995. Group A rotavirus G type prevalence in two regions of Hungary, *Arch Virol*, Vol 140, pp. 1693–703.

UNEP/WHO, 1991. *Assessment of the state of pollution of the Mediterranean Sea by pathogenic micro-organisms*, Document UNEP(OCA)/MED/WG.25/Inf.7, United Nations Environment Programme, Athens.

WHO, 1996. *Guidelines for drinking water quality*. Second Edition. Volume 2. Health criteria and supporting information. WHO, Geneva, 973 pp.

WHO, 1999. *The World Health Report 1999*. World Health Organization, Geneva. 136 pp.

WHO Collaborative study team on the role of breastfeeding on the prevention of infant mortality, 2000. Effect of breastfeeding on infant and child mortality due to infectious diseases in less developed countries: a pooled analysis. *Lancet*, Vol 355, pp. 451–454.

WHO/EEA, in press, *Water and Health*. WHO, Regional Office for Europe, Copenhagen.

WHO 1998, *Health for all data base: European Region* [Computer file]. WHO Regional Office for Europe, Copenhagen.

WHO 2001, on line at: http://www.who.int/home-page/index.en.shtml

Wilmoth, T.A. and Elder, J.P., 1995. An assessment of research on breastfeeding promotion strategies in developing countries. *Soc Sci Med*, Vol 41(4), pp. 579–594.

8. Foodborne diseases

Marco F.G. Jermini

Summary of existing knowledge
- Various bacterial and viral microorganisms, such as *Campylobacter* spp., pathogenic *Escherichia coli*, *Shigella* spp., *Salmonella* spp. and Norwalk-like viruses cause foodborne diseases.
- Infections due to pathogenic *E. coli* are thought to be the most frequent in both developed and developing countries.
- Children under 10 years of age are one of the most vulnerable groups at risk to foodborne pathogens.
- Young children also exhibit more severe symptoms because of their less developed immune systems.

Main challenges
- To prevent foodborne diseases in infants and children based on a multidisciplinary approach.

Action points
- Collect socio-cultural information and deliver it to the planners of educational programmes.
- Identify hazards at each step of the food chain, especially during the final food preparation stages, assessing the risks and determining the operations where control procedures can effectively reduce or eliminate hazards (the Hazard Analysis And Critical Control Point — HACCP — system).
- Educate family members and food handlers in food safety principles derived from the HACCP system.

8.1. Introduction

Food contamination ([2]) is one of the major contributors to diarrhoeal diseases and the associated malnutrition. Food safety is as important in the prevention of these diseases in infants and children as is breastfeeding and the provision of safe water supplies and sanitation. Food safety, i.e. all conditions and measures that are necessary during the production, processing, storage, distribution and preparation of food to ensure that it is safe, sound, wholesome and fit for human consumption, is often overlooked. The need to educate food handlers in food safety, particularly those who cook for the family and school canteen personnel, is often neglected. It should be regarded as an important tool in the prevention of foodborne diseases.

Newborn babies, infants and young children are very susceptible to foodborne diseases, because their immune systems are not fully developed and the microbial flora in their intestinal tract is not so competitive against pathogens (most of them with opportunistic character) as in adults. If they consume contaminated foods they may contract infections, toxi-infections and intoxications leading to illness and sometimes death (Kaufmann, 1997; Rolfe, 1991; Stern, 1987; Michaelsen *et al.*, 2000; Glass *et al.*, 1991).

Contaminants consist of a large variety of biological and chemical agents of disease, some of which can multiply in food, thus increasing their pathogenic potential. Although chemicals loom large in the eyes of the general public, they are actually less important as causes of foodborne illness than biological agents such as bacteria, fungi, viruses and parasites or the toxins produced by these agents.

8.2. Foodborne pathogens

Various pathogens have been identified as causing foodborne diseases. Some of these include bacteria such as *Campylobacter* spp., pathogenic groups of *Escherichia coli*, *Shigella* spp., *Salmonella* spp. and *Listeria monocytogenes*; protozoa such as *Giardia lamblia*, *Entamoeba histolytica* and *Cryptosporidium* spp., helminthes such as *Anisakis simplex* and *Trichinella spiralis*, and enteric viruses such as rotaviruses. In addition *Bacillus cereus*, *Clostridium perfringens*, *Staphylococcus aureus* and *Aeromonas* spp. are common foodborne pathogens that cause foodborne intoxications and toxi-infections which are frequently accompanied by diarrhoea.

Infections due to pathogenic *E. coli* are probably the commonest illnesses in developed and developing countries — they account for up to 25 % of all diarrhoeal episodes. Its transmission has been linked with contaminated complementary infant food. Infections due to verotoxin-producing *E. coli* (EHEC), especially those belonging to the serotype O157:H7, are emerging as a new problem in several countries worldwide. They are associated with haemolytic uraemic

(2) Only disease of biological origin is discussed in this chapter. Children's sensitivities to some chemical agents, such as pesticides and heavy metals, are discussed in separate chapters (see Chapters 4. and 10.).

syndrome, a disease of infancy and childhood, a leading cause of sometimes lethal, acute kidney failure in this age group. Not all countries have mandatory notification for EHEC or haemolytic uraemic syndrome, therefore the prevalence of this disease in Europe is unclear. However, reports from Denmark, Germany, the Netherlands, Sweden, United Kingdom and Switzerland indicate that this is a true emerging pathogen (WHO, 1997).

In several countries, *Aeromonas hydrophila* and other motile aeromonads have been incriminated in cases of human gastroenteritis, particularly in children under the age of two (WHO, 1997).

Clostridium botulinum is the pathogen, which causes infant botulism, the most common form of botulism. Infant botulism arises from ingestion of botulism spores rather than preformed toxin. It results from the colonisation and subsequent outgrowth and *in vivo* toxin production in the intestine. Possible sources of spores for infants are multiple, including food and dust. Honey, a food item fed to infants, often contains *C. botulinum* spores. All patients hospitalised to date with infant botulism have been between two weeks and one year of age; 94 % were six months old or less, and the median age at onset was 13 weeks. Cases of infant botulism have occurred in all major racial and ethnic groups. Adults with special bowel problems, leading to unusual gastrointestinal flora, may also be susceptible to 'infant-type' botulism. The illness has a wide spectrum of clinical severity, ranging from mild illness to sudden infant death. Various studies suggest that it may cause an estimated 5 % of cases of sudden infant death syndrome (Beneson, 1990). The fatality rate of hospitalised cases in the United States is 2 %. Without access to hospitals with paediatric intensive care units, more would die. Cases of infant botulism have also been reported from Europe although the actual incidence and distribution remain to be determined.

8.3. Sensitive populations: who is at the greatest risk?

In assessing the potential impact of foodborne disease, it is important to recognise that certain individuals may be at greater risk of serious illness than the general population. The outcome of exposure to infectious microorganisms depends on a number of host factors including:

- pre-existing immunity
- nutrition
- ability to elicit an immune response
- age (Kaufmann, 1997; Rolfe, 1991; Stern, 1987).

With enteric viruses, age plays a major role in the probability of developing clinical illness. It can vary from 5 % in children under five years of age to 70 % in adults (Hung *et al.*, 1984; Lednar *et al.*, 1985). Conversely, with rotaviruses children are more likely to develop gastroenteric symptoms than are adults (Hrdy, 1987). Age-dependent effects are also notable for salmonellosis, from both passive and active surveillance systems. Children under 10 years of age appear to be most susceptible and sensitive compared with other sectors of the population (CDC, 1997; Coleman and Marks, 1998). In the Netherlands, infections due to *Salmonella* Typhimurium occur most in children up to 10 years, especially in those under the age of five (median age is five), while those due to the antibiotic-resistant strain phagetype DT104 occur more often in children over five years of age (Van Pelt and Van Leuwen, 1998). The same was observed in some central European countries; for example, most of the salmonella cases in the Czech Republic were notified in babies under one year of age and in infants and young children under nine (Figure 8.1.).

Children may suffer more severe symptoms, but there are no data-based dose-response models that depict disease severity as a function of age.

Higher sensitivities of infants and young children towards infective pathogens may be attributed to the underdevelopment and instability of the gastrointestinal tract ecosystem (Drasar and Barrow, 1985; Hentges, 1983). With respect to this, breast milk is the safest and most nutritious food for newborn infants, and exclusive breastfeeding, i.e. giving the infant no fluid or food other than breast milk, protects against diarrhoea by minimising the infant's exposure to foodborne or waterborne pathogens (Motarjemi *et al.*, 1993).

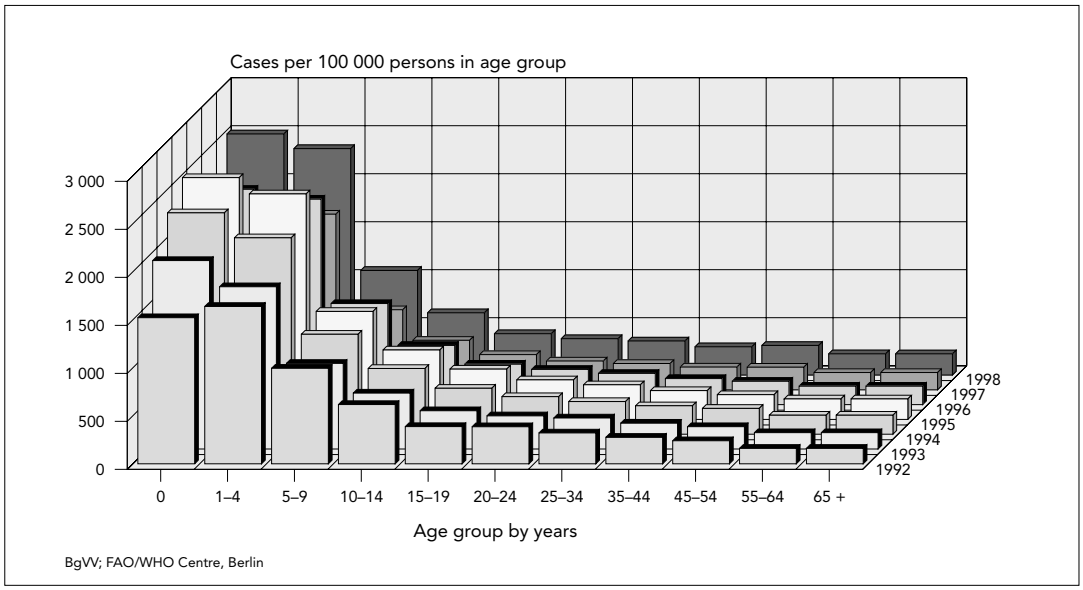
National breastfeeding and nutrition policies, as well as environmental factors such as type of food vehicle, consumption of the food as a meal or snack, indigenous microbial competitors in food, etc., may explain why the age distribution of pathogen isolates can differ from country to country. In

a survey of *Campylobacter* spp. seasonality in some European countries, the age distribution showed significantly fewer isolates in younger age groups, especially those aged one to four years, in Finland as compared to Denmark, Wales and Austria (Table 8.1.) (Nylen *et al.*, 1998).

Salmonellosis incidence rate by age groups, Czech Republic 1992–1998

Figure 8.1.

Source: Schmidt and Tirado, 2001



Age distribution, all Campylobacter isolates (n=50 036) reported in Finland, Denmark, Wales and Austria in the years 1993–97

Table 8.1.

Source: Modified from Nylen, 1998

Age group	% Finland 1995–97	% Denmark 1993-97	% Wales 1993–97	% Austria 1996-97
0–<1	0.5	2.6	3.7	0.7
1–4	3.3	16.4	10.1	16.2
5–14	4.8	9.5	7.6	21.0
Subtotal for infants and young children	**8.6**	**28.5**	**21.4**	**37.9**
15–24	14.6	20.8	13.7	13.9
25–34	25.3	19.4	18.8	15.7
35–44	19.4	10.9	14.1	7.4
45–54	15.5	8.7	12.2	6.2
55–64	9.0	5.1	8.0	6.7
65+	7.6	6.6	12.0	12.1

8.4. Outbreak investigations

Surveillance of outbreaks has proved useful in the rapid development of hypotheses for directed epidemiological research. It also provides valuable information for policy-makers who have to set priorities in the implementation of public health measures.

Overall data from the WHO Surveillance Programme for the Control of Foodborne Infections and Intoxications (Schmidt, 1995) indicates, that large proportions of diseases (36 %) are acquired in private homes (46.3 % of the outbreaks of which the place was known), while kindergarten and school canteens account for approximately 6 % (4 % of the outbreaks of which the place was known).

In some eastern European countries the latter figure can be higher. For example, 15.1 % of the outbreaks registered in Latvia between 1993 and 1998 (Table 8.2.) and 74.2 % of the outbreaks (corresponding to 35.1 % of the cases) registered in Belarus between 1994 and 1998 were acquired in school or kindergarten canteens (Table 8.3.) (Schmidt and Tirado, 2001).

Table 8.2. **Foodborne disease outbreaks by place where food was eaten, Latvia 1993–98**

Source: Schmidt and Tirado, 2001

Place	Year							
	1993	1994	1995	1996	1997	1998	1993–98	
	No of outbreaks						No	%
Canteen	-	27	-	-	17	-	**44**	**2.2**
School, kindergarten	-	64	105	76	40	7	**292**	**15.1**
Medical care facilities (hospital, nursery)	-	12	-	33	8	3	**56**	**2.9**
Private home	-	28	-	49	6	114	**197**	**10.2**
Other	86	60	83	110	58	1	**398**	**20.5**
Various places (two and more)	818	-	132	-	-	2	**952**	**49.1**
Total	**904**	**191**	**320**	**268**	**129**	**127**	**1 939**	**100**

Table 8.3. **Foodborne disease outbreaks, Belarus 1994–98**

Source: Schmidt and Tirado, 2001

Year	No of outbreaks	No of cases in outbreak	Place were food was contaminated or eaten or incriminated vehicle
1994	7	164	Mass catering
	3	635	Food-processing establishment
	2	228	Water
	25	416	Kindergarten or school
1995	1	298	Food-processing establishment
	1	199	Water
	22	320	Kindergarten or school
1996	1	39	Food-processing establishment
	11	186	Kindergarten or school
1997	4	72	Mass catering
	1	270	Food-processing establishment
	16	213	Kindergarten or school
1998	5	78	Mass catering
	6	384	Food-processing establishment
	2	195	Water
	21	250	Kindergarten or school
Total	**128**	**3 947**	

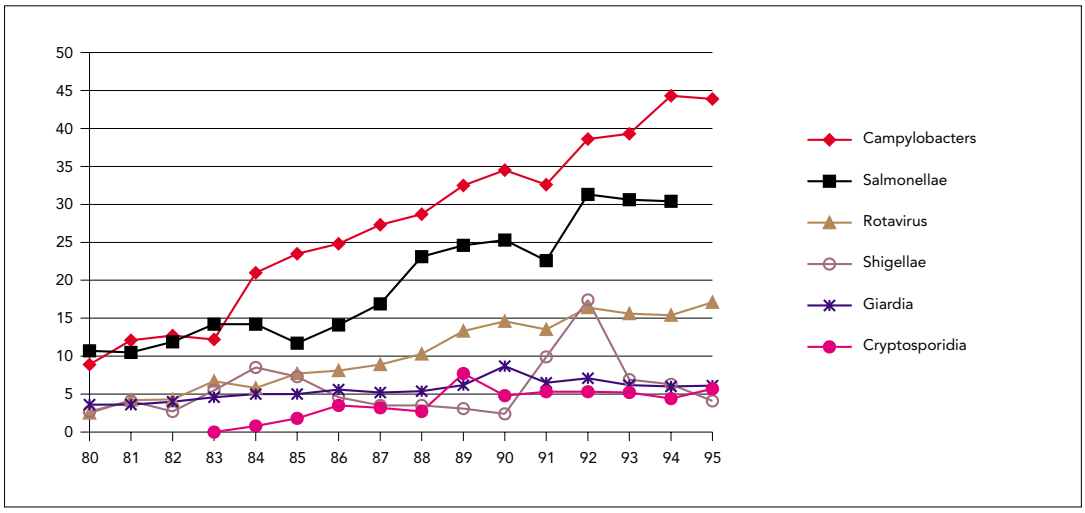
Worldwide, *Campylobacter* spp. takes first place among bacterial enteric pathogens (Phillips, 1995). Figure 8.2. compares the number of cases of *Campylobacter* spp. in England and Wales with other pathogens (WHO/ICD, 1999). This is a common trend in all European countries for the overall population; selected data relating to infants and children are not available. In general, most of the eastern European countries do not have a well-functioning surveillance system in place for this pathogen and only a few of them have data available.

Outbreak of campylobacteriosis in Germany

It is believed that most of the *Campylobacter* cases are isolated cases, but outbreaks have been recorded in some countries. Epidemiological investigations involving patients and staff working in the field of food production, combined with isolation and typing of agent strain from patient and food, were used in Germany to establish the source of infection and the route of transmission during outbreaks. Thirteen *Campylobacter* outbreaks have been investigated, among which a total of 900 patients were affected (Thurm and Dinger, 1998). As highlighted in Table 8.4., seven out of 13 outbreaks involved kindergartens, schools or children's homes.

Number of reported laboratory cases (per 1 000) of Campylobacter spp. and other pathogens in England and Wales in the years 1980–95

Figure 8.2.



Source: WHO/ICD, 1999

Besides the fact that most of the patients were children, raw milk was found to be the most frequent cause of *Campylobacter* outbreaks. This could be due to the tendencies of the populations of some European countries to consume food in a raw state. The specific lack of data on *Campylobacter* makes the evaluation of the consequences of the habit of drinking unpasteurised milk in some newly independent states (especially in rural areas) impossible.

Investigated outbreaks of foodborne campylobacteriosis in Germany 1991–97

Table 8.4.

Year	No of patients	Incriminated food	Place of food intake	Contributing factor
1991	82	Poultry meat	Kindergarten	Cross contamination
1992	25	Certified milk	Children's home	Direct intake
1994	289	Raw milk	Kindergarten and school	Insufficient heating
1995	91	Raw milk	Holiday camp	Direct intake
1996	13	Raw milk	School excursion to farm	Direct intake
1996	14	Unknown	Household	Unknown
1996	114	Raw milk	School excursion to farm	Direct intake
1996	19	Poultry meat	Kindergarten and school	Insufficient cooking
1996	29	Unknown	Household	Unknown
1996	6	Surface water	At play	Direct intake
1997	186	Raw milk	Kindergarten	Insufficient heating
1997	18	Certified milk	Household	Direct intake
1997	35	Pork meat	Firm celebration	Direct intake

Source: Modified from Thurm and Dinger, 1998

Outbreak of E. coli O157:H7 infections and haemolytic uraemic syndrome in Germany

Since 1988 outbreaks and isolated cases of severe diseases caused by EHEC have been reported from different geographical regions of Germany (Reida *et al.*, 1994). From October 1995 through March 1996 an epidemic with 43 cases of haemolytic uraemic syndrome was observed in Bavaria. In summer 1997 an increasing number of EHEC infections was noted. Four cases were associated with the consumption of raw milk, which led the local authorities to investigate 26 kindergartens and one day-care facility, all of which were supplied with certified raw milk from the same supplier. The investigators took stool samples from 1 697 children and were able to show implicit data correlation between typical EHEC and the consumption of raw milk. This indicated the possible role that milk had as vehicle of infection.

Outbreaks of E. coli O157:H7 and haemolytic uraemic syndrome in Switzerland

Preliminary results of an ongoing Swiss national surveillance system for rare paediatric disorders (Schmid *et al.*, 1998) showed an estimated annual incidence of 12 haemolytic uraemic syndrome cases per 100 000 in children under one year of age and four haemolytic uraemic syndrome cases per 100 000 in children between birth and four years, with no fatal outcome. The socio-demographic distribution of the cases showed that the patients' residences were frequently in rural areas, with possible contacts with cattle and/or their faeces, and the consumption of raw milk in the two weeks before the onset of the first prodromal symptoms.

Outbreaks of C. perfringens toxi-infection, B. cereus intoxication and listeriosis in Italy

Three different outbreaks of foodborne disease with gastrointestinal symptoms occurred in the Italian province of Turin between 1992 and 1997 in school catering facilities and affected approximately 3 000 children. The results of the epidemiological investigations carried out by Griglio *et al.* (1998) are shown in Table 8.5.

Table 8.5. **Epidemiological investigation of three outbreaks in school catering occurring in Piedmont, Italy, 1992–97**

Source: Modified from Griglio *et al.*, 1998

	Outbreak no 1	Outbreak no 2	Outbreak no 3
Number of consumers	1 100	10 760	2 750
Number of cases	500	900	1 500
Onset of symptoms	6–22 hrs	2–3 hrs	18–24 hrs
Symptoms	Diarrhoea Abdominal pain Vomiting	Vomiting Diarrhoea Abdominal pain	Abdominal pain Headache Nausea Diarrhoea
Food involved	Rice with tomato sauce Roasted veal Potatoes Fresh fruit	Vegetable soup with rice Surimi Potatoes	Pasta with tomato sauce Tuna and maize salad Fresh fruit
Results of investigation	*C. perfringens* toxin in stool specimens *C. perfringens* positive in roasted veal samples	*Bacillus cereus* positive in crabmeat surimi	*Listeria monocytogenes* isolated from blood of one patient Listeria monocytogenes isolated from kitchen environmental samples

Outbreak of variant Creutzfeld-Jacob disease (vCJD)

The new variant form of Creutzfeld-Jacob Disease (vCJD) is a new disease which differs from the traditional forms of CJD and was first described in 1996.

Although the cause of vCJD is not yet clear, it is possibly linked to exposure to the bovine spongiform encephalopathy agent. Transmission is thought to be through the intake of bovine-based food. The nature of the causal agent is not clear, but it has been suggested that it may be a self-replicating protein, called a prion.

In contrast to the traditional forms of CJD, the prevalence of vCJD is particularly high among young people, with the average age of affected patients being 29 years as opposed to 65 years for CJD (WHO, 2000). It was reported that of the 52 vCJD fatalities between mid-1995 and early 2000, almost half were between 20 and 29 years old and eight were aged 10–19 years (The Guardian, 2000). A search for vCJD was carried out among children in the United Kingdom with progressive intellectual and neurological deterioration detected within a prospective active surveillance since 1997. Out of the 885 cases with such deterioration, two fatal cases of vCJD and one case of probable vCJD were identified in 1999. The youngest ever case was a girl aged 12 years at the onset of the disease. No other children with clinical features of vCJD were found (Verity *et al.*, 2000). Overall, estimates for the years between 1994 and 2000 showed that the incidence of new onsets of vCJD increased by 23 % per year, and that the number of deaths increased by 33 % annually in the period 1995–2000 (Andrews *et al.*, 2000). Although the total number of cases is still low, the vCJD epidemic has to be managed cautiously.

8.5. Incidence of foodborne disease on the rise

Despite recent activities and initiatives, the incidence of foodborne diseases continues to increase. Diarrhoeal diseases have been traditionally associated with contaminated water supplies and lack of sanitation. A review of the impact of improving these environmental factors has shown that the rate of morbidity was reduced only by 27 % (Esrey, 1985; Nylen *et al.*, 1998). In northern and western Europe, where drinking water supplies and sanitation facilities are satisfactory, the incidence of foodborne diseases increased three-fold between the early 1980s and the late 1990s. It is believed that in some countries such diseases affect more than 10 % of the population, with children playing an important role.

This is due to the influence of different, often interrelated and changing, complex factors. These factors include the following:

Food supply system:

- New technologies have been employed in food production, processing and marketing which resulted in mass production and distribution, leading to opportunities for contamination and larger outbreaks.
- Intensive agriculture and animal husbandry practices have been introduced leading to increased contamination of raw foodstuffs, increased use of pesticides and veterinary drugs, and increased globalisation of the food industry.
- Trade liberalisation and international harmonisation of food standards and urbanisation have led to the trade of potentially contaminated foods, and longer food chains which introduce greater opportunities for contamination, growth and survival of pathogens.

Health and demographic situation:

- Population trends have led to an increase in the number of vulnerable persons, such as malnourished children and the elderly.
- Rapid urbanisation may result in insufficient infrastructure in some areas.

Social situation, behaviour and lifestyle:

- Patterns of food consumption have changed with increased consumption outside the home, increased travel and exposure to unsafe food, changes in food preparation habits, poverty and lack of education, lack of time and striving to increase economic profit.
- There has been a rapid increase in the number of food service establishments where food handlers do not have adequate training in food hygiene.

Health system and infrastructure:

- There has been a decrease in resources and a simultaneous increase in the number of businesses that require supervision, guidance and control.
- Weaknesses in the investigation and surveillance of foodborne diseases and monitoring of contaminants have led to incapacity to evaluate the impact of food safety.
- New technologies are available for the detection of foodborne hazards and food inspection, possibly leading to increased detection of emerging hazards.

Environmental conditions:

- Pollution, e.g. contamination with PCBs and dioxins, is environmental, caused by incineration or dispersion. Contamination by DDT and DDE is anthropogenic, due to the past abuse of this pesticide and the present global dispersion of the molecules.
- Climate conditions and climate changes.
- New foodborne hazards are emerging due to changes in the microbial and ecological system.

There are numerous reasons for the increasing trend of foodborne disease; however, outbreaks of foodborne illnesses are almost always caused by one or more errors during the food chain, frequently during the final preparation of food.

8.6. Prevention and control of foodborne diseases

To prevent foodborne illnesses, a multisectoral approach is needed. Measures such as improving environmental conditions may take a long time, and on their own they will not be enough to solve the problem. Food handlers, especially caterers and those cooking for the family, need to be educated on how to protect infants and children. Since the nutrition of infants and children depends closely on the education of their parents on food safety, this should be considered as one of the most important activities to

implement. A programme to educate parents on food safety principles should be considered an important part of every primary health care system. It should be incorporated into national infant- and child-feeding and nutrition programmes. Since socio-cultural settings vary among countries and even among the population of the same country it is suggested that education programme planners should consider an analysis of the hazards associated with food habits, the socio-economic situation and the technological facilities available in the target group or society. Two types of study are necessary for this approach:

- Collection of socio-cultural information and its delivery to the planner of educational programmes;
- Identification of hazards at each step of the food chain, but especially during final food preparation, assessing the risks and determining the operations where control procedures can be effective (the Hazard Analysis And Critical Control Point — HACCP — system).

In conclusion, it is clear that the prevention of foodborne diseases in infants and children requires a multidisciplinary approach, including the promotion of exclusive breastfeeding, the safe preparation and handling of complementary infant food, and the simultaneous education of parents and food handlers in food safety principles derived from the HACCP system.

Summary

Various pathogens cause foodborne diseases but infections due to pathogenic *E. coli* are thought to be the most frequent in both developed and developing countries. Children under 10 years of age appear to be most susceptible and sensitive to infection compared with other sectors of the population; they may also exhibit more severe symptoms.

Surveillance of outbreaks is an important tool to direct research and provide information to decision-makers.

Most infections are acquired in private homes and the consumption of raw milk has been identified as a frequent vehicle of infection.

Despite recent activities and initiatives, the incidence of foodborne diseases continues to increase, due to factors such as changes in the food supply system, as well as the health, demographic and social situation.

The prevention of foodborne diseases in infants and children requires a multidisciplinary approach, including the promotion of exclusive breastfeeding, the safe preparation and handling of complementary infant food, and the simultaneous education of parents and food handlers in food safety principles derived from the HACCP system.

References

Andrews, N.J., Farrington, C.P., Cousens, S.N. *et al.*, 2000. Incidence of variant Creutzfeld-Jacob disease in the UK, *Lancet*, Vol 356, pp. 481–2.

Beneson, A.S., ed, 1990. *Control of communicable diseases in man*, American Public Health Association, Washington, p. 62.

CDC, 1997. *Salmonella surveillance: Annual tabulation summary 1993–1995*, Center for Disease Control and Prevention, Atlanta, GA.

Coleman, M. and Marks H., 1998. Topics in dose-response modelling, *J Food Prot*, Vol 61, pp. 1550–9.

Drasar, B. and Barrow, P.A., eds, 1985. *Intestinal Microbiology*, American Society for Microbiology, Washington, DC.

Esrey, S.A., 1985. Interventions for the control of diarrhoeal diseases among young children: Improving water supplies and excreta disposal facilities, *Bulletin of the World Health Organization*, Vol 63, pp. 757–72.

Glass, R.I., Lew, J.F., Gangarosa, R.E. *et al.*, 1991. Estimates of morbidity and mortality rates for diarrhoeal diseases in American children, *J Pediatr*, Vol 118, pp. S27–33.

Griglio, B. *et al.*, 1998. Experience of the regional veterinary services in Piedmont about some important outbreaks of foodborne disease in school's catering, in *Proceedings of the 4th World Congress on Foodborne Infections and Intoxications*, Vol 2, pp. 661–5.

Hentges, D.J., ed, 1983. *Human intestinal microflora in health and disease*, Academic Press, New York.

Hrdy, D.B., 1987. Epidemiology of rotavirus infection in adults, *Rev Infect Dis*, Vol 9, pp. 461–9.

Hung, T., Chen, G.M., Wang C.G. *et al.*, 1984. Waterborne outbreaks of rotavirus diarrhoea in adults in China caused by a novel rotavirus, *Lancet*, Vol 2, No 8387, pp. 1140–2.

Kaufmann, S., 1997. The role of conventional and unconventional T cells in antibacterial immunity, *Am Soc Microbiol News*, No 63, pp. 251–5.

Lednar, W.M., Lemon, S.M., Kirkpatrick, J.W. *et al.*, 1985. Frequency of illness associated with epidemic hepatitis A virus infection in adults, *Am J Epidemiol*, Vol 122, pp. 226–33.

Michaelsen, K.F. *et al.*, 2000. *Feeding and nutrition of infants and young children,* WHO Regional Publication, European Series, No 87, Chapter 12, pp. 235, WHO Regional Office for Europe, Copenhagen.

Motarjemi, Y., *et al.*, 1993. Contaminated weaning food: A major risk factor for diarrhoea and associated malnutrition, *Bulletin of the World Health Organization*, Vol 71, pp. 79–92.

Nylen, G. *et al.*, 1998. Campylobacter seasonality in Europe, in *Proceedings of the 4th World Congress on Foodborne Infections and Intoxications*, Vol 1, pp. 293–7.

Phillips, C.A., 1995. Incidence, epidemiology and prevention of foodborne Campylobacter species, *Trends Food Sci Technol*, Vol 6, pp. 83–7.

Reida, P. *et al.*, 1994. An outbreak due to enterohemorragic *Escherichia coli* O157:H7 in a children's day care centre characterized by person to person transmission and environmental contamination, *Zbl Bakt*, Vol 281, pp. 534–43.

Rolfe, R.D., 1991. Population dynamics of the intestinal tract, in *Colonization control of human bacterial enteropathogens in poultry* (edited by L.C. Blankeship *et al.*), Academic Press Inc., New York, pp. 59–76.

Schmid, H. *et al.*, 1998. Epidemiology of haemolytic uraemic syndrome (HUS) in Swiss children: Preliminary results of a surveillance study, in *Proceedings of the 4th World Congress on Foodborne Infections and Intoxications*, Vol 2, pp. 880–3.

Schmidt, K., ed, 1995. *WHO Surveillance Programme for Control of Foodborne Infections and Intoxications in Europe*, 6th Report, BgVV Berlin.

Schmidt, K. and Tirado, C., 2001. *7th report of the WHO Surveillance Programme for Control of Foodborne Infections and Intoxications in Europe (1993–1998),* Federal Institute for Health Protection of Consumers and Veterinary Medicine, BgVV–FAO/WHO Collaborating Centre for Research and Training in Food Hygiene and Zoonoses, Berlin, 480 pp.

Stern, N.J., 1987. Host factors influencing colonization control of human enteropathogens, *Food Technol*, Vol 41, pp. 102–6.

The Guardian, 28 March 2000, online: http://www.newsunlimited.co.uk/Breaking News/UK/0,2478,92882,00.html

Thurm, V. and Dinger, E., 1998. Subtyping of outbreak-related strains as a useful method in the surveillance of *Campylobacter* infections, in *Proceedings of the 4th World Congress on Foodborne Infections and Intoxications*, Vol. 1, pp. 310–6.

Van Pelt, W. and Van Leuwen, W.J., 1998. Salmonella thypimurium phagetype DT104 in the Netherlands, in *Proceedings of the 4th World Congress on Foodborne Infections and Intoxications*, Vol 1, pp. 250–1.

Verity, C.M., Nicoll, A., Will, R.G. *et al.*, 2000. Variant Creutzfeld-Jacob disease in UK children: A national surveillance study, *Lancet*, Vol 356, pp. 1224–7.

WHO, 1997. *Prevention and control of enterohaemorragic Escherichia coli (EHEC) infections,* Report of a World Health Organization consultation, WHO/FSF/FOS/97.6, Geneva.

WHO/ICD, 1999. *Training course on HACCP. Principles and practice*, World Health Organization, Geneva.

WHO, 2000. *Variant Creutzfeld-Jacob disease (vCJD)*, Fact sheet 180, World Health Organization. http://www.who.int/inf-fs/en/fact180.html (in 2001).

9. Injuries

Ilona Koupilova, Martin McKee, David A. Leon, Dinesh Sethi and Anthony Zwi

Summary of existing knowledge
- Out of every 10 children (aged 1–14 years) who die in the European Region, between three and four die as a consequence of injury.
- The burden of health conditions is substantial, especially in central and eastern Europe and the former Soviet Union.

Main challenges
- To increase knowledge of the determinants of childhood and adolescent injuries in each country.
- To improve understanding of how specific beliefs, attitudes and types of behaviour affect the risk of injuries in children and adolescents.
- To evaluate the effect of different policies and interventions in a range of settings.
- To promote the adoption of the most appropriate policies and the implementation of relevant programmes.

Action points
- Develop national and regional capacity to collect and analyse data that can assess patterns of injury and their causes in each country and use these data to inform development of effective and locally relevant policies and interventions.
- Promote a culture that accepts the need to develop and effectively implement appropriate legislation and safety standards to create an environment in which there is a reduced risk of injuries.
- Promote appropriate education on ways of reducing risk of injury, while recognising that education alone is insufficient.
- Enhance health systems for managing injuries, including improved responses by emergency and trauma services and effective rehabilitation.

9.1. Introduction and definitions

The risk of childhood injury in a population reflects the physical, social and emotional environment within which children live. In the home, children are at risk from environmental hazards such as those associated with the absence of restraints to stop them falling, from fires caused by unsafe electrical connections which are then undetected because of absent smoke alarms, from dangerous chemicals and medicines in containers that lack childproof caps, from toys with small parts on which they can choke, and from falls in unlit and uneven passages. They are at risk on the roads as passengers, pedestrians and cyclists. In cars and buses, risks come from inadequate use of car safety seats and seat belts and from speeding drivers when speed limits are not enforced. As pedestrians they are at risk when roads are their only playground and when traffic and people are not physically separated. As cyclists, the absence of appropriate safety gear such as helmets may increase risk of severe injury. At school and at play they are at risk from unsafe equipment in playgrounds and from drowning in unfenced waterways. Wherever and whichever dangers exist in the physical environment, they frequently indicate an underlying failing in the social and emotional environment, in which designing a society that is safe for children is not seen as a priority (Zwi, 2000).

A first step in making something a priority is to make the scale of the problem visible. Although injuries are a major cause of premature death and their costs to society are high (Baker *et al.*, 1992) the scale of the problem they present is often underestimated. An understanding of the level and causes of childhood injuries in a population is central to any analysis of environmental threats to child health.

This chapter summarises the case for regarding injury as a major threat to the welfare of the children of Europe and one that is insufficiently recognised by politicians and other policy-makers. It also shows the enormous variation in rates of injury across the region, highlighting the scope for developing a Europe-wide initiative that would enable policy-makers to learn from best practice and thus to implement effective preventive policies.

First, it is necessary to provide some basic definitions. 'Injury' is a broad term covering a multitude of types of health problem each of which is associated with different factors and for which different types of interventions are possible.

The most basic classification of injuries is according to whether they are intentional or unintentional. Intentional injuries include homicide and interpersonal violence, wars and other forms of collective violence, and suicide and other forms of self-harm. Unintentional injuries are typically classified according to the means of their occurrence: poisoning, burns and scalds, drowning, falls and transport-related.

We deliberately avoid use of the term 'accident' in this chapter. Even when applied to unintentional injury it suggests that injury is in some way random, as illustrated by the saying 'accidents do happen', and by inference the resulting injuries are thought to be less amenable to systematic programmes of prevention than is in fact the case.

Finally, for most purposes, injuries can be considered as synonymous with the term 'external causes' that is used in statistics of mortality, consistent with the terminology used in the International Classification of Diseases.

9.2. The burden of disease

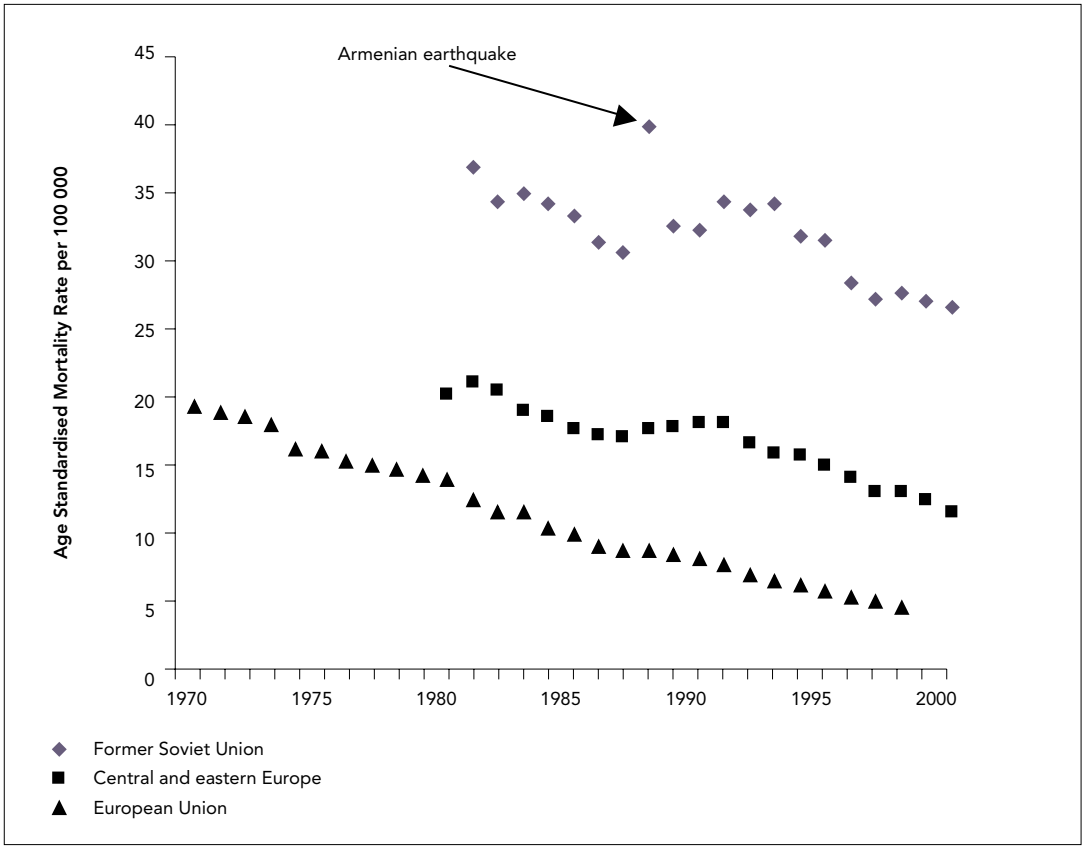
A regional overview

Out of every 10 children aged 1–14 years who die in the European Region, between three and four die as a consequence of injury. Injuries therefore make a much larger contribution to childhood mortality than do other leading categories of childhood death such as cancer or infectious disease. At a regional level the contribution is relatively consistent: in 1995 33 % of deaths of children aged 1–14 in the countries of the European Union were due to injuries, compared with 40 % in the countries of central and eastern Europe and 34 % in the countries of the former Soviet Union. However, as will be seen later, this disguises considerable variation between countries and, in the former Soviet Union, the figure is influenced by the relatively high mortality from infectious diseases in the central Asian republics, where the overall pattern of mortality resembles more closely that seen in developing countries.

The subsequent analyses are based primarily on mortality data supplied to WHO and, in particular, from the WHO Regional Office for Europe's Health for All database (WHO, 2002). Looked at over time there has been a striking fall in childhood deaths from injury in western Europe, with recently observed rates decreasing to around half what they were in 1970 (Figure 9.1.). The decline in central and eastern Europe has been much smaller and less consistent. The former Soviet Union saw little decline until the mid-1990s.

Trends by region in external cause mortality among children aged 1–14 year Figure 9.1.

Source: WHO, 2002

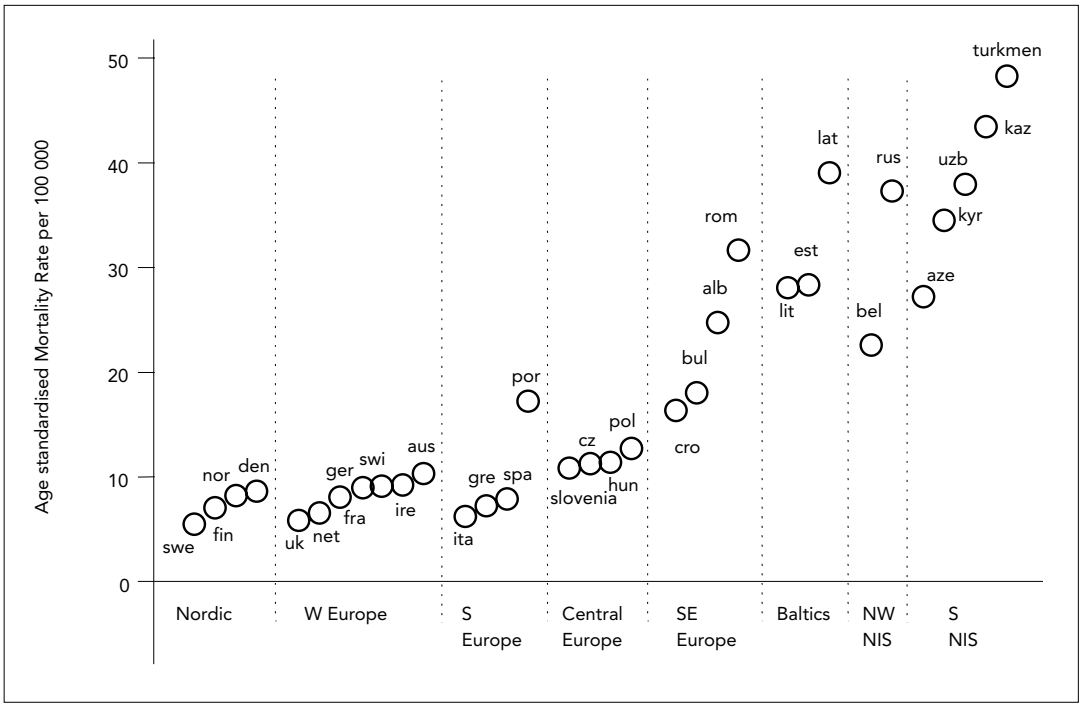


Countries also differ

A striking feature of the problem of injury mortality in Europe is the huge variation between countries. As expected, given the trends in Figure 9.1., there is a huge gap between east and west. This can also be seen in Figure 9.2. which provides more detail by dividing the eastern transition countries into five subregions: central Europe, south-eastern Europe, the Baltic states (Estonia, Latvia and Lithuania), the north-western newly independent states (the Russian Federation, Ukraine and Belarus) and the south-western newly independent states (Trans-Caucasian and Central Asian Republics). Western Europe has been divided into three subregions: the Nordic area, western Europe and southern Europe.

Figure 9.2. **Injury mortality rates from external causes among children aged 1–14 years by subregion (showing countries), 1993**

Source: WHO, 1998



Even within western Europe there is a two- to three-fold variation in mortality but this variation is relatively minor compared with the scale of the differences in eastern Europe. The extremely high rates seen in the former Soviet countries are particularly disturbing, reaching up to more than eight times higher than in the best-performing countries in western Europe. These very high rates are not confined to the Central Asian Republics, where there are some concerns about the quality of mortality data, but are also seen in the Baltic states of Estonia, Latvia and Lithuania that are hoping soon to join the European Union. The contribution of externally caused deaths to total childhood mortality is much higher in the Baltic States and the Russian Federation than in other countries in the east or west. In the Baltic states more than 60 % of male deaths in the age group 1–19 years are attributable to external causes, while among females it is more than 50 %. Among males aged 15–19 years 83 % of all deaths are accounted for by external causes, compared with less than 60 % in central or western Europe.

The pronounced variations in injury mortality rates between subregions of Europe are apparent for boys as well as girls as shown in Table 9.1. However, it is also clear that at every age and in every subregion injury mortality rates are higher in boys than girls and this sex difference becomes larger with age.

9.3. The contribution of injuries to the overall burden of disease

Injuries do not only kill children. They also cause disability, at times lifelong. No internationally comparable data exists on levels of non-fatal injuries for the European Region. However studies conducted in the United Kingdom, the Netherlands and the United States show that mortality from injuries represents the tip of a huge iceberg of morbidity. A recent national study of

injuries in the Netherlands in 1996 estimated that for every death from injury in children there were 160 hospital admissions, 2 000 accident and emergency visits and 6 200 non-fatal injuries of all types. Even if we assume that these estimates are too high by a factor of two, the levels of mortality found in this region still translate into an enormous number of serious injuries in children requiring hospital attention. Estimates range from 40 000 per year in Sweden, to 6.5 million children per year in the Russian Federation.

Mortality rates (per 100 000) from external causes by age, sex and subregion, 1992–93 Table 9.1.

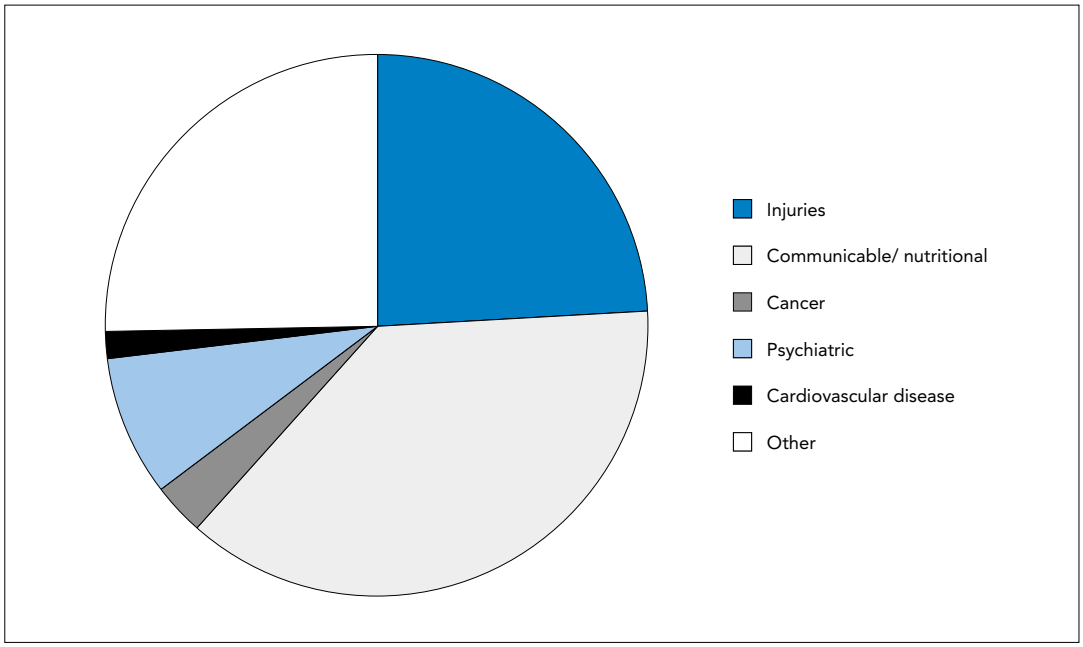
Source: WHO, 1998

Subregion	1–4 years		5–9 years		10–14 years		15–19 years	
	Male	Female	Male	Female	Male	Female	Male	Female
Southern NIS	75.4	58.7	34.6	18.2	33.4	13.6	75.2	25.9
North-western NIS	50.0	35.8	42.2	19.2	42.5	16.3	145.7	44.4
Baltic states	57.7	33.4	41.1	16.8	41.4	16.2	133.2	33.1
South-eastern Europe	44.8	31.9	30.2	14.9	28.6	10.7	60.2	18.7
Central Europe	18.6	13.1	13.4	7.1	15.7	6.5	63.5	17.5
Southern Europe	11.5	8.5	8.3	4.4	10.8	5.0	57.3	15.2
Western Europe	11.8	8.1	7.6	4.2	9.6	5.4	48.4	16.3
Nordic	8.3	5.2	9.9	3.5	8.8	4.7	45.8	15.3

Although making numerous assumptions and thus subject to many caveats, *The Global Burden of Disease* study (Murray and Lopez, 1996) has attempted to combine death and disability from leading causes by generating a measure called the disability adjusted life year in each of a number of world regions. Figure 9.3. shows the relative contribution made by the main groups of causes in the former socialist economies among those aged 1–14 years. Injuries account for almost a quarter of the total disease burden in this age group. The relatively large contribution by communicable diseases is driven by their high levels in the Central Asian Republics: as already noted, in countries of central and eastern Europe, the Russian Federation and its post-Soviet European neighbours the contribution by injuries is very much greater.

Contribution of major causes to overall burden of disease among children aged 0–14 in the former socialist economies, 1990 Figure 9.3.

Source: Murray and Lopez, 1996



The contribution to the east-west mortality difference

The scale of premature death from injuries in the east of the European Region is so great that if mortality rates from external causes in each of the transition countries could be reduced to the average of the western countries the east-west gap in total childhood mortality could be reduced considerably. In fact, the death rate among males aged 10–19 in central Europe would fall to the western European average. In the north-west former Soviet Union (the Russian Federation, Belarus, Ukraine) it would narrow by 80 % and in the Baltic states by 90 %. Because of the relatively greater contribution from communicable diseases in the southern part of the former Soviet Union and south-eastern Europe the gains would be smaller but still highly significant, with reductions in the gap with the west of between 20 % and 65 % depending upon age and sex. Another way of looking at the potential benefits of effective policies is that if death rates from external causes in transition countries in the 1990s had been reduced to the average for western Europe then about 32 000 fewer children and young adults (aged 1–19 years) each year would have died. Of course we recognise that if injury deaths were totally reduced children may then die from other causes, so the east-west gap may not be totally removed, but the fact that they could be so significantly reduced deserves our attention.

What contribution do different types of injury make?

Deaths from external causes can be thought of as falling into three categories:

1. transport injuries;

2. other external causes excluding violence (e.g. drowning, fires and falls);

3. suicide, homicide and other violence.

The contribution of these three categories is shown in Figures 9.4. and 9.5. by age and subregion and for males and females respectively.

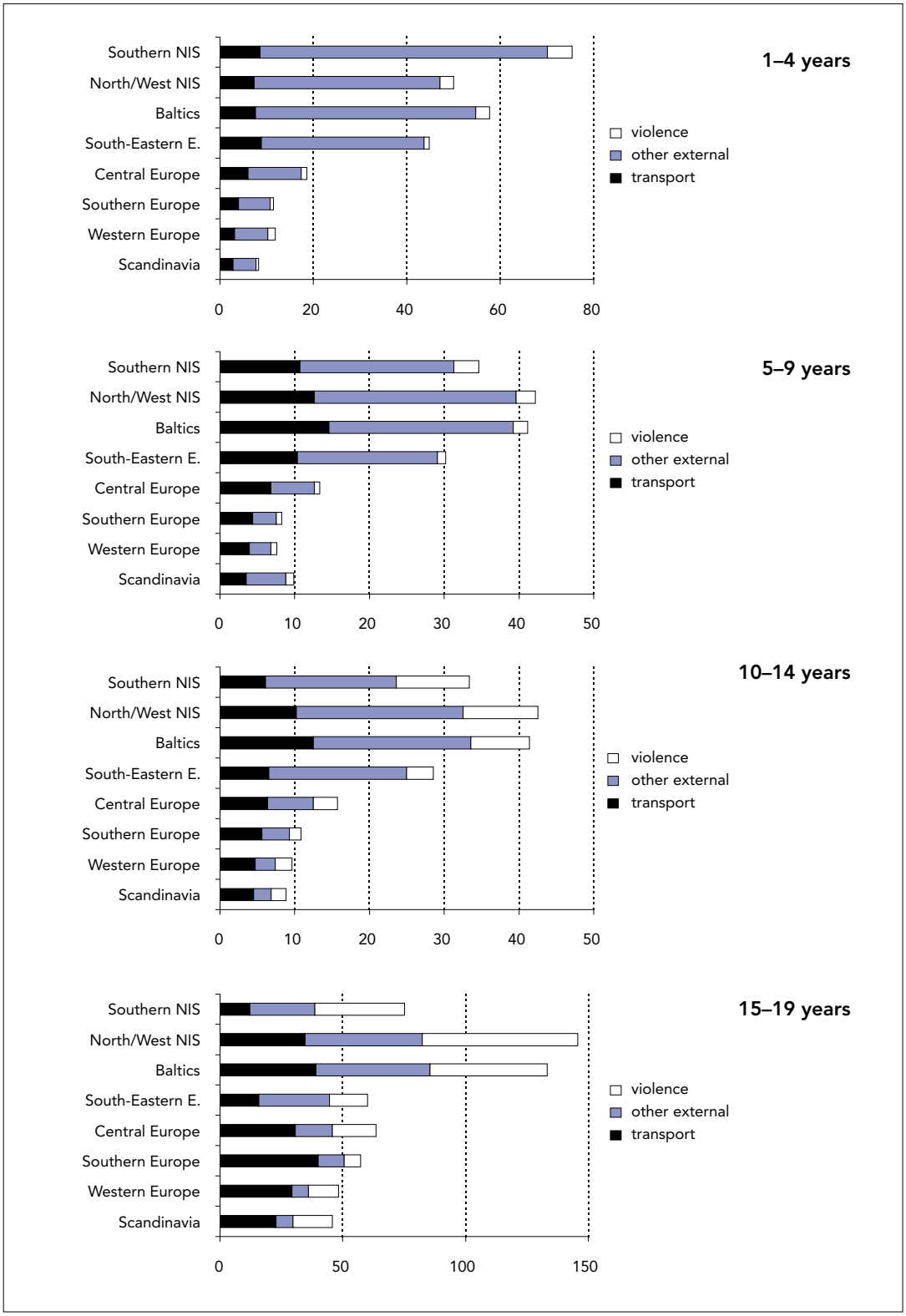
One of the most important implications of these figures is that they challenge the widely held assumption that deaths from injury among children in Europe are predominantly due to motor vehicle collisions. It is clear from Figures 9.4. and 9.5. that the east-west differences for external causes as a whole are driven mainly by the group of other external causes. These include drowning, accidental poisoning, fire and falls. There is a much more pronounced difference between the west and the transition countries for this group of causes than with mortality from either motor vehicle accidents or violence. For example, rates of motor vehicle deaths in Baltic countries such as Latvia are five times higher than in Sweden, but the figure is nine times higher for 'other external causes'.

Another notable contrast is that, for motor vehicle and violent deaths, there is a tendency for the highest rates to be in the Russian Federation and the Baltic states, with mortality from these causes in the southern former Soviet countries being relatively low. In contrast, the southern former Soviet countries tend to have the highest rates of all for the 'other external causes'. Thus in the former Soviet Union, mortality from motor vehicle injuries and violence is particularly associated with higher levels of urbanisation and industrialisation.

In every age group and both sexes, transport injuries (mainly related to motor vehicles) vary less between east and west than the aggregate of other external causes (excluding violence). This group of other external causes in the transition countries, however, becomes proportionally less important with increasing age, as deaths from violence become more important. The increase in mortality from violence with age is particularly steep in the Baltic states and the north-west part of the former Soviet Union. The relative differences between males and females are in general rather similar in each subregion at each age.

Mortality rates (per 100 000) from external causes by category among males by age and subregion, 1992–93

Figure 9.4.

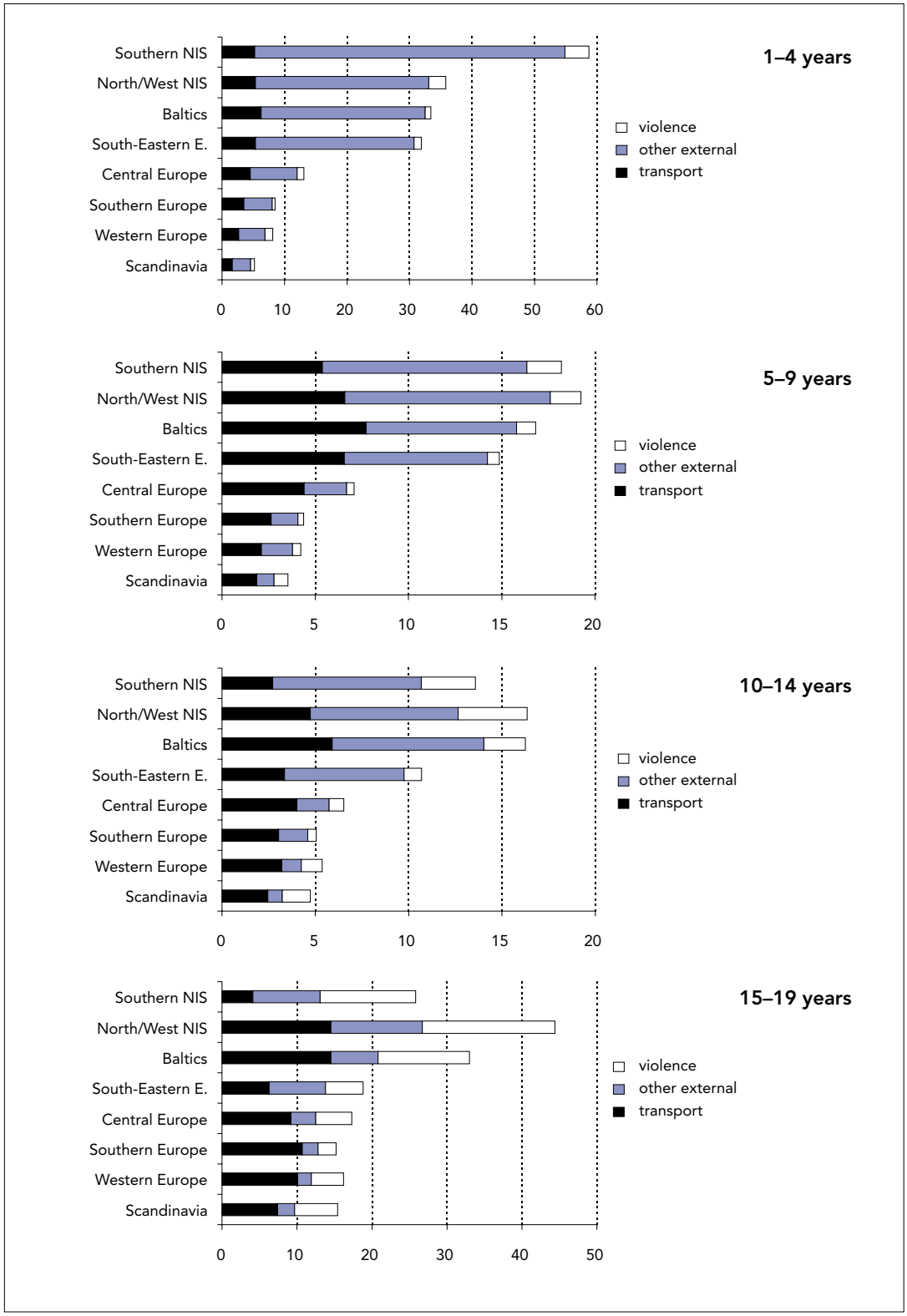


Source: WHO, 1998

Note: Scale for mortality rates varies by age group

Figure 9.5. **Mortality rates (per 100 000) from external causes by category among females by age and subregion, 1992–93**

Source: WHO, 1998



Note: Scale for mortality rates varies by age group

Transport injuries

Although transport collisions are not the main cause of the east-west gap in injury mortality, there are notable differences between subregions, particularly under the age of 10 years. Death rates among children in transition countries are between two and three times higher than in Scandinavia. In the oldest age group (15–19 years), however, there is no consistent pattern between east and west. For example, while rates in southern Europe among young men are

higher than in any of the transition countries, rates in the southern part of the former Soviet Union among 15–19 year olds are the lowest of any subregion.

What can explain the variation by age in the broad east-west pattern? In the oldest age group, a substantial proportion of deaths from motor vehicle collisions are among passengers in vehicles. At younger ages, children dying are more likely to be pedestrians. Although there are no reliable data on vehicles and mileage driven for each of the subregions, it is very likely that the number of vehicles in transition countries in 1992–93 and the mileage driven per head of population was lower than in the west, although it increased steeply after the end of the Cold War. It therefore seems most likely that the absence of a clear east-west difference at age 15–19 could reflect the lower access to vehicles in the east. Of course, this may conceal a situation in which a lower rate of vehicle use is associated with a much higher rate of fatalities per mile driven in transition countries. For young children, however, even a relatively low number of vehicles on the roads may pose a major hazard to pedestrians. There is clearly a great need to understand much better the relative contribution to overall deaths on the roads of unsafe driving, lack of road regulation, absence of enforcement, poor quality of roads and vehicles, lack of supervision or road safety training for children, or even weaknesses in emergency services or trauma care. The particular role of public transport vehicles, which may be more amenable to public policy interventions, also deserves attention. This must be a priority for future research, which could be undertaken relatively easily.

Drownings, accidental poisonings, fires and falls

The group of 'other external causes' consists of deaths from drowning, fires, falls, unintentional poisoning, drugs causing adverse effects, misadventures during medical care and 'other accidents including late effects'.

One of the most surprising findings is that deaths from drowning show some of the largest and most consistent east-west differences, particularly in the age range 5–14 years. It is, however, still unclear whether these deaths are mainly in rivers or in poorly supervised swimming pools. The higher rates of drowning in the youngest age group (1–4 years) compared with older children (5–14 years) in the Baltic republics and the southern part of the former Soviet Union suggests that unsupervised access to unfenced expanses of water or wells may play a role.

Interventions that improve swimming skills, while of great benefit for many reasons, are unlikely to have a major impact on drowning in this youngest age group. Other interventions such as fencing off unprotected areas and providing supervised areas for recreational swimming are likely to be of value. Among adolescents it is plausible that many cases of drowning are associated with alcohol intoxication, especially in view of the substantially higher rate among males in the Baltic republics and the north-west part of the former Soviet Union.

In absolute terms, deaths from falls and fire do not contribute greatly to the east-west difference, although rates are higher in all parts of the former Soviet Union. Deaths from accidental poisoning in most of the transition countries are many times more frequent than in the west, particularly in children under five years of age.

Violent deaths

Deaths from violent causes in childhood (1–14 years) are relatively rare in the transition countries, but are nevertheless still more common than in the west. In the former Soviet Union approximately 1 in 10 000 boys aged 10–14 years died from violent causes in 1992–93 — a rate five times higher than in Scandinavia, western or southern Europe. Under the age of 10 most violent deaths are from homicide or it is undetermined whether they were intentional or not. Suicide rates only become important from the age of 10 upwards, where they rise particularly steeply for males. The much higher rates of violent deaths among 15- to 19-year-old males in all subregions are due to steep increases in deaths from homicide as well as suicide. Homicide rates in young men are particularly high in the Baltic and the newly independent states. This is reflected in the fact that in these parts of the former Soviet Union between 30 % and 40 % of violent deaths in young men and women are due to homicide, while in Scandinavia and western Europe homicides make up between 5 % and 15 % of violent deaths in young men and women.

9.4. What we do not know

This chapter has drawn extensively on routinely collected mortality data, largely because it is one of the few sources available to describe the scale of the problem. There is, however, a great need for a much better understanding of the scale of the problem, its underlying causes, and the scope for effective action. Specifically, a detailed understanding of the epidemiology of childhood and adolescent injuries is missing in many countries, including the settings in which injuries occur and the risk factors and risk situations that contribute to them. What research does exist has been undertaken predominantly in a few western countries. There is also little research on the contribution of, and interaction between, specific beliefs, attitudes, and practices to the rate and pattern of injuries in many countries.

9.5. Control measures

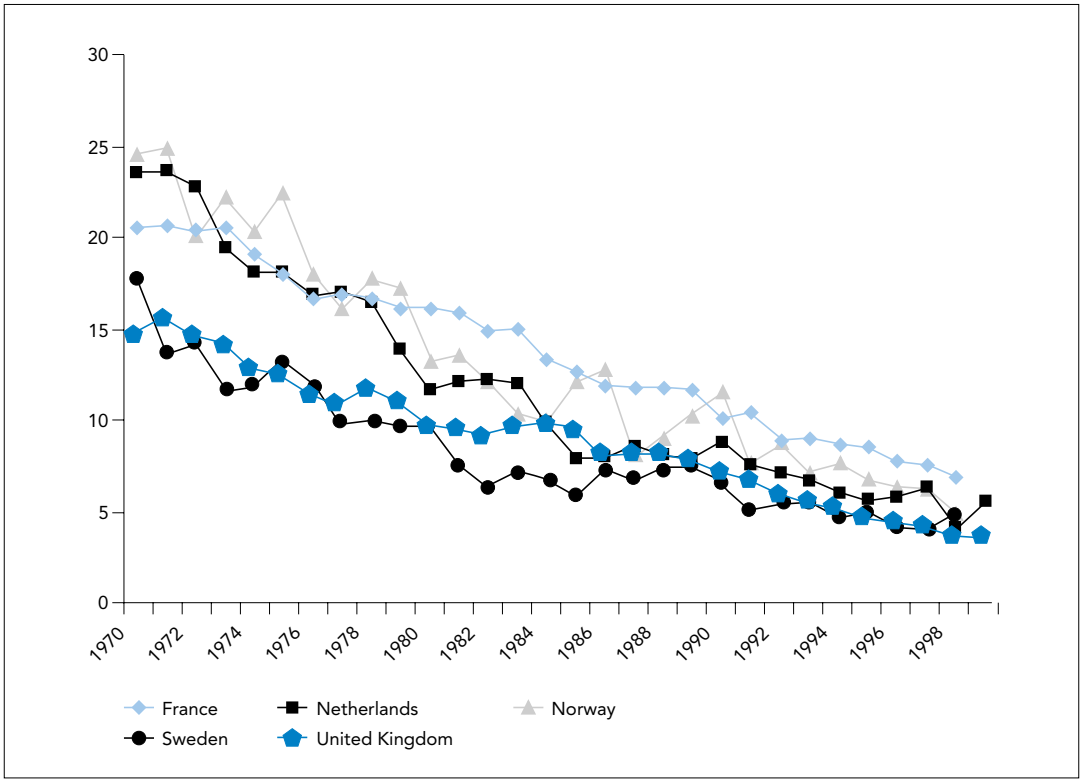
The evidence presented in this chapter highlights the substantial burden of injuries in children and adolescents in the transition countries of the east. It also powerfully demonstrates the contribution they make to the mortality gap between east and west, and highlights the urgent need for appropriate public health and social policy responses.

While there are always competing claims for the attention of policy-makers, the problem of injuries in children and adolescents in the transition countries of Europe has many features that should move it up the policy agenda. The scale of morbidity and the now-documented resultant loss of life, the associated use of health services and disability in a vulnerable age group, once they become clearly recognised, will be difficult to ignore. But it is not only the scale of the problem that speaks in favour of action; it is that effective injury reduction strategies exist and have already been implemented in many countries.

Several countries in western Europe have achieved considerable success in reducing deaths from injury (Figure 9.6.).

Figure 9.6. **Trends in deaths from external causes, per 100 000, age 0–14, in selected countries)**

Source: WHO, 2002



These societies have also demonstrated some of the many features of effective policies from which other countries can learn: the importance of raising the public profile of injuries; the central role of concerned civil society organisations; and the critical role of research in making the issue visible, assessing effectiveness of interventions and instituting solutions.

The evidence of effectiveness has been brought together in a number of recent reviews, a particularly good example being the report on prevention of unintentional childhood injuries by the United Kingdom Centre for Reviews and Dissemination (CRD, 1996). Some of its key points are as follows.

- Reduction of road injuries can be achieved through area-wide urban safety programmes, in particular where they are part of an integrated transport strategy that reduces car use and physically separates pedestrians from vehicles.
- Safety education aimed at drivers or children may increase knowledge but has little effect on injury rates. Instead, given the clear link between speed and severity of injury, traffic calming measures may be more effective.
- The use of cycle helmets reduces the probability of a serious head injury but making helmet-wearing compulsory is controversial because of fears that it could reduce the overall amount of cycling. Appropriate use of car restraints for young children also reduces the extent of injury.
- In the home, safety can be considerably enhanced by improved design, such as childproof containers, coiled power leads on electric kettles, and installation of smoke detectors. Targeted home visits by appropriately trained staff can increase the use of such devices but programmes on general home safety have had disappointing results.
- Community-based interventions, if targeted using relevant information on local patterns of injuries and their causes, have also been shown to reduce rates of injuries.

A word of caution is required. Most of the studies of interventions to prevent injuries have been carried out in a small number of advanced industrialised countries (CRD, 1996), and more work is required to be sure about their transferability to the often rather different context in central and eastern Europe. Policies and interventions need to be fine-tuned to local contexts: public health practitioners need to play a part in adapting good practice derived elsewhere to the social, political and health system structures in other settings (Zwi, 1996).

Even now it is possible to anticipate some potential problems with specific interventions that have been used successfully elsewhere (Forjuoh, 1996). Many aspects of enforcement of road safety depend upon the existence of a well-trained, highly motivated, and above all, uncorrupted police force. Thus, mobile radar control, which has been successfully used in many countries to enforce speed controls, may be less effective in other circumstances. Similarly the free distribution of smoke alarms, as a means of reducing childhood deaths from fires, may be considered unaffordable in some countries' economic circumstances. Successful drowning prevention programmes in western countries have used a combination of pool fencing, early swimming lessons and increased supervision (Modell, 1993; Kemp and Sibert, 1992). The balance between these different interventions will need to be closely attuned to the magnitude, form and distribution of drowning and may need to concentrate, for example, far more on open swimming areas such as wells, dams, lakes, rivers and beaches than on swimming pools and the need to fence them off. However, whatever the injury, the success of effective interventions from the west should stimulate countries with high mortality rates from injuries to intensify their efforts to reduce them.

Further research on the applicability of evidence on effectiveness of interventions in transition countries is needed to inform the policy process and to ensure that changes are based on evidence whenever possible. Unfortunately, in most parts of central and eastern Europe and the former Soviet Union, injuries have yet to get on to the health policy agenda (McKee *et al.*, 2000).

Summary

The contribution of injuries to the overall burden of disease in children and adolescents in the European Region is substantial. Injuries do not only kill children, they also cause disability, at times lifelong. Out of every 10 children aged 1-14 years who die in Europe, between three and four die as a consequence of injury. The mortality rates from external causes are particularly high in the former Soviet Union countries, reaching up to more than eight times higher than in the best-performing countries in western Europe. Road-traffic accidents represent the first cause of injuries across Europe, but the east-west differences are driven mainly by drowning, accidental poisoning, fire and falls. In the former Soviet Union, mortality from motor vehicle injuries and violence is particularly associated with higher levels of urbanisation and industrialisation.

The scale of the problem, particularly in the transition countries of Europe, speaks in favour of immediate action. Effective injury reduction strategies exist and have already been implemented in many countries. They include urban safety programmes, safety education aimed at drivers, use of cycle helmets and appropriate use of car restraints for young children, home safety programmes and community-based interventions using relevant information on local patterns of injuries and their causes. Further research on the applicability of this evidence on effectiveness of interventions in different settings is needed to inform the policy process.

Acknowledgement

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References

Baker, S.P., O'Neill, B., Ginsburg, M.J. *et al.*, 1992. *The injury fact book*, 2nd edition, Oxford University Press, New York.

CRD, 1996. Unintentional injuries in young people, Centre for Reviews and Dissemination, *Effective Health Care Bulletin*, Vol 2, pp. 1–16 http://www.york.ac.uk/inst/crd/ehc25.pdf

Forjuoh, S.N. and Li, G., 1996. A review of successful transport and home injury interventions to guide developing countries, *Soc Sci Med*, Vol 43, pp. 1551–60.

Kemp, A. and Sibert, J.R., 1992. Drowining and near drowning in children in the United Kingdom: Lessons for prevention, *British Medical Journal*, Vol 304, pp. 1143–6.

McKee, M., Zwi, A., Koupilová, I. *et al.*, 2000. Health policy-making in central and eastern Europe: Lessons from the inaction on injuries? *Health Policy Planning*, Vol 15, pp. 263–9.

Modell, J.H., 1993. Drowning, *N Engl J Med*, Vol 328, pp. 253–6.

Murray, C.J. and Lopez, A.D., 1996. *The global burden of disease*, World Bank, Harvard School of Public Health and World Health Organization, Harvard Press, Boston, MA.

WHO. (accessed 1998) *Mortality database,* online at: http://www.who.int/whosis/mort/download.htm#datafiles, Geneva, Switzerland.

WHO, 2002. *Health for all data base:* European Region (Computer file). WHO Regional Office for Europe, Copenhagen.

Zwi, A.B., 1996. Injury control in developing countries: Context more than content is crucial, *Injury prevention*, Vol 90, pp. 593–5.

PART III:
Environmental exposures associated with multiple health effects

Andreas Schürmann (age 13), Switzerland

10. Environmental tobacco smoke

Carol M. Courage
Contributing authors: Giorgio Tamburlini, Ondine S. von Ehrenstein

Summary of existing knowledge

- Both environmental tobacco smoke and maternal smoking during pregnancy, increase the risk of sudden infant death syndrome, low birth weight, reduced lung function, asthma, lower respiratory illness and middle ear infection.
- The health burden in Europe is substantial, given the high smoking rates in many European countries.

Main challenges

- To eliminate children's exposure to environmental tobacco smoke.
- To create a smoke-free environment from the beginning of fetal development.

Action points

- Implement legislation and other effective measures at the appropriate government level for systematic protection of children from exposure to environmental tobacco smoke.
- Institute public health policy and actions that aim at the elimination of exposure to tobacco smoke pollution by creating smoke-free environments for everyone.
- Implement educational and promotional campaigns to facilitate compliance with this legislation and also to encourage smoke-free homes.
- Develop an integrated multisectoral response involving, among others, the health, environment and education ministries as well as appropriate non-governmental organisations.

10.1. Introduction

Environmental tobacco smoke (ETS) is an aged, diluted mixture of mainstream smoke, that is smoke exhaled by smokers, and sidestream smoke, that is smoke emitted from the burning tip of the cigarette. The inhalation of ETS is known as 'involuntary smoking' or 'passive smoking'. More than 4 000 compounds have been identified in laboratory-based studies as components of mainstream smoke and at least 42 of these were classed as carcinogenic to laboratory animals, many of them known or suspected human carcinogens (NRC, 1986).

Children are exposed to ETS when people smoke, be it at home, visiting friends' homes or at other venues where people smoke. It is not possible at present to measure exposure to ETS directly because of its complexity. However, two approaches are used to estimate exposure to ETS. Firstly, data on the smoking habits of people in environments where the child spends time, for instance in the home, can be collected by questionnaire. The second approach involves measurement of components of ETS, or their metabolites; the most frequently used is cotinine, a metabolite of nicotine, which can be measured in the blood, serum, urine, saliva or hair. Cotinine levels increase with increased exposure to ETS (Henschen *et al.*, 1977).

10.2. Health effects of environmental tobacco smoke

Fetal and perinatal effects

Tobacco smoking has been associated with adverse changes in the fertility of women and in reductions in sperm number and quality that may impact on the reproductive competence of would-be parents (Kulikauskas *et al.*, 1985; Davis, 1991; Tuormaa, 1995; CA EPA, 1997; Ji *et al.*, 1997).

Active smoking by mothers has been shown to significantly reduce the rate of fetal growth in a dose-dependent manner, resulting in the birth of small-for-age babies; reported reductions in weight vary but are approximately 10 % for mothers who smoke heavily throughout pregnancy (Charlton, 1994). DiFranza and Lew (1995) calculated an odds ratio of 1.82 for the association between maternal smoking and low birth weight (<2 500 grams) using data from 23 studies; other studies have shown that smoking mothers may have up to a three-fold increased risk of having a small-for-gestational-age baby. Consumption of caffeine and alcohol are also known to retard fetal growth and these effects have been shown to be synergistic with the intrauterine growth retardation caused by maternal smoking during pregnancy (Olsen *et al.*, 1991; Andersen *et al.*, 1992). The risk of intrauterine growth retardation associated with maternal smoking appears to increase with maternal age, from two-fold for mothers aged 17 years to five-fold for mothers aged 35 years (Charlton, 1994). Although smoking throughout pregnancy is known to affect birth weight, there is some evidence that the final trimester may be particularly important (Charlton, 1994; Tuormaa, 1995). In some studies, babies of smoking mothers have been reported to be shorter and to have

smaller head circumferences at birth than babies of non-smoking mothers (Elwood *et al.*, 1987; Charlton, 1994).

In addition to the observed intrauterine growth retardation resulting in small-for -age babies, there is some evidence of an association between maternal smoking and premature birth (Tuormaa, 1995), though not all studies demonstrate this. Maternal smoking during pregnancy has also been associated with increases in miscarriage (up to 28 weeks gestation) and perinatal mortality (up to 28 days after birth, including stillbirth), of around 25 % or more (Charlton, 1994; Gidding *et al.*, 1994; DiFranza and Lew, 1995; Table 10.1.). Studies reviewed by Tuormaa (1995) showed increases of 5–70 % in miscarriage in smoking mothers. The role of ETS in ectopic pregnancies, however, is not yet clear.

Table 10.1. **Summary of pooled relative risks from meta-analysis of studies of fetal and perinatal effects of exposure to tobacco products**

Endpoint	Risk measure	Number of studies
Low birth weight	RR = 1.82 (95 % CI 1.67–1.97)	23 studies
Perinatal mortality	RR = 1.26 (95 % CI 1.19–1.34)	23 studies
(inc. stillbirth)	OR = 1.23 (95 % CI 1.21–1.41)	2 studies
Miscarriage	RR = 1.24 (95 % CI 1.19–1.30)	7 studies
	OR = 1.32 (95 % CI 1.18–1.48)	6 studies

Source: Di Franza and Lew, 1995

Exposure of pregnant women to ETS, usually from their smoking partner or other household member, has only been investigated in a few studies. In some, but not all, a reduction in mean birth weight or an increase in the risk of having a low-birth-weight baby was observed in the mother's exposure to ETS, although the effect was always smaller than for actively smoking mothers. Some of the studies showed no significant effects of maternal exposure to ETS during pregnancy and others failed to control for variables such as gestational age or alcohol consumption (Martin and Bracken, 1986; Haddow *et al.*, 1988; Lazzaroni *et al.*, 1990; Zhang and Ratcliffe, 1993; Charlton, 1994; Mainous and Hueston, 1994; Martinez *et al.*, 1994; Eskenazi *et al.*, 1995).

Regardless of cause, low birth weight is associated with higher risks of mortality and morbidity in infancy and early childhood (Royal College of Physicians, 1992) but the risk of perinatal mortality for babies of smoking mothers has been reported to be 25–56 % higher than for babies of non-smoking mothers for all birth-weight categories (Gidding *et al.*, 1994).

Postnatal effects of ETS exposure

The relative contribution of prenatal or postnatal ETS exposure to the adverse health effects observed postnatally cannot usually be determined. Where attempts have been made to obtain such information, this has usually been done by including in the studies mothers who have given up smoking during pregnancy but have started again after the birth of the child.

Sudden infant death syndrome

Sudden infant death syndrome (SIDS) is defined as unexplained mortality occurring in the post-neonatal period (1–12 months). The association between maternal smoking and SIDS is firmly established: typically, there is approximately a two- to three-fold increase in risk for prenatal smoking with a slightly smaller effect for postnatal smoking only. However, distinguishing the relative importance of the two time periods is quite difficult since there is generally a high correlation between smoking during and after pregnancy. Dose-response effects have been observed for both prenatal and postnatal maternal smoking (Couriel, 1994; Gidding *et al.*, 1994; DiFranza and Lew, 1995; Anderson and Cook, 1997; Table 10.2.). Although Thornton and Lee (1998a) argue that much of the association between SIDS and maternal smoking could be explained by residual confounding, most reviewers consider the association to be causal. Given the magnitude of association and the consistency across studies, it is unclear what, as yet unidentified, risk factor could explain the association.

Table 10.2. **Summary of pooled relative risks from meta-analyses of SIDS**

Source: Di Franza and Lew (1995); Anderson and Cook (1997)

Reference	Risk measure	Comment
DiFranza and Lew (1995)	RR = 2.98 (95 % CI 2.51–3.54) (12 studies)	Maternal smoking
Anderson and Cook (1997)	OR = 2.08 (95 % CI 1.83–2.38) (19 studies) OR = 1.94 (95 % CI 1.55–2.43) (4 studies)	Prenatal maternal smoking (adjusted for variety of confounders) Postnatal maternal smoking

Respiratory illness including asthma

Children exposed to ETS are more likely to suffer from respiratory illness (bronchitis, pneumonia, cough and wheeze) and to be hospitalised because of the illness than unexposed children (Etzel, 1994; DiFranza and Lew, 1996; CA EPA, 1997; SCOTH, 1998). There is evidence of a dose-response relationship between exposure to parental smoking and lower respiratory illness in infants; pooled risk estimates are typically in the range 1.5 to 2.5 (DiFranza and Lew, 1996; Strachan and Cook, 1997). Respiratory illness in the first year of life has been reported to significantly increase even if the mother smokes only after and not during pregnancy (Gidding *et al.*, 1994; Jedrychowski and Flak, 1997). Bottle-fed infants exposed to maternal smoke have been reported to have higher odds ratios for respiratory illness than breastfed infants (Woodward *et al.*, 1990). The associations between exposure to ETS in children and both lower respiratory illness and respiratory symptoms are likely to be causal given the statistical significance, consistency of findings and evidence of dose-response (Cook and Strachan, 1997). The raised risk in households where people other than the mother smoke suggests that postnatal rather than prenatal exposure to ETS is responsible for the effect (Cook and Strachan, 1997). Furthermore, there is evidence that exposure to ETS leads to increased infant mortality from respiratory illnesses as well as increased morbidity (DiFranza and Lew, 1996).

Several studies suggest that exposure to ETS can cause small decreases in lung function and increases in bronchial hyper-responsiveness in schoolchildren, although the data are limited (Cook *et al.*, 1998; Cook and Strachan, 1998). Very low-birth-weight babies exposed to ETS may have even further reduced respiratory function (Doyle *et al.*, 1996), but evidence is limited.

Asthma is a common, chronic illness among children and the incidence and exacerbation of this disease has been investigated in children exposed to ETS. Meta-analysis of a number of studies has shown that maternal smoking is associated with an increase in infant and child asthma prevalence, although causality has yet to be established (Table 10.3.; DiFranza and Lew, 1995; Cook and Strachan, 1997; Strachan and Cook, 1998a). Studies of infants and older children have produced conflicting results about the association between paternal smoking and asthma prevalence (Cook and Strachan, 1997; Strachan and Cook, 1998a) (see also Chapter 3).

The question of the severity of asthma attacks being increased by exposure to ETS has also been investigated (DiFranza and Lew, 1996; Strachan and Cook, 1998a). No formal meta-analyses were carried out because of the variety of different methods and measures used: for example, frequency of wheezing episodes, persistence of symptoms between attacks, need for medication, use of health services or interference with daily activities, and some studies used a severity score compiled from the different indices. DiFranza and Lew (1996) reported that all seven studies they identified showed significant increased risk of exacerbated existing asthma by ETS exposure. Strachan and Cook (1998a) reported that of 13 studies (six also covered by DiFranza and Lew, 1996), six showed a significant positive association with exposure to ETS, and three others showed a non-significant positive association. They concluded that ETS was likely to be a co-factor provoking wheezing attacks, rather than a cause of the underlying asthmatic tendency.

As respiratory illness and asthma in children are more closely associated with maternal smoking than smoking of other household members, this may reflect the greater amount of time spent with their mother in the home, especially by infants and younger children. The association between ETS and asthma and atopic disorders is discussed in detail in Chapter 3.

Table 10.3. **Summary of pooled risks from meta-analyses[1] and individual risk estimates from studies of respiratory illness**

Reference	Endpoint	Risk measure	Comment
DiFranza and Lew (1996)	Asthma prevalence Cough incidence LRI	OR = 1.46 (95 % CI 1.14–2.85) RR = 1.43 (95 % CI 1.31–1.56) RR = 1.36 (95 % CI 1.26–1.46) OR = 2.50 (95 % CI 1.86–3.36) RR = 1.46 (95 % CI 1.33–1.60)	Children, all ages Aged 6–19 years Aged less than 5 years
Cook and Strachan (1997)	Asthma prevalence Wheeze prevalence Cough prevalence Phlegm prevalence Breathlessness prevalence	OR = 1.21 (95 % CI 1.10–1.34) OR = 1.24 (95 % CI 1.17–1.31) OR = 1.40 (95 % CI 1.27–1.53) OR = 1.35 (95 % CI 1.13–1.62) OR = 1.31 (95 % CI 1.08–1.59)	Maternal smoking greater effect than paternal; both significant Clear dose-response School-age children
Strachan and Cook (1998a)	Asthma prevalence	OR = 1.37 (95 % CI 1.15–1.64) OR = 1.59 (95 % CI 1.27–1.99)	Infants, case-control studies; Mothers only, no significant effects for fathers
Maier *et al.* (1997)	Asthma prevalence Current wheeze	OR = 1.6 (95 % CI 0.9–2.7) OR = 1.7 (95 % CI 0.9–3.1)	Household tobacco smoker
Margolis *et al.*(1997)	LRI incidence	RR = 1.5 (95 % CI 1.1–2.0) RR = 2.2 (95 % CI 1.3–3.8)	≤10 cigarettes/day >10 cigarettes/day
Lam *et al.* (1998)	Cough and phlegm incidence	OR = 1.19 (95 % CI 1.01–1.47) OR = 1.38 (95 % CI 1.07–1.79) OR = 1.85 (95 % CI 1.19–2.85)	1-smoking household member 2-smoking household members 3-smoking household members

Source: See references in Table 10.3.

LRI= lower respiratory infection.

[1] The pooled estimates from meta-analyses are from DiFranza and Lew (1996); Cook and Strachan (1997); Strachan and Cook (1997).

Middle-ear disease and adenotonsillectomy

The most frequent cause of deafness in children is middle-ear effusion commonly known as 'glue ear'. This condition often requires surgery to insert grommets and it can result in problems with language development and educational progress (Charlton, 1994). There is strong evidence for modest increases in middle-ear disease (glue ear) among children exposed to tobacco smoke, with children under five years of age being the most susceptible (Table 10.4.; DiFranza and Lew, 1996; SCOTH, 1998; Strachan and Cook, 1998b). Strachan and Cook (1988b) report a range of odds ratios of 1.0–1.6 for studies of acute middle-ear disease; a formal meta-analysis was not possible because of the lack of quantitative information on parental smoking activity. The limited data available suggest that adenoidectomy or tonsillectomy may be up to twice as likely in children exposed to ETS than unexposed children (Table 10.4.; DiFranza and Lew, 1996; Strachan and Cook, 1998b). The California Environmental Protection Agency estimated that the impact of ETS on acute and chronic middle-ear infections accounts for 700 000 to 1.6 million visits to doctors per year in the United States (CA EPA, 1997).

Table 10.4. **Summary of pooled risks from meta-analyses of ear disease and adenotonsillectomy**

Reference	Risk measure	Comments
Strachan and Cook (1998b)	OR = 1.48 (95 % CI 1.08–2.04) OR = 1.38 (95 % CI 1.23–1.55) OR = 2.07 (95 % CI 1.82–2.35)	Recurrent middle-ear disease Middle-ear effusion Adenoidectomy, tonsillectomy or adenotonsillectomy
DiFranza and Lew (1996)	OR = 1.58 (95 % CI 1.11–2.24) RR = 1.19 (95 % CI 1.05–1.35) OR = 2.06 (95 % CI 1.42–2.99)	All middle-ear disease Tonsillectomy and adenoidectomy; only two studies included

Source: Strachan and Cook (1988b); Di Franza and Lew (1996)

Postnatal growth and development

Association of prenatal exposure to ETS with effects on postnatal development is very difficult because children exposed prenatally are also likely to be exposed postnatally. Data from numerous studies show that reductions in height associated with maternal smoking during pregnancy persist into childhood (Fox *et al.*, 1990; Rush, 1992). It is likely that some of this association is related to postnatal exposure to ETS.

Although associating behavioural problems with one potential cause is difficult, a

number of studies have attempted to investigate associations between exposure to tobacco smoke products and mental and social development of children. Children of mothers who smoked during and after pregnancy have been reported to have small reductions in functions of mental development (for example, cognitive ability, spelling, reading, oral language, verbal comprehension) and more behavioural problems (for example, hyperactivity, distractability) (Naeye and Peters, 1984; Sexton *et al.*, 1990; Baumann *et al.*, 1991; Fried, 1992; Weitzman *et al.*, 1992). Two of these studies also reported that children of mothers who smoked after, but not during, pregnancy had lower mental and social development than children without this exposure to ETS (Baumann *et al.*, 1991; Weitzman *et al.*, 1992). These studies provide evidence that both prenatal exposure to tobacco products and postnatal exposure to ETS may be associated with reductions in mental and social development.

Cancer

A number of studies have investigated whether exposure to tobacco products either prenatally, from either an actively or passively smoking mother, or postnatally from parental smoking, increases the risk of childhood cancers (Trédaniel *et al.*, 1994; Sorahan *et al.*, 1995; CA EPA, 1997; Ji *et al.*, 1997; Thornton and Lee, 1998b). Most studies have found a non-significant slightly increased risk of cancer, although many of the studies did not look at a large number of cancer cases and may have required a longer follow-up (Trédaniel *et al.*, 1994). However, other evidence suggests that exposure to tobacco smoke products may carry an increased risk to children. Increased DNA-adducts have been found in blood samples from newborn babies exposed to tobacco products *in utero* (e.g. Everson *et al.*, 1986; Coghlin *et al.*, 1991; Hansen *et al.*, 1992). The combined evidence suggests that the exposure to environmental tobacco smoke products may be causally associated with childhood cancer, as is also pointed out in Chapter 5 on cancer.

10.3. Policies to protect children from exposure to ETS

The revised WHO *Air quality guidelines for Europe* conclude: 'ETS has been found to be carcinogenic in humans and to produce a substantial amount of morbidity and mortality from other serious health effects ... Acute and chronic respiratory health effects on children have been demonstrated in homes with smokers ... and even in homes with occasional smoking ... There is no evidence for a safe exposure level.' The WHO International Consultation on Environmental Tobacco Smoke and Child Health (Geneva, 11–14 January 1999) called for 'Swift action to highlight the need for strong public policies to protect children from exposure to tobacco smoke'.

The Framework Convention on Tobacco Control

The paramount importance of tobacco as a factor affecting health has been recognised by the World Health Assembly (WHA), which in resolutions adopted in 1999 and 2000 has set forth the process for Member States to negotiate the Framework Convention on Tobacco Control and to present it for adoption by the WHA in 2003. The framework convention will be an international legal instrument that will circumscribe the global spread of tobacco and tobacco products. The scope of the framework convention is subject to intensive negotiations between Member States, and ETS is one of the items on the agenda. The instrument will be developed by WHO's 191 Member States so that their concerns are adequately reflected throughout the process (WHO, 1999).

In January of 2001, the Chair's text of the Framework Convention on Tobacco Control noted that the national policies and measures should include the 'implementation of legislation and other effective measures at the appropriate governmental level that provide for systematic protection from exposure to tobacco smoke in indoor work places, enclosed public spaces, and public transport, with particular attention to special risk groups such as children and pregnant women'.

The second round of the global negotiations on the framework convention was held at the end of April 2001 in Geneva, Switzerland.

Lisbon Working Group

A WHO meeting, convened in Lisbon, Portugal, from 29 to 30 May 2000, reviewed the present approaches to protecting populations from ETS exposure implemented in the Member States (WHO, 2000). The reports submitted from the Member States describing current policies to deal with exposure to ETS indicate that the approaches vary widely across the countries.

Some level of smoking restriction is most common for schools, day-care centres, public transportation and public entertainment places (theatres, etc.). However there are still several countries with no such restrictions, and in those with regulations, the restrictions are not comprehensive and compliance is often poor. In six out of 22 reporting countries, smoking is not restricted at hospitals. Workplace regulation does not exist or is unclear in eight countries (out of 26 reporting), and in a further eight it covers only state or other public enterprises, but not private workplaces. More than half of the reporting countries have no restrictions on smoking in restaurants, cafeterias and other catering facilities. In all countries, there are problems with the effectiveness of the existing regulations in preventing exposure to environmental tobacco smoke. A summary view of the existing policies and regulations is reported in Table 10.5.

Number of countries with restrictions on tobacco smoking in public places mentioned in reports from 28 European countries

Table 10.5.

Source: WHO, 2000

	Banned / restricted	Partial restrictions	Unclear regulations	No restrictions	No information
Workplaces	10	8[1)]	8	-	2
Schools	19	2	-	-	7
Day-care centres	6	1	-	-	21
Hospitals	17	4	6	-	1
Urban transport	19	-	-	2	7
Long-distance transport	14	-	-	-	14
Restaurants, etc.	11	3	-	12	2
Entertainment centres, etc.	23	-	-	3	2

[1)] Smoking regulations in public (not private) workplaces only.

The meeting emphasised that actions against environmental tobacco smoke are probably the best way to reduce *active* smoking. It has been observed that the four most significant predictors of progress towards people quitting smoking are:

- smoke-free workplace
- smoke-free home
- thinking second-hand smoke is dangerous, particularly to children
- cessation assistance based on counselling and other non-medical methods.

In this respect, restrictions on smoking in the workplace are a potent tool for decreasing active smoking: smokers quit because of the inconvenience and the decreasing social acceptance of smoking. It was also reported that the latest evidence suggests that children of parents who smoke outside are less likely to start smoking themselves. Community-level action aimed at educating and mobilising non-smokers so that they will demand realisation of their right to clean air is an important tool in achieving reductions in ETS exposure. An important determinant of effective action is to make the message clear that it is the smoke, not the smoker, that is the enemy. Also, proper appraisal of the economic consequences of smoking bans is necessary. For example, contrary to the claims made by the tobacco industry, there was no decrease in restaurant revenues related to the introduction of smoking bans in restaurants (WHO, 2000).

There was a general agreement of the group that enforced legislation is required and that voluntary policies are not sufficient to deal effectively with ETS exposure. To generate and implement this legislation, local action for educating and mobilising people to demand smoke-free environments might be necessary in many countries. The approach aiming at reduction of exposure to ETS in homes should focus on children's health as a priority and as instrumental for eliminating exposure to tobacco smoke of the other members of the households also. The main conclusions and recommendations of the meeting are summarised in Box 10.1.

Box 10.1. Key recommendations from a WHO meeting on ETS (WHO, 2000)

Public health policy and actions should aim at the elimination of exposure to tobacco smoke pollution by creating smoke-free environments for everyone.

This goal should be achieved through a combined programme of legislation and education. Legislation is necessary to create smoke-free workplaces and public places, including restaurants, educational institutions, day-care centres and hospitals. Voluntary arrangements are not sufficient. For such legal instruments to be effective, they should have viable means of enforcement, be supported through educational and promotional programmes, and be equipped with appropriate sanctions for non-compliance.

Legal actions should be taken using existing laws to protect non-smokers and to require smoke-free environments. These actions should be supported to use existing laws and legal systems to protect the rights of non-smokers most effectively. Countries are encouraged to take appropriate action to hold the tobacco industry accountable for damage caused by second-hand smoke.

Educational and promotional campaigns should be implemented to facilitate compliance with this legislation and also to encourage smoke-free homes. States should educate the population regarding the right to smoke-free air, existing laws and dangers of involuntary smoking, including the fact that there is no safe level of exposure. Educational efforts on the particular dangers of second-hand smoke to children should be used as a critical part of educational campaigns designed to achieve smoke-free homes. These educational programmes should address parents, children, child health professionals and family doctors.

An integrated multisectoral response should be developed involving, among others, the health, environment and education ministries as well as appropriate non-governmental organisations.

References

Anderson, H.R., Bland, J.M. and Peacock, J.L., 1992. The effects of smoking on fetal growth: evidence for a threshold, the importance of brand of cigarette, and interaction with alcohol and caffeine consumption, in *Effects of smoking on the fetus, neonate and child*, (edited by D. Poswillo and E. Alberman), Oxford University Press, Oxford, pp 89–95.

Anderson, H.R. and Cook, D.G., 1997. Health effects of passive smoking. 2. Passive smoking and sudden infant death syndrome: Review of the epidemiological evidence, *Thorax*, Vol 53, pp. 1003–9.

Baumann K.E., Flewelling, L.R. and LaPrelle, J., 1991. Parental cigarette smoking and cognitive performance of children, *Health Psychol*, Vol 10, pp. 282–8.

CA EPA, 1997. *Health effects of exposure to environmental tobacco smoke*, Office of Environmental Health Hazards Assessment, California Environmental Protection Agency. http://www.oehha.org/air/environmental_tobacco/index.html

Charlton, A., 1994. Children and passive smoking: A review, *J Fam Pract*, Vol 38, pp. 267–77.

Summary

It is often difficult to separate the possible adverse health effects resulting from prenatal exposure to tobacco products and postnatal exposure to ETS. Many studies have therefore investigated health endpoints at the perinatal or infant stages.

There is strong evidence that prenatal exposure to tobacco smoke products increases the risk of low-birth-weight infants and reduces mean birth weight for gestational age by about 10 %. Data are consistent regarding a small effect on miscarriage and stillbirth. Strong associations are also observed with sudden infant death syndrome (SIDS) based on a large number of studies, with relative risks of two- to three-fold. Consistent associations and clear dose-response relations with childhood respiratory illnesses, especially in infants, have been observed in a large number of studies. Similar findings are found for middle-ear disease. Asthma severity is also increased by exposure to ETS, and some health authorities have concluded that the incidence of asthma relates to ETS exposure. A few studies have observed associations with childhood cancer, but confirmation in larger studies is needed. Effects on child development, either physical or cognitive, or behaviour, have not been established, though there are numerous suggestive studies. Thus the main risks caused by prenatal and/or childhood exposure are reduced birth weight, increased risk of SIDS and respiratory and middle-ear infections, and exacerbation of existing asthma.

Public health policy and actions should aim at the elimination of exposure to tobacco smoke pollution by creating smoke-free environments for everyone.

An integrated multisectoral response should be developed involving, among others, the health, environment and education ministries as well as appropriate non-governmental organisations.

Coghlin, J., Gann, H.P., Hammond, K.S. *et al.*, 1991. 4-Aminobipheny1 hemoglobin adducts in fetuses exposed to the tobacco smoke carcinogen in utero, *J Natl Cancer Inst*, Vol 83, pp. 274–80.

Cook, D.G. and Strachan, D.P., 1997. Health effects of passive smoking. 3. Parental smoking and prevalence of respiratory symptoms and asthma in school age children, *Thorax*, Vol 52, pp. 1081–94.

Cook, D.G. and Strachan, D.P., 1998. Health effects of passive smoking. 7. Parental smoking, bronchial reactivity and peak flow variability in children, *Thorax*, Vol 53, pp. 295–301.

Cook, D.G., Strachan, D.P. and Carey, I.M., 1998. Health effects of passive smoking. 9. Parental smoking and spirometric indices in children, *Thorax*, Vol 53, pp. 884–93.

Couriel, J.M., 1994. Passive smoking and the health of children, *Thorax*, Vol 49, pp. 731–4.

Davis, D.L., 1991. Paternal smoking and fetal health, *Lancet*, Vol 337, p. 123.

DiFranza, R.J. and Lew, A.R., 1995. Effect of maternal cigarette smoking on pregnancy complications and sudden infant death syndrome, *Fam Pract*, Vol 40, pp. 385–94.

DiFranza, R.J. and Lew. A.R., Morbidity and mortality in children associated with the use of tobacco products by other people, *Pediatrics*, Vol 97, 1996, pp. 560–68.

Doyle, L.W., Ford, G.W., Olinsky, A. *et al.*, 1996. Passive smoking and respiratory function in very low birthweight children, *Med J Australia*, Vol 164, pp. 266–9.

Elwood, P.C., Sweetnam, P.M., Gray, O.P. *et al.*, 1987. Growth of children from 0–5 years: With special reference to mother's smoking in pregnancy, *Ann Human Biol*, Vol 14, pp. 543–57.

Eskenazi, B., Prehn, A.W. and Christianson, R.E., 1995. Passive and active smoking as measured by serum cotinine: The effect on birthweight, *Am J Public Health*, Vol 85, pp. 395–8.

Etzel, R.A., 1994. Environmental tobacco smoke, *Indoor Air Poll*, Vol 14, p. 62.

Everson, R.B., Randerath, E., Santella, M.R. *et al.*, 1986. Detection of smoking-related covalent DNA adducts in human placenta, *Science*, No 231, pp. 54–7.

Fox, N.L., Sexton, M. and Hebel, R.J., 1990. Prenatal exposure to tobacco: I. Effects on physical growth at age three, *Epidemiology*, Vol 19, pp. 66–71.

Fried, P.A., 1992. Clinical implications of smoking: Determining long term teratogenicity, in *Maternal substance abuse and the developing nervous system*, Academic Press Inc, pp. 77–96.

Gidding, S.S., Morgan, W., Perry, C. *et al.*, 1994. Active and passive tobacco exposure: A serious pediatric health problem, *Circulation*, Vol 90, pp. 2581–90.

Haddow, J.E., Knight, G.J., Palomaki, G.E. *et al.*, 1988. Second-trimester serum cotinine levels in nonsmokers in relation to birth weight, *Am J Obstet Gynecol*, Vol 159, pp. 481–4.

Hansen, C., Sorensen, L.D., Asmussen, I. *et al.*, 1992. Transplacental exposure to tobacco smoke in human-adduct formation in placental and umbilical cord blood vessels, *Terato Carcino Mutagen*, Vol 12, pp. 51–60.

Henschen, M., Frischer, T., Pracht, T. *et al.*, 1977. The internal dose of passive smoking at home depends on the size of the dwelling, *Environ Res,* 72, pp. 65–71.

Jedrychowski, W. and Flak, E., 1997. Maternal smoking during pregnancy and postnatal exposure to environmental tobacco smoke as predisposition factors to acute repiratory infections, *Environmental Health Perspectives*, Vol 105, pp. 302–6.

Ji, B., Shu, X., Linet, S.M. *et al.*, 1997. Paternal cigarette smoking and the risk of childhood cancer among offspring of nonsmoking mothers, *J Natl Cancer Inst*, Vol 89, pp. 238–44.

Kulikauskas, V., Blaustein, D. and Ablin, J.R., 1985. Cigarette smoking and its possible effects on sperm, *Am Fertil Soc*, Vol 44, pp. 526–8.

Lam, T.H., Chung, S.F., Betson, C.L. *et al.*, 1998. Respiratory symptoms due to active and passive smoking in junior secondary school students in Hong Kong, *Int J Epidemiol* , Vol 27, pp. 41–8.

Lazzaroni, F., Bonassi, S. and Manniello, E., 1990. Effect of passive smoking during pregnancy on selected perinatal parameters, *Int J Epidemiol*, Vol 19, pp. 960–6.

Maier, W.C., Arrighi, H.M., Morray, B. *et al.*, 1997. Indoor risk factors for asthma and wheezing among Seattle school children, *Environ Health Perspect*, Vol 105, pp. 208–14.

Mainous, A.G. and Hueston, W.J., 1994. Passive smoking and low birthweight: evidence of a threshold effect, *Arch Family Med*, Vol 3, pp. 875–8.

Margolis, P.A., Keyes, L.L., Greenberg, R.A. *et al.*, 1997. Urinary cotinine and parent history (questionnaire) as indicators of passive smoking and predictors of lower respiratory illness in infants, *Pediatric Pulmonology*, Vol 23, pp. 417–23.

Martin, T.R. and Bracken, M.B., 1986. Association of lowbirth weight with passive smoke exposure in pregnancy, *Am J Epidemiol*, Vol 124, pp. 633–42.

Martinez, F.D., Wright, A.L. and Taussig, L.M., 1994. The effect of paternal smoking on the birthweight of newborns whose mothers did not smoke, *Am J Public Health*, Vol 84, pp. 1489–91.

Naeye, R.L. and Peters, E.C., 1984. Mental development of children whose mothers smoked during pregnancy, *J Am College Obstet Gynecol*, Vol 64, pp. 601–7.

NRC, 1986. *Environmental tobacco smoke: measuring exposures and assessing health effects*, Washington DC, National Academy Press.

Olsen, J., Pereira, A. and Olsen, S., 1991. Does maternal tobacco smoking modify the effect of alcohol on fetal growth? *Am J Public Health*, Vol 81, pp. 69–73.

Royal College of Physicians, 1992. *Smoking and the young*, Royal College of Physicians of London, London.

Rush, D., 1992. Exposure to passive cigarette smoking and child development: An updated critical review, in *Effects of smoking on the foetus, neonate and child* (edited by D. Poswillo and E. Alberman), Oxford University Press, Oxford, pp. 150–70.

SCOTH, 1998. *Report of the Scientific Committee on Tobacco and Health*, Scientific Committee on Tobacco and Health, Stationery Office, London.

Sexton, M., Fox, N.L. and Hebel, J.R., 1990. Prenatal exposure to tobacco: II Effects on cognitive functioning at age three, *Int J Epidemiol*, Vol 19, pp. 72–7.

Sorahan, T., Lancashire, R., Prior, P. *et al.*, 1995. Childhood cancer and parental use of alcohol and tobacco, *Epidemiology*, Vol 5, pp. 354–9.

Strachan, D.P. and Cook, D.G., 1997. Health effects of passive smoking. 1. Parental smoking and lower respiratory illness in infancy and early childhood, *Thorax*, Vol 52, pp. 905–14.

Strachan, D.P. and Cook, D.G., 1998a. Health effects of passive smoking. 6. Parental smoking and childhood asthma: Longitudinal and case-control studies, *Thorax*, Vol 53, pp. 204–12.

Strachan, D.P. and Cook, D.G., 1998b. Health effects of passive smoking. 4. Parental smoking, middle ear disease and adenotonsillectomy in children, *Thorax*, Vol 53, pp. 50–6.

Thornton, A.J. and Lee, P.N., 1998a. Parental smoking and sudden infant death syndrome: A review of the evidence, *Indoor Built Environ*, Vol 7, pp. 87–97.

Thornton, A.J. and Lee, P.N., 1998b. Parental smoking and risk of childhood cancer: A review of the evidence, *Indoor Built Environ*, Vol 7, pp. 65–86.

Tredaniel, J., Boffetta, P., Little, J. *et al.*, 1994. Exposure to passive smoking during pregnancy and childhood, and cancer risk: The epidemiological evidence, *Paediatr Perinatal Epidemiol*, Vol 8, pp. 233–55.

Tuormaa, T.E., 1995. The adverse effects of tobacco smoking on reproduction and health: A review from the literature, *Nutr Health*, Vol 10, pp. 105–20.

Weitzman, M., Gortmaker, S. and Sobol, A., 1992. Maternal smoking and behavior problems of children, *Pediatrics*, Vol 90, pp. 342–9.

WHO, 1999. *The Framework Convention on Tobacco Control: A primer*. WHO/NCD/TFI/99. 8 rev. 3, online at: http://tobacco.who.int/repository/stp41/primeren.pdf

WHO, 2000. *Policies to reduce exposure to environmental tobacco smoke*, Report on WHO Working Group Meeting Lisbon, 29–30 May 2000, WHO Regional Office for Europe, Copenhagen (document EUR/00/5020495).

Woodward, A., Douglas, R.M., Graham, N.M.H. *et al.*, 1990. Acute respiratory illness in Adelaide children: Breast feeding modifies the effect of passive smoking, *J Epidemiol Comm Health*, Vol 44, pp. 224–30.

Zhang, J. and Ratcliffe, J.M., 1993. Paternal smoking and birthweight in Shanghai, *Am J Public Health*, Vol 83, pp. 207–10.

11. Pesticides

Cristina Tirado

Summary of existing knowledge

- Childhood patterns of behaviour often lead to increased levels of pesticide exposure compared with adults ('hands-to-mouth', certain eating habits).
- Possible health effects include immunological effects, endocrine-disrupting effects, neurotoxic disorders and cancer.

Main challenges

- To develop and implement effective strategies to prevent the risks for children of exposure to pesticides.

Action points

- Regulate the rational use of pesticides to reduce environmental pollution and residues in food and water.
- Establish maximum residue limits for pesticides in food and water that protect children.
- Develop adequate methodologies for risk assessment of chronic and acute hazards posed by pesticide residues to infants and children.

11.1. Introduction

Pesticides are extensively used worldwide for agriculture and for non-agricultural purposes. Currently more than 800 pesticides are registered in the European Union (EU). Harmful pesticide residues can contaminate the environment and accumulate in ecosystems, thus entering the human food chain. Some of these pesticides may cause cancer or damage the nervous, respiratory, reproductive, endocrine or immune systems.

Children and young infants are exposed to pesticides daily by three routes, namely ingestion, dermal absorption and inhalation. Children can ingest pesticides residues present in food (including baby foods and), drinking-water, breast milk and sometimes in soil. In addition, children can be exposed to pesticides used and/or found in households, schools, on pets, in swimming areas, rural environments, parks, etc. The large number of potential exposure sources and pathways is of particular relevance because it can lead to high cumulative exposure.

Because their bodies are still developing, fetuses, infants and children can be more vulnerable to toxic compounds than adults, and their diet and special behaviour patterns often result in greater exposure to pesticides. Pesticide-specific data on prenatal and postnatal developmental toxicity and exposure are lacking for many of the currently used pesticides. Risk assessments currently undertaken to establish acceptable daily intakes (ADIs), acute reference doses (ARfDs) where relevant and to evaluate proposed maximum residue limits (MRLs) for pesticides in food often do not take into account these important considerations so as to fully ensure the health and safety of infants and children.

This chapter presents an overview of the differences between infants and children compared with adults with respect to sensitivity as well as exposure to pesticides and it addresses the need to consider these differences in order to develop risk assessment methodologies and risk management strategies to protect these vulnerable populations.

11.2. Pesticides use and residues data in the European Region

Despite international efforts to promote sustainable use of pesticides in agriculture, and the actual reduction in use in several countries, since 1995 there has been no significant overall reduction in pesticide use in the World Health Organization (WHO) European Region. Pesticide groups most commonly used in the region from 1986 to 1997 were fungicides, herbicides, insecticides and plant growth regulators, particularly dithiocarbamates, inorganics, phenoxy hormone products, urea derivates, triazine, organophosphates and carbamates among others (FAOSTAT, 2000).

Information about the actual presence of pesticide residues in food in the European Region is very limited. Monitoring programmes have only recently been started in some countries. For the first time the European Union (EU) and Norway collected common data on pesticide residue levels in fruit and vegetables in 1996 and in fruit, vegetables and cereals in 1997 and 1998 (EEC, 1998; EEC, 1999; EEC, 2000). In the 1998 EU and Norway monitoring programme, pesticide residues were present in 36 % of the vegetable, fruit and cereal samples; MRLs were exceeded in 3.3 % of the

cases, mainly in fruit and vegetables, and multiple residues were detected in about 14 % of the positive samples. Most often found in the 1996–98 EU and Norway monitoring programmes were residues from fungicides followed by insecticides (i.e. iprodione, vinclozolin, procymidone, thiabendazole, carbendazim, imazalil, captan, chlorothalonil, folpet, methamidophos, dithiocarbamates, endosulfan, chlorpyriphos, and methidathion). Some of these pesticides are considered to be highly hazardous, to cause acute toxicity, neurotoxicity, developmental toxicity and eventually irreversible health effects (WHO/PCS, 1998; Tomlin, 1997; EPA, 1997a) Results from the EU special coordinated monitoring programmes in 1996, 1997 and 1998 ([3]) showed that the commodities in which MRLs were most often exceeded in 1996 were lettuce, followed by grapes, strawberries, apples and tomatoes. In 1997 they were beans followed by mandarins and bananas, and in 1998 spinach followed by peaches, carrots and oranges. It is noteworthy that some of these fruit (particularly mandarins, apples, grapes, peaches and bananas) are very common in children's diets (Wiles *et al.*, 1998).

In the Netherlands, a consumer organisation, Consumentenbond, has recently conducted a large analysis of pesticide residues in food, in response to the request of the Codex Committee on Pesticides Residues in Foods (CCPR) during its 32nd session for information on which pesticides are of particular concern for infants and children (Consumers International, 2001). The analysis was based on a cumulative risk assessment of 40 organophosphorus and carbamate pesticides consumed by Dutch children aged one to six years, using national government monitoring data and probabilistic methods ([4]). Results from this analysis revealed that pesticides of particular concern (considering relative toxicity and exposure) for infants and children were, in order of importance: parathion ethyl and dimethoate (together these pesticides accounted for 55 % of the total exposure to acetylcholinesterase-inhibiting compounds), mevinphos, phoslaone, monocrotofos, pyrazofos, methyl parathion, azinphos methyl and chorpyrifos. The three food commodities that contributed most to children's exposure to acetylcholinesterase-inhibiting compounds in this study were spinach from the Netherlands, apples from France and grapes from Italy and Greece.

Similar data from other countries on the actual presence of residues in foods consumed by children are necessary in order to provide CCPR and the Joint Food and Agriculture Organization of the United Nations (FAO)/WHO Meeting on Pesticides Residues (JMPR) with the best information on which to base their selection of the pesticides that should be assessed as potential hazards to children in the European Region.

11.3. Age-related variations in susceptibility and unique patterns of exposure to pesticides

Differences between the susceptibility of children and adults to pesticide toxicity and their unique patterns of exposure have been addressed by the US National Research Council (US NRC, 1993). This study was the scientific basis for the US Food Quality Protection Act, which strengthens the public health basis for regulating dietary and non-dietary exposure to pesticides. This study has also been reviewed by the EU Scientific Committee for Food (EU SCF, 1997; EU SCF, 1998) when expressing its opinion on an MRL of 0.01 milligrams per kilogram (mg/kg) for pesticides in foods intended for infants and children.

Age-related variation in susceptibility

Compared to adults, children and particularly fetuses and infants, are in a stage of rapid development and growth. During this development process, fetuses, infants and children have unique development periods of high vulnerability or critical windows of exposure. The ability of a developing organism to absorb, metabolise and eliminate xenobiotic compounds frequently differs from that of adults. Also, a number of the systems designed to protect the body from toxic chemicals (e.g. the blood brain barrier and the immune system) are still immature. All these factors can cause

(3) In 1996, seven pesticides and two groups of pesticides (benomyl group and dithiocarbamates) were analysed in apples, tomatoes, lettuce, strawberries and grapes. In 1997, five commodities (mandarins, pears, bananas, beans and potatoes) were analysed for 13 pesticides. In 1998 four commodities (oranges, peaches, carrots and spinach) were analysed for 20 pesticides.

(4) Residues data 1997–99 from the Dutch Health Inspectorate (Quality Agricultural Products Database) and consumption data from the Dutch National Consumption Survey of 1997–98. The Monte Carlo analysis was contracted to the State Institute for Quality Control of Agriculture Products (RIKILT).

toxic effects in exposed infants and children to be different from those in similarly exposed adults.

Differences in the toxicity of pesticides between children and adults have been found to be quantitative and occasionally qualitative (US NRC, 1993). Quantitative differences are partially due to age-related differences in absorption, metabolism, detoxification and excretion of toxic compounds. Differences in size, immaturity of biochemical and physiological functions in major body systems, and variation in body composition (water, fat, protein and mineral content) can all influence the extent of toxicity. Qualitative differences in toxicity may result, for example, during developmental periods of high susceptibility when exposure to a toxic agent can permanently change the structure or function of an organ system (US NRC, 1993). Of special concern is that susceptibility of the developing fetus, neonate, infant or child to delayed functional toxicity — as a result of exposure to apparently sub-toxic doses of pesticides during a critical window — may not become manifest until adulthood (EU SCF, 1997). Developmental functional toxicity is especially relevant for the developing central nervous system, and also applies to the endocrine, reproductive and immune systems. For example, perinatal exposure to any of the major classes of synthetic insecticides often results in perturbations in the nervous system, which may affect the behaviour of the developing organism (Mactutus and Tilson, 1986). In particular, some organophosphate pesticides such as methyl parathion and chlorpyrifos have been found to be more toxic to fetal and neonatal animals than to adults (Pope *et al.*, 1991; Pope and Chakraborti, 1992; Whitney *et al.*, 1995).

Current knowledge about age-related differences in susceptibility to specific pesticides is very limited and most of the testing protocols do not adequately address the toxicity and metabolism of pesticides in neonates and adolescent animals or the effects of exposure during early developmental stages and their sequelae in later life (US NRC, 1993; EU SCF, 1997). The EU Scientific Committee for Food (SCF) has expressed some concerns regarding the limitations of the standard toxicological tests and the currently used data packages and recommended that the issue of age-related differences in susceptibility to pesticides should be addressed on a case-by-case basis (1997).

Age-related differences in exposure

Fetuses, infants and children also differ both quantitatively and qualitatively from adults in their exposure to pesticides. The fetus's environment is clearly unique and the characteristic behavioural patterns and diets of infants and children also differ from those of adults.

Childhood patterns of behaviour often lead to increased levels of pesticide exposure compared with adults. For example, among toddlers and young children hands-to-mouth behaviour is an important mechanism of potential exposure to certain pesticides. Also, infants and children spend more time at home than adults, often crawling or playing at ground level where pesticide residues in household air, dust, carpets and even toys may be higher (Wallinga, 1998). Pesticides residues persistent in household soil and dust have been considered significant sources of exposure for young children (Lewis *et al.*, 1994). Children who live in or near farms will ingest significant amounts of pesticides by playing and crawling at ground level and by touching surfaces inside the home which contain pesticides either from window dust, from nearby lawns or from indoor applications (Simcox *et al.*, 1995; Zartain *et al.*, 1995).

The main difference in the exposure of adults and children to pesticides is in their respective diets. Children consume more food per kilogram of body weight than do adults. Their diet is less diverse and they thus have a relatively higher intake of some food items than do adults. In addition, average water consumption, both as drinking-water and as a food component, is relatively higher in children than in adults.

Breast milk and infant formula can be also contaminated with pesticide residues. Organochlorine pesticide residues have been found in women's breast milk at levels which may raise concerns about the nursing infant (Schutz *et al.*, 1998). Commercial baby food has been identified as the dominant source of residues of organophosphate pesticides for infants of 6–12 months of age in the United States (Wiles *et al.*, 1998). Multiple residues present in baby foods represent an additional concern, especially for pesticides that share a common mechanism of toxicity (e.g. cholinesterase inhibitors such as carbamates

and organophosphates). For example, in a group of the baby foods most commonly sold in the United States, up to 16 different pesticides were found, and many of the baby foods tested contained multiple pesticides (Wiles *et al.*, 1995). A later analysis ([5]) based on more than 80 000 US government laboratory tests from recent years and detailed data on children's food consumption, revealed that every day, 9 out of 10 American children between the ages of six months and five years are exposed to combinations of 13 different organophosphate insecticides in the foods they eat (Wiles *et al.*, 1998).

11.4. Concerns regarding the adequacy of the toxicological tests for risk assessment of pesticide toxicity in children

In many countries the introduction of pesticides in the market requires the submission of toxicological data to derive the ADI and most recently the ARfD where appropriate. The toxicological tests relevant to risk assessment in infants and young children ([6]) are included in the core toxicological dossiers required for new applications for EU authorisations for pesticides under the Council Directive 91/414/EEC (EEC, 1991) and in the data package necessary for allocating ADIs by JMPR. However, the EU SCF in its 1998 opinion stated that it is not in a position to know whether all the core tests relevant to risk assessment in infants and young children have been conducted for every pesticide currently in use in the EU or in countries outside the EU.

The EU SCF considers that there are relatively new areas of pesticide toxicity that deserve special attention in relation to infants and young children such as developmental neurotoxicity, immunotoxicity and endocrine and reproductive toxicity. Core toxicological tests may indicate a potential impact on the developing nervous, immune, reproductive or endocrine systems and suggest further studies may need to be undertaken in order to establish an appropriate ADI. However, some pesticides may have effects on these systems in the absence of any sign from the results of existing core studies (EU SCF, 1998). Thus, even if core studies are routinely done, they do not fully ensure pesticide safety to infants and children.

Developmental neurotoxicity of pesticides

Currently, developmental neurotoxicity tests are rarely conducted on chemicals in general, including pesticides. For example, behavioural, memory and learning deficits are rarely examined in conventional studies, and delayed toxicity resulting from exposure to low levels of a toxicant during a particularly sensitive developmental period may not always be adequately addressed by current testing procedures (EU SCF, 1997). In fact, neurotoxicity testing in adult animals has only been mandatory for some neurotoxic pesticides such as organophosphates and carbamates which inhibit acetylcholinesterase in the nervous system. Fetal and neonatal animals are often more sensitive than adults to the neurotoxic effects of some organophosphates (US NRC, 1993; Whitney *et al.*, 1995). This sensitivity includes increased susceptibility to acute and chronic cholinesterase effects and other potentially more serious brain and nervous system damage. Infants may be particularly vulnerable to reductions in brain acetylcholinesterase given that acetylcholine plays an important role in normal brain development, and resting levels of plasma and erythrocyte (and therefore probably brain) cholinesterase do not reach adult values until 6–12 months of age (EPA 1997a).

Additionally, there appears to be other mechanisms of toxic action besides cholinesterase inhibition. Exposure to some organophosphates can produce long-term behavioural and functional damage to the nervous system in the absence of observable signs of toxicity and with little correlation with cholinesterase levels (EPA, 1997a). For example, the administration of chlorpyrifos to developing rats — in doses that do not evoke overt toxicity — decreased DNA synthesis and caused a shortfall in cell numbers in brain regions enriched with cholinergic innervation (Slotkin, 1999). Furthermore, chlorpyrifos has been found to evoke non-cholinergic disruption of cell development by interfering with cell signalling by adenyl cyclase, leading to widespread disruption that is not limited to cholinergic systems (Slotkin, 1999).

(5) This study was based on a Monte Carlo cumulative exposure assessment for organophosphate insecticides.
(6) Multigeneration tests, developmental toxicity (teratology) tests, short-term toxicity and long-term chronic toxicity/carcinogenicity studies and neurotoxicity tests. NB: neurotoxicity is not always part of the core data set.

In the United States the developmental neurotoxicity test has been proposed as part of the core toxicology database and the Environmental Protection Agency (EPA) is now requiring registrants to conduct developmental neurotoxicity studies for a number of neurotoxic pesticides. In the EU the SCF recommended that this issue be addressed by appropriate experts with a view to setting criteria which can be applied in the future to decide when developmental neurotoxicity studies are necessary (EU SCF, 1998).

Endocrine and reproductive toxicity

Some chemicals have been shown to interfere with normal chemical-signalling and endocrine functions even at extremely small doses (EPA, 1997b). These are the so-called 'endocrine-disrupting chemicals', which include a number of pesticides. For example, dieldrin, toxaphene, chlordane and DDT have been found to be estrogenic, as has endosulfan, a pesticide still used in agriculture (Soto *et al.*, 1994). The possibility is that interactions of pesticides with specific endocrine receptors during fetal and infant development may have profound effects on the morphological and functional development of the child. For example, there is increasing evidence that exposure to certain synthetic compounds, including dioxins and polychlorinated biphenyls, during the perinatal period can impair normal thyroid function and also learning, memory and attentional processes in offspring (Hauser *et al.*, 1998). This raises the question whether the current toxicological database for pesticides is sufficient to fully assess potential developmental adverse effects.

Most data packages for pesticides include a multigeneration study in one species and developmental toxicity (teratology) studies in two species. These are adequate to identify substances acting as reproductive toxicants in adults and substances causing malformations or affecting growth, postnatal survival and reproductive capacity in offspring, but they are not adequate to detect all endocrine-disrupting effects (EU SCF, 1998). The Organisation for Economic Co-operation and Development (OECD) test guidelines for both the two-generation reproductive study and for the teratogenicity study (with a new title 'Prenatal developmental toxicity') are in the process of being updated to cover these issues.

Immunotoxicity

Numerous pesticides, including dieldrin, aminocarb, captan, carbaryl, lindane, malathion and dichlorophos, can induce changes in the immune system (US NRC, 1993; Barnett and Rogers, 1994). In 1993 the NRC concluded that the immune systems of infants and children showed an increased sensitivity to the toxic effects of chemicals. It has been recommended that in the context of risk assessment for infants and young children, immunotoxicity to infants and children needs to be addressed since some chemicals may interfere with the developing immune system and give rise to persistent adverse effects, such as reduced ability to respond to immune challenge (EU SCF, 1998; Wallinga, 1998). The OECD test guideline for 90-day oral toxicity stud studies in rodents is being updated to place additional emphasis on immunological concerns. Despite this, the EU SCF noted the need to consider the criteria that might trigger a requirement for immunotoxicity studies in developing animals (EU SCF, 1998).

11.5. Strategies to reduce the risks of children's exposure to pesticides

Particular policies to reduce the risks of pesticide exposure differ between countries. There are two general strategies used by national authorities to prevent or reduce children's exposure to harmful pesticides: regulation of the rational use of pesticides; and the establishment of MRLs that protect children for pesticides in food and water. In this context, the development of adequate methods for risk assessment of chronic and acute hazards posed by pesticide residues to infants and children is essential.

Regulation of the rational use of pesticides

The first step to protect infants' and children's health from exposure to harmful pesticides should be using pesticides in a way that minimises environmental pollution and residues in food and drinking-water. In this context the benefits of banning pesticides that are potentially dangerous to infants and children in crops grown for use in infant foods should be considered. For example, the United States prohibition of the use of methyl parathion in 36 crops (including 'risk-driving foods' such as peaches, apples, pears, green beans and grapes) in 1999 has effectively eliminated dietary risks while requiring only a modest reduction in the use of this economically important chemical

(Consumers Union, 2001). The EPA regulation of this chemical has been considered a model of rational and efficient risk management (Consumers Union, 2001).

At the international level there are initiatives to reduce the risks of pesticide use such as the OECD's pesticides risk reduction programme and the FAO's programme on integrated pest management (IPM), among others. However, although IPM methods have been recognised to be effective in the control of pests, in the reduction of pesticide use and hence in the levels of residues in food, IPM is not considered in the actual concept of good agriculture practices used to establish current MRLs. In the EU, Council Directive (CD) 91/414/EEC (EEC, 1991) on the placing of plant protection products on the market refers to the application of good plant protection practices and IPM methods in agriculture, and Council Regulations 2092/91 and 2078/92 are legislative instruments to reduce the use of pesticides by promoting organic farming.

Establishment of MRLs to protect infants and children

Currently there is no international consensus on how to address the risks of pesticide residues in foods for infants and children. The EU has introduced a precautionary measure to account for the present doubts on the adequacy of the existing ADIs for the protection of infants' and children's health and has adopted a limit of 0.01 mg/kg for every individual pesticide for processed cereal-based foods and infant formulae, pending toxicological evaluation of the substances. New provisions to CD 91/321/EEC on infant formulae and follow-on formulae, and to CD 96/5/EEC on processed cereal-based foods and baby foods for infants and young children (EEC, 1996a; EEC 1996b) regulate the levels of pesticides in these products in the EU. These two Council directives refer to the requirement of severe limitations in the use of pesticides and the careful selection of raw materials intended for baby food and infant formula in order to produce products with very low levels of pesticide residues. Furthermore, processed cereal-based foods, baby food, infant formulae and follow-on formulae should be free of those particular pesticides for which even the MRL of 0.01 mg/kg is exceeded under the worst-case intake conditions, and should be produced without the use of these pesticides.

Other countries such as the United States do not establish specific MRLs for foods intended for infants and children, and a case-by-case approach is used. To account for potential higher toxicity of some pesticides to infants and children or in the absence of complete and reliable data on pre and postnatal toxicity and exposure to a pesticide, the EPA must apply an additional ten-fold margin of safety to MRLs (FQPA, 1996).

The feasibility of establishing specific MRLs for cereal-based foods and infant formulae at the international level is currently under discussion at CCPR. Some countries have requested that WHO/FAO convene an expert consultation to make recommendations to CCPR on specific aspects related to risk assessment and other risk management considerations for dealing with risks from pesticide residues to infants and children (CX/PR 00/9).

Development of adequate methodologies for risk assessment of chronic and acute hazards posed by pesticide residues to infants and children

The 1997 Geneva Joint FAO/WHO Consultation on Food Consumption and Exposure Assessment of Chemicals recognised the importance of issues such as aggregated exposure (i.e. multiple routes of exposure and multiple residues) and additive effects of pesticides with common toxicity (i.e. cholinesterase inhibitors such as carbamates and organophosphates), and that these should be considered by both risk assessors and risk managers (WHO, 1997). In addition to estimating dietary intake, other possible sources of exposure such as drinking-water, occupational and environmental exposure should also be considered. The report recognised the greater exposure of children to pesticides and recommended that dietary exposure assessments should be based on the best use of available data and, where appropriate, risk assessors and risk managers should consider differences in food consumption patterns and in vulnerabilities to toxicities across and within populations, and potential human health consequences resulting from exposures to chemicals in foods. Methodologies to address the above-mentioned issues to adequately assess the risks to infants and children have not been resolved yet at the international level and several countries are re-evaluating their national risk assessment procedures.

In this context, the issue of acute toxicity ([7]) is especially relevant for infants and children considering their greater exposure (on a mg/kg body-weight basis) and the fact that they consume widely varying quantities of individual foods with widely varying residue levels. The 1997 Geneva consultation developed a methodology for performing acute dietary exposure assessment (WHO, 1997) and recommended the use of a 97.5 percentile residue value in the edible portion for dietary assessment and a 97.5 percentile consumption for eaters only when evaluating acute risk. Particularly interesting is the new United Kingdom technical policy on the estimation of acute dietary intake of pesticide residues which takes into account the variability of residues between individual commodities (PSD, 1999). The methodology for acute dietary exposure assessment is still being refined, additional data on consumption have been requested and new procedures for acute risk assessment and management are currently being discussed by JMPR, CCPR and at the EU level. Since organophosphates and carbamates are of special concern regarding acute toxicity to children, several countries have requested JMPR to establish ARfD for these pesticides.

During the 32nd session of CCPR, the EU and consumer representatives opposed the advancement of any MRLs above the limit of determination when there were acute and chronic exposure concerns.

Summary

Pesticide exposure of infants and children and their susceptibility to toxicity from ingesting pesticide residues can differ from that of adults. In comparison to adults, infants and children can be more susceptible to some pesticides (e.g. organophosphates), they have greater exposure to pesticides in their diets (on a mg/kg body-weight basis), their diet is less diverse and potential sources of exposure are broader.

Current risk assessment methodologies do not specifically consider infants and children and the wide range of exposure patterns that exist within this population. Consequently, variations in dietary and environmental exposure to pesticides (aggregated exposure) and health risks related to age and particular sensitivity are not addressed when establishing ADIs, ARfDs and MRLs.

It is questionable whether all existing pesticide ADIs have been set using databases which include the tests now considered necessary for risk assessment for infants and young children. In fact, there are limitations on the adequacy of toxicological testing regimes to identify risks to infants and young children.

In particular, more attention should be given to parameters that adequately address developmental toxicity and the function of the nervous, reproductive, endocrine and immune systems. Appropriate toxicological tests to assess perinatal and childhood toxicity should be developed.

The main step to reduce the risks of exposure to harmful pesticides is the rational use of pesticides.

The international scientific community has recognised the need to improve methods to assess the risk of chronic and acute hazards posed by pesticide residues to infants and children and to revise the actual procedures to establish MRLs to safeguard their health. An expert consultation has been recommended in the framework of Codex to address risk assessment policy and risk management recommendations to protect infants and children from pesticides residues. In the interim a precautionary approach has been recommended for pesticides that pose particular concern for infants and children to ensure that they are adequately protected.

(7) For pesticides that have acute toxic effects or may be able to induce long-term effects after a single dose, short-term dietary intakes should be considered and compared with the toxicological effects that are of concern from short-term exposures (i.e. an ARfD has to be used instead of an ADI).

References

Barnett, J. and Rogers K., 1994. *Pesticides. Immunotoxicity and immunopharmacology* (edited by J.H. Dean, *et al.*), 2nd edition, Raven Press, New York, pp. 191–231.

Consumers International, 2001. *Response of Consumers International to CL 2000/27-PR*, Part 3 http://www.ecologic-ipm.com

Consumers Union, 2001. *Success and failures in implementing the US Food Quality Protection Act*, a report card for EPA, New York http://www.ecologic-ipm.com

EEC, 1991. Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market.

EEC, 1996a. Commission Directive 96/4/EC of 16 February 1996 amending Directive 91/321/EC on infant formula and follow-on formulae.

EEC, 1996b. Commission Directive 96/5/EC of 16 February 1996 on processed cereal-based foods and baby foods for infants and young children.

EEC, 1998. *Monitoring for pesticide residues in the EU and Norway*, Report 1996.

http://europa.eu.int/comm/food/fs/inspections/fnaoi/reports/pesticides/mon_rep/index_en.html (in 2001).

EEC, 1999. *Monitoring for pesticide residues in the EU and Norway*, Report 1997.

http://europa.eu.int/comm/food/fs/inspections/fnaoi/reports/pesticides/mon_rep/index_en.html (in 2001).

EEC, 2000. *Monitoring for pesticide residues in the EU and Norway*, Report 1998 http://europa.eu.int/comm/food/fs/inspections/fnaoi/reports/pesticides/mon_rep/index_en.html (in 2001).

EPA, 1997a. *Background document on cholinesterases*, Attachment 4E presented to Environmental Protection Agency Scientific Advisory Panel Meeting of June 3–4, 1997, Arlington, Virginia.

EPA, 1997b. *EPA special report on endocrine disruption*, Environmental Protection Agency http://www.epa.gov./ORD/whatsnew.htm (in 2001).

EU SCF, 1997. *Opinion on a maximum residue limit (MRL) of 0.01 mg/kg for pesticides in foods intended for infants and young children* (expressed on the 19 September 1997), EU Scientific Committee for Food http://europa.eu.int/comm/dg24/ (in 2001).

EU SCF, 1998. *Further advice on the opinion of the Scientific Committee for Food expressed on the 19 September 1997 on a maximum residue limit (MRL) of 0.01 mg/kg for pesticides in foods intended for infants and young children* (adopted by the SCF on 4 June 1998), EU Scientific Committee for Food. http://europa.eu.int/comm/dg24/ (in 2001).

FAOSTAT, 2000. *Agriculture. Pesticides consumption*, Food and Agriculture Organization http://www.fao.org (in 2001).

FQPA, 1996. Food Quality Protection Act, Section 408(b)(2)(C)(ii)(II).

Hauser, P., McMillin, J.M. and Bhatara, V.S., 1998. Resistance to thyroid hormone: Implications for neurodevelopmental research of the effect of thyroid hormone disruptors, *Toxicology and Industrial Health*, Vol 14, pp. 85–101.

Lewis, R.G., Fortmann, R.C. and Camman, D.E., 1994. Evaluation methods for monitoring the potential exposure of small children to pesticides in the residential environment, *Archives of Environmental Contamination and Toxicology*, Vol 26, pp. 37–46.

Mactutus, CF, and HA Tilson. 1986. *Psychogenic and neurogenic abnormalities after perinatal insecticide exposure.* In Riley, EP, and CV Vorhees (eds.), Handbook of behavioral teratology. New York: Plenum Press.

Pope, C.N. and Chakraborti, T.K., 1992. Dose-related inhibition of brain and plasma cholinesterase in neonatal and adult rats following sublethal organophosphate exposures, *Toxicology*, Vol 73, pp. 35–43.

Pope, C.N., Chakraborti, T.K., Chapman, M.L. *et al.*, 1991. Comparison of *in vivo* cholinesterase inhibition in neonatal and adult rats by three organophosphorothioate insecticides, *Toxicology*, Vol 68, pp. 51–61.

PSD, 1999. *The registration handbook*, part III/A3/appendix 1B, Pesticides Safety Directorate, UK.

Schutz, D., Moy, G.G. and Kaferstein, F.K., 1998. *GMS/Food. International dietary survey: Infant exposure to certain organochlorine contaminants from breast milk — a risk assessment*, Food Safety Unit, World Health Organization, Geneva.

Simcox, N.J., Frenske, R.A., Wolz, S.A. *et al.*, 1995. Pesticides in the household dust and soil exposure pathways for children of agricultural families, *Environmental Health Perspectives*, Vol 103, pp. 1126–34.

Slotkin, T.A., 1999. Developmental cholinotoxicants: Nicotine and chlorpyrifos, *Environmental Health Perspectives*, Vol 107 (suppl 1), pp. 71–80.

Soto, A.M., Chung, K.L. and Sonnenschein, C., 1994. The pesticides endosulfan, toxaphene, and dieldrin have estrogenic effects on human estrogen-sensitive cells, *Environmental Health Perspectives*, Vol 102, pp. 380–3.

Tomlin, C.D.S., ed, 1997. *The pesticide manual*, 11th edition, British Crop Protection Council.

US NRC, 1993. *Pesticides in the diets of infants and children*, US National Research Council, National Academy Press, Washington DC.

Wallinga, D., 1998. *Putting children first. Making pesticide levels in food safer for infants & children*, National Resources Defense Council, Washington, DC http://www.nrdc.org

Whitney, K.D., Seidler, F.J. and Slotkin, T.A., 1995. Developmental neurotoxicity of chlorpyrifos: Cellular mechanisms, *Toxicology and Applied Pharmacology*, Vol 134, pp. 53–62.

WHO, 1997. *Food consumption and exposure assessment of chemicals*, Report of an FAO/WHO consultation (10-14 February 1997), World Health Organization, Geneva.

WHO/PCS, 1998. *The WHO recommended classification of pesticides by hazard and guidelines to classification 1998-1999*, World Health Organization, Geneva.

Wiles, R. and Davies, K., 1995. *Pesticides residues in baby food*, Environmental Working Group, Washington DC http://www.ewg.org

Wiles, R., Davies, K. and Campbell, C., 1998. *Overexposed. Organophosphate insecticides in children's food*, Environmental Working Group, Washington DC http://www.ewg.org

Zartain, V.G., Streicker, J., Rivera, A. *et al.*, 1995. A pilot study to collect micro-activity data of two-to-four year-old farm labor children in Salinas Valley, California, *Journal of Exposure and Analytical Environmental Epidemiology*, Vol 5, pp. 21–34.

12. Ultraviolet radiation

Eva A. Rehfüss and Ondine S. von Ehrenstein

Summary of current knowledge
- Frequent sun exposure and a history of sunburn during childhood and adolescence are major risk factors for the development of skin cancer and cataracts.
- UV radiation may suppress some immunological responses.
- Measures to reduce children's UV radiation exposure can significantly decrease adverse health effects and health care costs.

Main challenges
- To increase knowledge of the effects of UV radiation on the eye and the immune system.
- To increase knowledge on the cost-effectiveness of educational programmes.

Action points
- Promote and support studies to investigate children's special vulnerability to the effects of UV radiation on the skin, eyes and immune system.
- Promote a change in public awareness about personal sun protection and develop comprehensive school programmes involving students and teachers as well as families and the wider community.
- Establish and measure markers to evaluate the effectiveness of UV radiation control programmes, including indicators to assess the cost-effectiveness of interventions.

12.1. Introduction

Children's exposure to ultraviolet (UV) radiation is a major public health issue, not only because overexposure during childhood increases the risk of skin cancer later in life. It may also increase the risk of retinal injury in childhood and the risk of cataract of the eye later in life, and may suppress immunological responses. Immune suppression is thought to have implications for the progression of skin cancer, the development of certain infections and in vaccine responses (AAP, 1999).

Ultraviolet (UV) radiation is one component of the many different types of radiation emitted by the sun (solar spectrum). The UV region covers the wavelength range 100–400 nanometres (nm) and is divided into three bands: UVA (315–400 nm), UVB (280–315 nm) and UVC (100–280 nm). As sunlight passes through the atmosphere, all UVC and approximately 90 % of UVB radiation are absorbed by ozone, water vapour, oxygen and carbon dioxide. UVA radiation is less affected by the atmosphere. Therefore, the UV radiation reaching the earth's surface is largely composed of UVA with a small UVB component.

The UV level on earth is influenced by:

- Sun height: the higher the sun in the sky, the higher the UV level. Thus UV levels vary with time of day and time of year, with maximum levels occurring when the sun is directly overhead at around midday during the summer months.
- Latitude: the closer the equator, the higher the UV levels.
- Cloud cover: UV levels are highest under cloudless skies — even with cloud cover, the scattering of UV radiation by water molecules and fine particles in the atmosphere can result in high UV levels.
- Altitude: at higher altitudes, a thinner atmosphere filters less UV radiation; with every 1 000 metres increase in altitude, UV levels increase by 10 to 12 % (Blumthaler *et al.*, 1994).
- Ozone: ozone absorbs some of the UV radiation that would otherwise reach the earth's surface; ozone levels vary over the year and even through the day.
- Ground reflection: UV radiation is reflected or scattered to varying extents by different surfaces, e.g. snow can reflect as much as 80 % of UV radiation, dry beach sand about 15 % and sea foam about 25 % (Sliney, 1986).

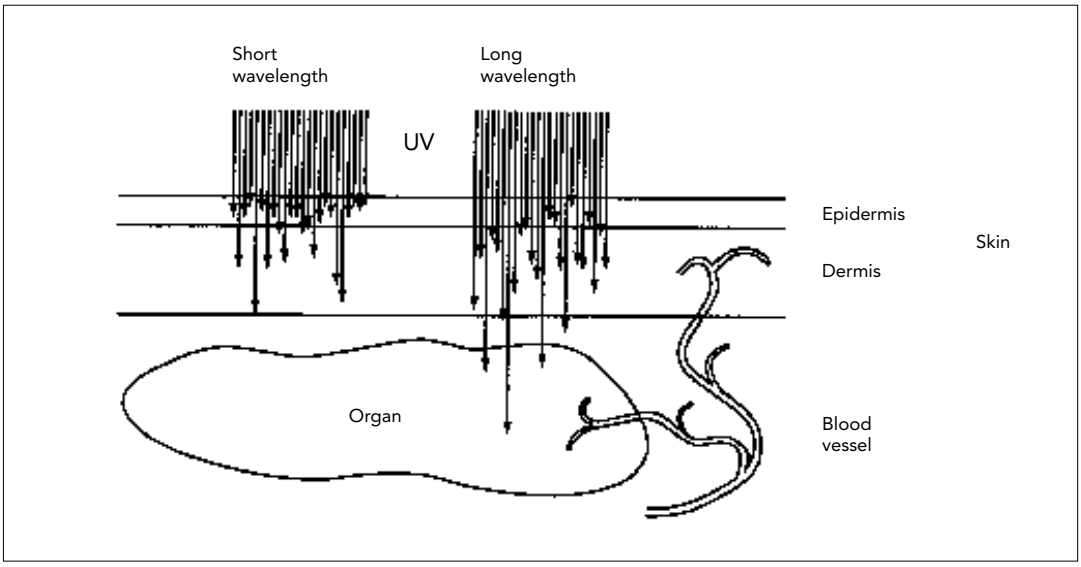
An increasing number of people are also exposed to artificial sources of UV radiation used in industry and commerce and in recreational activities such as tanning lamps and sunbeds.

12.2. Biological and health effects

Ultraviolett radiation causes different biological effects depending on its intensity and wavelength. These include erythema (skin reddening) and carcinogenesis. Experimental studies have shown that UVB is three to four times as effective as UVA in causing erythema in humans and skin cancer in animals (IARC, 1992); however, UVA can penetrate into the deeper layers of the skin (Figure 12.1.).

Figure 12.1. **Depth of penetration of short- and long-wavelength UV radiation through the skin**

Source: Christensen, 2000



Ultraviolett radiation must be absorbed by a molecule, i.e. a chromophore, to initiate chemical changes. UV radiation can induce biological effects by directly causing DNA damage. UV-induced mutations include single- and double-strand breaks and mutations in individual bases, as well as large-scale genetic alterations such as chromosome breakage. DNA seems to be the primary chromophore in the induction of erythema, a reddening of the skin, leading to the release of various inflammatory mediators such as cytokines and adhesion molecules (Césarini, 2000). Indirect biological effects and additional chromophores gain importance with increasing wavelength. The absorption of longer wavelength UV radiation, mostly in the UVA range, by a chromophore leads to the generation of reactive oxygen intermediates. These radicals can lead to changes in the permeability of membranes and the activity of proteins, and may have genotoxic and mutagenic effects.

The carcinogenicity of UV radiation has been evaluated by the International Agency for Research on Cancer (IARC) which concluded that 'there is sufficient evidence for humans for the carcinogenicity of solar radiation. Solar radiation causes cutaneous melanoma and non-melanocytic skin cancer' (see Table 12.1.). UV radiation may also indirectly influence cancer development through increased cell proliferation and changes in the immune system (IARC, 1992; WHO, 1994).

Table 12.1. **Evaluation of the carcinogenic risks to humans of solar and UV radiation**

Source: IARC, 1992

Agent	Degree of evidence of carcinogenicity		Overall evaluation of carcinogenicity to humans
	Human	Animal	
Solar radiation	S	S	1
Broad-spectrum UV radiation		S	
UVA radiation		S	2A
UVB radiation		S	2A
UVC radiation		S	2A
Fluorescent lighting	I		3
Sunlamps and sunbeds, use of	L		2A

S = sufficient evidence; L = limited evidence; I = inadequate evidence.
Group 1: the agent is carcinogenic to humans; Group 2A: the agent is probably carcinogenic to humans; Group 3: the agent is not classifiable as to its carcinogenicity to humans.

Short-term health effects

The most common acute effects of excessive UV radiation exposure are sunburn and tanning. Erythema, which represents the mildest form of sunburn, is caused by vasodilation of capillary vessels and various histological alterations. Strong sunburn may cause the skin to blister and peel. UV-induced tanning occurs in two phases: immediate pigment darkening is thought to be caused by the oxidation and redistribution of melanin in the skin upon exposure to UVA. This immediate tan begins to fade within a few hours of cessation of exposure. Delayed tanning has its maximal effectiveness in the UVB range, and is caused by the production of new melanin over a period of approximately three days. Furthermore, thickening of the outermost layers of the skin attenuates penetration of UV radiation to the deeper layers of the skin and thus serves as a protective mechanism against further damage. Depending on their skin type, individuals vary greatly in their skin's initial threshold for erythema and their ability to adapt to UV radiation exposure.

Acute effects on the eye include photokeratitis and photoconjunctivitis. These inflammatory reactions are comparable to sunburn of the very sensitive skin-like tissues of the eyeball and eyelids. Both are reversible and are not thought to result in any long-term damage to the eye. An extreme form of photokeratitis is snow blindness.

Long-term health effects

Beneficial effects of UV radiation

Exposure to UVB stimulates the production of vitamin D in the skin. Vitamin D increases calcium and phosphorus absorption from food and plays a crucial role in skeletal development, immune function and blood cell formation. Vitamin D deficiency is unlikely for most people as, for example, a 10- to 15-minute daily exposure of face, forearms and hands to normal northern European summer sun is sufficient to maintain vitamin D levels (McKie, 2000).

Artificial sources of UV radiation have been used to treat several diseases and dermatological conditions, including rickets, psoriasis, eczema and jaundice. Therapeutic treatment takes place under medical supervision, and the beneficial effects of UV radiation exposure usually outweigh harmful side-effects. Use of tanning lamps or sunbeds for cosmetic purposes is not recommended (EURO*SKIN*, 2000).

Adverse effects of UV radiation on the skin

Chronic exposure to UV radiation accelerates skin ageing, and the gradual loss of the skin's elasticity results in wrinkles, dry, coarse skin and skin discolouration (WHO, 1994; Wei *et al.*, 1994). UV radiation also causes a number of degenerative changes in the cells, fibrous tissue and blood vessels of the skin, e.g. the induction of freckles and nevi.

Between 2 and 3 million non-melanoma skin cancers (WHO, 2001) and 132 000 melanoma skin cancers occur globally each year. Estimates of melanoma incidence rates for the European Region vary between below 1 case per 100 000 in the central Asian area and above 10 cases per 100 000 in some Scandinavian countries (see Table 12.2.). Since the early 1960s, the incidence of skin cancers has increased by between 3 % and 7 % in most fair-skinned populations (Armstrong and Kricker, 1994).

Non-melanoma skin cancers (NMSCs) comprise basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). BCC represents the commonest skin cancer but is rarely fatal, while SCC can metastasise and be fatal if left untreated. NMSC is most frequent on parts of the body that are commonly exposed to the sun, such as ears, face, neck and forearms. This implies, particularly for SCC, that long-term, repeated UV radiation exposure is a major causal factor (WHO, 1994).

Malignant melanoma (MM), although far less prevalent than NMSC, is the major cause of death from skin cancer. A large number of studies indicate that the risk of MM correlates with genetic and personal characteristics and a person's UV radiation exposure behaviour (WHO, 1994). High, intermittent exposure to solar UV radiation, especially during childhood, has been identified as a significant risk factor for the development of MM (WHO, 1994).

Table 12.2. **Melanoma incidence in countries in the European Region, 2000 estimates**

Source: Adapted from Ferlay *et al.*, 2001

Country	Total population (000)	Age-standardised incidence rate per 100 000	
		Male	Female
Albania	3 134	4.78	4.38
Armenia	3 787	0.60	0.51
Austria	8 080	8.82	10.35
Azerbaijan	8 041	0.54	0.47
Belarus	10 187	4.46	3.51
Belgium	10 249	5.82	6.83
Bosnia and Herzegovina	3 977	4.33	3.97
Bulgaria	7 949	3.59	3.73
Croatia	4 654	4.95	4.38
Czech Republic	10 272	8.20	8.30
Denmark	5 320	10.59	13.03
Estonia	1 939	3.82	6.37
Finland	5 172	7.47	7.85
France	59 238	6.77	7.96
Georgia	5 262	2.09	2.01
Germany	82 017	6.53	7.08
Greece	10 610	1.88	2.00
Hungary	9 968	7.63	6.75
Iceland	279	7.61	11.61
Ireland	3 803	7.85	10.22
Israel	6 040	9.44	9.81
Italy	57 530	4.57	5.50
Kazakhstan	16 172	4.67	4.22
Kyrgyzstan	4 921	0.93	0.72
Latvia	2 421	3.27	4.34
Lithuania	3 696	2.98	4.33
Luxembourg	437	5.13	7.19
Malta	390	3.98	5.82
Netherlands	15 864	9.38	12.87
Norway	4 469	14.12	15.89
Poland	38 605	5.58	6.68
Portugal	10 016	2.48	3.62
Republic of Moldova	4 295	3.58	3.15
Romania	22 438	3.02	3.89
Russian Federation	145 491	5.39	4.73
Slovakia	5 399	5.12	5.42
Slovenia	1 988	8.12	7.40
Spain	39 910	2.83	4.47
Sweden	8 842	12.60	13.34
Switzerland	7 170	9.26	10.11
Tajikistan	6 087	0.46	0.45
The Former Yugoslav Republic of Macedonia	2 034	7.15	7.05
Turkey	66 668	1.00	0.87
Turkmenistan	4 737	2.50	2.79
Ukraine	49 568	4.96	4.72
United Kingdom	59 415	6.14	7.65
Uzbekistan	24 881	0.53	0.44
Yugoslavia	10 552	4.07	3.79

Skin cancer risk is generally greater among fair-skinned populations whose natural protection by pigmentation is much lower than in naturally brown or black populations. In addition, the skin varies in its ability to adapt to UV radiation exposure, i.e. tanning and skin thickening.

Some individual risk factors for skin cancer are:

- fair skin
- blue, green or hazel eyes
- light-coloured hair
- tendency to burn rather than suntan
- history of severe sunburn
- many moles
- freckles
- a family history of skin cancer.

Adverse effects of UV radiation on the eye

Long-term health effects of UV radiation exposure on the eye include age-related cataract, pterygium, photodermatitis and eye cancer. Cataract is caused by a clouding of the lens and is responsible for 12–15 million cases of blindness, making it the leading cause of blindness in the world. Even though cataracts appear to different degrees in most individuals as they age, sun exposure, in particular exposure to UVB, appears to be a major risk factor for cataract development. According to WHO estimates, up to 20 % of cases of cataract-related blindness may be caused or enhanced by sun exposure (WHO, 1994). As the world's population ages, cataract-induced visual dysfunction and blindness are on the increase; reducing ocular exposure to UV radiation and preventing people from smoking are the only interventions that can reduce cataract risk (Brian and Taylor, 2001). Infants and children may be at particular risk of retinal injury since the transmissibility of the lens to UV radiation is greatest during childhood (AAP, 1999).

Adverse effects of UV radiation on the immune system

There is increasing evidence of a suppressive effect of both acute high-dose and chronic low-dose UV radiation exposure on the human immune system (Duthie *et al.*, 1999). Exposure to environmental levels of UV radiation alters the activity and distribution of some of the cells responsible for triggering immune responses in humans. Consequently, sun exposure may enhance the risk of disease resulting from viral, bacterial, parasitic or fungal infections and may modify the course of disease progression in both animals and humans (Halliday and Norval, 1997; Yamamoto *et al.*, 1999; Yamamoto *et al.*, 2000). Furthermore, especially in countries of the developing world, high UV levels may reduce the effectiveness of vaccinations. (Halliday and Norval, 1997; Duthie *et al.*, 1999). On the other hand, ecological studies indicate that UV radiation may play a protective role in some autoimmune disorders such as multiple sclerosis, insulin-dependent diabetes mellitus and rheumatoid arthritis (van der Mei *et al.*, 2001; Ponsonby *et al.*, unpublished data). However, these observations need further confirmation with non-aggregated data and experimental studies.

Animal experiments have demonstrated that UV radiation can modify the course and severity of skin tumours (Fisher and Kripke, 1977). Also, people treated with immunosuppressive drugs have a greater incidence of SCC than the normal population, with almost all of the tumours occurring on sun-exposed body sites. Consequently, beyond its role in the initiation of skin cancer, sun exposure may reduce the body's defences that normally limit the progressive development of skin tumours (WHO, 1994).

Childhood UV radiation exposure and skin cancer

Both melanoma and non-melanoma skin cancers rarely occur in childhood. Only 2.8 % of all childhood cancers diagnosed in the United States during 1975–95 were melanomas (Bernstein and Gurney, 1999). However, melanoma has become the most common US cancer in the 25–29 age group, and the third most common cancer among 20- to 24-year-old Americans (Ries *et al.*, 2001). In Europe, the cumulative incidence rate of melanoma among 0- to 14-year-olds is approximately 2 per 100 000 per year (Parkin *et al.*, 1998).

Sun exposure during childhood and adolescence appears to set the stage for the development of both melanoma and non-melanoma skin cancers (IARC, 1992). Light skin colour, freckling in childhood, a history of severe childhood sunburn and recreational sunlight exposure in childhood and adolescence have been identified as major risk factors for basal cell carcinoma (Gallagher *et al.*, 1995; Kricker *et al.*, 1994). Exposure to high levels of sunlight and a history of one or more incidents of sunburn

during childhood can significantly increase the risk for melanoma later in life (Whiteman *et al.*, 2001; Westerdahl *et al.*, 1994). Melanoma risk due to childhood sun exposure is aggravated by high sun exposure during adulthood (Autier and Doré, 1998; Elwood and Jopson, 1997). An association was found between the number and type of melanocytic nevi and the development of melanoma; the presence of congenital nevi greater than 1.5 cm in diameter is considered to increase the risk for melanoma. Furthermore, dysplastic melanocytic nevi may be a response to solar injury and are considered precursor lesions that increase the risk, as has been summarised by the American Academy of Pediatrics (AAP, 1999). Furthermore, an increased melanoma risk for young people related to the popular habit of artificial tanning in sunbeds was found in Sweden (Wester *et al.*, 1999).

12.3. Global environmental change and UV-related damage

Stratospheric ozone is a particularly effective UV radiation absorber. Decreased ozone levels will persist for many years to come, and the corresponding increases in UV radiation reaching the earth's surface are likely to exacerbate adverse health effects in all populations of the world. Computational models predict that a 10 % decrease in stratospheric ozone could cause an additional 300 000 non-melanoma and 4 500 melanoma skin cancers and between 1.6 and 1.75 million more cases of cataract worldwide every year (WHO, 1994).

Climate change may also influence people's exposure to sunlight. As clouds have a large effect on the amount of UV radiation reaching the earth's surface, reduced cloud cover could significantly increase people's UV radiation exposure. Furthermore, with increasing temperatures people are likely to spend more time outdoors thus adding to both their cumulative UV radiation exposure and their risk of sunburn (Hill and Boulter, 1996). In northern Europe global warming may well have a greater impact on people's sun exposure than ozone depletion (Diffey, 2000).

12.4. Behaviour and UV radiation exposure: protection measures to reduce children' s UV radiation exposure

Skin cancer is largely preventable. Between 65 % and 90 % of melanomas are caused by UV radiation exposure (Armstrong and Kricker, 1993) and could be prevented by limiting exposure to the sun and artificial sources of UV radiation. People's behaviour in the sun is the main cause of the rise in skin cancer rates in recent decades. An increase in popular outdoor activities and changed sunbathing habits often result in excessive UV radiation exposure. Many people consider intensive sunbathing to be normal and, unfortunately, even many children and their parents perceive a suntan as a symbol of attractiveness and good health. A change in people's behaviour towards effective sun protection is therefore essential to reduce UV radiation exposure, and could eliminate more than 70 % of skin cancers (Stern *et al.*, 1986).

Box 12.1. Ozone depletion

'The thickness of the ozone layer above Europe has decreased significantly since the beginning of the 1980s and is declining at a rate of up to 8 % per decade. The gradual fall in chlorine concentrations in the troposphere (on their way to the stratosphere) shows that international policies to control ozone-depleting substances are having success. Production and sales of ozone-depleting substances in EEA member countries have fallen significantly since 1989. However, the long life of these substances in the atmosphere means that recovery of the ozone layer may not be complete until after 2050. The remaining policy challenges for European countries are to tighten control measures, to reduce the production and use of HCFCs and methyl bromide, to manage banks of existing ozone-depleting substances, and to support developing countries in their efforts to reduce their use and subsequent emissions of ozone-depleting substances' (EEA, 1999).

British residents receive approximately 30 % of their annual UV radiation exposure during a two-week summer holiday (Diffey, 1996). This is likely to be similar for other northern and middle European countries. Where people spend their summer holiday will critically determine their overall sun exposure. Therefore, the most important factor increasing the need for sun protection even further is likely to be the rapid growth in overseas holidays (Diffey, 2000).

The importance of sun avoidance during childhood and adolescence

Sun avoidance during childhood and adolescence may have a greater impact on risk reduction than sun protection during adulthood (Autier and Doré, 1998). The majority of a person's lifetime exposure takes place before age 18 (Wakefield and Bonett, 1990; Marks *et al.*, 1990). Schoolchildren were shown to receive almost half their daily UV radiation dose during school-related

outdoor activities, especially if they did not seek shade during breaks (Moise *et al.*, 1999).

Nevi represent an important risk factor for skin cancer and are a major risk factor for melanoma. Their development occurs mostly before adolescence, and UV radiation exposure increases the number of nevi (Armstrong, 1997). Sun protection, in particular the use of clothes, appears to be an effective way to prevent the proliferation of nevi (Autier *et al.*, 1998).

Shade, clothing and hats provide the best protection for children (Box 12.2.) — applying sunscreen becomes necessary on those parts of the body that remain exposed like the face and hands. Sunscreen should never be used to prolong the duration of sun exposure (IARC, 2001).

Box 12.2. WHO recommends the following simple protection steps (WHO, 2001)

- Always keep infants of less than 12 months in the shade.
- Limit children's time in the midday sun.
- Cover up with protective clothing, a hat and sunglasses.
- Apply broad-spectrum sunscreen of SPF 15+ generously.
- Avoid sunlamps and tanning parlours.
- Remember that sun protection is necessary in all outdoor settings.

12.5. Strategies and programmes

Reducing both the occurrence of sunburn and cumulative UV radiation exposure can prevent damage to the skin, eyes and immune system, and significantly reduce health care costs. Long-term strategies are required in order to change people's sun exposure habits and the current societal view that associates a tan with good health. Action should be taken through a comprehensive approach including policy measures, information and education, and structural changes in the environment.

The SunSmart campaign of the Anti-Cancer Council of Victoria, Australia (ACCV, 1999), has made significant achievements in raising awareness of the issues of sun protection and skin cancer as well as encouraging changes in sun-related lifestyle. Recent evaluations of the programme show that fewer people see tanning as desirable or attractive and more people wear hats, use sunscreen and cover up to avoid the sun. Most significantly, research over the past decade has revealed an 11 % decrease in the incidence of common skin cancers among 14- to 50-year-olds (Staples *et al.*, 1998).

Beyond the health benefits, effective programmes can significantly decrease costs in the health system and strengthen the economy. Current prevention campaigns in Australia invest approximately USD 0.08 per person per year, while the direct costs of skin cancer treatment have been estimated at USD 5.70 per head of the population during the same period of time (Carter *et al.*, 1999).

School programmes

During the first 18 years of life children spend a significant proportion of their time at school or as part of school-based activities. Schools, therefore, are vitally important settings to promote sun protection among children, adolescents and the people taking care of them. Skills-based health education helps individuals to develop knowledge, attitudes, values and the life skills needed to make and act on the most appropriate and positive health-related decisions. Schoolchildren are especially susceptible to fashion trends suggesting that a suntan is healthy, and skills-based health education can help them to resist peer pressure. Individuals who develop such skills at a young age are more likely to adopt and sustain a healthy lifestyle during schooling and for the rest of their lives (FRESH, 2000).

Intersun, WHO's global UV project, has identified the development of a framework for children's sun protection education and practical educational resources as one of its priority activities (WHO, 2001). The curricular content and related activities on sun protection must be culturally and geographically relevant. While it is a personal decision to adopt sensible sun behaviour, positive choices can be supported through adequate structural and policy measures (WHOa, in press) such as the provision of shaded areas in the school environment. The availability of shade structures at schools and day-care centres is likely to reduce children's UV radiation dose significantly (Moise *et al.*, 1999). As a health issue with a very specific risk factor, sun protection is an ideal entry point to becoming a health-promoting school (WHO, 2000) which fosters health and learning through school health education, a healthy school environment, school health services, community and family involvement and outreach, and health promotion for school staff (WHOa, in press).

The role of health professionals

Parents who are knowledgeable about the hazards of sun exposure and practise sun protection are more likely to protect their children (Buller *et al.*, 1995). Pregnant women and young parents are particularly responsive to the sun protection message. Health professionals, especially gynaecologists and paediatricians, represent an important avenue for information dissemination about the health risks of UV radiation exposure and adequate sun protection. Similarly, due to their frequent interaction with patients and their families, general practitioners and nurses can play a key role in both primary and secondary prevention of skin cancer. It is crucial that they are adequately trained to recognise the risk factors and precursors of skin cancer to allow for correct referral to a dermatologist.

The role of local authorities

Local authorities have a responsibility to ensure that their community is safe and healthy for its residents, businesses and visitors. They can make a significant contribution to skin cancer control by creating a physical environment that provides shade at bus stops, in school grounds, and over benches and barbecue sites in parks. A supportive regulatory environment can influence policies and practices in schools and recreation centres, or ensure commercial sunbed establishments are run professionally. Local authorities should take adequate steps to reduce health risks associated with outdoor programmes where participants and staff may be at risk of high sun exposure.

The UV index represents a vehicle that can help to inform the public about UV health risks and sun protection (ICNIRP, 1995; WHOb, in press). The UV index describes the level of solar UV radiation at the earth's surface. The values of the index range from zero upwards — the higher the index value, the greater the potential for damage to the skin and eye, and the less time it takes for harm to occur. Local authorities in cooperation with the educational sector and the media can influence knowledge, attitudes and behaviour of residents in their municipalities.

Summary

Overexposure to ultraviolet (UV) radiation from the sun and artificial sources is of considerable public health concern, because it plays an important role in the development of skin cancer and cataracts, and may suppress certain immunological responses. Frequent sun exposure and a history of sunburn during childhood and adolescence are major risk factors for the development of skin cancer later in life. Prevention efforts to change children's knowledge, attitudes and behaviour regarding sun protection can significantly decrease adverse health effects and health care costs.

A reduction in UV radiation exposure during childhood and adolescence may significantly reduce the risk of adverse health effects later in life, and is likely to have a greater impact on risk reduction than sun protection during adulthood. Therefore, prevention efforts should focus on this critical age group and work towards changing children's knowledge, attitudes and behaviour in relation to sun protection.

Policy measures, information and education, and structural changes in the environment represent key components of an effective prevention programme. Schools, health professionals and local authorities play an important role in reaching out to children and the people taking care of them.

References

AAP, 1999. *Handbook of pediatric environmental health*, Committee on Environmental Health, American Academy of Paediatrics, Elk Grove Village, IL.

ACCV, 1999. *Skin cancer control program, related research and evaluation*, SunSmart Evaluation Studies No 6, Anti-Cancer Council of Victoria, Victoria.

Armstrong, B.K., 1997. Melanoma: Childhood or lifelong sun exposure, in *Epidemiology, causes and prevention of skin diseases* (edited by J.J. Grob, R.S. Stern, R.M. MacKie *et al.*), 1st edition, Blackwell Science, London, pp. 72–7.

Armstrong, B.K. and Kricker, A., 1993. How much melanoma is caused by sun exposure? *Melanoma Res*, Vol 3, pp. 395–401.

Armstrong, B.K. and Kricker, A., 1994. Cutaneous melanoma, *Cancer Survey*, Vol 19/20, pp. 219–40.

Autier, P. and Doré, J.F., 1998. Influence of sun exposures during childhood and during adulthood on melanoma risk, EPIMEL and EORTC Melanoma Cooperative Group, European Organization for Research and Treatment of Cancer, *Int J Cancer*, Vol 77, pp. 533–7.

Autier, P., Doré, J.F., Cattaruzza, M.S. *et al.*, 1998. Sunscreen use, wearing clothes, and number of nevi in 6- to 7-year-old European children, European Organization for Research and Treatment of Cancer Melanoma Cooperative Group, *J Natl Cancer Inst*, Vol 90, pp. 1873–80.

Bernstein, L. and Gurney, J.G., 1999. Carcinomas and other malignant epithelial neoplasms, in *SEER program 1975–1995. SEER paediatric monograph, 1975–1995* (edited by L.A.G. Ries, M.A. Smith, J.G. Gurney *et al.*), National Cancer Institute, SEER Program, NIH, Pub. No 99-4649, Bethesda, MD.

Blumthaler, M., Webb, A.R., Seckmeyer, G. *et al.*, 1994. Simultaneous spectroradiometry; a study of solar UV irradiance at two altitudes, *Geophys Res Lett*, Vol 21, pp. 2805–8. http://seer.cancer.gov/Publications/PedMono (in 2001)

Brian, G. and Taylor, H., 2001. Cataract blindness — challenges for the 21st century, *Bulletin of the World Health Organization*, Vol 79, pp. 249–56.

Buller, D.B., Callister, M.A. and Reichert, T., 1995. Skin cancer prevention by parents of young children: Health information sources, skin cancer knowledge, and sun-protection practices, *Oncol Nurs Forum*, Vol 22, pp. 1559–66.

Carter, R., Marks, R. and Hill, D., 1999. Could a national skin cancer primary prevention campaign in Australia be worthwhile? An economic perspective, *Health Promotion International*, Vol 14, pp. 73–82.

Césarini, J.P., 2000. Biological effects and health consequences, in *Non-ionizing radiation. Executive summary of the 4th International non-ionizing radiation workshop Kyoto, Japan, May 22–25, 2000* (edited by R. Matthes, J.H. Bernhardt and M. Taki), International Commission for Non-Ionizing Radiation Protection, ICNIRP 9/2000, pp. 77–80.

Christensen, T., 2000. Radiation risks to children, in *Children and radiation. Selected topics raised at an international conference* (edited by T. Christensen and S. Stephens), Norwegian Centre for Child Research, Trondheim, pp. 15–29.

Diffey, B., 1996. Population exposure to solar UVA radiation, *Eur J Dermatol*, Vol 6, pp. 221–2.

Diffey, B., 2000. Personal protection: The way forward, *Radiation Protection Dosimetry*, Vol 91, pp. 293–6.

Duthie, M.S., Kimber, I. and Norval, M., 1999. The effects of ultraviolet radiation on the human immune system, *Br J Dermatol*, Vol 140, pp. 995–1009.

Elwood, J.M. and Jopson, J., 1997. Melanoma and sun exposure: An overview of published studies (Review), *Int J Cancer*, Vol 73, pp. 198–203.

EEA, 1999. *Environment in the European Union at the turn of the century*, European Environment Agency, Copenhagen.

EURO*SKIN*, 2000. *Recommendations from an international conference towards the promotion and harmonization of skin cancer prevention*, European Society for Skin Cancer Prevention, Hamburg.

Ferlay, J., Bray, F., Pisani, P. *et al.*, 2001. *GLOBOCAN 2000: Cancer incidence, mortality and prevalence worldwide*, Version 1.0, IARC CancerBase No 5, IARC Press, Lyon. (On line at: http://www-dep.iarc.fr/dataava/infodata.htm)

Fisher, M.S. and Kripke, M.L., 1977. Systemic alteration induced in mice by ultraviolet light irradiation and its relationship to ultraviolet carcinogenesis, *Proc Natl Acad Sci USA*, Vol 74, pp. 1688–92.

FRESH, 2000. *A FRESH start to improving the quality and equity of education*, Focusing Resources on Effective School Health, WHO, UNESCO, UNICEF, World Bank, Education International.

Gallagher, R.P., Hill, G.B., Bajdik, C.D. *et al.*, 1995. Sunlight exposure, pigmentary factors, and risk of nonmelanocytic skin cancer. I. Basal cell carcinoma, *Archives of Dermatology*, Vol 131, pp. 157–63.

Halliday, K.E. and Norval, M., 1997. The effect of UV on infectious diseases, *Reviews in Medical Microbiology*, Vol 8, pp. 179–188.

Hill, D. and Boulter, J., 1996. Sun protection behaviour: Determinants and trends, *Cancer Forum*, Vol 20, pp. 204–10.

IARC, 1992. *IARC monographs on the evaluation of carcinogenic risks to humans — Solar and ultraviolet radiation*, Vol 55, International Agency for Research on Cancer, WHO, Lyon, France.

IARC, 2001. *IARC monographs on cancer prevention — Sunscreens*, Vol 5, International Agency for Research on Cancer, WHO, Lyon, France.

ICNIRP, 1995. *Global solar UV index*, International Commission on Non-Ionizing Radiation Protection, Oberschleissheim.

Kricker, A., Armstrong, B.K and English, D.R., 1994. Sun exposure and non-melanocytic skin cancer (Review), *Cancer Causes Control*, Vol 5, pp. 367–92.

Marks, R., Jolley, D., Lectsas, S. *et al.*, 1990. The role of childhood exposure to sunlight in the development of solar keratoses and non-melanocytic skin cancer, *Med J Australia*, Vol 152, pp. 62–6.

McKie, R.M., 2000. Effects of ultraviolet radiation on human health, *Radiation Protection Dosimetry*, Vol 91, pp. 15–8.

Moise, A.F., Buttner, P.G. and Harrison, S.L., 1999. Sun exposure at schools, *Photochem Photbiol*, Vol 70, pp. 269–74.

Parkin, E.M., Kramarova, E., Draper, G.J. *et al.*, eds, 1998. *International incidence of childhood cancer*, Vol II, International Agency for Research on Cancer, Lyon.

Ponsonby, A.L., McMichael, A. and van der Mei, I., unpublished data.

Ries, L.A.G., Eisner, M.P., Kosary, C.L. *et al.*, eds, 2001. *SEER cancer statistics review, 1973–1998*, National Cancer Institute, Bethesda, MD.

Sliney, D.H., 1986. Physical factors in cataractogenesis: Ambient ultraviolet radiation and temperature, *Invest Ophthalmol Visual Sci*, Vol 27, pp. 781–90.

Staples, M., Marks, R. and Giles, G., 1998. Trends in the incidence of non-melanocytic skin cancer (NMSC) treated in Australia 1985–95: Are primary prevention programs starting to have an effect? *Int J Cancer*, Vol 78, pp. 144–8.

Stern, R.S., Weinstein, M.C. and Baker, S.G., 1986. Risk reduction for nonmelanoma skin cancer with childhood sunscreen use, *Archives of Dermatology*, Vol 122, pp. 537–45.

van der Mei, I.A., Ponsonby, A.L., Blizzard, L. *et al.*, 2001. Regional variation in multiple sclerosis prevalence in Australia and its association with ambient ultraviolet radiation, *Neuroepidemiology*, Vol 20, pp. 168–74.

Wakefield, M. and Bonett, A., 1990. Preventing skin cancer in Australia, *Med J Australia*, Vol 152, pp. 60–1.

Wei, Q., Matanosky, G.M., Farmer, E.R. *et al.*, 1994. DNA repair and susceptibility to basal cell carcinoma: A case-control study, *Am J Epidemiol*, Vol 140, pp. 598–607.

Wester, U., Boldemann, C., Jannsson, B. *et al.*, 1999. Population UV-dose and skin area — do sunbeds rival the sun? *Health Phys*, Vol 77, pp. 436–40.

Westerdahl, J., Olsson, H. and Ingvar, C., 1994. At what age do sunburn episodes play a crucial role for the development of malignant melanoma (Review), *Eur J Cancer*, Vol 30A, pp. 1647–54.

Whiteman, D.C., Whiteman, C.A. and Green, A.C., 2001. Childhood sun exposure as a risk factor for melanoma: A systematic review of epidemiologic studies (Review), *Cancer Causes Control*, Vol 12, pp. 69–82.

WHO, 1994. Ultraviolet radiation, *Environmental Health Criteria*, No 160, World Health Organization, Geneva.

WHO, 2000. *Local action: Creating health-promoting schools*, WHO Information Series on School Health, World Health Organization, Geneva.

WHO, 2001. *Intersun. The global UV project*, Fact sheet 261, World Health Organization. http://www.who.int/inf-fs/en/fact261.html (in 2001)

WHOa, in press. *Sun protection: An essential element of a health-promoting school,* WHO Information Series on School Health, World Health Organization, Geneva.

WHOb, in press. *Global solar UV index — A practical guide,* World Health Organization, Geneva.

Yamamoto, K., Ito, R., Koura, M. *et al.*, 1999. Increased susceptibility of mice to malarial infection following UVB irradiation, *J Epidemiol*, Vol 9, pp. S93–6.

Yamamoto, K., Ito, R., Koura, M. *et al.*, 2000. UVB irradiation increases susceptibility of mice to malarial infection, *Infection and Immunity*, Vol 68, pp. 2353–5.

13. Electromagnetic fields

Kristie L. Ebi
Contributing authors: Ondine S. von Ehrenstein, Katja Radon

Summary of existing knowledge
- The classification of power-frequency electromagnetic fields (EMF) as a possible human carcinogen is partially based on studies of childhood leukaemia.
- Available evidence suggests that exposure to power-frequency EMF is not associated with childhood brain tumours.
- The possible adverse health effects in children associated with radiofrequency fields have not been fully investigated.

Main challenges
- To improve understanding of the effect of EMF on children's health, particularly in early development.
- To determine the biological mechanism of action.
- To determine relevant exposure and improve knowledge of all sources of exposure.

Action points
- As any population-level effect is likely to be small, prudent avoidance is one approach to dealing with the uncertainty.

13.1. Introduction

Public concern continues about the possible negative health consequences of exposure to power-frequency and radiofrequency electromagnetic fields (EMF). Modern industrial development has resulted in everyone being exposed to a complex mix of electric and magnetic fields and radiation, with exposure beginning before birth. The possible health outcomes associated with power-frequency EMF were recently reviewed by national and international agencies, including the International Agency for Research on Cancer (IARC), the National Radiological Protection Board (NRPB), the US National Institute of Environmental Health Sciences (NIEHS) and others (NRPB, 2001; WHO, 2001; Tenforde, 2000; Portier and Wolfe, 1998). One priority issue was the association between power-frequency fields and childhood leukaemia. All reviews noted that more than 20 years of research have not resolved scientific questions about the possible adverse health effects of EMF exposure and that evaluations of exposure assessment and epidemiological studies were made more difficult because of the lack of knowledge of what, if any, is the biologically relevant exposure and the lack of a biological mechanism. The following chapter gives an overview of EMF, and then summarises research on the association between EMF and adverse health effects in children.

13.2. Physical characterisation

Electromagnetic radiation is the transportation of energy through space. The electromagnetic spectrum spans a very large range of frequencies — more than 15 orders of magnitude. It ranges from below power-frequency fields to ionising radiation. This spectrum can be divided into three broad bands based on their frequency or wavelength: electromagnetic fields and radiation (0 hertz (Hz) to 300 gigahertz (GHz), where 1 000 Hz = 1 kilohertz (kHz), 1 000 kHz = 1 megahertz (MHz) and 1 000 MHz = 1 GHz); infrared and optical radiation; and ionising radiation (Figure 13.1.). Electromagnetic fields and radiation are further broken down (Table 13.1.) into: extremely-low-frequency (ELF) EMF (between 30 and 3 000 Hz); radio frequencies, which range from the very low frequencies of television sets and visual display units (about 30 kHz) to the high frequencies of FM radio (about 300 MHz); and microwaves, which are at the high end of this spectrum (up to 300 GHz). Power-frequency EMF falls into the ELF range of the spectrum; the frequency depends on the power source. Power systems operate at frequencies of either 50 or 60 cycles per second (50 or 60 Hz).

Electromagnetic fields and their sources Table 13.1.

Source: NRPB, 2001

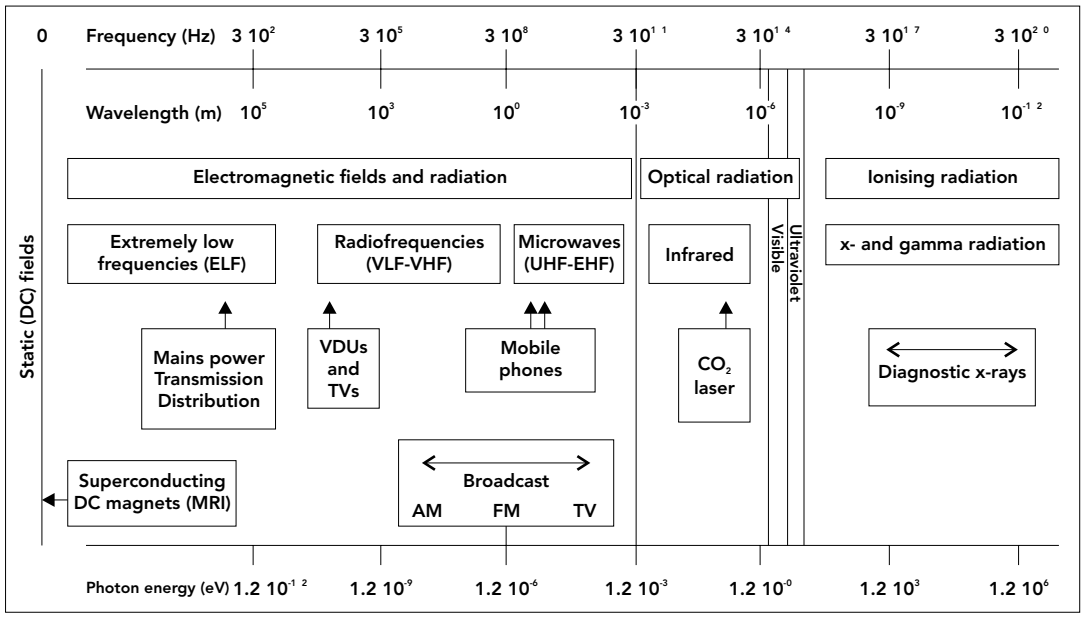
Frequency	Wavelength	Description	Band	Sources
0 Hz		Static		Earth's field Magnets, DC supplies
		Sub-extremely low frequency	SELF	
30 Hz 50 Hz	10 000 km 6 000 km	Extremely low frequency	ELF	Electric power lines and cables Domestic and industrial appliances
300 Hz	1 000 km	Voice frequency*	VF	Induction heaters
3 kHz	100 km	Very low frequency	VLF	Television sets Visual display units
30 kHz	10 km	Low frequency	LF	AM radio
300 kHz	1 km	Medium frequency	MF	Induction heaters
3 MHz	100 m	High frequency	HF	RF heat sealers
30 MHz	10 m	Very high frequency	VHF	FM radio
300 MHz	1 m	Ultra high frequency	UHF	Mobile phones Television broadcast Microwave ovens
3 GHz	10 cm	Super high frequency	SHF	Radar Satellite links Microwave communications
30 GHz	1 cm	Extra high frequency	EHF	Point-to-point links
300 GHz	1 mm	Infrared		

*Radiofrequencies equivalent to speech (sound) frequencies.

Note: 1000 Hz = 1 kHz; 1000 kHz = 1 MHz; 1000 MHz = 1 GHz.

Electromagnetic spectrum Figure 13.1.

Source: NRPB, 2001



13.3. Extremely-low-frequency electromagnetic fields (ELF-EMF)

An electromagnetic field is composed of two components, the electric and the magnetic fields. The electric field is created by the presence of an electric charge and is determined by the voltage. Whenever electricity is generated, transmitted or used, magnetic fields are created from the presence and motion of electric charges. The current determines the magnitude of a magnetic field. Magnetic fields are three-dimensional (described by the directional components x, y, z) and time-varying vector quantities that can be described by a number of parameters, including their frequency, phase, direction and magnitude. Electric and

magnetic fields have different properties that are of importance when considering possible biological effects. Essentially all materials, including clothing, easily shield power-frequency electric fields. In contrast, the properties of magnetic fields are such that they pass through nearly all materials, including living tissues, building structures and the earth. The primary determinants of magnetic field exposure are source geometry and distance from the source to the measurement location. One consequence is that the magnitude of a magnetic field decreases fairly rapidly with distance from an isolated source. In general, magnetic fields from transmission and distribution lines decrease with the inverse square of the distance, while the fields from appliances decrease with the inverse square to the inverse cube of the distance. The strength of a magnetic field is usually designated by its magnetic flux density or B field measured in tesla (T). Magnetic field exposures from power frequency fields are in the range of μT (1×10^{-6} T).

Sources and magnitude of exposure

Major sources of EMF exposure include electrical power generation, transmission and use in residential and occupational settings, and telecommunications and broadcasting. Most devices that have electrical wires are potential sources of power-frequency EMF. Although the predominant exposure is to alternating current waveforms, humans are also exposed to a mixture of frequencies, including switching events that generate abrupt spikes of high-frequency transients that can extend into radio frequencies. Residential exposures include power-frequency exposures, radio frequencies and microwave sources.

Magnetic field exposures from power lines are dependent on the current carried on the line, the geometry of the system, the number of consumers, the distance to the nearest electrical equipment (often substation or transformer), the grounding practices, and the season (Johnsson and Mild, 2000). Typical magnetic field exposures directly under transmission lines are: 40 μT under a 400-kilovolt (kV) line, 22 μT under a 275-kV line and 7 μT under a 132-kV line (NRPB, 2001). Exposures 25 metres away from these same lines typically are 8, 4 and 0.5 μT, respectively.

Table 13.2. summarises children's personal magnetic field exposures in six studies (Foliart *et al.*, 2001). Some of these studies were of childhood leukaemia and others were surveys. The 24-hour mean time-weighted average measurements ranged from 0.10 to 0.14 μT, with 10–14 % of children having exposures above 0.2 μT. Typically, high-voltage transmission lines account for a minority of high exposures. For example, in Germany, only 29 % of all higher magnetic field exposures were attributable to high-voltage transmission lines (Schütz *et al.*, 2000).

The high visibility of overhead power lines has resulted in most concern about EMF exposure being associated with them. A frequently proposed solution is undergrounding of transmission and distribution lines. However, exposures from underground cables may be higher due to the properties of magnetic fields and the constraints in building an electrical supply system. Electricity is carried in three separate phases (seen as the three conductor bundles carried on transmission lines). The spatial arrangement of these phases will cancel some amount of the magnetic field (compared with a single conductor). The amount of cancellation is determined by the configuration of and distance between these phases. Transmission and distribution lines require a minimum ground clearance to prevent flashover hazards; this clearance is often more than 7 metres. Undergrounding cables are individually insulated and placed much closer together than overhead conductors. This close physical spacing results in more field cancellation than occurs with overhead lines. However, underground wires are often buried at a depth of 1 metre, placing the magnetic field source closer to an individual than an overhead source (Figure 13.2.).

Besides overhead power lines, residential EMF exposures arise from current flowing in conducting pipework and the ground, and from appliance use. Away from power lines, background magnetic field levels arise because the load current a particular house draws is rarely exactly balanced by the current returning via the neutral conductor. In the United Kingdom, residential exposures away from power lines are mostly in the range of 0.01 to 0.2 μT, with very few exposures exceeding 0.3 μT (Swanson and Kaune, 1999). Different operating characteristics and wiring practices result in higher exposures in the United States. For most people, their highest magnetic field

Children's personal magnetic field exposures by study[1] Table 13.2.

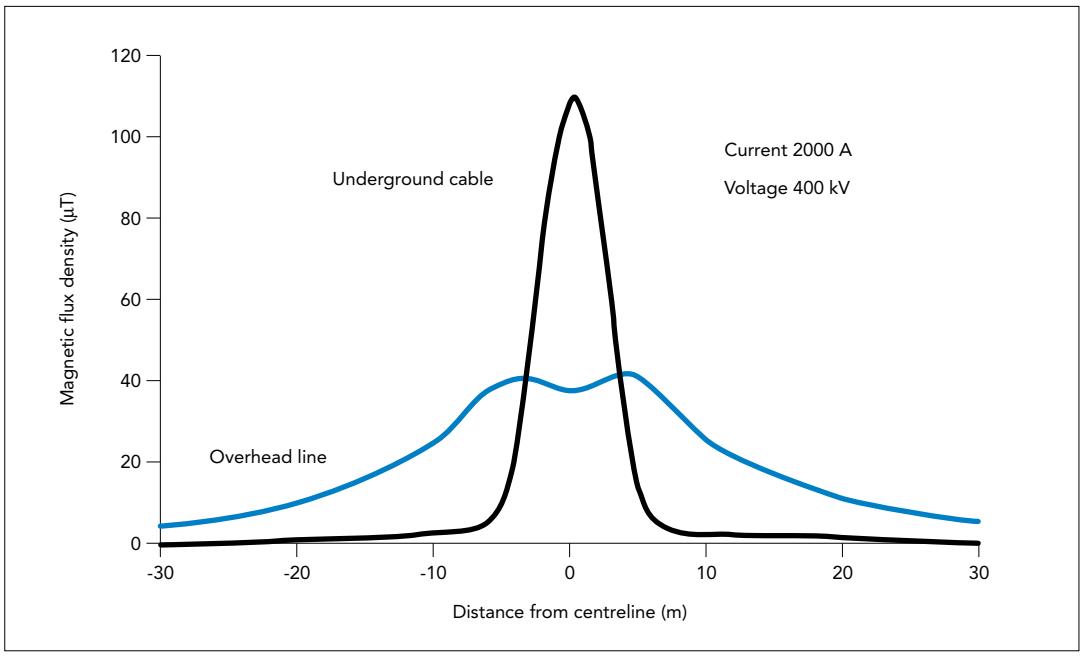
Source: Foliart *et al.*, 2001

Study (age range)	N	24-hour time-weighted average mean (μT)	24-hour time-weighted average ≥ 0.2 μT	Geometric mean (μT)	Geometric standard deviation	Median (μT)
Childhood leukaemia survival (case study: 0–15 years)	356	0.115 (0.104)[2]	10.1 %	0.075	2.30	0.073 μT
EMF-RAPID 1 000 person (0–18 years) (Zaffanella and Kalton, 1998)[3]	138	0.106	12.3	0.077	2.19	0.069
NCI – Washington, DC pilot (0–8 years) (Kaune *et al.*, 1994)	29	0.13	14.3[4]	0.105	1.89	n/a
EPRI – Enertech study (0–18 years) (Kaune and Zaffanella, 1994)	31	0.14	13	0.097[5]	2.46	n/a
NCI – cases (<15 years) (Linet *et al.*, 1997)	615	0.104	11.4	0.077	2.09	0.072
BCCA study – controls (0–14 years) (McBride *et al.*, 1999)	329		12.8[6]			

1) Includes studies reporting exposures among children.
2) Excludes outlier associated with night-time use of portable fan.
3) Includes 138 children up to the age of 17: the 24-hour time-weighted average exposures were 0.11 μT for children less than 5 years and 0.10 μT for children 5–17 years of age.
4) Per cent ≥ 0.25 μT.
5) At-home average for combination of two days.
6) Lifetime predicted exposure; contemporaneous measurements yield 15.3 %.

Magnetic fields from overhead lines and underground cables Figure 13.2.

Source: NRPB, 2001



exposures arise from the use of domestic appliances that incorporate motors, transformers or heaters (NRPB, 2001). For example, at 3 centimetres (cm) distance, the magnetic field exposures from hair dryers and can openers may be several hundred microtesla.

Exposure assessment

One goal of exposure assessment is to choose a summary measure that is both physically meaningful and biologically relevant. Challenges include the facts that residential (and most occupational) exposure is not perceptible by humans; the sources of EMF are ubiquitous in modern urban life making it difficult to predict circumstances that might lead to particularly high exposures; EMF are highly variable in time and space, which means that measurements can be subject to large random variations; and there is no generally accepted biophysical mechanism and no established biomarker of exposure or response (Portier and Wolfe, 1998). Various approaches have been used to summarise EMF exposure over time within groups of individuals. There is no scientific consensus on which exposure metrics (if any) are related to biological responses.

One commonly used exposure surrogate in studies of childhood cancers is the time-weighted average. Another surrogate is called a wire or wiring code, which combines information on the identifying characteristics of the distribution and transmission lines visible from outside a home and the distance from the home to the wires. Wire codes were primarily used in studies conducted in the United States.

Biological interactions

As the issues of concern for children are leukaemia (specifically acute lymphocytic leukaemia) and brain cancer, the following discussion will focus on the association between exposure to ELF-EMF and cancer development and progression. The full range of possible biological effects associated with power-frequency fields has been extensively reviewed by NRPB, NIEHS and others (NRPB, 2001; Tenforde, 2000; Portier and Wolfe, 1998).

Experimental studies relevant to carcinogenesis

A large number of papers have been published describing cellular and animal studies designed to determine whether or not electric or magnetic fields are capable of carcinogenesis. The focus of recent studies has been cancer promotion or progression as earlier studies demonstrated that ELF-EMF fields do not contain enough energy to directly cause DNA damage and, therefore, are not genotoxic (Murphy *et al.*, 1993; McCann *et al.*, 1993). A comprehensive review of fields below 1 μT also concluded that these fields are not mutagenic (Lacy-Hulbert *et al.*, 1998).

The 2001 NRPB review concluded that: 'At the cellular level, there is no clear evidence that exposure to weak ELF electromagnetic fields (of less than 1 μT) can affect biological processes. Studies are often contradictory and there is lack of confirmation of positive results from different laboratories using the same experimental conditions.' The review also concluded that there were three areas with suggestive evidence where further investigation is needed: possible enhancement of genetic change caused by known genotoxic agents; effects on intracellular signalling, particularly calcium flux; and effects on specific gene expression. The results that claim to demonstrate positive effects tend to show small changes with uncertain biological consequences; also, these positive effects are generally at field levels much higher than those found in residences.

In addition to NRPB and NIEHS, Boorman *et al.* (2000) and McCann *et al.* (2000) extensively reviewed the animal carcinogenic studies. The studies investigated the possible effects of exposure to mostly power-frequency fields on spontaneous and chemically induced tumour incidence, and on the growth of transplanted tumour cells. Most of the recent large-scale studies found no evidence of carcinogenicity. Specifically, four large-scale studies of the effects of lifetime exposures on spontaneous tumour incidence in rats and mice were mostly negative (Mandeville *et al.*, 1997; Yasui *et al.*, 1997; Boorman *et al.*, 1999; McCormick *et al.*, 1999). Several studies investigated the possible effects on brain cancer or on leukaemia, the childhood cancers of concern. The reviews concluded that most studies reported a lack of effect of power-frequency magnetic fields on leukaemia or lymphoma in rodents (mostly mice). Two of the studies used transgenic mice that develop a disease with some similarities to childhood acute lymphocytic leukaemia (Harris *et al.*, 1998; McCormick *et al.*, 1998). Other studies found no effect of EMF on the progression of transplanted leukaemia cells in mice or rats.

The most marked effect reported in only one study was an increase in lymphoid hyperplasia and lymphoma in mice exposed over three generations (Fam and Mikhail, 1996); however, NRPB concluded that there were a number of deficiencies that made it difficult to place a high degree of confidence in the result (NRPB, 2001). Although there is no natural animal model of spontaneous brain tumour, a recent large-scale study in female rats found no effect of EMF exposure on chemically induced nervous system tumours (Mandeville *et al.*, 2000). Other large-scale rat studies reported a low incidence of brain cancers (Mandeville *et al.*, 1997; Yasui *et al.*, 1997).

Epidemiological studies of childhood cancers

IARC, NRPB and US NIEHS reviewed the scientific literature regarding possible evidence for an association between exposure to ELF-EMF and cancer development (NRPB, 2001; WHO, 2001; Portier and Wolfe, 1998). All used a similar process of expert judgment for evaluation of the scientific evidence and IARC and US NIEHS summarised their findings according to the strength of the overall evidence using the IARC categories. IARC and US NIEHS concluded that the scientific evidence, in particular the evidence as it relates to childhood leukaemia, suggests that power-frequency EMF is possibly carcinogenic to humans (category 2B). The decisions were based on the evaluations that there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. NIEHS concluded that there was inadequate evidence of carcinogenicity with respect to childhood nervous system tumours.

There is a considerable body of epidemiological research on the association between power-frequency EMF and childhood leukaemia dating from 1979 (Wertheimer and Leeper, 1979). NIEHS, NRPB and others have extensively reviewed the epidemiology studies of ELF-EMF and childhood leukaemia (NRPB, 2001; Portier and Wolfe, 1998). The strengths of the reported associations between residential exposure to power-frequency magnetic fields and childhood leukaemia vary in the studies from no association to about a two-fold increased risk of childhood leukaemia among children with higher exposure. A number of methodological issues make interpretation of these studies difficult; these include exposure assessment, confounding and selection bias. The exposure assessment issue revolves around the question of the appropriate metric to be used as a surrogate for exposure. As noted above, unknowns include the possible mechanism of action of power-frequency magnetic fields, the aspect of the fields that is of biological relevance and the etiologically relevant time period. An additional difficulty arises from the problem of estimating exposures prior to disease diagnosis. The variety of metrics used to estimate exposure are not able to capture the hourly, daily, weekly, seasonal and long-term fluctuations in magnetic-field strength.

In addition, as little is known about the etiology of childhood cancers, studies have searched for factors that could confound the reported associations between EMF and childhood leukaemia. Recent reviews, including NIEHS and NRPB, conclude that confounding is unlikely to be an explanation for the reported results (NRPB, 2001; Portier and Wolfe, 1998). Langholz used the mathematics of confounding to explore factors that could explain the reported associations between wire codes and childhood leukaemia in three major case-control studies conducted in the United States (Langholz, 2001). Very few potential explanatory factors were identified (age and type of home, and magnetic fields). The question of selection bias arises because some of the studies conducted in the United States used methods to choose controls that may have resulted in controls not being representative of the population from which the cases arose. However, other studies, particularly those conducted in Scandinavian countries, were unlikely to suffer from selection bias because individual-level morbidity and mortality data are available across the population.

The NIEHS and NRPB reviews concluded that there is limited evidence that residential exposure to ELF magnetic fields is carcinogenic in children (NRPB, 2001; Portier and Wolfe, 1998). The NIEHS stated that 'although the exposure metrics used as surrogates for exposure to magnetic fields are of varying precision, it is difficult to find an explanation other than exposure to magnetic fields for the consistency of the reported excess risks for childhood leukaemia in studies conducted in different countries under different conditions, with different study designs' (Portier and Wolfe, 1998).

Two recent studies conducted pooled analyses of magnetic fields and childhood leukaemia (Ahlbom *et al.*, 2000; Greenland *et al.*, 2000). Original data were used in both analyses. Ahlbom *et al.* (2000) based their re-analysis on nine studies with comparable cases and controls that used direct measurements of exposure. Exposure assessment in these studies was based either on magnetic field measurements of 24 to 48 hours (studies in Canada, Germany, New Zealand, the United Kingdom and the United States), or on calculated field exposures (studies in Denmark, Finland, Norway and Sweden). There were 3 203 cases, of whom 83 % had acute lymphocytic leukaemia, and 10 388 controls. Exposure categories were defined *a priori* as < 0.1 μT (baseline for comparison); 0.1 to < 0.2 μT; 0.2 to < 0.4 μT; and ≥ 0.4 μT. There were 44 cases and 62 controls in the highest exposure category of ≥ 0.4 μT. In the measurement studies, the summary relative risk (RR) for all types of leukaemia in the highest exposure category was 1.83 (95 % CI 1.08–3.11; p = 0.01). In the calculated field studies, the relative risk in the highest exposure category was 2.13 (95 % CI = 0.93–4.88; p = 0.04). The summary relative risk in all studies combined was 2.00 (95 % CI = 1.28–3.13; p = 0.002). Relative risks in the intermediate exposure categories were close to unity for both measured and calculated fields. Continuous analysis estimated the relative risk at 1.15 (95 % CI 1.04–1.27) per 0.2 μT (p = 0.004). Adjustment for potential confounding variables did not appreciably change the results. The percentage of children in the highest exposure category varied by country. The results for acute lymphocytic leukaemia were essentially the same. The authors pointed out that the results mean that the 99.2 % of children residing in homes with exposure levels < 0.4 μT had estimates compatible with no increased risk, while the 0.8 % of children with exposures ≥ 0.4 μT had a relative risk estimate of about two. This increased risk is unlikely to be due to random variability.

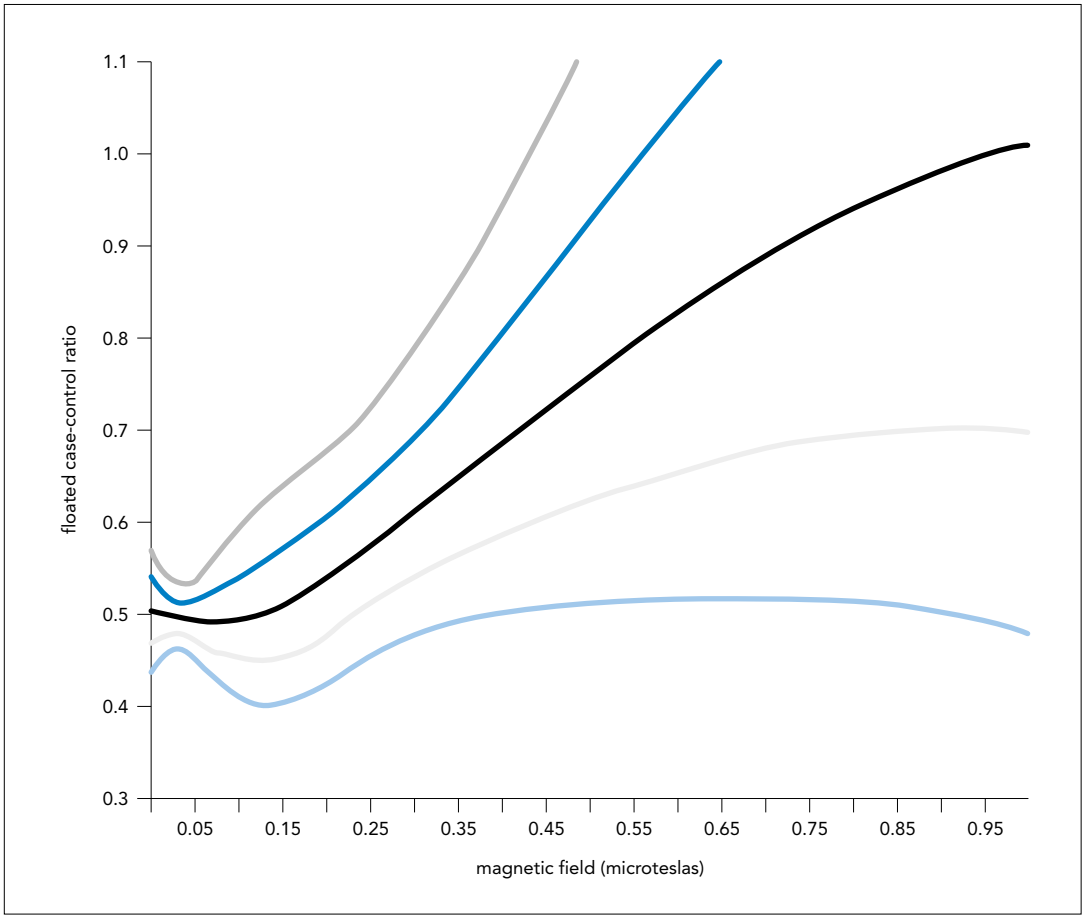
Greenland *et al.* (2000) re-analysed the data from 12 studies of childhood leukaemia. Eight of the studies were included in the Ahlbom *et al.* (2000) re-analysis. As much as possible, calculated historical fields or averages of multiple measurements were used. The target metric was each child's time-weighted average exposure up to three months prior to diagnosis. The cut-off for the highest exposure category was ≥ 0.3 μT. The results were similar to those reported by Ahlbom *et al.* (2000); the summary odds ratio (OR) for those in the highest exposure category was 1.7 (95 % CI 1.2–2.3) compared with exposure to 0 to 0.1 μT. There also was evidence of increasing risk with increasing exposure to magnetic fields above 0.15 μT (Figure 13.3.). Controlling for various potentially confounding variables made little difference in the risk estimates. The authors calculated that for the population of the United States, the population-attributable fraction of childhood leukaemia associated with residential exposure might have been 3 % (95 % CI –2 % to +8 %). The authors concluded 'both our categorical and trend analyses indicate that there is some association comparing fields above 0.3 μT to lower exposures'. However, they caution that 'the inconclusiveness of our results seems inescapable'.

The NRPB review supports the possible small effect of magnetic field exposures on the incidence of childhood leukaemia (NRPB, 2001). Among children up to 14 years of age, about 430 cases of leukaemia (all types) are registered each year in England and Wales. The UK Childhood Cancer Study found that 0.4 % of children are exposed to ≥ 0.4 μT. Assuming a doubling of risk at this exposure level, then annually about two cases of leukaemia would occur anyway and a further two cases might be attributable to EMF exposure. If regression dilution were concealing a relative risk of 1.5 for children exposed to between 0.2 and 0.4 μT, then the annual number of attributable cases might be six or seven.

These reviews are supported by a recent population-based case-control study in West Germany that included 24-hour measurements of magnetic field exposures for 514 cases of acute lymphocytic leukaemia and 1 301 controls (Schütz *et al.*, 2001). The analysis compared exposures above and below 0.2 μT. Only 1.5 % of the study population had exposures above 0.2 μT. The strongest association was found for night-time exposures (OR = 3.21, 95 % CI 1.33–7.80). A dose-response relationship was observed after combining the data of all German studies on childhood leukaemia and magnetic field exposures (OR rising to 4.28 (95 % CI 1.25–14.7) in the highest exposure category of ≥ 0.4 μT). The authors note that even if the observed association were confirmed, the impact would be small in Germany.

Floated case-control ratios from 3-degree-of-freedom quadratic-logistic spline model fit to pooled magnetic field data, with adjustment for study, age, and sex. Inner dotted lines are pointwise 80 % confidence limits; outer dotted lines are pointwise 99 % confidence limits

Figure 13.3.



Source: Greenland *et al.*, 2000

However, further analyses of the United Kingdom Childhood Cancer Study, a population-based case-control study covering the whole of England, Scotland and Wales, found no association between any childhood cancers, including acute lymphocytic leukaemia, and residential proximity to electricity supply equipment, distances to high-voltage lines, underground cables, substations and distribution circuits (UK Childhood Cancer Study Investigators, 2000). Magnetic field exposures were calculated from this equipment using distance, load and other circuit information for 3 380 cases and 3 390 controls. There was no evidence that either proximity to electrical installations or the magnetic field levels they produce were associated with increased risk of childhood leukaemia or any other cancer.

A review of the epidemiological evidence of an association between exposure to ELF-EMF and childhood brain tumours concluded that there is no support for an overall association (Kheifets *et al.*, 1999).

The NIEHS concluded that the limited data on maternal exposure to ELF-EMF during pregnancy or paternal exposure before contraception do not suggest an exposure-related increased risk of spontaneous abortion or adverse outcomes of pregnancy (Shaw, 2001). However, two new studies suggest an association (Lee *et al.*, 2002; Li *et al.*, 2002). Lee *et al.* (2002) conducted a nested case-control study of residential and personal magnetic field exposures and spontaneous abortion. The study included 177 cases and 550 controls. A variety of exposure metrics were assessed at 30 weeks of gestation (or the equivalent point relative to the onset of pregnancy for women who had a spontaneous abortion), including rate of change, maximum value and time-weighted average. Women in the second through fourth quartiles were generally associated with a more than 50 % increased risk of spontaneous abortion. Spontaneous abortions were not associated with either spot measurements or with time-weighted average exposures over 0.2 µT. Li *et al.* (2002) conducted a population-based prospective cohort study of personal magnetic field

exposures during pregnancy. The study included 969 women with a positive pregnancy test at less than 10 weeks of gestation. Personal magnetic field exposure data were collected over a 24-hour period. No association was observed between spontaneous abortion and average magnetic field exposure. Magnetic field exposures over 1.6 μT were statistically significantly associated with spontaneous abortion (RR = 1.8, 95 % CI 1.2–2.7) when compared with exposures less than 1.6 μT. The association was stronger for spontaneous abortions that occurred at less than 10 weeks (RR = 2.2, 95 % CI 1.2–4.0) and for women with multiple prior fetal losses or with subfertility (RR = 3.1, 95 % CI 1.3–7.7). In a commentary published with the papers, Savitz concluded that: 'These two new studies provide fairly strong evidence against an association with time-weighted average magnetic fields and moderately strong evidence for an association with other indices; both of these findings may be due to an artifact resulting from a laudable effort to integrate behavior and environment' (Savitz, 2002). Savitz suggested that behavioural differences between the study groups could introduce differential misclassification of exposure. Further research is needed on the question of whether there is an association between magnetic field exposure and spontaneous abortion.

Protection against ELF

The International Commission on Non-Ionizing Radiation Protection (ICNIRP) publishes EMF guidelines for general public exposure to time-varying electric, magnetic and electromagnetic fields up to 300 GHz (ICNIRP, 1998). These guidelines are based on shock hazards, not cancer or other health effects. The current recommendations for 50/60-Hz electric fields are 2 milliamperes per square metre (mA/m^2) current density to prevent effects on nervous system function; for 50-Hz power-frequency fields, this translates to 5 000 volts per metre (V/m) for electric fields and 100 μT for magnetic fields. Some countries have legally implemented these guidelines (SVDB, 1996). Several governmental authorities have issued statements proposing action to reduce exposure to EMF, e.g. the Swedish Board for Safety recommended avoiding the placement of schools and day-care centres in environments where the magnetic fields exceed 0.2–0.3 μT (Johnsson *et al.*, 2000).

Faced with the uncertainties regarding a potential causal association between exposure to ELF-EMF fields and adverse health outcomes, some have suggested that 'prudent avoidance' of EMF exposure may be justified (Johnsson *et al.*, 2000; WHO, 1998; Kheifets *et al.*, 2001). The NIEHS report concluded that: 'In summary, the NIEHS believes that there is weak evidence for possible health effects from ELF/EMF exposure, and until stronger evidence changes this opinion, inexpensive and safe reductions in exposure should be encouraged' (Portier and Wolfe, 1998). These are 'no regrets' options that are inexpensive, safe and easy to implement. Further research is needed to clarify these issues.

13.4. Radiofrequency fields

The term radiofrequency (RF) is not strictly defined, but often indicates the part of the electromagnetic spectrum ranging from 100 kHz to 300 GHz; this is the part of the spectrum below the frequencies of visible light and above ELF fields. RF fields have higher frequency (shorter wavelength) than ELF-EMF. An RF wave used for radio communication is referred to as a carrier wave. The information it carries (speech, computer data, etc.) has to be added to the carrier wave in some way, a process known as modulation. The information can be transmitted in either analogue or digital form. The RF spectrum includes, in approximate order by increasing frequency: amplitude modulation (AM) radio, frequency modulation (FM) radio, very-high-frequency (VHF) radio and television, ultra-high frequency (UHF) television and cellular telephone transmissions, and microwave ovens, radar and satellite communications. Natural exposure to RF fields is negligible.

RF is usually expressed as a power density measured in watts per square metre (W/m^2) (or milliwatts per square centimetre (mW/cm^2)) and for dosimetry as specific absorption rates (SARs). SARs are the basis for virtually all RF exposure guidelines. The SAR is defined in watts per kilogram (W/kg) and is the rate of absorption of RF energy in a unit mass of tissue. As such, the SAR represents the energy actually absorbed. The SAR cannot be readily measured in routine exposure assessment, but requires special techniques to determine it. SAR levels are specified for whole body and for partial body or localised exposure. A variety of physical,

biological and environmental factors can affect the SAR. These include the frequency, polarisation, modulation, power density, tissue properties, size (of person or animal), orientation relative to fields, temperature, humidity and other factors (Polk and Postow, 1996). Unlike ELF electric fields, most common household materials do not block RF fields.

Sources and magnitude of exposure

RF field sources in the home include microwave ovens, mobile telephones, burglar alarms, video display units and television sets. Most RF fields in the environment originate from radio and television broadcasting and telecommunication facilities. Studies of RF conducted at frequencies exceeding 1 MHz are of exposures that do not relate to everyday life exposures. When considering mobile telephones, one has to distinguish between continuous exposure from base stations and voluntary exposure to the telephones themselves. The maximum field intensity at 2.2 cm from the antenna of a telephone (the distance at which calculations are made) is about 200 W/m^2; actual exposures depend on telephone characteristics (Polk and Postow, 1996). This is about one-quarter of the intensity of the sun's radiation on a clear summer day, although the frequency of the emissions from a telephone is a million or so times smaller (IEGMP, 2000). This field intensity compares with a maximum intensity of 0.01 W/m^2 typically found around base stations (IEGMP, 2000).

Exposure assessment

RF exposure assessment is limited as measurements are rarely available. Exposure has been based on work site, distance from transmitters and other facilities, number of minutes of cellular telephone use, etc. Unlike ELF-EMF, RF measurement instrumentation is not available to conduct personal monitoring. For most studies, there is limited information on other factors that may relate to the health outcome.

Biological interactions

The depth of penetration of the RF field into the tissue depends on the field frequency and is greater for lower frequencies (WHO, 1998). The interactions of RF fields and biological systems are complex. One categorisation of these interactions is as thermal and non-thermal. Thermal effects result from the heating of biological materials due to energy deposition and absorption. Non-thermal effects are defined as alterations in biological/biochemical functions at RF energy levels not sufficient to heat biological systems. There is a growing body of scientific evidence that exposure to RF fields at intensities far less than levels required to produce measurable heating can cause effects in cells and tissues (RSCHC, 1999). These effects are often at the cellular membrane and enzyme activity level, coupled with other exposure conditions (presence of other chemicals, modulation of RF fields, etc.)

The rate of tissue temperature rise at any body location depends on the rate of energy absorption at that location. RF fields below 1 MHz do not produce significant heating, but they may induce electric fields in tissues. RF fields between 1 MHz and 10 GHz penetrate tissues and may cause tissue heating (increases in tissue or body temperature by $\geq$ 1 °C) (IEGMP, 2000). RF fields above 10 GHz are absorbed at the skin surface with very little energy penetrating into underlying tissues. Adverse health effects such as eye cataracts and skin burns occur from RF fields above 10 GHz; these are generated by power densities above 1 000 W/m^2 and are not found in everyday life.

The research on RF interactions with biological systems is extensive. Numerous biological systems or health end-points have been studied, including: chromosome-genetic, membrane or cell function, carcinogenesis, reproduction, nervous system, cardiovascular system, immune system and ocular effects. An Expert Panel Report prepared at the request of the Royal Society of Canada for Health Canada concluded: 'Scientific studies performed to date suggest that exposure to low intensity non-thermal RF fields do not impair the health of humans or animals. However, the existing scientific evidence is incomplete, and inadequate to rule out the possibility that these non-thermal biological effects could lead to adverse health effects' (RSCHC, 1999).

Experimental studies relevant to carcinogenesis

A review of the literature suggests that RF fields are unlikely to be mutagenic based on many negative results from *in vitro* studies on DNA damage, mutation frequency and chromosome aberration frequency (Michaelson and Lin, 1987). An ICNIRP review of animal studies concluded that exposure to RF fields is unlikely to initiate

carcinogenesis (ICNIRP, 1998). There are various experimental results that are consistent with biological effects, some of which may be related to carcinogenic mechanisms at RF field strengths below those that produce thermal effects. For example, a number of studies reported some evidence of an effect of RF on intracellular levels of ornithine decarboxylase (ODC), an enzyme implicated in tumour promotion (tumour promoters increase ODC synthesis) (Michaelson and Lin, 1987). However, the results are inconsistent and no clear mechanism has been shown.

In 1997, an animal study of genetically susceptible mice exposed to pulsed RF fields of 900 MHz observed a more than two-fold increase in lymphoma compared with control mice (RR = 2.4, 95 % CI 1.3–4.5) (Repacholi *et al.*, 1997). This experiment was designed to assess exposures that would be encountered with the use of digital cellular telephones. The exposures were in the range 2.6–13.0 W/m^2 (0.26–1.3 mW/cm^2), yielding a range of SARs of 0.13–1.4 W/kg. These SARs are near the maximum levels of existing standards. The authors encouraged caution in the interpretation of their study: 'While the increase in the incidence of lymphoma found here was highly statistically significant, and the exposure conditions were designed to mimic the fields generated by a digital mobile telephone, the implications of the study for the risk of carcinogenesis in humans are unclear. It is difficult to extrapolate directly from mice to humans due to differences in their absorption of energy from RF fields.'

Epidemiological studies

Elwood recently reviewed the epidemiologic studies of RF field exposures and human cancers (Elwood, 1999). He categorised the studies into: studies of cancer clusters; studies of general populations exposed to television, radio and similar emissions; studies of occupational groups with exposure to such fields; and case-control studies. Several studies looked at associations with childhood cancers. Although there are suggestions of an association between RF exposures and childhood leukaemia (Figure 13.4.), Elwood concludes: 'The studies individually are weak and, as a consequence, the results cannot be easily interpreted in terms of cause and effect. The major impression from these studies is their inconsistency. There is no type of cancer that has been consistently associated with RF exposure.'

As noted in the Canadian review, certain subgroups such as children are more susceptible than healthy, young adults to various environmental health hazards (RSCHC, 1999). They note that susceptible subgroups has received very little study with respect to RF exposure, and the studies that have been conducted have not been particularly rigorous in their design and have studied group rather than individual-level data. Consequently, these studies are not particularly informative about potential RF health risks.

Results were recently published from two case-control studies and one cohort study of cellular telephone use and cancer (Muscat *et al.*, 2000; Inskip *et al.*, 2001; Johansen *et al.*, 2001). None found evidence of a link between cellular telephone use and increased brain cancer risk. The cohort study found no excess risk for cancers of the salivary glands, leukaemia or other site-specific cancers (Johansen *et al.*, 2001). Although the length of follow-up on these studies was relatively short, if RF exposure is assumed to act by promoting the growth of underlying cancers, then the recent intense use of cellular telephones (as considered in these studies) may be of more importance than latency or long-term use considerations. Additional studies are under way that may further clarify the relation between the use of mobile telephones and cancer.

The level of energy absorption in children while using mobile telephones is comparable to the levels found for adults; however, due to the larger number of ions contained in the tissue of children, the specific tissue absorption rate is considered to be higher (Schonborn *et al.*, 1998). Given their growing tissues, the fetus and the child may be more susceptible than adults to any adverse effects of RF.

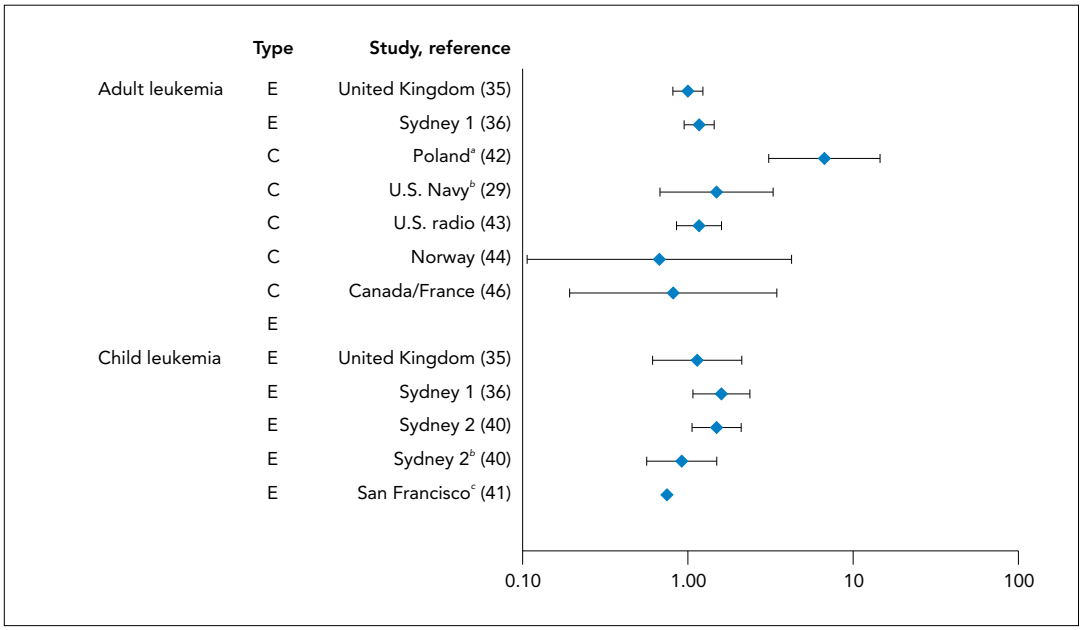
The advisory Scientific Committee on156, Ecotoxicity and the Environment (SCTEE) to the European Commission recently updated its opinion on the possible health effects of mobile telephone use (SCTEE, 2001). The committee was asked specifically to consider the long-term exposure to low non-thermal levels. It was also asked to review whether or not the European safety limits for exposure to mobile telephone emissions, as set by ICNIRP, are still valid considering the latest scientific knowledge. The SCTEE concluded: 'The additional information which has become available on carcinogenic and other

non-thermal effects of radiofrequency and microwave radiation frequencies in the last years does not justify a revision of exposure limits set by the Commission on the basis of the conclusions of the 1998 opinion of the Steering Scientific Committee.'

Relative risks and 95 % confidence limits for studies of leukemia in adults and in children. Type of study: C, occupational cohort; E, ecological

Figure 13.4.

Source: Elwood, 1999



[a]All lymphatic and hematopoietic-total leukemia not given.
[b]Excluding Lane Cove area. [c]No confidence limits given; nonsignificant.

The Independent Expert Group on Mobile Phones (IEGMP, 2000) concluded:

'First, the balance of the evidence available does not suggest that RF radiation from mobile telephones or base stations causes cancer or other disease. However, there is now evidence that effects on biological functions, including those of the brain, may be induced by RF radiation at levels comparable to those associated with the use of mobile telephones. There is, as yet, no evidence that these biological effects constitute a health hazard but at present only limited data are available. This is one reason why we recommend a precautionary approach.'

'Second, concerns have been expressed that the pulsed nature of the signals from mobile telephones and masts may have an impact on brain function. This is an intriguing possibility, which deserves further research, particularly if pulsed signals continue to be used in the third generation of telephones and related technologies. Research should concentrate on signal modulations representative of present and future telephone technology.'

In addition to direct effects, there can be indirect effects of RF. For example, an association between mobile telephone use while driving and an increased risk of traffic accidents has been shown in experimental as well as epidemiological studies (Redelmeier and Tibshirani, 1997).

Protection against RF

The guidelines for protection against adverse health effects in the optical and radiofrequency region are largely directed at limiting living tissue temperature rise due to absorption of thermal energy. Safety standards were developed following a review of RF-associated thermal and non-thermal effects by the International Commission on Non-Ionizing Radiation Protection (ICNIRP, 1988). The safety limits recommended are well above the RF exposures found in the daily environment. The basic restriction for whole body exposure is an SAR of 0.4 W/kg for occupational exposure and 0.08 W/kg for general population exposure. The ICNIRP review shows that the threshold for irreversible effects in the most sensitive tissues is more than 4 W/kg under normal environmental conditions (ICNIRP, 1988). Higher limits were set for exposure of smaller body parts. The standards do not take into

account the effects of RF exposures on the fetus and the developing child.

The SCTEE concluded: 'Thus current knowledge is insufficient for the implementation of measures aimed at the identification and protection of a highly sensitive sub-group of the population.' (SCTEE, 2001). The Independent Working Group on Mobile Phones recently stated that: 'If there are currently unrecognised adverse health effects from the use of mobile phones, children may be more vulnerable because of their developing nervous system, the greater absorption of energy in the tissues of the head, and a longer lifetime of exposure.' (IEGMP, 2000) The group believes 'that the widespread use of mobile telephones by children for non-essential calls should be discouraged'.

Protection against RF and ELF

Because there are suggestions that RF exposure may be more hazardous for the fetus and child due to their greater susceptibility, prudent avoidance is one approach to keeping children's exposure as low as possible.

Summary

Extremely low frequency (ELF) electromagnetic fields (EMF) are classified as a 'possible carcinogen' (IARC category 2B) primarily based on epidemiological studies of childhood leukaemia. High exposure to ELF-EMF is relatively rare in the general population (a few per cent of the population). Summary studies suggest that there is about a two-fold increased risk of childhood leukaemia among highly exposed children. There is no or little evidence for other health effects of ELF-EMF exposure in children. Adverse health effects following exposure to radio frequencies have not been consistently identified. Prudent avoidance is one approach to dealing with uncertainty concerning exposure in this portion of the electromagnetic spectrum. Recent reviews encourage the reduction of exposure through 'no regrets' options that are inexpensive, safe and easy to implement. Further research is needed to clarify the potential risks of ELF-EMF and radiofrequency fields for children's health.

References

Ahlbom, A., Day, N., Feychting, M. *et al.*, 2000. A pooled analysis of magnetic fields and childhood leukaemia, *Br J Cancer*, Vol 83, pp. 692–8.

Boorman, G.A., McCormick, D.L., Findlay, J.C. *et al.*, 1999. Chronic toxicity/ oncogenicity evaluation of 60 Hz (power frequency) magnetic fields in F344/N rats, *Toxicol Pathol*, Vol 27, pp. 267–78.

Boorman, G.A., Rafferty, C.N., Ward, J.M. *et al.*, 2000. Leukaemia and lymphoma incidence in rodents exposed to low-frequency magnetic fields, *Radiation Res*, Vol 153, pp. 627–36.

Elwood, J.M., 1999. A critical review of epidemiologic studies of radiofrequency exposure and human cancers, *Environmental Health Perspectives*, Vol 107(suppl 1), pp. 155–68.

Fam, W.Z. and Mikhail, E.L., 1996. Lymphoma induced in mice chronically exposed to very strong low-frequency electromagnetic field, *Cancer Lett*, Vol 105, pp. 257–69.

Foliart, D.E., Iriye, R.I., Tarr, K.J. *et al.*, 2001. Alternative magnetic field exposure metrics: Relationship to TWA, appliance use, and demographic characteristics of children in a leukemia survival study, *Bioelectromagnetics*, Vol 22, pp. 574–80.

Greenland, S., Sheppard, A.R., Kaune, W.T. *et al.*, 2000. A pooled analysis of magnetic fields wire codes, and childhood leukemia, *Epidemiology*, Vol 11, pp. 624–34.

Harris, A.W., Basten, A., Gebski, V. *et al.*, 1998. A test of lymphoma induction by long-term exposure of E-PIM1 transgenic mice to 50 Hz magnetic fields, *Radiation Res*, Vol 149, pp. 300–7.

ICNIRP, 1998. Guidelines for limiting exposure to time-varying electric, magnetic, and electromagnetic fields (up to 300 GHz), International Commission on Non-Ionizing Radiation Protection, *Health Physics*, Vol 74, pp. 494–522.

IEGMP, 2000. *Mobile phones and health*, Independent Expert Group on Mobile Phones. http://www.iegmp.org.uk (in 2001)

Inskip, P.D., Tarone, R.E., Hatch, E.E. *et al.*, 2001. Cellular-telephone use and brain tumors, *N Engl J Med*, Vol 344, pp. 79–86.

Johansen, C., Boice, J.D. Jr., McLaughlin, J.K. *et al.*, 2001. Cellular telephones and cancer — a nationwide cohort study in Denmark, *J Natl Cancer Inst*, Vol 93, pp. 203–7.

Johnsson, A. and Mild, K.H., 2000. Electromagnetic fields — a threat to children's health? in *Children and radiation. Selected topics raised at an international conference* (edited by T. Christensen and S. Stephens), Norwegian Centre for Child Research, Trondheim, Norway, pp. 53–86.

Kaune, W.T. and Zaffanella, L.E., 1994. Assessing historical exposures of children to power-frequency magnetic fields. *J Expo Anal Environ Epidemiol* Vol 4, pp. 149–70.

Kaune, W.T., Darby, S.D., Gardner, S.N. *et al.*, 1994. Development of a protocol for assessing time-weighted-average exposures of young children to power-frequency magnetic fields, *Bioelectromagnetics*, Vol 15, pp. 33–51.

Kheifets, L.I., Sussman, S.S. and Preston-Martin, S., 1999. Childhood brain tumors and residential electromagnetic fields (EMF), *Rev Environ Contam Toxicol*, Vol 159, pp. 111–29.

Kheifets, L.I., Hester, G.L. and Banerjee, G.L., 2001. The precautionary principle and EMF: Implementation and evaluation, *J Risk Research*, Vol 4, pp. 113–25.

Lacy-Hulbert, A., Metcalfe, J.C. and Hesketh, R., 1998. Biological responses to electromagnetic fields, *FASEB Journal*, Vol 12, pp. 395–420.

Langholz, B., 2001. Factors that explain the power line configuration wiring code-childhood leukemia association: What would they look like? *Bioelectromagnetics* (suppl 5), pp. S19–31.

Lee, G.M., Neutra, R.R., Hristova, L. *et al.*, 2002. A nested case-control study of residential and personal magnetic field measures and miscarriages, *Epidemiology*, Vol 13, pp. 21–31.

Li, D.K., Odouli, R., Wi, S. *et al.*, 2002. A population-based prospective cohort study of personal exposure to magnetic fields during pregnancy and the risk of miscarriage, *Epidemiology*, Vol 13, pp. 1–3.

Linet, M.S., Hatch, E.E., Kleinerman, R.A. *et al.*, 1997. Residential exposure to magnetic fields and acute lymphoblastic leukemia in children, *N Engl J Med*, Vol 337, pp. 1–7.

Mandeville, R., Franco, E., Sidrac-Ghali, S. *et al.*, 1997. Evaluation of the potential carcinogenicity of 60 Hz linear sinusoidal continuous-wave magnetic fields in Fischer F344 rats, *FASEB Journal*, Vol 11, pp. 1127–36.

Mandeville, R., Franco, E., Sidrac-Ghali, S. *et al.*, 2000. Evaluation of the potential promoting effect of 60 Hz magnetic fields on N-ethyl-N-nitrosourea induced neurogenic tumours in female F344 rats, *Bioelectromagnetics*, Vol 21, pp. 84–93.

McBride, M.L., Gallagher, R.P., Theriault, G. *et al.*, 1999. Power-frequency electric and magnetic fields and risk of childhood leukemia in Canada, *Am J Epidemiol*, Vol 149, pp. 831–42.

McCann, J., Dietrich, F., Rafferty, C. *et al.*, 1993. A critical review of the genotoxic potential of electric and magnetic fields, *Mutation Res*, Vol 297, pp. 61–95.

McCann, J., Kavet, R. and Rafferty, C.N., 2000. Assessing the potential carcinogenic activity of magnetic fields using animal models, *Environmental Health Perspectives*, Vol 108, pp. 79–100.

McCormick, D.L., Ryan, B.M., Findlay, J.C. *et al.*, 1998. Exposure to 60 Hz magnetic fields and risk of lymphoma in PIM transgenic and TSG-p53 (p5s knockout) mice, *Carcinogenesis*, Vol 19, pp. 1649–53.

McCormick, D.L., Boorman, G.A., Findlay, J.C. *et al.*, 1999. Chronic toxicity/ oncogenicity evaluation of 60 Hz (power frequency) magnetic fields in B6C3F1 mice, *Toxicol Pathol*, Vol 27, pp. 279–85.

Michaelson, S.M. and Lin, J.C., 1987. *Biological effects and health implications of radiofrequency radiation*, Plenum Press, New York.

Murphy, J.C., Kadan, D.A., Warren, J. *et al.*, 1993. Power frequency electric and magnetic fields: A review of genetic toxicology, *Mutation Res*, Vol 296, pp. 221–40.

Muscat, J.E., Malkin, M.G., Thompson, S. *et al.*, 2000. Handheld cellular telephone use and risk of brain cancer, *JAMA*, Vol 284, pp. 3001–7.

NRPB, 2001. *ELF electromagnetic fields and the risk of cancer*, Report of an Advisory Group on Non-Ionising Radiation, Vol 12, No 1. National Radiological Protection Board, Chilton, UK.

Polk, C. and Postow, E., 1996. *Biological effects of electromagnetic fields*, CRC Press, Boca Raton, FL.

Portier, C.J. and Wolfe, M.S., eds, 1998. *Assessment of health effects of exposure to power-line frequency electric and magnetic fields*, National Institutes of Health working group report, NIEHS.

Redelmeier, D.A. and Tibshirani, R.J., 1997. Association between cellular-telephone calls and motor vehicle collisions, *N Engl J Med*, Vol 336, pp. 453–8.

Repacholi, M., Basten, A., Gebski, V. *et al.*, 1997. Lymphomas in Eμ-*Pim1* transgenic mice exposed to pulsed 900 MHz electromagnetic fields, *Radiation Res*, Vol 147, pp. 631–40.

RSCHC, 1999. *A review of the potential health risks of radiofrequency fields from wireless telecommunication devices*, An expert panel report prepared at the request of the Royal Society of Canada for Health Canada, Ottawa, RSC EPR 99–1.

Savitz, D.A., 2002. Commentary: Magnetic fields and miscarriage, *Epidemiology*, Vol 13, pp. 9–20.

Schonborn, F., Burkhardt, M. and Kuster, N., 1998. Differences in energy absorption between heads of adults and children in the near field of sources, *Health Physics*, Vol 74, pp. 160–8.

Schütz, J., Grigat, J-P., Strmer, B. *et al.*, 2000. Extremely low frequency magnetic fields in residences in Germany. Distribution of measurement, comparison of two methods for assessing exposure, and predictors for the occurrence of magnetic fields above background level, *Radiat Environ Biophys*, Vol 39, pp. 233–40.

Schütz, J., Grigat, J-P., Brinkmann, K. *et al.*, 2001. Residential magnetic fields as a risk factor for childhood acute leukaemia: Results from a German population-based case-control study, *Int J Cancer*, Vol 91, pp. 728–35.

SCTEE, 2001. *Opinion of possible effects of electromagnetic fields (EMF), radio frequency fields (RF) and microwave radiation on human health*, Scientific Committee on Toxicity, Ecotoxicity and the Environment, adopted 30 October 2001. http://europa.eu.int/comm/health/ph/programmes/pollution/ph_fields_index.html

Shaw, G.M., 2001. Adverse human reproductive outcomes and electromagnetic fields: A brief summary of the epidemiologic literature, *Bioelectromagnetics* (suppl 5), pp. S5–18.

SVDB (Sechsundzwanzigste Verordnung zur Durchfürhung des Bundes-Immissionsschutzgesetzes), 1996. *Verordnung über elektromagnetische Felder*, 16. December, Germany.

Swanson, J. and Kaune, W.T., 1999. Comparison of residential power-frequency magnetic fields away from appliances in different countries, *Bioelectromagnetics*, Vol 20, pp. 244–54.

Tenforde, T.S., 2000. Biological interactions and potential health effects of static and ELF fields, in *ICNIRP. Non-ionizing radiation. Executive summary of the 4th International Non-ionizing Radiation Workshop Kyoto, Japan, May 22–25, 2000* (edited by R. Matthes, J.H. Bernhardt and M. Taki), pp. 29–32.

UK Childhood Cancer Study Investigators, 2000. Childhood cancer and residential proximity to power lines, *Br J Cancer*, Vol 83, pp. 1573–80.

Wertheimer, N. and Leeper, E., 1979. Electrical wiring configurations and childhood cancer, *Am J Epidemiol*, Vol 109, pp. 273–84.

WHO, 1998. *International EMF project*, World Health Organization. http://www.who.int/peh-emf/index.htm (in 2001)

WHO, 2001. Fact Sheet 263: *Electromagnetic Fields and Public Health: Extremely Low Frequency Fields and Cancer*. http://www.who.int/inf-fs/en/fact263.html.

Yasui, M., Kikuchi, T., Ogawa, M. *et al.*, 1997. Carcinogenicity test of 50 Hz magnetic fields in rats, *Bioelectromagnetics*, Vol 18, pp. 531–40.

Zaffanella, L.E. and Kalton, G.W., 1998. Survey of personal magnetic field exposure: 1000-person survey, *EMF RAPID Engineering Project No 6. Final report*, Enertech Consultants.

PART IV:
Issues of principles, methods and policies

Ieva Vaivaraite (age 13), Lithuania

14. Environmental justice: an issue for the health of the children of Europe and the world

Carolyn Stephens and Simon Bullock

Summary of current knowledge
- There is growing evidence that the most disadvantaged groups suffer from the worst environmental conditions and that industrialised nations impose disproportionate environmental burdens on the poorest countries as well as on future generations.

Main challenges
- To tackle the difficulties of implementing and enforcing a rights approach to environmental injustice.

Action points
- To improve our knowledge of the current situation of environmental injustice in the European Region.
- To implement policies to reduce environmental injustice as well as income inequalities.

14.1. Introduction

This chapter covers in brief some aspects of the growing community-based and academic work on 'environmental justice'. It provides the conceptual background and relates this to the issue of children's health. A number of cases taken from European countries are described to illustrate the existing situation and suggestions are made as to the policy responses needed to combat the problems identified.

14.2. Environmental justice: the background

'Environmental justice' articulated in its current form is most prominent in the United States. Since the 1980s a network of 5 000 black, Hispanic and indigenous grass-roots communities has organised strong political opposition to the siting of environmentally hazardous industrial facilities in predominantly black neighbourhoods and indigenous people's reservations. This movement has made substantial progress. In 1994, President Clinton ordered that 'each Federal agency shall make achieving environmental justice part of its mission' (Committee on Environmental Justice, 1999).

The US Environmental Protection Agency defines environmental justice as:

'The fair treatment and meaningful involvement of all people, regardless of race, ethnicity, income, national origin or educational level with respect to the development, implementation and enforcement of environmental laws, regulation and policies. Fair treatment means that no population, due to policy or economic disempowerment, is forced to bear a disproportionate burden of the negative human health or environmental impacts of pollution or other environmental consequences resulting from industrial, municipal and commercial operations or the execution of federal, state, local and tribal programs and policies.'

The US definition includes both 'substantive' and 'procedural' rights to a healthy environment. Thus, environmental justice can include both the right to a healthy environment and the right to participate in the decision-making process to obtain that right. This formulation is not unique to the United States. In fact, international human rights law has been modified since the Rio Summit of 1992 to reflect principles of environmental substantive and procedural rights and then, potentially, environmental justice. Box 14.1. shows the draft principles of the United Nations Sub-Commission on Human Rights and the Environment (Boyle, 1996). Boyle notes that the principles currently developed at international level draw heavily on existing human rights law and international environmental law (Boyle, 1996).

Although the United States has produced the clearest definition of environmental justice, most European countries have constitutions that could be used for the protection of environmental health. For example, the Spanish constitution contains a right to enjoy an 'environment suitable for the development of the person', and the Portuguese constitution states that 'everyone shall have the right to a healthy and ecologically balanced human environment and the duty to protect it' (Douglas-Scott, 1996). In addition, Europe also has several region-wide treaties that deal with

environment and health protection at the level of rights, including the European Convention on Human Rights dating from 1950. The World Health Organization (WHO) made inequalities its first target in its 'Health for All' strategy, aiming that 'the differences in health status between countries and between groups within countries should be reduced by at least 25 %, by improving the level of health of disadvantaged nations and groups' (WHO, 1992).

Box 14.1. Draft principles of the UN Sub-Commission on Human Rights and the Environment

International substantive rights

- Freedom from pollution, environmental degradation and activities that adversely affect the environment or threaten life, health, livelihood, well-being or sustainable development.
- Protection and preservation of the air, soil, water, sea-ice, flora and fauna and the essential processes and areas that are necessary to maintain biological diversity and ecosystems.
- The highest attainable standard of health.
- Safe and healthy food, water and working environments.
- Adequate housing, land tenure and living conditions in a secure, healthy and ecologically sound environment.
- Ecologically sound access to nature and the conservation and sustainable use of nature and natural resources.
- Preservation of unique sites.
- Enjoyment of traditional life and subsistence for indigenous peoples.

International procedural rights

- The right to information concerning the environment.
- The right to receive and disseminate ideas and information.
- The right to participation in planning and decision-making processes, including prior environmental impact assessment.
- The right of freedom of association for the purpose of protecting the environment or the rights of persons affected by environmental harm.
- The right to effective remedies and redress for environmental harm in administrative or judicial proceedings.

Source: Boyle, 1996

However, routine environmental exposures affecting child health, such as transport-related pollution and housing, occur without citizens being able to access environmental policy for justice. Further, in addition, past and recent environmental crises such as Chernobyl, the BSE affair and dioxin contamination have all occurred despite Europe's well-developed constitutional, environmental and human rights legislative frameworks (Lang, 1999; Ryder, 1999).

From a procedural perspective, too, there are some potential advances. For example, the United Kingdom's Independent Inquiry on Inequalities in Health (1998) has as a major recommendation 'as part of all health impact assessment, all policies likely to have a direct or indirect effect on health should be evaluated in terms of their impacts on health inequalities, and should be formulated in a way that by favouring the less well off they will, where possible reduce inequalities' (Acheson *et al.*, 1998).

So, there are strong calls for national 'environmental justice'. This national focus does however require expansion — for one country can impose environmental injustices upon another, and one generation can impose similar injustices on another. Both of these issues are growing in importance, as environmental problems become both more global and longer in timescale. As an example, current levels of greenhouse gas emissions are higher than the planet can tolerate — as has been agreed legally and internationally in the Kyoto protocol (UNEP, 1999). The majority of these gases are produced by Western countries, yet the majority of the negative impacts will be felt by future generations and people in Southern countries (UNEP, 1999). Other issues which reinforce the same point include nuclear waste, control of water resources and production of bio-accumulative and persistent chemicals.

'Environmental justice' is now a growing issue in Europe. It has at its heart the premise that the current disproportionate impacts of environmental hazards must be addressed, but it is also focusing on the availability and use of environmental resources (Stephens *et al.*, 2000). For example, in response to the difficult problem of how environmental resources should be distributed in a world of ecological limits, member groups of the environmental network Friends of the Earth have advocated the use of 'equal distribution of resource consumption between countries on a per capita basis' (Carley and Spapens, 1997). Friends of the Earth Scotland have launched a campaign for environmental justice on these lines. They argue that 'Our conception of environmental justice therefore brings together the need for global and intergenerational equity in resource consumption and ecological health, with a priority to act with those who are the victims of that inequality in the present. No less than a decent environment for all, no more than

our fair share of the Earth's resources' (Scandrett *et al.*, 2000).

There are therefore three areas to look at, from a European perspective:

- national: the state of environmental injustice within Europe and European countries;
- international: the extent to which Europe imposes injustice on other countries;
- generational: the extent to which Europe imposes injustices on future generations, in Europe and globally.

The next section looks at the existing situation and trends in these areas.

14.3. Environmental justice: the evidence

Within Europe

Even in rich countries in Europe there are major environmental impacts on people. These impacts are borne disproportionately. There is a lack of information, but the available evidence strongly suggests that it is poorer people who suffer from the worst environmental conditions. Box 14.2. documents some examples of substantive environmental injustice in the United Kingdom — a comparatively rich country in Europe. Policies as well as impacts can also be deeply unjust. Substantive injustices are caused, in part, by procedural injustices. For example, waste disposal policies are not designed to hurt poorer communities but can do so through the decision-making process if wealthier groups can access decisions more easily and avoid perceived harm. For example, in 1998, residents of Greengairs — a relatively poor community in Scotland — found that a local landfill operator was accepting toxic polychlorinated biphenyl (PCB) waste from Hertfordshire in England, a comparatively much richer area. Dumping of this waste is illegal in England, but regulations are less strict in Scotland. Community campaigning brought an end to the dumping and also secured other environmental and safety improvements (Scandrett *et al.*, 2000). But inadequate enforcement of regulations, derisory fines and poor identification of pollution levels are still major national problems (McBride, 1999).

There are gross health inequalities in the United Kingdom. The average standard mortality ratio for men in Social Class V is 806 per 10 000. For men in Social Class I the ratio is 280 (Acheson *et al.*, 1998). The UK government's health strategy states that 'During the 1980s and 1990s the gap between rich and poor widened and the health gap grew wider' (Her Majesty's Government, 1999). These health inequalities are the result of complex factors, but it is indisputable that the type of environmental injustices highlighted in Box 14.2. exacerbate

Box 14.2. Some examples of environmental injustice in the United Kingdom

Pollution

Factories emitting toxic pollutants are disproportionately located in poorer communities. Research comparing the government's data on polluting factories with income data for postcodes, showed that (McLaren and Bullock, 1999):

- There are 662 polluting factories in the United Kingdom in areas with average household income of less than £15 000, and only five in postcode areas where average household income is £30 000 or more.
- The more factories in an area, the lower the average income. In Teesside, one area has 17 large factories. Average income in the area is £6 200 — 64 % less than the national average.
- The poorest families (defined as household incomes of less than £5 000) are twice as likely to have a polluting factory in their immediate area as families with an income of £60 000 or more.
- In London, over 90 % of polluting factories are in areas with below average income, and in the north-east the figure is over 80 %.

Transport

- The recent UK government *Independent inquiry into inequalities in health report* notes that 'The burden of air pollution tends to fall on people experiencing disadvantage, who do not enjoy the benefits of the private motorised transport which causes the pollution'. As well as pollution, road accidents also affect the poorest people worst. Children in social class V are five times more likely to be killed in road accidents than children in social class 1 (Acheson *et al.*, 1998).

Housing

- Nearly 9 million households in the United Kingdom suffer from fuel poverty — the lack of affordable warmth. Fuel poverty exacerbates ill-health and is a major contributor to the 32 000 extra winter deaths in the United Kingdom each year. The main cause of fuel poverty is poor quality housing and homes with terrible levels of energy efficiency, and it is poorer people who live in the worst quality housing. Of households earning less than £4 500, 76 % are not able to heat their homes to minimum health-based heating standards and 460 000 households in England with an income of less than £4 500 have homes with an energy efficiency ('SAP' rating) of less than 10 out of 100 (DoE, 1996).
- The Independent Inquiry collates evidence that in the United Kingdom 40 % of all fatal accidents happen in the home. Almost half of all accidents to children are associated with architectural features in and around the home. Households in disadvantaged circumstances are more likely to be the worst affected.

the other inequalities faced by poorer people, and add to the burden of health inequalities.

Similarly, income and health inequalities are rife throughout Europe. And children in poorer countries, and of poorer families within wealthier countries, experience less healthy living, ambient and learning environments. Children go on to experience reinforcement of this cycle in their adulthood, with less access to remunerated, secure and rewarding employment. Within Europe, gross domestic product (GDP) per capita is typically 10 times higher in western Europe than in the rest of the region. In eastern Europe and central Asia, GDP fell by approximately 40 % as a result of the economic collapse of the early 1990s. Unemployment and under-employment has become a major issue throughout the world and affects Europe badly. Europe's large population of 872 million faces rising rates of unemployment: rates rose from 7.8 to 10.2 % between 1990 and 1995 (UNEP, 1999).

Unemployment is a major factor in the creation and perpetuation of social exclusion. Health inequalities result from social and economic inequalities between groups in most European states. The more egalitarian states have been shown to have better health overall (Wilkinson, 1996; Wilkinson, 1999).

Overall then, Europe still has major inequalities — between and within countries. In addition, the available evidence from the United Kingdom suggests that environmental problems in countries tend to be borne more heavily by poorer people, exacerbating these inequalities.

This leads to two conclusions — one, that tackling income inequalities will reduce health problems; two, that tackling environmental problems will reduce health inequalities, as poorer people tend to suffer from the worst environmental problems.

Global

Children in other countries are affected by European policies. For example, Europe produces 31 % of the world's carbon dioxide emissions, with only 13 % of the world's population (WRI, 1997). Further, in terms of per capita energy, the people of the United States consume five times more than the people of Europe (UNEP, 1999). The impacts of climatic change tend to be greater in poorer countries — which are vulnerable to extreme weather events and lack the financial resources to respond — for example, Hurricane Mitch in Central America and flooding in India and Bangladesh. The predictions of the Intergovernmental Panel on Climate Change and WHO increasingly link apparently 'natural' climatic events to changes created by the disproportionate consumption of the United States and Europe (UNEP, 1999; McMichael *et al.*, 1994).

Developing countries also suffer from the large appropriation of environmental resources by richer countries. Southern wood, land, minerals and metals are still being used predominately for further Western development, not Southern development, and raw commodity prices are low (Latouche, 1993). Poorer people outside Europe are not the main beneficiaries of the use of their country's resources, which is driven by a development model which is dominated and run by European and other northern hemisphere countries. According to the latest World Bank figures, increases in inequality over the last 130 years are gross: the ratio of income per capita in the richest countries to that in the poorest countries increased from 11 times as high in 1870 to 38 times in 1960 and to 52 times as high in 1985. More importantly, there has been a more profound concentration of income. Thus, the ratio between the average income of the world top 5 % of people and the world bottom 5 % increased from 78 to 1 in 1988, to 123 to 1 in 1993 (World Bank, 1999). Only 19 % of Europe's population are children; this proportion is 33 % for the rest of the world (WRI, 1997). Even colossal global economic growth is not enough to tackle poverty, as distribution is so unequal. People's needs must be met directly. More even access to the world's resources will be required to tackle these inequalities.

Southern countries also suffer from the imposition of outdated or dangerous Western technologies, processes and by-products. Waste which is too toxic for disposal in the West is routinely reported entering the South despite the Basel Convention. Pesticides produced in the West and banned for health and environmental reasons in the West are exported to and used in the South. Leaded petrol accounts for over 95 % of sales in Africa — in Europe Sweden has completely phased out this neurotoxin (WHO, 1997).

This all adds up to a large and increasing burden imposed by European and other Western countries on developing countries.

Generational

Current economic activities also tend to heavily undervalue the rights of future generations (McMichael *et al.*, 1994; McMichael, 1993; Smil, 1993; Attfield and Wilkins, 1992; Belsey, 1992).

A clear example is in the field of chemicals policy. Through heavily polluting industrial activities the entire global environment is now awash with persistent and bio-accumulative chemicals. The effects of this are uncertain, but many of these chemicals have now been found to have subtle and unanticipated adverse effects on wildlife. One class of chemicals — endocrine-disrupting chemicals — is known to affect the reproductive and developmental function of a wide range of creatures. The effects on humans are uncertain, but what is clear is that their and other chemicals' routine dispersal into the environment is an enormous and probably irreversible gamble with the health of children and future generations (Fur, 1999; Williams, 1998). In the face of grave uncertainties, the main current policy response is to wait for more evidence — this approach places the burden of proof of safety on to the public, rather than the chemical. It ensures that the concerns of those who benefit from the use of a process are weighted far higher than those who potentially suffer — particularly children and future generations. This has been described as 'toxic trespass', and this situation in effect means that 'there is a lack of consent among those who suffer the burden of 'acceptable risks'. This differs widely from medical ethics, where testing should only occur 'with the express permission of those involved and only where there is no alternative (Steingraber, 1999).

Chemicals policy is not the only example of these generational issues. Nuclear power is another technology where the benefits accrue to the current generation, but the majority of costs (through waste management) will have to be borne — perhaps in perpetuity — by future generations.

Part of the problem is that decisions are routinely made with discount rates such that costs in the future — beyond 10 years — have almost negligible impact on policy. But perhaps more important is the use of risk assessment models which consistently undervalue and often completely ignore uncertainties. Uncertainty is an unavoidable component of decisions involving environmental and public health harm (Steingraber, 1999). Decisions must be based on what is not known, as well as what is known.

Conventional risk assessments also fail to protect human rights in other ways. Williams notes that they are based on an 'average' human model — a white, European, healthy male — which is irrelevant to most of the world's population, in 'stark contrast to the human rights assumption that we should protect the most vulnerable' (Williams, 1998). Participants at the Wingspread conference on the precautionary principle argue that 'decisions about toxic chemicals should ask the basic question of whether exposure is safe for a six-week-old embryo; if not, then the activity should not occur' (Steingraber, 1999).

Trends

Globalisation is a major driving force affecting the economic and environmental context of Europe. The United Nations Environment Programme argues that globalisation, characterised by rapid movement of capital, skills, employment, ideas and technologies, 'is a concern at a number of levels. From a purely practical point of view, it drives global demand for an unsustainable level of consumption'. Further, 'the shift towards corporate globalization means that decision-making at transnational companies is often more influential than local and regional decision-making'. Finally, correlating with trends in social polarisation, globalisation is leading towards an 'attitude of survival in a declared context of inevitable economic war' between states, regions, communities and individuals. Globalisation is weakening the power of the state to regulate, and increasing economic and social fragmentation particularly of peripheral communities (UNEP, 1999).

Increasingly, evidence shows that the current economic processes within Europe have exacerbated inequality and not enhanced the economic conditions of the majority of the people of Europe. This is true across the region. For example, the latest report on health inequalities in the United Kingdom reports that 'average incomes grew in real terms by about 40 % between 1970 and

1994/5, but this growth was far greater (60–68 %) amongst the richest tenth of the population'. For the poorest tenth of the United Kingdom's population real incomes actually fell by 8 per cent (after housing costs) in the same period (Acheson *et al.*, 1998). Similarly, social polarisation is one of the key effects of the reforms in the Russian Federation and eastern Europe.

Since the current effects of globalisation are a strong counterweight to any attempts to reduce inequalities or environmental injustices, strong policies will be required to ensure that globalisation does not further exacerbate inequalities and damage the environment. Generational and international rights are a critical aspect of environmental justice (Stephens *et al.*, 2000; Dower, 1992).

14.4. Policy responses

Environmental rights

Every person's right to a healthy environment is a good guiding goal for policies. However, implementation and enforcement are difficult. For example, Boyle (1996) and several others note that a rights approach to environmental justice may be potentially problematic in practice. Often states in Europe and elsewhere have constitutions that maintain the 'right' to health and 'sufficient' environments. Some include procedural rights also. Yet articulation of these rights within current legal frameworks proves difficult (Boyle 1996).

The following chapters give brief examples of some responses necessary to move towards the end goal of a healthy environment for all.

Precautionary action

Traditional approaches to managing environmental risks have not worked — because they cannot adequately deal with uncertainties. A paradigm shift in environmental decision-making is needed, towards a precautionary approach.

A precautionary approach will be based on understanding that uncertainty becomes the reason for taking action to prevent harm and for shifting the benefit of the doubt to those beings and systems that might suffer harm. The process of applying the precautionary principle needs to be open, informed and democratic and must include potentially affected parties (Scandrett *et al.*, 2000; Cameron and McKenzie, 1996).

Taking a precautionary approach will ensure that the rights of future generations and the powerless are better incorporated into decision-making. It will also ensure that the interests of a wider range of people in the current generation are taken into account.

The right to know and the need for more information

Ensuring that all people have an enforceable right to know about decisions which may affect their health is a critical aspect of ensuring environmental justice. The preamble to the United Nations' Aarhus Convention recognises that 'in the field of the environment, improved access to information and public participation in decision-making enhances the quality and the implementation of decisions, contributes to public awareness of environmental issues, gives the public the opportunity to express its concerns and enables public authorities to take due account of such concerns'. Ratification and implementation of the Aarhus Convention should ensure that people have greater access to the environmental information to make informed decisions and choices.

Accountability and participation

It has been suggested that the people of Europe are gradually losing any rights they may have had to participate in the development, implementation and enforcement of environmental laws, regulation and policies (Lang, 1999). Social exclusion in Europe is a procedural injustice, when whole sections of the society cannot access decision-making processes (Cameron and Mackenzie, 1996). It could be argued also that all the peoples of Europe are losing their procedural rights as governments cede to organisations such as the World Trade Organization whose role is to advocate freedom of trade, doing so at the expense of environmental, social or health concerns (Koivusalo, 1999).

People should have the power to influence the decisions that affect them (Box 14.3.). The 'toxic trespass' of all our bodies, mentioned above, is a clear example of the current lack of control people exercise over decision-makers.

Box 14.3. The procedural injustices that lead to substantive environmental injustice

'When you say that it (incineration) is acceptable, it is acceptable to the more articulate sections of the population. From what you have said, the incinerator ends up in the less articulate sections of society. I do think we ought to make that quite clear.'
Lord Judd questioning Richard Mills of the United Kingdom National Society for Clean Air and Environmental Protection (Ryder, 1999).

Broadening decision-making is not only necessary — both from a rights and a precautionary perspective — it should also lead to better decisions. Those who are at risk of suffering from environmental degradation are much more likely to employ a common sense, precautionary approach than the government, which must defend its decisions in the courts, or those who stand to gain (either in the short or long term) from an activity (Scandrett *et al.*, 2000). Currently, though, people have little control. Where participation is offered, it is most often in the context of extremely unbalanced power arrangements. In some countries, like the United Kingdom, there is a presumption in favour of development, with little accountability of developers to local people.

Good neighbour agreements, used in the United States, could be one way to improve accountability — these are both legally binding and voluntary agreements between industry and community which can include clauses on community access to information, negotiated improvements in pollution prevention, and guarantees of good unionised jobs going to local people, or other local economic benefits. This is not local economic democracy, but is a certain improvement in the accountability of industry to other stakeholders as well as the traditional shareholders (Scandrett *et al.*, 2000).

High-level commitment

Active and high-level commitment to tackling inequalities and injustice will be required, if the current trends of globalisation are not to make these injustices worse. It will not be enough to have a 'level playing field' — the equal treatment of unequals will merely exacerbate injustice (Coates, 1998). Some governments are starting to make profound commitments. For example within the last year the United Kingdom government has pledged to eradicate child poverty in the United Kingdom within 20 years, to cancel (a large part of) its 'Third World' debt, acknowledged its overconsumption of fossil fuels and pledged to reduce carbon dioxide emissions by 20 % by 2010. If the United Kingdom and other European countries implement policies to meet these and other similar targets, and set about a systematic programme to target all types of inequality — national, international and generational — then Europe will be leading the way in tackling environmental justice in all its forms.

Summary

The concept of environmental justice was first articulated in the United States during the '80, starting from the opposition to the siting of environmental hazardous industrial facilities in predominantly black or indigenous communities. This means that no population should be forced to bear a disproportionate burden of environmental impacts of pollution or other environmental hazards. There is growing evidence throughout Europe that the most disadvantaged groups, and children and pregnant women among them, suffer from the worst environmental conditions. There is also growing concern about the disproportionate environmental burdens imposed by industrialised nations on the poorest countries as well as on future generations. From here the need to tackle income inequalities to reduce health problems and deal with environmental problems to reduce health inequalities.

Although implementation and enforcement are difficult, a rights approach to environmental injustice, starting from every person's right to a healthy environment, is a good guiding goal for policies. Ensuring that all people have an enforceable right to know and to participate in decisions which may affect their health is a critical aspect of ensuring environmental justice.

Active and high-level commitment to tackling inequalities and injustice will be required to prevent current trends of globalisation from making these injustices worse.

References

Acheson, D. *et al.*, 1998. *Independent Inquiry into Inequalities in Health report*, 1st edition, Stationery Office, London.

Attfield, R. and Wilkins, B., eds, 1992. *International justice and the Third World*, Routledge, London.

Belsey, A., 1992. World poverty, justice and equality, in *International justice and the Third World* (edited by R. Attfield and B. Wilkins), Routledge, London, pp. 35–50.

Boyle, A., 1996. The role of international human rights law in the protection of the environment, in *Human rights approaches to environmental protection* (edited by A. Boyle and M. Anderson), Oxford University Press/ Clarendon Press, Oxford, pp. 43–71.

Cameron, J. and Mackenzie, R., 1996. Access to environmental justice and procedural rights in international institutions, in *Human rights approaches to environmental protection* (edited by A. Boyle and M. Anderson), Oxford University Press/Clarendon Press, Oxford, pp. 129–53.

Carley, M. and Spapens, P., 1997. *Sharing our world*, Earthscan Publications, London.

Coates, B., 1998. *The developmental implications of the MAI: WDM critique of the Fitzgerald Report to the UK Department for International Development*, World Development Movement, Oxford.

Committee on Environmental Justice, 1999. *Towards environmental justice: research education and health policy needs*, Institute of Medicine, National Academy Press, Washington, DC.

DoE, 1996. *English house condition survey: Energy report*, Department of the Environment, Her Majesty's Stationery Office, London.

Douglas-Scott, S., 1996. Environmental rights in the European Union: participatory democracy or democratic deficit? in *Human rights approaches to environmental protection* (edited by A. Boyle and M. Anderson), Oxford University Press/Clarendon Press, Oxford, pp. 109–29.

Dower, N., 1992. Sustainability and the right to development, in *International justice and the Third World* (edited by R. Attfield and B. Wilkins), Routledge, London, pp. 93–117.

Fur, P.D., 1999. The precautionary principle: Applications to policies regarding endocrine-disrupting chemicals, in *Protecting public health and the environment. Implementing the precautionary principle* (edited by C. Raffensperger and J. Tickner), Island Press, Washington, DC.

Her Majesty's Government, 1999. *Saving lives: Our healthier nation*, HMSO, London.

Koivusalo, M., 1999. *World Trade Organization and trade-creep in health and social policies*, GASSP, STAKES, Geneva.

Lang, T., 1999. The new GATT round: Whose development? Whose health? *J Epidemiol Comm Health*, Vol 53, pp. 681–2.

Latouche, S., 1993. *In the wake of the Affluent Society — an exploration of post-development,* Zed Books, London.

McBride, G., 1999. *Scottish applications of environmental justice*, University of Edinburgh, Edinburgh.

McLaren, D. and Bullock, S., 1999. *The geographic relation between household income and polluting factories*, Friends of the Earth, London.

McMichael, A.J., 1993. *Planetary overload: Global environmental change and the health of the human species*, Cambridge University Press, Cambridge.

McMichael, A., Woodward, A. and van Leeuwen, R., 1994. The impact of energy use in industrialised countries upon global population health, *Medicine & Global Survival*, Vol 1, pp. 23–32.

Ryder, R., 1999. No-one ever died from dioxin. The dioxin problem in Britain, *The Ecologist*, Vol 29, pp. 369–74.

Scandrett, E., McBride, G. and Dunion, K., 2000. *The campaign for environmental justice in Scotland*, Friends of the Earth Scotland, Edinburgh.

Smil, V., 1993. *Global ecology. Environmental change and social flexibility*, 1st edition, Routledge, London, pp. 1–237.

Steingraber, S., 1999. Lessons from Wingspread, in *Protecting public health and the environment. Implementing the precautionary principle* (edited by C. Raffensperger and J. Tickner), Island Press, Washington, WC.

Stephens, C. *et al.*, 2000. Our view. Act local, think global? Or act local, act global? How international environmental and social justice can be achieved if local governments reach out to each other, *EG — Local Environment News*, No 4.

UNEP, 1999. *Global environment outlook GEO2000,* United Nations Environment Programme, Earthscan Publications, NairobiWHO, 1992. *Our planet, our health,* Report of the WHO Commission on Health and Environment, World Health Organization, Geneva.

WHO, 1997. *Health and environment in sustainable development — five years after the Earth Summit*, World Health Organization, Geneva.

Wilkinson, R.G., 1996. *Unhealthy societies — the afflictions of inequality*, Routledge, London.

Wilkinson, R., 1999. Income inequality, social cohesion and health: Clarifying the theory — a reply to Muntaner and Lynch, *Int J Health Serv*, Vol 29, pp. 525–43.

Williams, C., 1998. *Environmental victims: New risks, new injustice*, Earthscan Publications, London.

World Bank, 1999. *Inequality: Trends and prospects*, World Bank Group.

WRI, 1997. *World resources 1996–1997* (edited by the World Resources Institute), Oxford University Press, Washington, DC.

15. Searching for evidence, dealing with uncertainties and promoting participatory risk management

Giorgio Tamburlini and Kristie L. Ebi
Contributing author: David Gee

Summary of existing knowledge
- There are major difficulties in making accurate assessments of risks and hazards, as there may be uncertainties in the probability of an event, and in the scale and nature of its consequences.
- Risk assessments, exposure assessments and risk management protocols have generally not given sufficient consideration to developing organisms.

Main challenges
- To apply the precautionary principle in situations with uncertainties about potentially serious health threats, until adequate data are available for more scientifically based assessments.
- To involve stakeholders in the assessment process and develop mechanisms to ensure that children's interests are taken into consideration.

Action points
- Evaluate children's exposure from conception to adolescence in animal assays and epidemiological studies, taking into account children's specific susceptibility. Include parental exposure, when appropriate, in epidemiological studies.
- Promote a rational approach to participatory decision-making in children's environmental health issues.

15.1. Introduction

A growing body of evidence suggests that children are disproportionately vulnerable to many environmental hazards, and that the physical environment plays a role in a variety of adverse health effects from conception to adolescence. Considerable knowledge gaps exist as to whether there are adverse health effects associated with specific environmental factors. In addition, new methods need to be developed to aid this search. This chapter provides an overview of these issues. Specific attention is paid to the challenges of assessing risks for developing organisms. We review approaches proposed to deal with scientific uncertainties and discuss issues raised by the application of the precautionary principle. In addition, a rational framework is suggested for involving all interested parties in risk assessment, risk management and decision-making.

15.2. Searching for evidence: the assessment process

Approaches to evaluating the impacts of environmental risks to human health vary greatly depending on the extent of knowledge about the key variables of concern, such as exposure risk and susceptibility factors, and on the certainty and nature of the relationship between the risk and the potential outcome(s) (Bernard and Ebi, 2001). Probably the most familiar method is that of toxicological risk assessment which has been primarily applied to environmental agents, generally chemicals. The standard four-step risk assessment paradigm — hazard identification, dose-response assessment, exposure assessment and risk characterisation — is shown in Box 15.1. Under this paradigm, the evaluation of information on the hazardous properties of environmental agents and on the extent of human exposure to them results in a quantitative or qualitative statement about the probability and degree of harm to the exposed population(s). Policy judgements about the choice of scientific approach are made in each of the four steps. For example, the choice of one dose-response model over another is a 'science-policy' choice (Bernard and Ebi, 2001).

Box 15.1. The toxicological risk assessment process

Step 1. Hazard identification
Determine whether exposure to an agent has the potential to cause adverse health effects.

Step 2. Dose-response assessment
Determine the possible severity of the adverse effects at different levels of exposure to the agent.

Step 3. Exposure assessment
Estimate the exposure of individuals, including potentially sensitive groups such as children, to the agent.

Step 4. Risk characterisation
Combine the information from the previous steps to determine the level of potential risk to humans and the environment.

The limitations of risk assessment, as currently practised, should be recognised and understood. The assumptions underlying traditional risk assessment may limit its applicability to complex environmental problems (Bernard and Ebi, 2001). One of these assumptions is that a defined exposure to a specific agent (generally, a xenobiotic) causes a specific adverse health outcome to identifiable exposed populations, including specific people at particular risk. In general, the health outcome is distinctive and the association between immediate cause (e.g. asbestos exposure) and health impact (e.g. mesothelioma) can be fairly clearly determined. Even where the health outcomes are less specific than in the asbestos example, there may be data from animal or human studies demonstrating an increased risk associated with a well-defined exposure. However, most diseases associated with environmental exposures have many causal factors, which may be interrelated. These multiple, interrelated causal factors, as well as relevant feedback mechanisms, need to be addressed in investigating complex disease/exposure associations, because they may limit the predictability of the health outcome and even the ability to estimate the degree of uncertainty in any risk estimation (Bernard and Ebi, 2001).

While early risk assessments narrowly focused on determining the probability of harm, the general approach and philosophy are evolving and becoming more relevant to complex environmental problems. Recent efforts are considering social, economic and political factors in describing risk. Stakeholders are now expected to be involved throughout the risk assessment process to ensure that the risk characterisation addresses a broad range of concerns and that the context in which the assessment will be used is taken into account.

General difficulties of assessing risks and hazards

There are major difficulties in making detailed and accurate assessments of risks and hazards, as there may be uncertainty both in the probability of an event occurring and in the scale and nature of its consequences. These uncertainties may arise from a variety of factors (WHO EUR 1999a):

- lack of data: the large amount of new chemicals appearing on to the market makes comprehensive testing difficult and the data availability on existing chemicals may be very poor;
- biased sources of data: sometimes the main information available on the risks posed by a technology comes from those with an interest in promoting it;
- the emergence of new technologies (e.g. genetically modified organisms) for which there is not a sufficient body of experience;
- the complexity of the interactions between humans and the environment leads to many possible causes for any given effect, and to difficulties in establishing the role of each single factor;
- separation of cause and effect over space (e.g. widely dispersed pollution) and time (e.g. intergenerational effects) which makes it difficult to establish causal connections;
- synergistic and cumulative effects (e.g. failure to take into account pre-existing body burdens of toxic substances or of the combined effects of toxicants);
- unpredicted sources of hazards;
- varying susceptibilities among populations due to genetic, social or environmental factors.

Should risk assessment fail to explicitly address these issues, it may give the illusion of an objectivity which is not justified.

Issues of risk assessment for agents acting during early developmental stages

An important question for risk assessment is whether the current sources of information for hazard identification (animal bioassays and epidemiological studies) are adequate to identify agents that could pose particular risks for children during various developmental stages. One example of the weaknesses of animal evidence is the difference between the healthy young rats (which breathe through the nose) used in experiments and a mixed age and health status human population, who partly breathe through the mouth. These three differences (age, health status and mouth-breathing) were the main reasons experts in 1987 'dramatically' underestimated the health impact on humans of fine particles in polluted air, compared with 1997 (WHO, 1997).

Accumulating knowledge has changed our approaches. In a 1992 conference on risk assessment for children it was concluded that animal bioassays, which included perinatal exposures, were not able to detect carcinogens that were not identified through standard methods. A more recent review prepared by the US Environmental Protection Agency (EPA) for the Science

Advisory Panel, which is in charge of assessing the scientific basis for pesticide policies, came to the opposite conclusion (Buffler, 1999).

Most risk assessments have failed to incorporate explicit assumptions about children's exposure, which may differ from adults. We have seen in Part I that children breathe more air, eat more food and drink more water per unit of body weight than adults. They have a less diverse diet and their diet varies greatly with age. These differences may make children more or less susceptible than adults to any adverse consequences of exposure to a hazardous substance. Also, risk assessments usually only consider one route of exposure (e.g. air) to any given compound.

Steps 1 to 4 of the risk assessment process should be carefully reconsidered to include the following set of questions for substances dispersed in the environment.

For steps 1 and 2:

- Did the toxicity assessment include the reproductive and early developmental stages or did it extrapolate from data on adults?
- Did laboratory tests and epidemiological studies consider adequately sensitive end-points (e.g. the impact on learning capabilities when assessing potential neurotoxicants)?
- Have the long-term effects (e.g. cancer or cardiovascular disease or chronic lung disease) of exposure very early in life been evaluated?

To provide adequate answers to these questions, the scope of animal assays should be expanded to incorporate perinatal exposure and early developmental stages. Epidemiological studies on *in utero*, perinatal and childhood exposure are also needed. Data on whether children are more vulnerable to the adverse effects of a particular agent, including whether the target organ in children is more vulnerable, should be collected and incorporated into risk assessments (Roberts, 1992; McConnel, 1992).

For steps 3 and 4:

- Were exposure patterns at different stages of development, from conception to adolescence, included in exposure assessments?
- Did exposure assessment models and estimates specifically consider children's unique modes of exposure, such as children's hands-to-mouth behaviour and the additional time children spend on floors and on the ground?
- Were all sources of exposure, such as diet, water, home, day care and school, neighbourhood and working places (for parents) taken into consideration?
- Did the exposure assessments reflect 'real world' experiences, including factors such as multiple exposure, multiple routes of exposure, chemical mixtures, and additive or synergistic effects?

Risk assessments for agents to which children are exposed must be based on children's exposure patterns. Child inhalation rates and food and water consumption rates must be used. Food consumption surveys should include adequate sample sizes of ages with specific consumption patterns, such as less than 12 months, from 1–3 years, 4–10 years and 11–18 years.

New methods are being developed to assess the risk of combined exposure to a variety of substances and sources of exposure. For instance, an individual may be exposed to lead from many sources, such as contaminated drinking-water, lead-based paint and airborne lead in industrial and densely polluted areas. The exposure to all these sources should be combined in one measure for an assessment of combined risk.

Another important area for exposure assessment is the monitoring of toxic substances in humans, e.g. in blood and urine. This kind of bio-monitoring will identify population groups who are at higher risk, and will help determine whether exposures are changing in the population. Less costly methods for biological testing must be developed so that testing can become more widely applicable.

Finally, epidemiological tracking systems, particular over several decades, such as disease registers and tissue banks, are important for following trends in diseases that may be related to environment. These systems can help evaluate progress and identify areas that require interventions (US EPA, 2000; EEA, 2002).

15.3. Dealing with scientific uncertainties

Developing the scientific basis to protect children's health will require a sustained effort by many disciplines. When data are insufficient, the development of a sound basis to deal with uncertainty may be equally or more challenging. The recent focus on human rights as a framework for public health ethics (Dworkin, 1993) provided some guidance and support. International agencies recently incorporated this new perspective into their policies, including environmental matters (Boyle and Anderson, 1996).

A key issue to be addressed in dealing with public health is what level of proof is to be used when making a decision. The level of proof can vary from very high to low, depending on the issue being addressed. A sound scientific approach normally requires a high level of proof, such as that provided by the coexistence of:

- valid experimental studies;
- consistency and coherence of results among different studies on the same subject;
- evidence of a dose-response relationship (the greater the exposure, the greater the effect);
- a plausible biological rationale to explain the investigated causal link.

The above requirements are often not met due to a variety of factors, including the continuous development of new chemicals and technologies, the pressure by the industry and the public to introduce them on to the market before completing rigorous scientific scrutiny, and the difficulties entailed in this scrutiny. The result can be a high degree of scientific uncertainty on the actual hazard to health and/or the magnitude of the health impact produced by a new substance. This problem becomes particularly serious when the substance or technology has the potential to produce serious or irreversible damage. This applies both to risks posed by unplanned non-routine events (chemical or nuclear accidents) and to risks posed by ongoing exposure to environmental agents (ultraviolet radiation, lead, tobacco smoke). For this reason, there has been a growing movement to adopt 'precautionary approaches' to the management of health risks in the face of scientific uncertainty. In fact, much damage to health and/or the environment might have been avoided by applying precautionary approaches.

Within the declaration signed in London at the 1999 Third Ministerial Conference on Environment and Health, WHO was encouraged to take into account 'the need to rigorously apply the Precautionary Principle in assessing risks and to adopt a more preventive, pro-active approach to hazards' (WHO, 1999b).

The precautionary principle

The precautionary principle and its application to environmental hazards and their uncertainties only began to emerge as an explicit concept in the 1970s, when German scientists and policy-makers were trying to deal with 'forest death' and its possible causes, including air pollution. The main element they developed was a general rule of public policy action to be used in situations of potentially serious or irreversible threats to health or the environment, where there is a need to act to reduce potential hazards before there is strong proof of harm. A precautionary approach, however, requires much more than establishing the level of proof needed to justify action to reduce hazards. The German Clean Air Act of 1974, as elaborated in the 1985 report on the Clean Air Act (Boehmer-Christiansen, 1994; EEA, 2001) also included elements such as:

- research and monitoring for the early detection of hazards;
- a general reduction of environmental burdens;
- the promotion of 'clean production' and innovation;
- the proportionality principle, where the costs of actions to prevent hazards should not be disproportionate to the likely benefits;
- a cooperative approach between stakeholders to solving common problems via integrated policy measures that aim to improve the environment, competitiveness and employment;
- action to reduce risks before full 'proof' of harm is available if impacts could be serious or irreversible.

Since the 1970s, the precautionary principle has risen rapidly up the political agenda, and has been incorporated into many international agreements. This principle featured in the 1992 Rio Declaration on

Environment and Development as Principle 15 (UN, 1993):

'In order to protect the environment, the precautionary approach shall be widely applied by States according to their capabilities. Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation.'

The precautionary principle has been increasingly included in national legislation and international treaties as an appropriate foundation for environmental decision-making. For example, the European Treaties state that the 'Community policy on the environment shall be based on the precautionary principle'. An instance of adoption of the precautionary principle is the European Commission's decision to ban beef from the United Kingdom, with a view to limiting the risk of transmission of bovine spongiform encephalopathy. The European Court of Justice ruled that this decision was justified 'in view of the seriousness of the risk and the urgency of the situation, and having regard to the objective of the decision, the Commission did not act in a manifestly inappropriate manner by adopting the decision, on a temporary basis and pending the production of more detailed scientific information'.

On 2 February 2000, the European Commission approved a communication on the precautionary principle that provided guidelines for its application (CEC, 2000). Measures based on the precautionary principle should be:

- tailored to the chosen level of protection;
- non-discriminatory in their application, i.e. they should treat comparable situations in a similar way;
- consistent with similar measures already taken, i.e. they should be comparable in scope and nature to measures already taken in equivalent areas in which all scientific data are available;
- based on an examination of the potential benefits and costs of action or lack of action (including, where appropriate and feasible, an economic cost-benefit analysis);
- provisional in nature, i.e. subject to review in the light of new scientific data;
- capable of assigning responsibility for producing the scientific evidence necessary for a more comprehensive risk assessment.

In this definition, the precautionary principle is 'risk-oriented' in that it requires an evaluation of risk including cost-benefit considerations. It is clearly intended for use in drafting provisional responses to potentially serious health threats, until adequate data are available for more scientifically based responses. Thus, the application of the precautionary principle does not mean that a scientific approach is not required (Box 15.2.). The recent EU ban on phthalates is an example specifically related to children's health protection. Phthalates, a family of chemicals used to make polyvinyl chloride (PVC) plastic solid and flexible, can produce adverse effects on the developing male reproductive tract and may have a carcinogenic effect. Because phthalates are widely used in objects to which newborn babies, particularly premature and sick babies, may be exposed for long periods, such as pacifiers, intravenous catheters and tracheal tubes, a ban was decided until ongoing research provides more conclusive data.

Box 15.2. The precautionary principle and the scientific approach are not in opposition

'Supporters of precautionary action have often generalised their position to one that appears antagonistic to science, despite the fact that science has usually provided the initial information about the threat. This often reflects frustration at the slowness of the scientific process, the uncertainty of risk assessment and the fact that those opposing action overuse the argument that scientific research is needed before any action can be taken. Advocating action without waiting for definitive science has been interpreted by some as a reason to stop research. But the opposite should be the case: acting on the precautionary principle should automatically trigger research' (Goldstein, 1999).

Other cautionary policies

Several other policies promoting caution have been developed to address concerns about public, occupational and environmental health issues in the face of scientific uncertainty. These include precursors and variations of the precautionary principle such as prudent avoidance and the adoption of extra safety factors for the most vulnerable in establishing safety standards.

Prudent avoidance was initially developed as a risk management strategy for power-frequency electromagnetic fields (EMF). This approach advocates taking simple, easily achievable, low-cost measures to reduce EMF exposure. The terms 'simple', 'easily

achievable' and 'low-cost', however, lack precise definition. Generally, government agencies have applied the policy only to new facilities, where minor modifications in design can reduce levels of public exposure. It has not been applied to enforce modification of existing facilities, which is often very expensive. Defined in this way, prudent avoidance recommends taking low-cost measures to reduce exposure, in the absence of any scientifically justifiable expectation that these measures would reduce risk. This approach assumes that the time-weighted average (TWA) exposure is biologically relevant, with no threshold effects; that is, a reduction in an individual's TWA exposure will reduce the probability of experiencing any adverse health effects associated with the higher level of exposure. Major issues in EMF are that the relevant exposure and the mechanism of action are unknown. Prudent avoidance measures are generally applied as voluntary recommendations rather than fixed limits or rules.

Prudent avoidance (not necessarily identified as such) has been adopted in parts of the electrical sector in several countries. Measures that can be taken at 'modest cost' include routeing power lines away from schools, and phasing power-line conductors to reduce magnetic fields near the right of way.

'As low as reasonably achievable' (ALARA) is a conceptually different approach, as it is a policy used to minimise known risks, by keeping exposures as low as reasonably possible, taking into consideration costs, technology, benefits to public health, safety and other societal concerns. ALARA today is mainly used in the context of ionising radiation protection, where limits are not set on the basis of a threshold, but rather on the basis of the acceptable risk that can be presumed to exist even at levels below recommended limits, on the grounds that what constitutes 'acceptable risk' can vary widely among individuals.

When there are insufficient susceptibility and exposure data to support the identification of safety limits for children, one approach taken is that of considering extra safety factors for children**.** An example is the Food Quality Protection Act (USA, 1996) that authorises the EPA to add extra safety factors to protect children from dietary exposure to pesticides.

15.4. Promoting participatory risk management

Policy-makers as well as the scientific community should be aware of the need to involve interested parties in the assessment process: this is necessary to incorporate the views and experiences of the communities concerned and is a requisite for participatory decision-making (WHO, 1999a). It is also necessary to ensure that decision-making processes based on an assessment benefit from opinions that are independent of any commercial or political pressure. The scientific community has a particular responsibility in making the best assessment of risks and hazards, and in identifying the levels of uncertainty inherent in the assessment. The assessment process and its results must be made understandable to the interested parties if they are to share the decision on what should be done to protect health. In order to ensure transparency, the details of the studies evaluated in an assessment should be made available to the public. Unfortunately, the use of participatory methods based on available information (US EPA, 2000) is the exception rather than the rule. They should be used more extensively and the experiences shared.

While science provides the starting point for assessing risk, a decision on what constitutes an acceptable risk is essentially a value judgement. The acceptability of risk may depend on many factors besides the quantitative assessment, e.g. whether it is a chosen or imposed risk, whether the risk could be avoided and at what price, and whether the distribution of risks through the population correlates with the distribution of benefits. Even though part of the assessment process is a scientific exercise, the fact that assessing risks involves value judgements makes it essential to involve those who will bear the risk in the overall decision-making process. Various models have been used for bringing together experts, policy-makers and the public to debate risk management, such as consensus conferences and citizens' advisory committees. These models generally do not include mechanisms to ensure that children's interests are taken into consideration during the assessment process. Methods need to be developed on how to incorporate the views of children — should they have direct participation or should parents, educators and paediatricians be their representatives?

Policy-focused assessments are one approach to translating scientific information into timely and useful insights that inform policy and resource management in the face of uncertainties. Ultimately, assessments must help resource managers and other decision-makers determine what they should do differently — or the same — to respond to environmental exposures (Scheraga and Furlow, 2001). Policy-focused assessment is an ongoing process that engages both researchers and end-users in analysing, evaluating and interpreting information from multiple disciplines to draw conclusions that are timely and useful for decision-makers. This process provides stakeholders with the opportunity to participate in the process of evaluating acceptable levels of risk and appropriate responses. Throughout the process, key research gaps are identified and research needs prioritised to provide the information needed to inform future decisions. The process includes:

- ongoing collaboration between the research, assessment and stakeholder communities;
- a focus on stakeholder information needs;
- multidisciplinary approaches;
- use of scenarios (or 'what-ifs') to deal with uncertainties;
- evaluation of risk management options.

Although used in only a few instances to date, this approach is likely to be followed in many future assessments.

Several key questions should be posed when evaluating an assessment (Box 15.3.). They cover many of the issues discussed in this chapter and their sequence provides a rational approach to participatory decision-making in environmental health matters (EEA and WHO, 1999).

Box 15.3. Key questions for evaluating an assessment

- What is the nature and strength of the evidence for an adverse health effect and for the role of specific environmental factors in that effect?
- What is the nature of the impact (trivial or serious, reversible or irreversible, immediate or long-term, large or small numbers affected)?
- Are the health effects evaluated in highly vulnerable groups such as pregnant women or children?
- Are the specific circumstances considered that may increase exposure as well as the likelihood of cumulative exposure?
- Are exposure or effect avoidance measures available, and actors identifiable and willing to take action?
- What are the cost and benefits of action and inaction in both economic and health terms? Are the risks acceptable in view of the benefits?
- Who benefits? Who carries the risk? Are risks and benefits equally distributed among the population?
- Does the nature of the effect indicate the need for taking immediate action according to the precautionary principle?
- How are the consequences of action or inaction to be evaluated?
- How can informed consent and public involvement in acceptable risks be achieved?

Summary

Public health decision makers should use the best available scientific evidence. Establishing a causal link between environmental factors and adverse health effects poses many challenges. Risk assessment is one tool for evaluating the evidence. Environmental and public health policies have traditionally been determined primarily using data from adult animals or adult humans. The reproductive periods and children have rarely been considered. As a result, risk assessments, exposure assessments and risk management protocols do not cater sufficiently for children. There is an urgent need to evaluate children's exposure from conception to adolescence in animal assays and epidemiological studies, taking into account children's specific susceptibility. When appropriate, parental exposure should be included in epidemiological studies.

There often remains a high degree of scientific uncertainty and ignorance on the actual hazard to health and/or the magnitude of the health impact produced by a new substance. This problem becomes particularly serious when the substance or technology has the potential to produce serious or irreversible damage.

Several policies promoting caution have been developed to address concerns about public, occupational and environmental health issues in the face of scientific uncertainty. Various international agreements recommend using the precautionary principle where there may be serious and irreversible health impacts, but insufficient scientific proof of the risk. The precautionary principle is clearly intended for use in drafting provisional responses to potentially serious health threats until adequate data are available for more scientifically based responses. Other approaches include the establishment of extra safety factors for children and prudent avoidance of potentially dangerous exposures.

Policy-makers as well as the scientific community should be aware of the need to involve stakeholders in the assessment process: this is necessary to incorporate the views and experiences of the communities concerned, and is a requisite for participatory decision-making. A participatory risk management process should follow a rational approach including an evaluation of available evidence and, when feasible, a comprehensive cost-benefit analysis of the various policy options.

References

Bernard, S.M. and Ebi, K.L., 2001. Comments on the process and product of the Health Impacts Assessment component of the United States National Assessment of the potential consequences of climate variability and change, *Environmental Health Perspectives*, Vol 109 (suppl 2), pp. 177–84.

Boehmer-Christiansen, S., 1994. The precautionary principle in Germany: enabling government, in *Interpreting the precautionary principle*(edited by O'Riordan, T. and Cameron, J.), Cameron and May, London.

Boyle, A. and Anderson, M., 1996. *Human rights approaches to environmental protection*, Oxford University Press/Clarendon Press, Oxford.

Buffler, P.A., 1999. Carcinogen risk assessment guidelines and children, *Environmental Health Perspectives*, Vol 107, pp. 4784–8.

CEC, 2000. *Communication from the Commission on the precautionary principle*, Commission of the European Community, Brussels.

Dworkin, R., 1993. *Taking rights seriously*, Harvard University Press, Cambridge MA.

EEA and WHO, 1999. *Children in their environment: Vulnerable, valuable and at risk*, European Environment Agency and World Health Organization Regional Office for Europe, Copenhagen, 1999.

EEA, 2001. *Late lessons for early warnings: the precautionary principle, 1896-2000*, European Environment Agency, Copenhagen.

EEA, 2002. *Response to late lessons: some implications for information flows to decision-makers and the public*, European Environment Agency, Copenhagen.

Goldstein, B.B.D., 1999. Editorial: The precautionary principle and the scientific approach are not in opposition, *Environmental Health Perspectives*, Vol 107.McConnel, E.E., 1992. Comparative responses in carcinogenesis bioassays as a function of age at first exposure, in *Similarities and differences between children and adults* (edited by P.S. Guzelian, C.J. Henry and S.S. Olin), ILSI Press, Washington DC, pp. 66–78.

Roberts, R.J., 1992. Overview of similarities and differences between children and adults: Implications for risk assessment, in *Similarities and differences between children and adults* (edited by P.S. Guzelian, C.J. Henry and S.S. Olin), ILSI Press, Washington DC, pp. 11–5.

Scheraga, J. and Furlow, J., 2001. From assessment to policy: Lessons learned from the U.S. National Assessment, *Human and Ecological Risk Assessment*, Vol 7, pp. 1227–46.

UN, 1993. *Agenda 21: The UN programme of action from Rio*, United Nations, New York.

US EPA, 2000. *America's children and the environment: A first view of available measures.* US Environmental Protection Agency, Office of Children's Health Protection, Office of Policy Economics and Innovation and National Center for Environmental Economics.

USA, 1996. *Food Quality Protection Act*, US Public Law 104–70.

WHO, 1997. *Health and environment in sustainable development*, World Health Organization, Geneva.

WHO, 1999a. *Access to information, public participation and access to justice in environment and health matters*, document EUR/ICP/EHCO 02 02 05/12, WHO Regional Office for Europe, Copenhagen.

WHO 1999b *Declaration of the Third Ministerial Conference on Environment and Health*, London, 16-18 June1999, WHO Regional Office for Europe, Copenhagen.

16. Policy development

Joy Carlson and Giorgio Tamburlini

Summary of existing knowledge
- Developing organisms have different exposure patterns and susceptibilities to environmental toxicants, and this represents the basic rationale for specific protective policies.
- Environmental and health policy is essentially a multi-disciplinary and multi-sectorial field.

Main challenges
- To develop child-focused environmental and health policies based on specific risk assessment.
- To promote the active participation to environmental policy development of all sectors of society and of communities, including children and young people.

Action points
- To promote closer coordination among UN agencies, the EU, national governments and environmental and health agencies, non-governmental organisations to develop, implement and enforce child-focused environmental health policies.
- To promote the creation of databases and key indicators to enhance the development of child-focused protective policies and to help create an informed citizenry.

16.1. Introduction

This chapter provides general guidance for developing environmental policies that are specifically aimed at protecting reproductive and child health. The rationale for paying specific attention to children and the guiding principles adopted by WHO for environmental health policies are reviewed. From these premises, a basic framework for developing and assessing child-focused environmental policies is suggested. The principal actors and tools for policy development at international and national level are described, with particular emphasis given to the need to incorporate environmental child protection within national environmental health action plans (NEHAPs) and other relevant national programmes. In the light of this need, child-focused environmental indicators are recommended to monitor exposures and health outcomes and to track progress in policy implementation.

As policies are developed by and implemented through different agencies within the 51 countries in the WHO European Region, this chapter is meant to provide general guidance and suggestions. Each city, region and country can adapt these suggestions for use within its own institutional structure to address the specific health threats in its area.

16.2. Rationale and guiding principles for protective policies for children

From the scientific information on children's environmental health reviewed in this monograph, several basic conclusions can be drawn to form a rationale for any policy discussion.

- Children cannot be regarded as little adults because their behaviour, physiology, metabolism and diet are different.
- Children have different susceptibilities from adults due to their dynamic growth and to their biological systems which are not yet fully developed.
- Children have very different exposure patterns from adults.
- For children, the stage in their development when the exposure occurs is as important, if not more important, than the type and dose of exposure.
- Children are exposed to different types of toxicants in different combinations throughout their lives.
- Children can have very different health outcomes from adults exposed to the same toxicant; such health outcomes alter normal development and can be permanent.
- Children have more years during which they may be exposed to a variety of toxicants, which can lead to disease later in life.
- There is mounting evidence that certain types of childhood diseases may be related to environmental exposure, e.g. asthma and neurodevelopmental effects.

The fact that children cannot be regarded as 'little adults' has important implications for environmental health policy. Environmental policy decisions based on the need to protect adult health may, in fact, not be protective of children's health. Because of the serious potential impact on children's health due to environmental exposures, we have a responsibility to protect children now and in the future.

Three basic values form the ethical foundation of the WHO Health for All policy (WHO, 1999a):

- health as a fundamental human right;
- equity in health and solidarity in action between countries, between groups of people within countries and between genders;
- participation by and accountability of individuals, groups and communities and of institutions, organisations and sectors in health development.

These values are particularly relevant to environmental health policies aimed at protecting today's children as well as future generations for a number of reasons.

- Because children do not determine the environment into which they are born or in which they develop, it is the responsibility of the adults to ensure that a safe and healthful environment is created, promoted and maintained.
- In 1996, children were declared full citizens of the European Union (EU). As such, they have the right to full inclusion in public policies including protection in environmental policy.
- The WHO European Region includes some of the richest countries in the world and others that are extremely poor. Within most countries the differences in economic status are deepening. Such differences should be seen not only as a threat to social cohesion, but first of all in human rights terms. The persistent and even increasing discrepancies in health status and quality of life enjoyed by different populations, which are largely reflected in the health status of children, is unacceptable. Much stronger emphasis must be given to the promotion of equity in health and to solidarity among and within countries.
- One particular aspect of inequity is the inter-generation injustice created by the fact that future generations are going to bear the greatest burden of environmental deterioration.
- The concepts of participation and accountability lead to several other concepts and principles that are particularly important when developing environmental health policies for children. The right to know principle, for example, is crucial in that access to information represents the basis for the recognition of the special vulnerability of children and therefore for policies that take this into account.

There are several other principles stemming from the basic values that WHO has identified as underlying principles for policy development in the specific field of environmental health (WHO, 1999b). Among these, two are particularly relevant to environmental policies that aim to protect children:

- the precautionary principle which should inform policies aimed at protecting reproduction and early development from potentially harmful substances;
- the principle of sustainable development, meaning development that meets the needs of the present without compromising the ability of future generations to meet their own needs.

These guiding principles should inform any policy development and implementation.

16.3. Basic questions for use in policy development

Many different agencies, organisations, governmental structures and individuals may be involved in policy development and implementation in the European Region. This diversity requires a framework of questions which can help guide policy formulation and can be applied in different situations. Children's environmental health has far-reaching implications, certainly within the health and environment arenas, but it also touches upon public policy as seemingly distant as urban planning, transportation, manufacturing and building practices.

The following basic questions have been designed so that, if answered appropriately, they can help guide the development of public and environmental policies that will protect children and promote a healthy environment.

1. Have the unique vulnerabilities and exposure patterns of children been considered in assessing environmental risks?

2. Are current policies and regulations protective of children?

3. Are access to information and public participation ensured so that parents, professionals and particularly those

involved in child education and health, as well as communities at large, may make informed decisions related to environmental health risks and lifestyle choices and contribute to effective policies and interventions?

4. Do current and proposed policies promote a healthy environment for children, through intersectoral action?

5. Are explicit policies addressing the issue of environmental justice?

The following provides some examples of how these issues can be relevant when reviewing or developing environmental health policies aimed at protecting children and those of reproductive age. The appropriate level of responsibility in providing answers to these questions is also indicated.

1. Have the unique vulnerabilities and exposure patterns of children been considered?

Environmental and public health policies have traditionally been determined using data from adult animals or adult humans (males). Infants and children have not been part of the data equation. As a result, risk assessments, exposure assessments and risk management protocols have not included children. This general issue about risk assessment can be expressed through two main questions, as the answer involves two different levels of responsibility.

- Do risk assessments consider the unique vulnerabilities and susceptibilities of children and include children's exposure patterns at different times of development?

  This issue has been extensively discussed in the previous chapter. What matters here is to remember that most of the questions on the specific vulnerability of children, as well of pregnant women, have global relevance. As a consequence, the responsibility for providing scientifically sound answers belongs to the international scientific community. The duty and responsibility of policy-makers is to ensure that international and national research agencies have access to sufficient resources to respond to this commitment, that the scientific efforts are coordinated, that scientific information is made widely available, and that regions and countries with fewer resources benefit, in accordance with the principle of solidarity, from international assistance to answer specific information needs. For example, the consequences of the Chernobyl accident raised new questions about the effects of specific radiation exposures, and the international research community and international agencies cooperated in data-gathering and follow-up studies to quantify these effects. It is essential that countries with limited research capabilities and widespread problems of environmental pollution benefit from the research conducted at the international level on the health effects of pollutants and in particular on their potential harm to the reproductive functions and systems, since it has been shown that knowledge in this field is scarce and may require a great amount of resources. Policy-makers must understand that environmental health threats go beyond national boundaries and that collaborative research efforts and information-sharing are essential.

- Are children's exposures and environment-related health conditions assessed in different geographical areas, as well as in different population groups?

  As patterns of exposure are largely dependent on social and cultural factors, the answer to these questions must take into account regional and country peculiarities. Regional and country environmental and health agencies are responsible for carrying out exposure assessments that take into account the different local realities and circumstances. For example, children's exposure to lead or pesticides could differ greatly in countries that have similar environmental pollution levels of these toxicants, in terms of lead concentration in water, food and soil, depending on the different housing situations and lifestyles that can put children of one country at much higher risk of being contaminated than children from another country. Similarly, differences can also occur within different social and ethnic groups within the same country. Policy-makers must make sure that specific exposure assessments, which take into account the particular circumstances in which children and pregnant women live and develop, are carried out. Governmental and scientific institutions should also collaborate in establishing adequate data collection systems, particularly for conditions specifically

related to environmental threats such as congenital malformations, cancers or chronic respiratory diseases. Biomonitoring should be ensured in sample populations of children as well as in pregnant women exposed to hazardous substances. International solidarity and collaboration is also necessary to respond to these more country-specific information needs.

2. Are policies and regulations protective of children?

The specific needs of pregnant women and children have often been disregarded because of insufficient awareness about their particular and greater susceptibilities. Existing policies and regulations should be evaluated to ensure that they take into account these increased susceptibilities. Extra safety margins should be provided when data are insufficient. The basic questions to be asked here are therefore the following:

- Do existing environmental laws and regulations take into account child or reproductive-specific toxicity and exposure?

- When child- or reproductive-specific toxicity data or exposure data are insufficient, is an extra margin of safety employed or the substance disallowed for use until such data are available?

  A typical case where regulations must be adapted to cover the specific needs of children is that of lead, since we know that even levels that are considered safe for adults can produce harmful or irreversible damage in the developing brains of children. The phasing-out of added lead in petrol, to be accomplished by January 2005 within the EU, is an example of an exposure reduction policy. As added lead in petrol is not the only source of lead poisoning, other regulations are necessary. One example is provided by Denmark, the first country in the world to impose, in 2000, a wide-ranging ban on lead. Restrictions will apply also to cadmium, mercury and nickel, and pesticides.

  The issue of how to protect populations when data are insufficient was discussed in the previous chapter. An example of an extra safety factor introduced to protect children has been the Food Quality Protection Act issued in the United States in 1996. On the basis of the precautionary principle, in March 2000 the EU established a ban on phthalates, a family of chemicals used to make polyvinyl chloride (PVC) plastic soft and flexible. Exposure to phthalates can produce adverse effects on the developing male reproductive tract and in the long run have a carcinogenic effect. Phthalates are widely used in objects to which children, including very premature and sick babies, are intensively exposed, such as pacifiers, toys and catheters, and are widely dispersed in the environment so that children can undergo multiple exposures to them.

  In September 2000 the EU environment ministers reached a unanimous political agreement on a directive aimed at reducing ground-level ozone pollution, a toxicant for the respiratory tract to which children are particularly susceptible. The directive (October 2000) establishes that Member States will be allowed to exceed the WHO guideline of 120 micrograms per cubic metre on no more than 25 days each year by the year 2010. It also establishes that the alert threshold should be lowered to 240 micrograms from the previous 360 micrograms.

3. Are access to information and public participation ensured so that parents, professionals and particularly those involved in child education and health, as well as communities at large, can make informed decisions regarding environmental health risks and lifestyle choices and contribute to effective policies and interventions?

The Aarhus Convention, adopted in June 1998 and so far signed by 39 governments and by the European Community (UNECE, 1999), is currently the most significant regional framework for strengthening public rights of access to information, participation in decision-making and access to justice in the context of environment-related health. It outlines an imperative to seek and actively cultivate and inform local and national expertise, and to engage all community members in truly meaningful participation.

Some suggestions to create a more informed citizenry and a network of informed professionals include:

- Better information for the general public, by making available exposure assessment data and information about environmental

toxicants released into various media (i.e. soil, water, air), and by creating mechanisms for individuals and communities to have their questions and concerns answered and addressed by credible, independent experts.

- Educating policy-makers on the health threats to children from environmental exposures. Parents, community members and experts play a key role in this. Frequently they must advocate for the protection of children. Governments at all levels — local, regional, national and international — often need support and pressure from various constituency groups in order to move forward with an initiative. People who can articulate community experience, present epidemiological and clinical data, and discuss innovative technologies or systems are key figures in moving the children's environmental health initiative forward.

- Promoting a better understanding of environment and health throughout the education system. Pilot initiatives have been developed in various European countries, some of them under the umbrella of the Healthy School Initiative. Curricula for children have been developed in the United States by the Environmental and Occupational Health Sciences Institute at Rutgers University (http://www.eohsi.rutgers.edu). However, other agencies such as the family, the media and the entertainment industry (cinema, television, music) also influence children's knowledge and lifestyles. Effective policies must take into account these diverse and changing influences and address them with specific interventions.

- Incorporate environmental health topics into the training of health care professionals and other relevant professionals (scientists, engineers, urban planners, teachers, policy-makers). In 1999 the American Academy of Pediatrics produced a *Handbook of Pediatric Environmental Health* which summarises current knowledge and offers suggestions on how to deal with environmental health issues at individual and community levels. Training manuals on paediatric environmental health have been developed for medical and nursing faculties in the United States by the Children's Environmental Health Network (http://www.cehn.org). Postgraduate training in child environmental health should be ensured particularly for public health specialists and community paediatricians.

4. Is a healthy environment for children promoted, through action involving the different stakeholders and the agencies involved in child development and education?

Environmental health policies not only eliminate, reduce and/or prevent exposures to health hazards, they also serve as vehicles to promote, enhance and sustain our environments. Such policies must be based on multisectoral approaches, where the community is seen as a fully participating partner. A 'toxicological' approach to a safe environment for children is not sufficient and a broader approach is needed.

Developing child protective policies requires the thinking and skills of a variety of specialists including, but not limited to, medical and public health experts, toxicologists, epidemiologists, researchers, and child development and paediatric experts. It also requires the cooperation of engineers, architects, urban planners and transportation experts to help change our technologies, engineering and manufacturing systems, and promote a healthier approach to how we live and work. Last but not least, it requires the participation and input of community members, non-governmental organisations and parents.

Child protective environmental and public policies are greatly enhanced by the engagement of many perspectives and stakeholders. This collaboration between policy-makers, civil society and the private sector must be based on transparency and democratic engagement. Examples of economic sectors that may more directly affect health are transport and agriculture. Links between sustainable transport, health and environment networks, and the transport sector should be encouraged. Policies for transportation, zoning and planned growth, conservation of public lands, siting for parks and land use, and building construction are examples of policies that are particularly relevant for children's health. Sustainable agriculture can provide safer and healthier food products and on this basis successful partnership with farmers can be envisaged.

An integrated approach will also take into account the full range of benefits and cost of policy response. For example, policies designed to reduce air pollution from traffic by reducing traffic volumes will also yield substantial benefits from increased physical activity and from reduced noise and accidents.

Each country, city and locality may have its own particular way of creating multisectoral and multidisciplinary involvement. Strategies that have proved particularly productive include:

- stakeholder meetings, including the private sector (such as industry and transport), the educational system, local administrations and representatives of the community, including independent non-governmental organisations, as well as paediatricians, public health experts and scientists;
- formation of local, regional and national multisectoral coalitions or councils, again including various components of society;
- development and implementation of health and environment assessments at local level as a first step towards a shared analysis of specific situations and needs.

It is clear that directives, as well as national laws and regulations, can be enforced only where efficient monitoring mechanisms are in place and the general public has access to information.

5. Is environmental justice pursued, by prioritising the protection of those population groups that are at highest risk?

This issue has been discussed thoroughly in a previous chapter. As noted, environmental justice is not bound to one country. It is an international issue and can be seen in the problem of industrialised countries shipping toxic waste to developing countries, selling banned or restricted products to developing countries, or exporting toxic consumer products such as tobacco. These economic issues raise ethical and legal ones. As globalisation proceeds, there is an imperative for policy-makers to take responsibility not to continue this circle of poison and to strive for economic viability and sustainability for all nations. International trade regulations must consider the right to health alongside economic growth.

16.4. Actors and tools for policy development at international and national level: the role of international and national agencies and of NEHAPs

Policy development at the global level

Given the global, interdependent and transboundary nature of many environmental issues, including environmental sustainability and the moral obligation towards the protection of the less privileged, areas relating to children's environmental health must have a global arena for policy development. This global arena includes the international agencies such as those belonging to the United Nations system, international non-governmental organisations and the international scientific community. Only this global partnership can ensure that problems are appropriately evaluated in their global dimensions and that adequate policies and regulations are developed and enforced.

The 1997 Declaration of the Environmental Leaders of the Eight on Children's Environmental Health intensified their commitment to protecting children's health from environmental hazards. The environment ministers of the G8 countries acknowledged the special vulnerabilities of children and committed their countries to take action on several specific environmental health issues such as lead, poisoning, microbiologically safe drinking-water, endocrine-disrupting chemicals, environmental tobacco smoke and air quality.

The Declaration should serve as the framework for all European countries, especially regarding the policy approaches, which are described in Box 16.1.

The G8 called on financial institutions, WHO, the United Nations Environment Programme (UNEP) and other international bodies to continue ongoing activities and to pay increasing attention to children's environmental health, in particular the economic and social dimensions of children's health. In addition, they committed their countries to fulfilling and to promoting the Organisation for Economic Co-operation and Development (OECD) Declaration on Risk Reduction for Lead (UNECE, 1996). The Declaration of the Environmental Leaders of the Eight on Children's Environmental Health and in particular the policy approaches that it lays down (see

Box 16.1.) can serve as the framework for all European countries.

Box 16.1. Declaration of the Environmental Leaders of the Eight on Children's Environmental Health: policy principles

- Preventing exposure is the most effective way of protecting children's health from environmental threats. Governments should therefore develop policies that seek to prevent childhood diseases by preventing exposures to environmental agents, on the basis of the precautionary principle.
- National policies should take into account the specific exposure pathways and dose-response characteristics of children when conducting environmental risk assessment and setting protective standards.
- Research should be promoted in order to gain a better understanding of the particular exposure and sensitivities of infants and children to environmental hazards. Exchange of information on research results and the development of regulatory systems should also be promoted.
- Awareness of the environment and health should be promoted, so as to enable families to better protect their children's health.

The United Nations General Assembly Special Session on Children, to be held in May 2002, will review, expand and update the UN's agenda for children for the coming decade. Issues related to children's rights to better environmental health will be included in the new agenda (http://www.unicef.org).

A Global Convention on Persistent Organic Pollutants was agreed in December 2000 by negotiators from 122 countries. The convention phases out the use of 12 chemicals: eight hazardous pesticides, two industrial solvents (including PCBs) and two groups of secondary products from combustion processes (dioxins and furans). The treaty represents a first step to bridge the chasm between rich and poor nations to ensure that pollutants used on one shore do not surface on another. UNEP was the negotiating agency for this convention (http://www.irtpc.unep.ch/pops/indxhtms/status.html).

The role of WHO

In response to the above international mandates and to growing concerns among Member States, WHO is strengthening and integrating its activities relating to children's health and the environment.

In July 1999 the Department for the Protection of the Human Environment established a task force for the protection of children's environmental health. The task force is made up of members from WHO headquarters, WHO regional offices and WHO centres for environment and health, as well as many WHO programmes relating to children's health and environmental health. The objectives of the task force are:

- to raise the awareness of Member States and different sectors about priority issues identified at global, regional and national levels;
- to raise the awareness of the public using mass media and community-based education activities;
- to promote the recognition, assessment and studying of the main paediatric diseases linked to the environment, and their mitigation and prevention;
- to support the development and use of harmonised tools and methodologies for data collection, risk assessment and information dissemination;
- to promote preventive and educational activities for the community and sound public policies.

Policy development at the European level

The declaration of the Third Ministerial Conference on Environment and Health, (London, June 1999) represents the most authoritative policy statement addressing children's health and the environment at the European level. The declaration was signed by the ministers responsible for health and the environment of all the European Member States of WHO and includes:

- the identification of priority areas;
- the recognition of the influence of the social environment in the genesis of environmental disease, as well as the crucial importance of education;
- the identification of the need to highlight the particular needs of children within the NEHAP process.

The five priority areas are:

- preventive strategies and research on asthma and allergy;
- public health intervention on injuries;
- prevention of smoking and exposure to environmental tobacco smoke;
- promotion, on the basis of the precautionary principle, of public health measures in areas of emerging concern;

- development of a mechanism for monitoring and reporting progress throughout the region on the basis of key indicators of the state of children's health and the state of the relevant environmental conditions.

The conference also endorsed the document 'Children's health and the environment' (WHO, 1999c). The WHO Regional Office for Europe, within its new structure, established a new Unit for Children's Health and Environment to coordinate and promote activities in the area and respond to the mandate of the London conference. WHO and the European Environment Agency (EEA) are collaborating in the development of a periodical report on children's health and environment on the basis of key indicators.

The European Commission and the European Parliament are becoming increasingly important for environment and health policy development in the European Region, not only because the majority of the states in this region will soon belong to the EU but also because of the influence that EU policies can exert even beyond its geopolitical boundaries. The EEA aims to provide timely and relevant environmental information to policy-making agents, at the EU level as well as at the national level, and to the public.

Policy development at the national level: the role of NEHAPs

At the Second European Conference on Environment and Health (Helsinki, June 1994) the Member States and WHO launched a plan to develop national environment and health action plans (NEHAPs). The Third Ministerial Conference on Environment and Health (London, June 1999) recommended that 'the particular needs of children be highlighted and prioritised within the NEHAP process and other relevant national programmes'.

How can this be done? The document 'Implementing NEHAPs in partnership' (WHO EUR, 1999b), also endorsed by the London Conference, makes general recommendations for implementation strategies and identifies the main responsibility of central governments and their environmental and health agencies. Ideally, a specific programme should be established at country level to take care of children's environmental health, to assist the government in defining policies and interventions, in promoting public awareness and monitoring risks and exposures. In order to start highlighting and prioritising the specific needs of children it is also necessary that interdisciplinary task forces are formed at country level to build the necessary expertise, and that national multisectoral councils, again including representatives of various sectors of society, are promoted to contribute to policy development and implementation.

The recent development of child environmental health policy in the United States can provide a successful example. In April 1997, an Executive Order was issued on Children's Environmental Health and Safety that called upon all federal agencies to 'make it a high priority to identify and assess environment health risks and safety risks that may disproportionately affect children' and 'ensure that its policies, programs, activities, and standards address disproportionate risks to children that result from environmental health risks or safety risks'.

The Executive Order also created a high-level federal inter-agency Task Force on Environmental Health Risks and Safety Risks to Children. The task force is coordinating and sharing research information and results, mounting joint national initiatives and collaborating on a variety of activities.

In 1997, the US Environmental Protection Agency (EPA) formed an Office of Child Health Protection to assist that agency with integrating a child protective approach. A national Federal Advisory Committee was formed to help the agency in its work. This committee comprises many disciplines including experts on environmental justice issues, paediatricians, scientists, legal experts, representatives from environmental, public health and child-focused non-governmental organisations, communication experts, and industry officials and local policy-makers from different areas of the country. The committee recommends policy actions and reviews draft scientific, regulatory and policy documents for the EPA. This varied stakeholder involvement has helped the agency create more internal credibility for the issue and provides new and different perspectives and suggestions. It operates on a consensus basis and offers a model of how

multidisciplinary stakeholders can act effectively on children's environmental health issues.

The points in Box 16.2. were included in the agenda developed by the US EPA to ensure child protection from environmental risk (http://www.epa.gov).

Box 16.2. US EPA agenda for child environmental health

1. Ensure that all standards set are protective of the potentially heightened risks faced by children, and that the most significant current standards be re-evaluated as we learn more.
2. Identify and expand scientific research.
3. Expand research opportunities on child-specific susceptibility and exposure to environmental pollutants so that the best information can be employed in developing protection for children.
4. Develop new comprehensive policies to address cumulative and simultaneous exposures faced by children moving beyond the chemical-by-chemical approach of the past.
5. Expand the community right to know to allow families to make informed choices concerning environmental exposures of their children.
6. Provide parents with basic information so they can take individual responsibility for protecting their children in their homes, schools and communities.
7. Expand educational efforts with health and environment professionals to identify, prevent and reduce environmental health threats to children.
8. Commit to providing the necessary funding to address children's environmental health issues as a priority.

16.5. Monitoring health status and tracking progress: the need for child-specific environmental health indicators

Developing a policy agenda and monitoring progress is impossible without an adequate information basis. Information is needed for several reasons:

- to help identify and prioritise problems
- to inform the numerous groups of stakeholders
- to provide a rational framework for discussion and debate
- to define, evaluate and compare the actions
- to monitor the effects of these actions.

The need for information in environmental decision-making has been emphasised earlier in this chapter. A crucial step in the use of information for decision-making is the identification of appropriate indicators. Indicators are a crucial link in the process: measurements produce raw data; data are aggregated and summarised to provide statistics; and statistics are then converted into indicators, that is information of direct use to the decision-maker. Environmental health indicators have the potential to contribute to improved environmental health management and policy (WHO, 1999d). Child-focused indicators can make a crucial contribution to highlighting and prioritising the particular needs of children. Environmental health indicators can be categorised as health outcome indicators, to describe the health effects that are more closely related to environmental factors, and exposure indicator*s*, to describe the actual exposures to environmental hazards.

So, which indicators should be used? The choice of appropriate indicators is subject to several limitations, the main one being the quality and reliability of the information sources. If information is not complete or is unreliable, indicators will be of little or no use. Identifying suitable indicators is a difficult task: they must be meaningful to scientists, politicians and the general public. They should meet the criteria of scientific validity, political relevance and above all feasibility, e.g. they should rely as much as possible on available information, such as routine statistics, and only partially on ad hoc studies. Ideally, 'negative' indicators (e.g. describing air pollution or water contamination and their consequences) should be integrated with 'positive' indicators (e.g. availability of green spaces, infant food labelling, safe transport programmes).

The indicators suggested here (see Box 16.3.) represent a first attempt to identify health outcome and exposure indicators that meet these criteria. The proposed lists takes into account the extremely variable situation across the WHO European Region, recognising that some indicators may not be applicable in some countries because data are not available and yet be insufficient in other, more advanced countries. The list also includes some policy indicators**.** Policy indicators fail to meet many of the requisites of a good indicator: they are mainly qualitative and therefore in most instances they cannot be expressed by numbers, rates and percentages. Defining precise criteria to

establish whether a policy is or is not implemented is a difficult matter and somewhat arbitrary judgements are frequently needed in the assessment. Nevertheless, it is useful to consider a short list of social and environmental policies that are relevant to child health as a general guide to assess the commitment of national or local authorities.

Policy-makers should also determine who should collect data and how, through the establishment of and ongoing support to current statistical offices, registries and research centres. Suggestions to encourage data collection and research include:

- establishing data registries for environment-related health outcomes, such as birth defects, asthma, learning disabilities and cancer;
- collecting not only exposure assessment data but also biomonitoring data so that actual body burdens of toxicants in children can be identified, recorded and mitigated;
- ideally, the development of centres for children's environmental health research and data collection.

The EPA's Office of Children's Health protection, in collaboration with EPA's National Centre for Environmental Economics, has developed a report which describes trends in levels of environmental contaminants in air, water, food, and soil; concentrations of lead measured on children's bodies; and childhood diseases that may be influenced by environmental factors (EPA, 2000). The report is a good example of how available information can be collected and used as a starting point for discussions among policy makers and the public.

16.6. The role of children and of child-focused non-governmental organisations

There is one last point that needs to be strongly emphasised at the end of a section devoted to the development of environmental protective policies for children. It concerns the importance, for the successful outcome of these policies, of establishing partnerships that include sectors of the society which take responsibility for or are addressed to children, as well as the children themselves.

Box 16.3. Some suggested indicators for child environmental health

Health outcome indicators (in children under 15 years)
- Acute respiratory infection (ARI) mortality
- ARI morbidity including asthma (*)
- Diarrhoea mortality
- Diarrhoea morbidity (*)
- Mortality due to poisoning
- Morbidity due to poisoning (*)
- Mortality due to external causes
- Hospital admissions for injuries
- Accidents in working children (ILO)
- Incidence of childhood cancer

(*) hospital admissions

Exposure indicators
- Indoor air pollution (percentage of homes relying on biomass consumption for cooking and heating)
- Outdoor air pollution (percentage of cities with concentration > 40 parts per million of PM_{10})
- Excreta disposal facilities (percentage of households with access to)
- Safe drinking-water (percentage of houses with access to)
- Pesticide use per hectare (major groups such as DDT, organophosphates, PCBs)
- Tobacco use (percentage of households with children where parents smoke)
- Environmental lead (percentage of children with blood levels above 10 micrograms per decilitre (µg/dl)

Policy indicators
- Policies to ensure universal access to safe drinking-water
- Policies to ensure universal access to excreta disposal
- Safe housing programmes
- Lead-free gasoline policy
- Food labelling policy
- Water monitoring programme
- Hazardous waste disposal programme
- Sun protection measures/programmes
- Smoke-free policy at least for public places attended by children
- Safe transport and independent mobilty programmes for children
- Educational programmes focusing on environmental and health issues
- Training programmes in environmental health for child health and public health professionals

Representatives of children and youth should be given a voice in the international arenas where issues related to children's health and the environment are discussed. Examples of such participation are increasingly seen in international and particularly national meeting and initiatives.

The active involvement of non-governmental organisations representing the rights and views of children and young people is also needed and governments should establish periodic consultation practices with them, as well as ensuring full access to information about ongoing plans and programmes in the relevant fields.

This kind of partnership is also needed at the local level. The active engagement and support of the various sectors of civil society is at the same time more important and more feasible, as shown by many successful examples of engaging the public in initiatives that promote environmentally safer, health-enhancing and economically sustainable policies such as mobility plans to reduce traffic load and exposure to traffic-related pollution. The point of view and best interests of children have often been at the very core of these initiatives, and children have directly participated in some instances to identify problems and solutions.

Children have been recognised as full citizens of Europe and are fully entitled to represent their views and give their contribution to the transition towards environmentally sound and sustainable development that represents their future.

Summary

Children and infants have different exposure patterns and susceptibilities to environmental toxicants from adults, and this represents the rationale for specific policies to protect the fetus and the child from harm, and to promote a healthy environment.

Health as a human right, equity and solidarity, participation and accountability, the right to know, sustainable development and the precautionary principle are the basic guiding values and principles for policy development.

Five questions form a suggested framework for policy development and assessment:

- Have the unique vulnerabilities and exposure patterns of children been considered in assessing environmental risks?
- Are current policies and regulations protective of children?
- Are access to information and public participation ensured so that parents and professionals, as well as communities at large, may make informed decisions and contribute to effective policies and interventions?
- Do current and proposed policies promote a healthy environment for children, through intersectoral action?
- Are explicit policies addressing the issue of environmental justice?

The UN agencies, the EU, national governments and environmental and health agencies, and child and environment-focused non-governmental organisations are the main actors of policy development and assessment. Environmental and health policy is a multidisciplinary and multisectoral field. Policy development is greatly enhanced by the active participation of community members and of a variety of disciplines and experts. The educational sector can contribute in the development and implementation of child-focused policies by promoting awareness and participation among students and teachers. Environmental and health topics should be increasingly incorporated in the training of a variety of professionals and particularly of child health professionals.

The creation of databases, registries and key indicators will enhance the development of protective public policy and will also help create an informed citizenry.

Children and young people should be given a voice when issues related to child environmental health are discussed.

References

Environment Leaders' Summit of the Eight, *Declaration of the Environment Leaders of the Eight on Children's Environmental Health*, Miami FL, 5-6 May 1997.
URL: http://www.g7.utoronto.ca/g7/environment/1997miami/children.html

Organisation for Economic Co-operation and Development, OECD, 1996, *Resolution of OECD the Council Concerning the Declaration on Risk Reduction for Lead*, OECD Document No C(96)42/FINAL, adopted by the Council on its 869th Session of 20 February 1996 [C/M(96)4/PROV].

United Nations Economic Commission for Europe, UNECE, Environment and Human Settlements Division, 1998, *Convention on access to information, public participation in decision-making and access to justice in environmental matters*, Aarhus, Denmark, June 1998.

US EPA, 2000, *America's children and the environment: A first view of available measures.* US Environmental Protection Agency, Office of Children's Health Protection, Office of Policy Economics and Innovation and National Center for Environmental Economics.

WHO, 1999a, *Health21: The health for all policy framework for the WHO European Region,* European Health for All Series No.6, WHO Regional Office for Europe, Copenhagen.

WHO, 1999b, *Implementing National Environmental Health Action Plans in partnership,* document EUR/ICP/EHCO 02 02 05/10, WHO Regional Office for Europe, Copenhagen.

WHO, 1999c, *Children's health and the environment,* document EUR/ICP/EHCO 02 02 05/16, WHO Regional Office for Europe, Copenhagen.

WHO, 1999d, *Environmental health indicators: framework and methodologies,* document WHO/SDE/OEH/99.10, World Health Organization, Geneva.

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