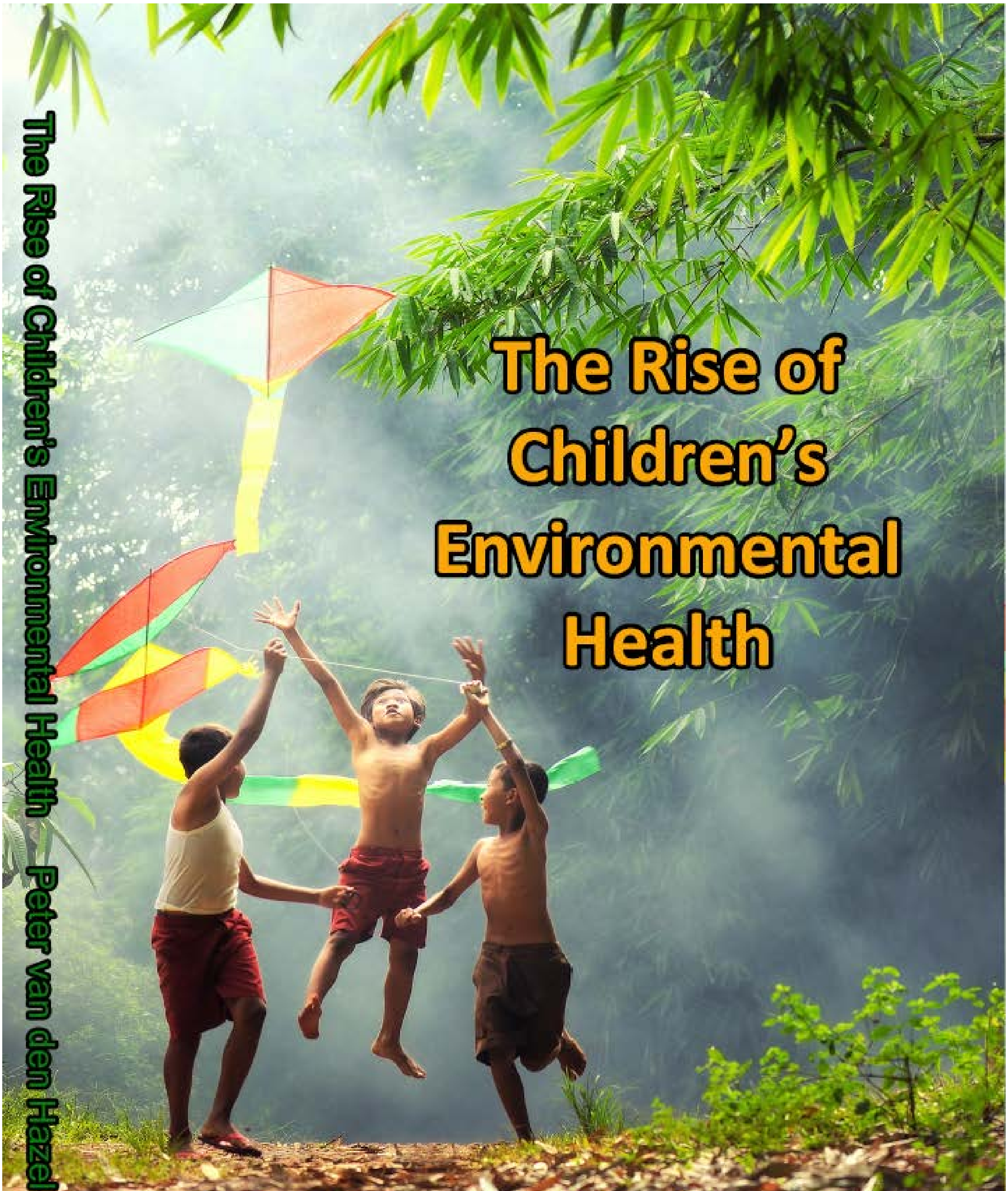
The Rise of Children's Environmental Health Peter van den Hazel
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The rise of children's environmental health

Proefschrift ter verkrijging van de graad van doctor

aan de Radboud Universiteit Nijmegen

op gezag van de rector magnificus prof. mr. S.C.J.J. Kortmann,

volgens besluit van het college van decanen

in het openbaar te verdedigen op vrijdag 8 november 2013

om 13.00 uur precies

door

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Cover design: Peter van den Hazel
Cover photo: Gregorius Suhartoyo. www.GregoriusSuhartoyo.com
Language editing Chapters 1 & 10: Radboud in'to Languages
Printing: Ipskamp Drukkers Nijmegen
ISBN/EAN: 978-94-6191-804-8

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Doctoral Thesis to obtain the degree of doctor

from the Radboud University Nijmegen

on the authority of the Rector Magnificus prof. dr. S.C.J.J. Kortmann,

according to the decision of the Council of Deans

to be defended in public on Friday, November 8, 2013

at 13.00 hours

by

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Contents

CHAPTER 1 INTRODUCTION

This thesis focuses on knowledge about children's environmental health and analyses the role that knowledge plays in policy development. Various aspects are considered. First, the rise of the children's environmental health domain during the last two decades in Europe, secondly a validation of the knowledge in this field, thirdly an assessment of its relevance to policy making by providing recommendations on its use by policy makers, and fourthly an analysis of how this knowledge is used through networking between scientists, policy makers and other stakeholders.

Historical perspective

Environment and health have a long-standing relationship. The impact of the physical environment on health has been known for centuries[1]. Nevertheless, research in this domain has only developed since the occurrence of large environmental incidents in the 20th century. Revolutions in chemistry increased pollution and the technology revolution linked the environment even more to health. From the health perspective, comprehensive models of health do help explain the relationships between the determinants of health. Evans and Stoddart defined the determinants of health and how these interrelate, with the healthcare system being just one factor among many[2,3]. This 'field' model builds on the earlier health field framework of Lalonde[4] as shown in Figure 1[5]. The physical and social environments are one of the key determinants of health in this model. Exposure to environmental stressors is conceptualised within the key determinant of physical and social environment, which is equal to the healthcare system, lifestyle, and biological and genetic factors.

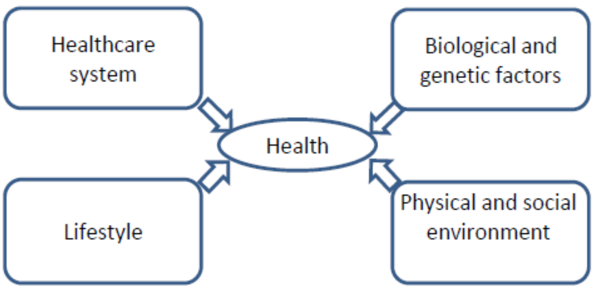

Figure 1. Basic health field model, after Hancock[5]

The effect of environmental stressors on human health falls within the domain of environmental health. Many new environmental stressors have arisen over the past 100 years[6,7] which pose major challenges for health, social development and well being. Environmental stressors harm health through many pathways, acting via ecosystem change and by altering other health determinants. Over the last four decades, increasing knowledge about the influence of the environment on health has been instrumental in setting the policy agenda on environment and health at different levels of governance[8]. However, the health effects of different forms of environmental exposure to different groups within the general population, including children, are less explored and understood.

Environment and health

The most frequently used definition of environmental health was developed by the World Health Organization: “Environmental health addresses all the physical, chemical, and biological factors external to a person, and all the related factors impacting behaviours. It encompasses the assessment and control of those environmental factors that can potentially affect health. It is targeted towards preventing disease and creating health-supportive environments. This definition excludes behaviour not related to the environment, as well as behaviour related to the social and cultural environment, and genetics”[9].

The following definition of 'Environmental Health' suggests an additional aspect of the policy discourse with:

“Environmental health comprises those aspects of human health, including quality of life, that are determined by physical, chemical, biological, social and psychosocial factors in the environment. It also refers to the theory and practice of assessing, correcting and preventing those factors in the environment that can potentially adversely affect the health of present and future generations”[10]. In contrast to the WHO definition this version includes social and psychosocial factors. Powis[11] argues that the inclusion of the social as well as the bio-physical within environmental health reflects the growing understanding that while all humans, irrespective of their social, economic, cultural, ethnic or geographical background, are subject to environmental risk factors, their vulnerability varies. The health effects of environmental change are clearly unequal, reflecting social stratification under which the poor and disadvantaged are subject to disproportionate vulnerability[11].

Children's environmental health

Several incidents and environmental disasters have stimulated the production of scientific knowledge of acute paediatric health effects since the 1960s[12]. This has triggered the development of a new scientific domain, 'children's environmental health'. In addition to acute child health effects, science has paid more attention to low dose environmental stressors whose existence was neither known nor suspected a few decades ago[13]. Children are a specific and often more vulnerable group to environmental stressors compared with adults[14,15].

However, policy makers did not include this knowledge on children in the early agenda setting for the environment and health policy domain. Actually, children have been a forgotten group despite the increasing realisation that environmental stressors harm human health. This lack of recognition has led to a demand in society over the past two decades for more knowledge and the validation of the knowledge available. Furthermore, this responsiveness refers to making this scientific knowledge relevant.

Once science recognised that the topic of children was underexplored in the knowledge production field, different stakeholders have brought forward the need to raise awareness in the policy domain about the environmental hazards for children. Consequently, the particular awareness of children's specific position in the knowledge production field has also highlighted the fact that a bridge between science and policy in children's environmental health was lacking[6,16-19].

Although the broad context mentioned in the MacArthur definition has influenced the agenda setting of children's environmental health, the key part of this definition on the physical, chemical and biological determinants in the environment also provides the narrow scope for dealing with the physical environment in this thesis, and not with the social environment. This limitation has the advantage that it focuses on issues which are unique to children, whereas the social and psychosocial factors also relate to adults. Besides, knowledge on the impact of these physical, chemical and biological determinants is more available than that on the broader social context. The European Commission has been interested to know what the impact of these physical environmental determinants on children is so that it can develop policies according to the WHO definition[20], thus legitimising the limitation to physical, chemical and biological determinants.

Since the late 1990s, the agenda setting on environment and health has resulted in changing thoughts and ideas, or discourses, including the acknowledgment of the specific position of children. These emerging new discourses have resulted in more research and political activities related to children's environmental health. These activities include knowledge production and validation, followed by knowledge utilisation and the interaction between science, politics and society. The work for this thesis has been part of these multiple activities. It has been done over several years in the context of two EU funded environmental health research projects: the Fifth Framework Programme (FP5) EU PINCHE project with a focus on knowledge production and validation, and the Sixth Framework Programme (FP6) EU HENVINET project with a focus on knowledge utilisation[21,22].

This thesis uses the term *children's health and the environment* when a link or relation to some form of policy is implied. The term children's environmental health is meant to refer to the scientific field of health and the environment, related to physical factors. Environmental health threats indicate that potential health effects can be attributed to the environment, being the overall quality of specific stressors within the environment.

Science and policy interface in children's environmental health

Each new scientific field sees changes in scientific knowledge production when facing and studying problems. The field of children's environmental health has made an epistemological shift from the Modern or Positivistic Model towards Post-Normal Science[23]. Scientists have produced objective and universal knowledge driven by curiosity and independent from politics. Policy makers are informed by scientists and sort out the values and preferences in order to formulate the correct and rational policy[24]. At the birth of each domain there is no intervention in the knowledge production process and no interaction between science and policy besides linear knowledge transfer (Figure 2). Science and policy are two separate entities. The science domain still focuses on theory and has a long-term perspective, while the policy domain is practice oriented with a short-term perspective.

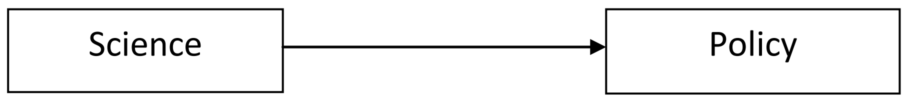

Figure 2. Science and Policy: The Strong Positivistic Model, after Stassen[8].

When several incidents occurred in children's environmental health, science and policy had some interaction. This can be visualised by the Modern Model, which assumes that policy makers pose questions to the scientific community and that scientists inform policy makers by producing valid, objective and reliable knowledge. It is the role of intermediaries to bridge the gap between science and policy (Figure 3).

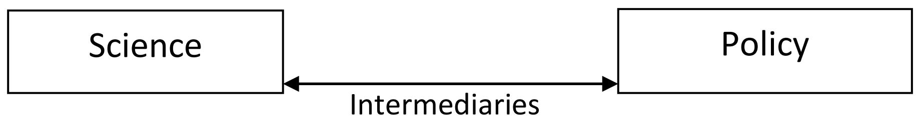

Figure 3. Science and Policy: The Modern Model, after Stassen[8].

The Modern Model, however, is limited in its applicability in cases where scientists disagree, or if scientists are stakeholders themselves, or when the problems are too complex or have irreducible uncertainties[24]. Post-Normal Science emphasises the uncertainties and the value-laden character of policy-related science under conditions of complexity. Post-Normal science accepts a plurality of perspectives with science as one part of the review process and stakeholders as another part participating in an open dialogue on the validity and relevance of evidence. This application of Post-Normal Science in children's environmental health fits the processes of putting children's environmental health on the policy agenda, as this Post-Normal Science is attempting to characterise a methodology of inquiry that is appropriate for cases where "facts are uncertain, values in dispute, stakes high and decisions urgent"[25].

From knowledge production to knowledge utilisation

In the 1990s, the scientific community had become aware that quite a few studies in environmental health dealt with topics related to children's environmental health. Scientists recognised that knowledge of the impact of the environment on children's health was fragmented and incomplete. This recognition prompted the emergence of children's environmental health as a separate scientific domain.

At the International Society of Environmental Epidemiology (ISEE) conference in 1997, the Children's Environmental Health Network noticed that a significant part of the scientific community was engaged with research related to children[19]. More than 25% of the ISEE conference papers were related to children[19]. In the 1990s, the scientific community recognised that with regard to the sensitivity to environmental factors, a distinction had to be made between different groups or entities within the population. Children were one of those groups.

Up to the late 1990s the results of studies on children's environmental health were hardly used for any policy making. Several reasons can be brought forward to explain this: 1) the problems are too complex or unstructured to be used in the policy arena before more studies are conducted; 2) the available knowledge is not sufficiently validated to convince policy makers to undertake action; 3) the scientific and policy community are not capable to translate their study results into policy recommendations.

According to the typology of policy problems used by Hisschemöller[26], environmental health problems are considered complex, unstructured, clouded with uncertainty and ill defined (Table 1). This is even more so for environmental health problems in children, where relevant child-specific norms and values are lacking and where knowledge on low-dose exposure and specific age groups is uncertain.

		Certainty about Relevant Knowledge	
		+	-
Consensus on Relevant Norms and Values	+	Structured Problem	Moderately Structured Problem
	-	Moderately Structured Problem	Unstructured Problem

Table 1. Typology of policy problems, after Hisschemöller[26]

The character of these problems therefore makes knowledge a necessary, yet insufficient resource to put children's environmental health onto the political agenda.

The first observation that the available knowledge is not sufficiently validated to convince policy makers to undertake action can be linked to the issue that science and policy are two separate domains. The science domain produces knowledge that is not necessarily used by the policy domain and the policy domain is not interested in knowledge that is not yet validated.

The second observation relates to the fact that knowledge validation belongs to the science domain and not to the policy domain. The respective representatives of these domains have difficulty in understanding each other's language and in communicating about the relevance of issues. To make a bridge from science to policy, children's environmental health knowledge has to be made relevant in order to be utilised in the development of proper policies. This knowledge validation (close to science) and the knowledge utilisation (close to policy) are bridged by the process of making knowledge relevant as shown in Figure 4.

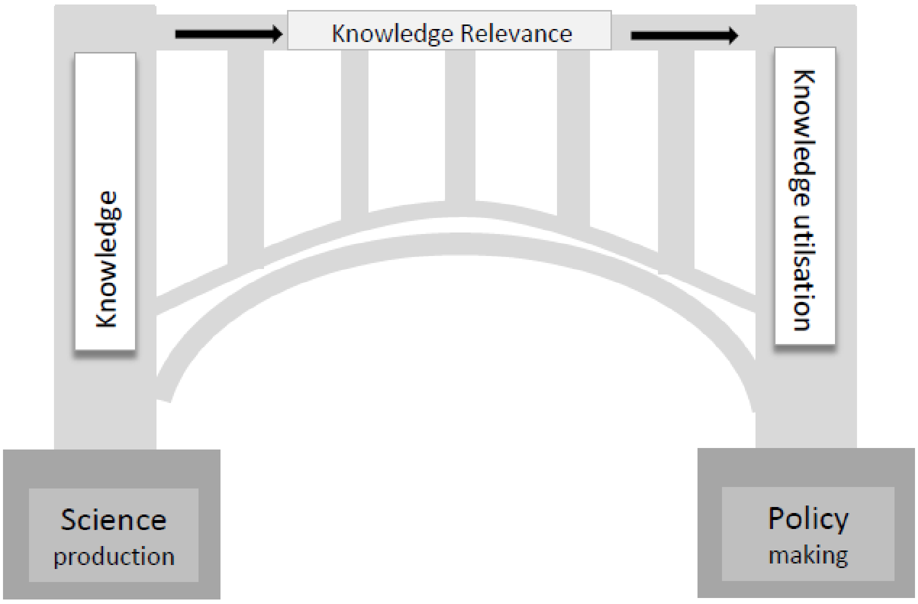

Figure 4. Science policy bridge

An epistemological shift, as described above, also comprises an organisational shift from a monodisciplinary, reductionist, fragmented organisation of science towards one in a post-normal sense, crossing disciplinary boundaries and with interaction, leading to transdisciplinary knowledge production[8]. Wiesmann gives a definition for transdisciplinary research: "transdisciplinary research is research that includes cooperation within the scientific community and a debate between research and the society at large[27]. The science-policy bridge had to be built in children's environmental health. Part of that work has been initiated and undertaken during the past two decades, as I will describe in the rest of this chapter.

Knowledge validation

Knowledge validation can be distinguished as internal or external validity. Internal validity is a property of scientific studies, which reflects the extent to which a conclusion based on a study is warranted. For example, the constructs 'children's environmental health' or 'children's vulnerability' need to be valid concepts. These constructs have been discussed and proved valid in scientific studies. External validity is about the extent to which the results of a study can be generalised to other situations and to other people[28]. The knowledge validation in this thesis points mainly to the concept of external validity as a generalisation based on specific scientific studies.

Results from studies possess high degrees of external validity if they can reasonably be expected to apply:

(a) to the target population of the study (i.e. from which the study sample itself was drawn), or from the target population (e.g. validated results for adults) as generic results re-validated for another population (e.g. children). Regarding validation as the specification of generic knowledge, studies were done in the 1980s and 1990s in which children are specifically seen as victims that should have been protected from environmental harm. Examples relate to the Chernobyl accident, the lead problem, the mercury problem (Minimata disease), the DES problem or air pollution[12,29]. Besides examples from incidents, there were results from some studies which show an impact of environmental factors specifically on children, e.g. from lead or benzene in low dose exposure in the 1980s and 1990s. Also, increasing asthma rates and diarrheal diseases are among the study results showing the health impact on children in many parts of the world (geographical spread). A lack of knowledge on exposure data in children has been identified as well as on the cause-effect chain in children's environmental health for many environmental exposure factors, both accidental and chronic. These examples deal with the knowledge validation in the form of specification of generic knowledge, as these studies originate from adult studies (including low dose studies).

(b) to the universe of other populations (e.g. across time and space). This kind of validation deals with generalisation of specific data (e.g. on pollutants). In the knowledge validation on children's environmental health several key issues are identified to illustrate these forms of validation. The studies on children affected by pesticides serve as an early example[15].

Since the NRC report[15] (1993) on children and pesticide exposure there has been a growing recognition within the scientific community that children differ from adults in their response (reaction) to environmental stressors. However, the knowledge base explaining these differences is limited[30]. Sometimes results can be generalised for a range of other pollutants. While the growth in scientific knowledge related to children's environmental health is beyond dispute, there still remains a gap in specific knowledge on the consequences of the variation in vulnerability and sensitivity as seen in the many time-windows of exposure in children. Compared to adults, research on children lags behind in knowledge on dose-response relationships. Only a limited amount of knowledge is available on the issues of low dose exposure, geographical spread and exposure data related specifically to children. These issues are costly to society[31,32]. The European Commission wanted the knowledge on these issues to be validated.

Many studies have been used to support the development of legislative standards and norms on compounds which have not been developed to protect children[33]. Policy makers want to know whether validated results of these studies can be used to protect children in general regulatory processes.

Since the NRC report in 1993, scientists in the environment and health field, first in the USA and later in Europe, have realised that there was a need to fill the gaps in knowledge[15]. This realisation has been used by different governance levels to support the scientific community to validate the knowledge available and to specify it in the children's environmental health domain. Since the emergence of children's environmental health on the scientific agenda, policy makers have pushed for the validation of the results of studies on children, as policy makers wanted to know which knowledge could be used to make policy and how this should be done. Policy makers have asked the scientific community to show the relevance of the available knowledge and how to apply this knowledge to bridge the science policy gap. This is discussed below. PINCHE was established to analyse and validate the available knowledge to see whether it could underpin certain policy actions.

The complex web of sources, environmental stressors, exposures and their multiple health effects appears to have different effects on children, which even differ per age group. The production and organisation of scientific knowledge is challenging because of the dealing with complexity and multiple, cumulative and uncertain impacts of environmental stressors[34]. Throughout the multiple processes of agenda setting, validation, utilisation etcetera, as analysed in this thesis, this complexity of children's environmental health has had consequences for the validation of knowledge related to emerging problems. Examples are children's exposure to radiation, electromagnetic fields or cocktails of chemicals. Another activity in the knowledge validation process is that the fragmentation of available knowledge on these complex issues is analysed. The available knowledge is combined, accumulated and validated to see how it could fit in specific knowledge which is sometimes difficult to generalise.

The role of international bodies in knowledge validation

Two organisations in particular have been instrumental in the process of knowledge validation. The World Health Organization (WHO) became involved in the work on children's environmental health in the late 1990s. The WHO recognised children's environmental health as a global issue. The problems of sanitation and air pollution for children are widespread, causing many children under the age of 5 years to die. The WHO joined the First International Conference on Children's Health and Environment in August 1998 and, around that time, started an expert group to look into the issues related to children's environment.

The European Commission has looked for ways of developing policies, not on a wide scope of issues, but rather on a selected number of priorities. The Fifth Framework Programme of DG Research of the European Commission installed Thematic Networks on different themes. The Commission has asked for a coordinated thematic project in the field of scientific knowledge and the science-policy interface in children's environmental health. As a result, the aforementioned Policy Interpretation Network on Children's Health and Environment (PINCHE) was established in 2004[20]. Several activities have been identified in the knowledge validation process by this Thematic Network.

Furthermore, one activity of PINCHE has been to analyse the main causes of childhood diseases as part of the validation of scientific knowledge. This has included the available knowledge on exposures to a range of chemical compounds and their health effects.

The role of international bodies in this field is further elaborated in chapter 2 of this thesis.

Knowledge relevance

Knowledge relevance forms the bridging structure between knowledge validation and knowledge utilisation. It is built upon several pillars related, for example, to costs and benefits[31], social construct[35], interaction of disciplines[34], data availability and participation of stakeholders (extended peer community)[36]. This is illustrated in the science policy bridge model (Figure 5). These concepts have been dealt with in the PINCHE project but are not further explored in this thesis.

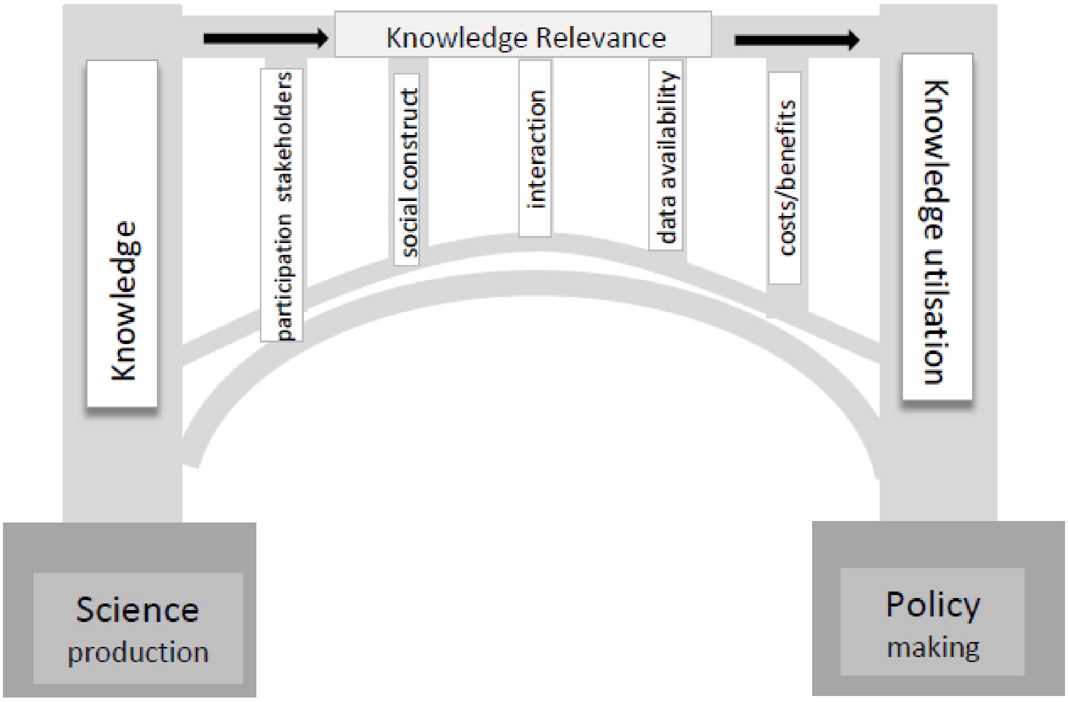

Figure 5. Science policy bridge with pillars for knowledge relevance

Until 1993, the scientific community was unable to use the valid information produced by the results of its studies to influence policy makers[15]. A few individuals started to mobilise experts from different disciplines, including policy makers, to take a deeper look at the consequences of the early studies. The scientific community demonstrated that children are exposed to environmental stressors during different phases in their life, including their intrauterine life, yet with different health outcomes. For example, the stressors children are exposed to during their short time in the womb can cause health damage which has financial and social consequences to society in economic, social and healthcare systems[37].

PINCHE had a role in bringing the relevance of knowledge on children's vulnerability forward to enable the policy domain to make adequate choices. Moreover, new emerging issues had to be studied and to be judged for their policy relevance, e.g. exposure to endocrine disruptors or to electromagnetic fields[38]. The European Commission wanted to know more about the gaps in knowledge on exposures to different factors so that it could steer the research agenda on children's environmental health[20].

Furthermore, the EU's strategy has been to have the PINCHE consortium analyse the existing scientific data for policy relevance. This analysis has been based mainly on existing knowledge. Part of PINCHE's strategy was not to summarise the growing amount of scientific knowledge in the field of children's environmental health and not to produce new knowledge on environmental stressors, but rather to provide information on the relevance of existing validated knowledge. This strategy has culminated in a practical approach and activities to support solutions for identified problems in children's environmental health. What matters is not the scientific state-of-the-art knowledge in itself, but its relevance to society and policy. Some scientific results from the healthcare sector have already raised policy awareness and action during the early development of the field of environmental health. A good example is the lead problem, for which the scientific community has shown the relevance of reducing the exposures of leaded petrol in order to reduce the burden of disease in children[39-41].

The key issues to which these activities in PINCHE were directed are: 1) identification of new emerging issues in children's environmental health; 2) identification of gaps in knowledge; 3) promotion of the use of available knowledge relevant on children's environmental health; 4) prioritisation of known problems in children's environmental health; 5) support of policy making in children's environmental health.

The relevance of state-of-the-art studies was therefore conveyed to the policy community.

Knowledge utilisation

Knowledge utilisation follows on from knowledge relevance in the structure of bridging science and policy. The policy domain uses knowledge to make satisfactory policies in most science-policy models. Four major dimensions of knowledge utilisation are suggested by the literature[42]. The first of these is the dissemination source*:* the agency, organisation, or individual responsible for creating the new knowledge or product, and/or for conducting dissemination activities. Second is the content or message that is disseminated, which can be the new knowledge or product, as equally any supporting information or materials. Third is the dissemination medium, in other words how the knowledge or product is described, "packaged," and transmitted. Fourth is the user or intended user of the information or product to be disseminated. Figure 6 illustrated the interaction of these four elements[42].

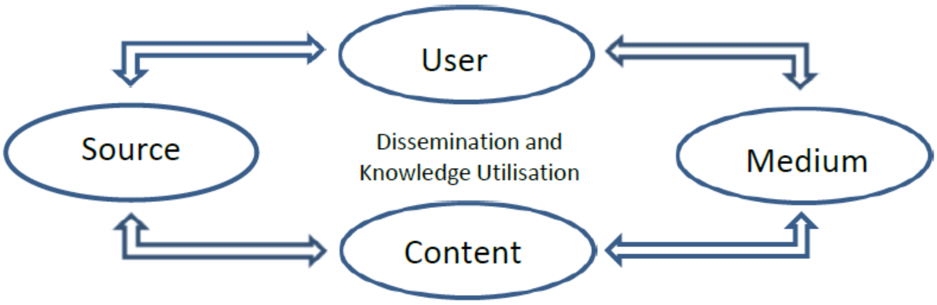

Figure 6. Dimensions of the Dissemination Utilisation Process[39]

De Goede et al.[43] produced an overview of different utilisation models. In general, these models share the common goal of explaining the apparent gap between research and policy. They distinguish six types of knowledge utilisation models. Four models assume a linear sequence from supply of knowledge to utilisation by decision makers, which does not satisfactorily describe knowledge utilisation in children's environmental health. Two models involve communication between scientists and policy makers: the 'two communities' model and the 'explanation' model[43]. These two models are not linear and are a better fit because policy makers have been asking questions of the scientific community on children's environmental health.

The 'two communities' model is elaborated by Caplan[44]. It emphasises the cultural gap between researchers and policy makers. According to De Goede[43], Caplan argues that research outcomes need to be framed so that these fit in the niche and culture of policy makers. Moreover, Caplan's 'two communities' model implies that policy makers need to be involved with research agendas and design[44]. Nevertheless, a critique of this argument states that "the two communities alone is an inadequate basis for attempts to change the way research and policy relate to each other"[45]. De Goede[43] raises the question: "whether the model captures important determinants like the rejection or acceptance of research by advocacy coalitions during policy development based on their core values and beliefs, the influence of institutional structures within policy networks and the perspective that researchers are already a part of the policy makers domain and that the so-called 'gap' does not exist"[43].

The 'explanation' model focuses on the interaction between researchers and policy makers. The interaction explains how knowledge is utilised during the policy development process.

The 'two communities' model seems to fit knowledge utilisation in children's environmental health, with the EU directing the research agenda and the science community steering the policy recommendations. The 'explanation' model seems to fit the role of NGOs as a linkage mechanism better.

Application of the 'two communities' model in PINCHE

The key issue at stake is the fact that knowledge on children's environmental health has to be made comprehensible and ready for policy makers to use. So far, policy makers do not have the knowledge to make decisions based on the main problems. PINCHE had to make policy recommendations based on scientific knowledge in the children's environmental health field as requested by the European Commission. PINCHE analyses the knowledge from which recommendations are made to strengthen children's environmental health in the policy domain. These recommendations had to be used by policy makers for the development of the next EU Framework Programme and for the further development of the EU Environment and Health Action Plan. These recommendations were related to content (exposure reduction measures, additionally needed research topics) and to the process of knowledge dissemination (data availability, data accessibility). Furthermore, PINCHE prioritised the results from children's environmental health studies in order to make it feasible for policy makers to make choices based on a risk evaluation in children's environmental health. The PINCHE network therefore made a set of recommendations that will lead to a better incorporation of science in the policy domain of children's environmental health.

The PINCHE thematic network project incorporated the involvement of disciplines, such as lobbyists and industry representatives, but focuses mainly on the interaction between scientists and policy makers. After PINCHE, a network for policy makers and scientists in children's environmental health has not been continued. However, the EU-funded project

HENVINET (Health and Environment Network)[22], has looked at the mechanisms of institutionalisation of the domain environment and health (not only focused on children). The network building activities from the HENVINET project are analysed in this thesis to see whether a network of scientists and policy makers can support the continuation of policy making based on knowledge provided by the scientific community in the domain of environment and health. As the focus on children is considered too narrow by DG Environment, the HENVINET project has examined the entire field of environment and health.

The FP6 coordination action Health and Environment Network HENVINET has aimed to create a permanent network of professionals, in order to provide policy relevant scientific advice, and to tackle communication gaps in environment and health. A role for different networks in policy integration is needed for building a strong, continuous environment and health field, e.g. by a network of scientists, a science and policy network, societal groups and science networks. HENVINET has focused on the network between scientists and policy makers, but also on an interdisciplinary framework of cooperation[22]. The goals, communication and knowledge utilisation are a few aspects which make the formation of interdisciplinary networks difficult. More specifically the HENVINET project analysed how and under what conditions increased social networking between scientists and policy makers would enhance the quality of both problem knowledge and problem solving by means of facilitating actions between a diversity of actors. Interdisciplinary and transdisciplinary networks are considered to be useful strategic means for enhancing communication and cooperation between different actors in order to raise the problem-solving potential of both scientists and policy makers.

This thesis explores the practical possibilities for bringing science and policy together in a network, taking on board the options to communicate to the entire field of stakeholders in environmental health. Practical methods have been used in HENVINET to explore the functioning of trans- and multidisciplinary networking.

Objective and research questions

This thesis has four objectives:

1) to analyse the rise of the children's environmental health domain during the last two decades in Europe;
2) to assess the validation of knowledge in this field;
3) to assess the relevance of this knowledge to policy making by providing recommendations on its use by policy makers;
4) to analyse how networking techniques support the provision of knowledge to policy makers and their utilisation of this knowledge.

Research questions

The research performed and reported on in this thesis has a strong practical focus. It was work performed in response to a request by the European Commission in support of its upcoming research programmes. The following questions are central in this thesis.

1) Which mechanisms and actors have played a role in the agenda setting of children's environmental health during the last two decades in Europe?
2) How has the children's environmental health domain developed in the last two decades?
    - How did the validation of knowledge in the children's environmental health field contribute to the development of this field?
    - How did making the knowledge in the field of children's environmental health relevant contribute to this field's development?
    - How did the utilisation of knowledge in the children's environmental health field contribute to the development of this field?

These questions are answered in the following chapters.

Outline of the thesis

The first chapter is the introduction to this thesis. The second chapter of this thesis deals with the agenda setting of children's environmental health in the European policy field. The interaction between the scientific community and the policy domain, and the roles of different stakeholders are discussed. The third chapter provides a review on children's vulnerability and sensitivity to environmental stressors. It underlines the importance of

looking at children and also provides background information on the latest knowledge about children's vulnerability, as part of knowledge validation.
These last two chapters are followed by five chapters (chapters 4 – 8) that deal with the results of the Policy Interpretation Network on Children's Health and Environment (PINCHE) as a research intervention in the children's environmental health domain:

1) a chapter on the importance of prominent health effects and diseases in children in relation to environmental pollution (knowledge validation);

2) a chapter with a specific example of the effects on children from exposure to lead as an environmental stressor (knowledge validation);

3) a chapter with a range of recommendations to support the development of a strategy on children's environmental health at different levels of governance: international, national, regional, and local (knowledge relevance);

4) a chapter on the science policy related results of the EU-funded network PINCHE. The project has collected scientific data on children's environmental health, has validated these data and translated these into policy recommendations (knowledge relevance);

5) the last PINCHE-related chapter provides results and identifies priorities on children's environmental health which are used as input for additional EU policy actions (knowledge utilisation).

The last part of the thesis brings forward the results of network building activities between scientists and policy makers from another EU-funded project HENVINET, which serves as a follow-up of PINCHE. This is described in the ninth chapter. The role of networks and other tools in supporting the science-policy interface to strengthen a new policy domain are analysed (knowledge utilisation). The questions to be answered relate to the needs, content, structure and dissemination of a network of professionals. The last chapter of the thesis gives conclusions to the main findings and insights, discusses these, and then formulates recommendations for both research and policy in this field.

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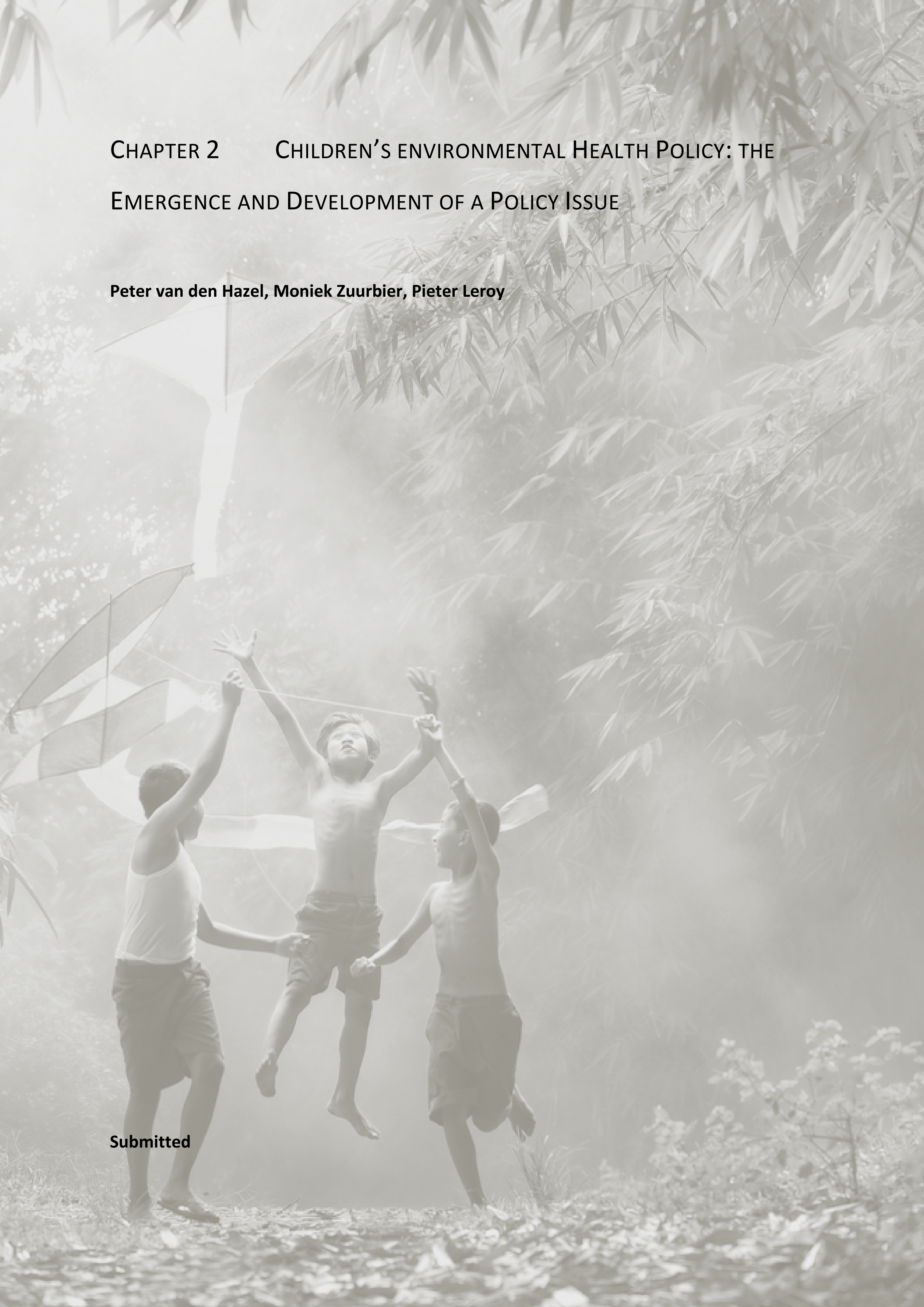

CHAPTER 2 CHILDREN'S ENVIRONMENTAL HEALTH POLICY: THE EMERGENCE AND DEVELOPMENT OF A POLICY ISSUE

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Submitted

Abstract

Objectives

The emergence of children’s environmental health upon the political agenda in Europe is analysed, and the identification of the triggering mechanisms thereof.

Methods

Official policy and political documents from governments, EU, WHO and NGOs were used to analyse. Documents were found using keywords children, environment, policy, science-policy interface, declarations and agenda setting on internet (Google search) and by using Scopus and Pubmed.

Study design

The agenda setting processes and the strategic behaviour of actors involved is studied based on the barrier model by Bachrach and the policy streams approach of Kingdon. Scientific literature, Declarations, Conference statements and alike were used as sources.

Results

The WHO Environment and Health conferences are considered as the start of the European agenda-setting process. The availability of scientific information and the forging of a coalition of actors and agencies from different spheres increased the agenda formation. Scientific knowledge was used to endorse and legitimise further research and policy claims, and managed to successfully transfer it to political arenas and translate it into decision-making in a new domain of children’s environmental health. The EU-SCALE initiative gave a strong push to designing and implementing policies. Children got a fixed spot on the agenda of Ministerial Conferences on Environment and Health. Complexity and uncertainty that goes with less obvious issues of the environment-health relation in children hindered the institutionalisation.

Conclusions

The agenda-setting of children’s environmental health is seen as successful. Its institutionalisation seems only halfway and might stagnate over the foreseeable future.

Keywords: Children, environmental health, policy, agenda setting, institutionalisation

Introduction

In the late 19th century, it was public health concern that triggered the demand for environmental hygiene. In the early days of the 1970s health concerns were among the driving forces to produce environmental policies. Only the last five decades environmental health emerged as a more or less distinguishable policy domain. However, children were not included as an involved target group of this policy domain until the last two decades. This chapter looks at the emergence of a sub-domain within the latter: the attention to environmental health related to children. Over the last decades, children's health has received more attention, both as a result from and as a trigger for more scientific research. Environment studies resulted into new insights, relating to children's enhanced vulnerability and susceptibility to the appearance of health effects after exposure to environmental stressors. Besides the role of new scientific insights the efforts of leaders of NGOs, from the field of health practitioners and politicians who advocated for environmental health policies, with specific goals and standards particularly relating to children, needed analysis.

This chapter aims to document the emergence of children's environmental health upon the political agenda in Europe and to identify the mechanisms thereof and, briefly, its gradual institutionalisation. As to the former, the consecutive agenda setting processes and the strategic behaviour of the actors involved, including their discursive and networking strategies were analysed. As to the latter, the chapter assessed the gradual institutionalisation of goals and standards, of resources and rules, in brief, the coming into being of a novel policy domain.

The first section briefly presents the theoretical stance, with some basic concepts on agenda setting and institutionalisation, and the methodology. The context is outlined: European environmental policies, from which the environmental health gradually emerged, mainly provoked by World Health Organisation (WHO) initiatives. The subsequent section identifies in more detail the agenda setting of children's environmental health, with the role of the actors involved and the strategies deployed. The analysis concludes on the respective share of scientific insights (related to children) on the one hand and societal and political mobilisation on the other in the processes of agenda setting and institutionalisation of children's environmental health.

Methods

Agenda Setting

Policy analysis has different approaches to agenda setting, yet two approaches dominate the field. The first is Bachrach and Baratz[1] well-known 'barrier model', the other the seminal 'policy streams' approach of Kingdon[2]. Bachrach and Baratz[1] suggest that, for an issue to be put on the political agenda, a series of barriers need to be surmounted: the issue needs identification, recognition, support and priority before it ever gets to political decision making. From this perspective, the success or failure of an agenda setting process largely depends upon the capacities of agencies advocating the issue to surmount these consecutive barriers. Throughout that process, the mobilisation of resources, either in terms of supporters, funding, expertise, access to decision-makers etc., plays a crucial role.

Kingdon's approach assumes the juxtaposition of three streams of variables: problems, policies and political context. Problems might be unclear or even wicked, policies may include solutions that do not fit to present problems, and the political context may be furthering or hindering specific issues to raise and/or to be recognised. In brief, successful agenda-setting needs a fruitful interaction between these three streams, in what is called a policy window: an opportunity to create a policy change. While 'policy entrepreneurs' are ascribed a crucial role in the creation and exploitation of such opportunities, Kingdon leaves a huge role for unpredictable 'policy windows' to open, for instance in the aftermath of a crisis, a shocking event, etc. In other words: successful agenda-setting largely depends on circumstances beyond a particular agency's voluntarism.

Institutionalisation

Institutions and institutionalisation are key concepts in social sciences. We cannot fully report on their origins and significance here. Yet we refer to institutions here as (a) the phenomenon whereby, over time, day to day actors' behaviour solidifies into patterns, which (b) in turn structure actors' day to day behaviour[3]. Institutions, therefore, have both a stabilising and a changing aspect: while the persistence of institutions assures social stability, the emergence of new actors, new ideas, new scientific insights, might result into a gradual or rapid change of patterns, resulting, in our case, into the coming into being of a new policy domain.

Methodological Account

The analysis used a series of documents in order to reconstruct (a) the development of European environmental health policy, and (b) the shift in attention to children's environmental health. The documents studied comprehend policy documents, scientific articles and publications of different sorts originating from the World Health Organisation, the European Environment Agency (EEA), the European Commission, and from a series of societal, scientific and non-governmental organisations, all since the 1970s. For a systematic analysis of these texts and documents automated search tools were used to look for children's environmental health and the agenda setting thereof. In addition to this comprehensive document analyses, a number of seven experts in environmental health policy have been questioned about their role in and/or their view on the agenda setting. The responses provided by these specialists were validated by so called 'member checking', in which the factual authenticity and interpretive validity of the analysis was checked. Simultaneously, this served as a check on the reliability of the interpretation. The experts checked their own and their institution's role in the process of the agenda setting on children's environmental health.

Results

The political Context: European environmental (Health) Policies

The institutionalisation of environmental policy at national as well as at European level has been studied extensively[4,5,6]. Based on the literature three phases of European environmental policy making can be distinguished. The first phase had its start in 1972, the same year the club of Rome published its 'Limits to growth' [7], and was formalised in the first Environmental Action Programme (1973). It was triggered by the fear for distortions of the internal market by national environmental regulations on the one hand, and by the then emerging environmental concern, fuelled by a series of environmental catastrophes on the other. It resulted in a long series of ad hoc regulations and standards on separate pollutants, and into the establishment of environmental organisations and institutions, such as the European Consumer Protection Service and the DG Environment itself in 1981. In this period, mainly some environmental 'leader' states, such as Denmark, Germany and the Netherlands, tried to push European environmental policy forward.

The second phase started with the Single European Act coming into force (1987), marking the enclosure of the objectives of the community's environmental policy into the EEC Treaty, and thereby providing a legal basis for the EU's environmental policies. This partly reflected the entrance of three other progressive environmental countries joining the EU: Austria, Sweden and Finland. In turn, it led towards a more comprehensive, evidence-based and plan-wise approach to environmental policy. The seminal Dutch National Environment Policy Plan (1989) strongly influenced the European and different national environmental plans, and the European Environment Agency was established. Next to environmental standards, also policy-making processes were harmonised, and environmental interest groups were increasingly acknowledged as partners. Yet throughout the eighties, environmental health as part of environmental policy was hardly mentioned.

The gradual emergence of environmental health

Environmental health is defined by the World Health Organisation (WHO) as those aspects of human health and disease that are determined by factors in the environment. It includes direct pathological effects of chemicals, radiation, and some biological agents, and the effects on health and wellbeing of the broad physical, psychological, social and aesthetic environment which includes housing, urban development, land use and transport[8]. Health is seen here as a public health aspect in contrast with individual health care.

The promulgation of this definition almost coincided with the third phase of European environmental policies, starting with the establishment of the Maastricht and Amsterdam treaties in 1992 and 1997 respectively[9,10]. In the Maastricht treaty, the precautionary principle was included for the first time in a European policy document[5], including its application to protect both environment and human health. In the Amsterdam treaty, article 152 reads*:* "A high level of human health protection shall be ensured in the definition and implementation of all Community policies and activities. Community action, which shall complement national policies, shall be directed towards improving public health, preventing human illness and diseases, and obviating sources of danger to human health. Such action shall cover the fight against the major health scourges, by promoting research into their causes, their transmission and their prevention, as well as health information and education" [9,10]. This statement gave the EU a commitment to ensure human health protection and to include it in its environment policies. Again it was considered as part of public health, meaning it concerned the health of the general population.

This shift had also its impact on concrete regulations and standards. Even though some early European environmental policies touched upon human health - e.g. the first EU policy on toxic compounds dates from 1967 -, the first public health action programmes have been implemented after the 1992 Maastricht treaty only. These led to the Community Action Plan on Pollution-related Diseases in 1999 (EU, Decision No 1296/1999/EC)[11]. This latter programme aimed at improving knowledge of health effects of pollutants, and at improving the understanding of management and assessment of pollution related diseases. Table 1 provides an overview of environmental health related EU policies.

European regulatory measures on environmental health were established, but there hardly existed any complementary legislation to protect children's environmental health. The EU Directive on air pollution mentioned that member states could take more stringent measures to protect children from exposure to NOx, PM (particulate matter), CO (carbon monoxide) and lead, but no limit values for children or children's settings were given (Directive 1999/30). The Directive on the use of flame retardants and heavy metals indicated the danger to children's health, and this directive solely gave a special limit value for the use of mercury in toys (Directive 88/378). The EU Directive on the restriction of use of Bisphenol A in plastic infant feeding bottles served as a second example[12].

All in all, till the early 1990s, children were not considered a priority group to be included as a vulnerable group in whatever policy strategy or Directive.

Directive 96/62/EC	Ambient air quality management and assessment
Directive 96/61/EC	Integrated pollution prevention and control : IPPC Directive
Directive 98/8/EC	Concerning the placing of biocidal products on the market
Decision 1296/1999/EC	Community action on pollution-related diseases
Council Directive 1999/30/EC	Relating to limit values for sulphur dioxide, nitrogen dioxide and oxides of nitrogen, particulate matter and lead in ambient air *(First Daughter Directive)*
Com (1999) 706	Community Strategy for Endocrine Disrupters - a range of substances suspected of interfering with the hormone systems of humans and wildlife
Directive 2000/69/EC	Relating to limit values for benzene and carbon monoxide in ambient air *(Second Daughter Directive)*.
Council Decision of 4 April 2001	Protocol on Heavy Metals
Communication COM(2001)583;	Community strategy for dioxins, furans and polychlorinated biphenyls. Second progress Report {SEC(2007) 955}
Com (2001) 262	On the implementation of the Community Strategy for Endocrine Disrupters
Regulation (EC) No 466/2001	Maximum levels for certain contaminants in food stuffs
Directive 2002/49/EC	Assessment and management of environmental noise
Directive 2002/3/EC	Relating to ozone in ambient air *(Third Daughter Directive)*.
Directive 2004/107/EC	Relating to arsenic, cadmium, mercury, nickel and polycyclic aromatic hydrocarbons in ambient air *(Fourth Daughter Directive)*.
Directive 2007/51/EC	Relating to restrictions on the marketing of certain measuring devices containing mercury. Amending Council Directive 76/769/EEC
Directive 2008/50/EC	New air quality objectives for PM2.5 (fine particles)
Directive 2011/8/EU	Amending Directive 2002/72/EC as regards the restriction of use of Bisphenol A in plastic infant feeding bottles

Table 1. Main EU policy on environmental health

Children's environmental health

The increasing awareness on environmental health paved the way for the increasing concern about children's environmental health. Can we identify the role and contribution of different agencies and factors in surmounting the barriers to agenda-setting, and to indicate the particular circumstances that favoured or disfavoured that process? The initiating role of the WHO and its impact on Europe stands out if the shift to the inclusion of children's environmental health on the agenda of Ministerial conferences is considered. In addition, the role of (new) scientific insights, from the US and within Europe are analysed. Although influential, neither of these factors would have been sufficient for the agenda-setting without a coupling between scientists, practitioners and policy makers. Among others, NGOs played an important role in creating a transdisciplinary context that favoured the further agenda-setting of children's environmental health. Some observations about the present situation and an educated guess about the foreseeable future, however, make clear that a lasting institutionalisation of this issue is not yet guaranteed.

The initiating role of the WHO and its impact on the EU

In 1989 the World Health Organisation (WHO) increased the awareness on the necessity to integrate the fields of environment and health in Europe by initiating the First Ministerial Conference on Health and Environment in Frankfurt. This was needed to deal with emerging and worsening problems, such as the Chernobyl accident, increasing air pollution, lead pollution, etc. The agenda was mainly driven by the environment actors, whereas the input from the health domain was not very prominent. The mobilisation of resources, according to the 'barrier model', in term of funding and expertise was enough to keep environment issues on the policy agenda, but not yet environmental and health. It was followed by the Second Ministerial Conference (Helsinki, 1994)[14] during which the ministers of environment and health decided that all countries had to make National Environment and Health Action Plans, NEHAPs. Based, among others, upon the experiences in the environmental policy domain, these NEHAPs should, firstly, describe the current state of environment and health, and secondly, present a programme to strengthen environment and health[14,15]. These first two conferences were clearly informed by the environmental approach, hence the items discussed and the solutions sought for were the obvious environmental issues, such as air and water pollution. However, at the second Ministerial Conference the integration discourse was set. Stassen[16] argues that this discourse was acknowledging:

a) the need for closer cooperation between health-related environmental, and research areas in order to develop a community system that integrates information on the state of the environment, ecosystems, and human health;

b) the importance of institutionalizing environmental health as a policy domain; and

c) the intent to improve cooperation between the European-, national-, and local-level processes[16].

The Third Ministerial Conference in London in 1999 opted for further implementation of the NEHAPs, by the initiation of Local Environment and Health Action Plans, LEHAPs[17]. Here, children are mentioned for the first time in the context of environmental health at a governmental level. In the Declaration of the conference, the ministers stated: “we are determined to develop policies and implement actions to provide children with a safe environment, including during prenatal and postnatal development, towards the highest attainable level of health” [17]. The London Ministerial Conference of 1999 also identified the need for more scientific information in order to support the policy making at a member state level and to overcome the lack of specific child related standards or norms. This identification was furthering the agenda setting in member states, as it reduced the barrier for funding research and the access of other organisations to decision-makers. This latter point was supported by the outcome of the Aarhus Conference on Access to Information, Public Participation in Decision-Making and Access to Justice in Environmental Matters[18]. The outcome of the Third Conference was that the European Environment and Health Committee (EEHC), as the preparatory committee installed by the WHO, prepared and set the agenda of the upcoming ministerial conferences. In 2001 it decided to focus on children on the Fourth Ministerial Conference on Health and Environment in Budapest in 2004[19], and to make this topic prominent on the agenda. At this conference the particular vulnerability of children and reproductive health to environmental threats was made explicit.

Later again, the EU shared the WHO’s recognition of the problem in its Environment Action Programme[20], that contained the plans for European environmental policy for the next ten years. This document clearly prioritised ‘Environment and Health’ (EU, Decision No 1600/2002/EC)[21]. Within another few years, one evolved from ‘recognition of the problem’ to the next barrier, 'demand for political action'. The latter is the case at WHO level in the Children's Environment and Health Action Plan for Europe[22], presented at the Fourth Ministerial Conference on Environment and Health in Budapest (2004)[19]. At EU level, the 6th Environment Action Programme[20] represented a strong backing to develop policies on children's environmental health.

In other words, from 1999 onto 2004 one sees children's environmental health to overcome the barriers of recognition and demand for action, both at the level of the WHO-Europe and the EU. This discourse was set by 1) the mobilization of resources in terms of support by participating NGOs; 2) the increase in research funding by the EU; 3) the prioritization by the politicians; and 4) the integration of environment, health and children into a policy framework such as the Children's Environment and Health Action Plan for Europe (CEHAPE)[22]. The Fifth Ministerial Conference on Environment and Health in Parma clearly reconfirmed the issue on the political agenda[23].

In the meantime, in June 2003, the SCALE initiative was launched[24]. SCALE (Science, Children, Awareness, Legislation and Evaluation), part of a more comprehensive European Environment and Health Strategy, aimed at scaling up efforts to protect human health, particularly for the most vulnerable groups in society, such as children. It is important to notice that SCALE was largely based on input from the WHO, from NGOs and from the scientific community. The EU Commission was instrumental in providing an opportunity to bring together three streams of Kingdon's model: 1) the political will was there by the initiative of the EU Commissioner; 2) the recognition of problems by the research community; and 3) the policies and urgent declarations at different governance levels. Therefore, SCALE did not only set priorities, it also mobilized a network of organisations and expertise to further both research and policy. SCALE was a common initiative of DG Environment, DG Health and DG Research, in cooperation with the Consumer Protection Service, and actually prepared the action plan for the aforementioned Fourth Ministerial Conference (2004)[19,24]. While SCALE was the first clear EU Commission activity that focused on children's environmental health, it flagged the end of the first and second phases of agenda setting: in the first phase, both the WHO and the EU signalled environmental health as a general issue of concern, reaching its apogee on the Third Ministerial conference in 1999[17]. Thus, setting the political context furthering children's environmental health as a specific issue. The second phase reflects a more particular political awareness regarding children's specific vulnerability, reaching its apogee with the SCALE initiative to list a series of interrelated problems and to set priorities. The policy change was created.

The role of Science

Although the input of science was a main driver in the agenda-setting process, science did not provide solutions that politicians had to implement. The scientific community did show what the problems were in children's environmental health. Furthermore, science provided evidence that, behind the often visible problems of insulated environmental stressors having specific health effects, there was a larger and more complex problem: vulnerable groups in society, children in particular, being exposed to a cocktail of environmental stressors, with largely unknown or uncertain effects. This signal from science was transported from the medical field to the policy makers. Early reports on lead intoxication, pesticides or radiation focused only on particular stressors and effects. Moreover, they were all written from a paediatric viewpoint and linked to the curative health sector. The report from the US National Research Council (NRC) on 'Pesticides in the Diets of Infants and Children' [26] was the first official report that placed children as a specific target group in the limelight for political decision making. This was clearly a success factor of the agenda setting process depending on the capacity of the agency involved and what surmounted the first barrier according to Bachrach and Baratz [1]. The US government was quick to respond to this scientific knowledge and took a range of political decisions to support children's environmental health. Major recommendation of the NAS committee (within the NRC) was to create child-protective safety factors which became a central provision of the Food Quality Protection Act[27]. Specifically, the FQPA, motivated in part by the committee's report, called for the application in risk assessment of an additional margin of safety to protect children's health in two circumstances: a) in the absence of data demonstrating assurance of safety, and b) in the presence of data showing children to be at greater risk to a particular chemical than adults[27]. Since the NRC report, both the curative health sector with leading paediatricians and the public health sector together with NGOs recognised the need for more research in the domain of children's environmental health.

As indicated above, environmental issues were part of scientific awareness since the 1970s. While the health effects thereof got less attention by environmental scientists, this was much more prominent an issue for the WHO, that in fact functioned as an information exchange platform. Thus, mobilising human resources in support of the children's environmental health field. Among scientists, environmental health issues were exchanged on international conferences since the 1980s. While the US clearly was a pioneer in the field, the work done there was rapidly transferred to Europe. Therefore, the early claims on children's environmental health in Europe are largely based upon scientific work done in the USA. This applies to the 1993 NRC report in particular, yet it applies to initiatives taken by the US Environment Protection Agency (EPA) and to some actions from NGOs[28,29]. These US initiatives have been very instrumental in the development of activities in Europe, largely thanks to a series of exchanges between American and European scientists (ISEE conferences)[30]. For example a conference in Poland in 1996, sponsored in part by the National Institute of Environmental Health Sciences, scientists from Western Europe and the United States, met to share information regarding paediatric environmental health in Central and Eastern Europe, to consider methodological issues in the design and conduct of such studies, and to discuss preventive strategies[31]. These exchanges of scientific knowledge triggered, among others, the aforementioned initiatives set up by the WHO in Europe, where children's environmental health were put upon the agenda somewhere between the second and third Ministerial Conferences on Environment and Health, in Helsinki 1994 and London 1999 respectively[13,17]. The role of science is also clear from the fact that several scientists acted as prominent speakers at these conferences.

Transdisciplinary Cooperation

From the above, it may be clear that the collection of scientific knowledge on the impact of pollutants on human health in general and the higher susceptibility of children for these risks, was a necessary condition to overcome the first barrier of agenda-setting: the recognition of the problem. Scientific knowledge is necessary, yet not sufficient to further agenda-setting. Scientifically underpinned claims need to be societally and politically supported by a range of relevant agencies, in this case by medical practitioners, societal groups, NGOs and politicians themselves. A gradually increasing interaction between scientists, professionals, policy-makers and NGOs was a decisive pre-condition to stabilise the agenda setting and build a possible institutionalisation of children's environmental health.

Sometimes scientists co-worked with NGOs to put their issues on the tables. Examples are the International Society for Doctors on the Environment, which was a fine example of interdisciplinary activities within one NGO[30]. Together with other international NGOs, like Women in Europe for a Common Future (WECF), besides some national NGOs, like the Danish Ecological Council, scientists played a role in setting the agenda and making children more prominent in the decision making process of European authorities[32].

The gradual establishment of links between science, society and politics in this field, though, dates from the late 1990s, when a variety of organisations originating from these different spheres shared a basic recognition of the problem. At the first International Conference on Children's Health and Environment in 1998, the International Network on Children's Health, Environment and Safety (INCHES) was founded[33]. This co-incided with activities from the WHO and the Third Ministerial Conference in London[17]. One can regard 1998 as a turning point, since it flagged the moment from which European scientists, medical doctors, NGOs and policy makers showed a lasting interest in the adverse health effects in children caused by environmental pollution and that at international governance level the politics and policy field made decisions to work on children's environmental health in an integrative manner.

It has been seen from other health cases, that scientific uncertainty and complexity may hinder political agenda-setting[34]. In the aftermath of the London conference, though, the participation of the European Environment Agency (EEA) side by side with NGOs within the European Environment and Health Committee (EEHC), clearly contributed to the selection of children as the central theme for the Fourth Ministerial Conference in Budapest[19]. While the period until 1998 was characterised as the era of agencies, scientists in the first place, pushing the issue of children's environmental health to overcome the consecutive barriers of agenda-setting, the period 1999-2004 is characterised as the period of coming together of the streams of problems, policies and context, creating a window of opportunity to create a real policy change.

Although not in Kingdonian terms, the 1999 London conference pointed at the need to what was called 'bridge the gap between science and policy' in the field of children's environmental health. The scientific community had to be given resources to further raise the children's environmental health issue. Based on the recommendations by a special workgroup initiated by the then Commissioner for the Environment Wallström in 2001 the European Commission decided to finance the project Policy Interpretation Network on Children's Health and Environment (PINCHE) in 2002[35]. This project started in 2004, aimed at (1) the systematic organisation of available scientific knowledge and its interpretation for the policy field, and at (2) the identification of policy recommendations to protect children's health from environmental exposures, such as air pollution, carcinogens and neurotoxic compounds. PINCHE was one of the thematic networks set up by the European DG Research. It can be regarded, on the one hand, as a formalisation of the pre-existing cooperation crossing the borders of the scientific, societal and political spheres and, on the other hand, as a clear example of organising a transdisciplinary approach to a largely undiscovered domain in both science and politics. PINCHE indeed led to the formal establishment of a network of scientists, health and environment NGOs, industry, patient and consumer organisations and policy makers. PINCHE, therefore, can be considered a major step in translating scientific insights into implementable policies. PINCHE developed policy recommendations targeting the European as well as the national policy level.

Through the funding of this project, the European Commission, firstly, formally confirmed the agenda setting of the issue, and acknowledged the initiatives undertaken so far by an informal yet well-functioning coalition of actors that was sketched above. Secondly, and even more important from an institutionalisation perspective, the Commission attributed additional resources to this network, thereby endorsing and strengthening its organisational capacities in terms of personnel, expertise and funding. The European Commission wanted a transdisciplinary approach of these Thematic Networks with involvement of different stakeholders including NGOs, industry and policymakers. Through the increased organisational capacity, PINCHE and related projects gave more institutes and organisations access to scientific and policy relevant information on children's environmental health, thereby in turn strengthening their own stakeholders' position. Altogether, it enabled a more systematic identification and exploration of problems and possible solutions at different levels and targeting different organisations in countries across Europe. Thirdly, the European Commission allocated formal status and additional resources to the network, thereby greatly endorsing its activities and furthering its pertinence. The EC committed itself to the case of children's environmental health, by fully recognising the issue as a clear policy priority.

The EU confirmed the importance of the topic by identifying environment and health as one of the four priority areas in the 6th Environmental Action Programme, and by addressing research calls specifically to children's environmental health[20]. From their part, the SCALE initiative, the Framework Programme for Research and Technological Development, and the European Environment and Health Action Plan 2004-2010, all looked for an integrated approach to collect and use information on environment and health, as well as to improve the assessment of environmental impact on human health and the stakeholder involvement[25].

As a result, between the conference in London and the aforementioned SCALE initiative[25] the EU Commission became fully involved. The topic of children's environmental health became part of the DG Research Framework programmes since 2003. This, in turn, reinforced the interest for the topic within the research community at national levels, either at universities or research institutes, and gave rise to even more insights in scientific and policy related issues, and the interrelations between those. The step was taken from international governance level, through the EU and the WHO, to the governance level of member states.

From Agenda Setting to Policy Making

The agenda-setting reached yet another stage as a large part of the resources in Europe was used to build upon the Children's Environment and Health Action Plan for Europe (CEHAPE)[22]. As the EU member states started to produce their own Children's Environment and Health Action Plan (CEHAP), from 2004 onwards, they involved more scientific and professional disciplines, and invited more governmental departments and ministries, agencies, NGOs and others involved in health and environment at national, regional and local level than ever to take part in the designing of these action plans. Public and political attention for the sake of children's environmental health seemed to have reached its apogee here. Since this time it is seen that agenda setting items were translated into policies. These environmental health discourse affected the involved actors at European and national levels. It boosted environmental health research and policy making, making health effects of environmental exposure a trans-boundary issue[16], and giving cross-overs between diverse policy areas. However, the question was if the science-policy interface and the integration of research results in children's environmental health policy making could last.

The figure 1 shows the timeline of the different actions and the participation of the European Commission, the World Health Organisation or societal organisations.

The present and the foreseeable Future

With the consecutive Ministerial Conferences, the establishment and funding of projects that bridged between science and policy, all indicators seemed to point at the coming into being or a gradual institutionalisation of a new domain in science-and-policy: children's environmental health domain. Yet two indicators were hindering a merely optimistic conclusion. One was that, while member states worked on the follow-up of their CEHAPEs and while also the last Ministerial Conference in Parma (2010)[23] had sessions on children's environmental health, the field was not (yet?) institutionalised at national level. Whereas member states largely diverged in the extent they had organised environmental health as a recognisable and distinguishable policy domain[36], they hardly started to organise children's environmental health as a specific domain.
The second indicator dealt with the 7th Framework Programme of the EU which reduced the focus on children's environmental health by not mentioning research items on children in relation to the environment anymore[37]. The latter clearly contrasted with the USA, where large monitoring programmes were conducted, while the EU shifted the research focus away from children's environmental health.

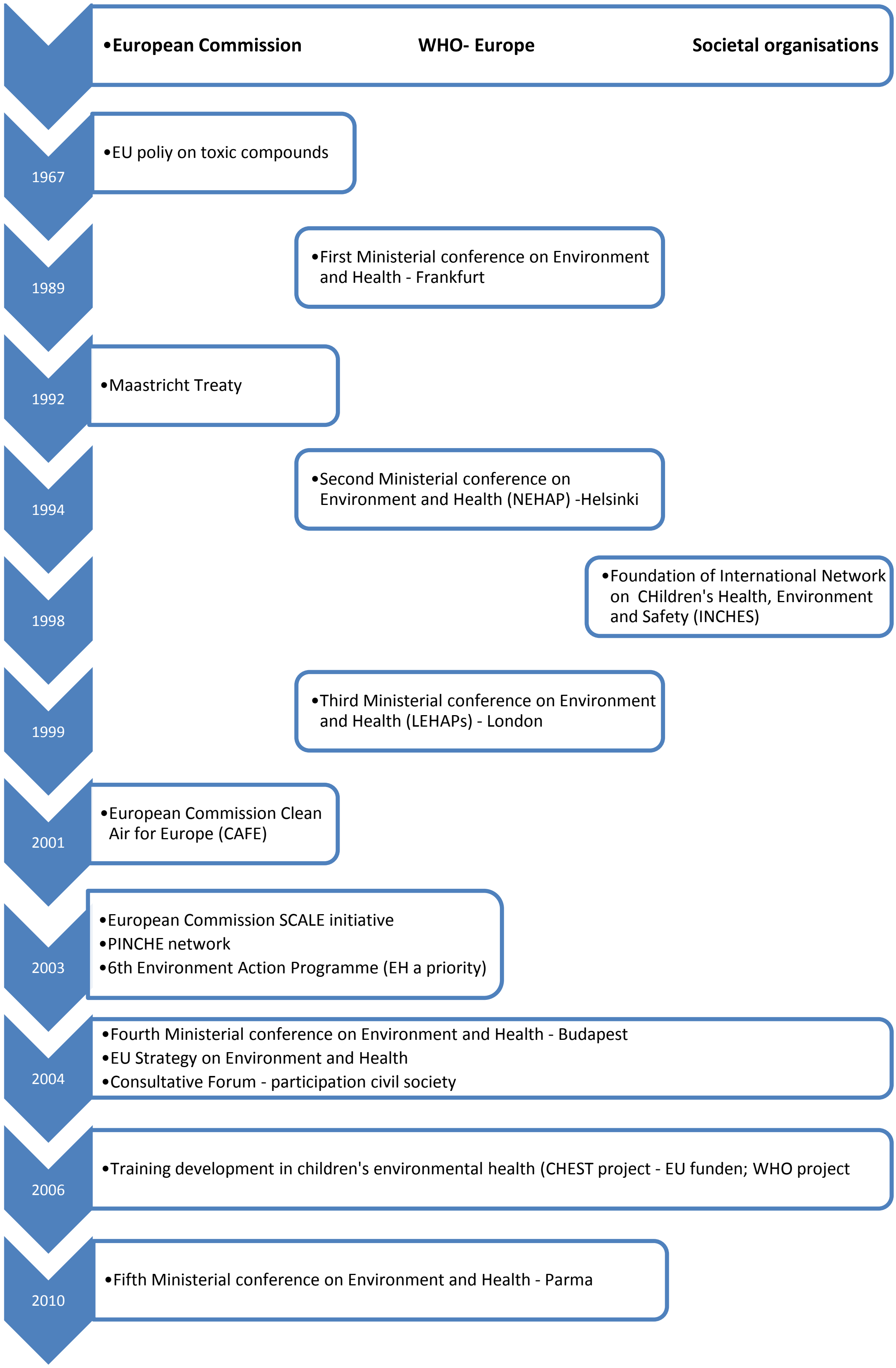

Figure 1. Stakeholder participation

It has been argued in some EU-projects that certain institutional changes would support the development in environmental health towards more institutionalisation. For example, environmental health policy would be strengthened by installing a separate institution for this field of policy, a 'DG Environment and Health', and in national settings a 'Ministry of Environment and Health'.

Discussion

This paper's main question was to assess which factors can explain the emergence of children's environmental health on the policy agenda in Europe, either at community and national level, and its gradual institutionalisation as a distinguishable domain of knowledge-and-policy making.

Although one might be somewhat doubtful about its future path - which we come back to in a moment -, the main observation is that of the agenda-setting of the issue of children's environmental health over the last 15 years or so. The analysis looked for the policy window by which the agenda setting of children's environmental health emerged. The juxtaposition of three streams of variables occurred between 1997 and 2003 in Europe

The first stream dealt with the problem identification. While somewhat belated in comparison to the USA, the European agenda-setting has undoubtedly been successful. As to the former, one has to bear in mind that, whereas in the USA both NGOs (CEHN) and governmental bodies (e.g. NRC, EPA) were publishing on children's environmental health since the 1980s, organisations in Europe were inactive till the late 1990s[28,29,38,39]. While information was exchanged between American and European scientists and NGOs, it was not until 1997 that some activities were deployed in Europe, based on the identification of problems in children's environmental health. The WHO initiated Environment and Health conferences, the first one in 1989, which is regarded as the start of the European agenda-setting process. The Third Ministerial Conference included children's environmental health as a topic. This initiated the second stream on the political context. The third stream, the policy context, happened when the EU produced the SCALE initiative. From that point onwards, the agenda-setting went on rapidly and successfully with a transdisciplinary approach.

In retrospect, two factors have been decisive: the availability of scientific information on the one hand and, even more important it seems, the forging of a coalition of actors and agencies from different spheres on the other. This coalition not only shared and communicated the available scientific knowledge, it also used it to endorse and legitimise research and policy claims, and managed to successfully transfer it to political arenas and translate it into decision-making.

As to the role of scientific knowledge, the US EPA was able to add a few well-known health effects in relation to environmental exposures, such as air pollution and respiratory diseases, or lead exposure and neuro-developmental disorders to the G8 agenda[40]. These concrete insights rapidly penetrated the political arena, hence many countries developed regulations on environmental health policies with regard to the protection of children. The banning of lead in petrol and the banning of lead pipes for the drinking water system proved to be a success story in reducing the exposure and health effects in children[41]. For lead, even a specific norm to protect children for health effects became available.

While these obvious examples helped to convince politicians about the importance of policies to protect children, they have not been transferred or multiplied onto other children's environmental health issues. This is partly due to the complexity and uncertainty that goes with less obvious issues of the environment-health relation in children. In some cases, scientific information was not complete, and even not sufficiently convincing to inform political action. In other cases, additional policy measures might have been too expensive while their effectiveness was unclear. The latter, therefore, had less political support. In addition, one should state that, even though the scientific community was rather univocal in its claims, there was not always consensus on the evidence of environmental health problems and on the political priorities therein. For example, within the SCALE process, a minority viewpoint was published on the topic area of childhood cancer and children's vulnerability.

While scientific information and evidence was a necessary factor in the agenda-setting, the constant communication over these insights is regarded as the decisive factor in this successful agenda-setting. The WHO has played a crucial role in increasing the concerns within scientific and professional communities. By providing joint actions and projects, WHO Europe gradually established informal collaboration with NGOs, e.g. INCHES and member states in Europe. Simultaneously, the European Environment and Health Committee[1] was able to get children and environmental health a fixed spot on the agenda of the Ministerial Conferences on Environment and Health, initiated by the WHO Europe: organising special sessions on children's environmental health on these conferences became very instrumental, not only in distributing scientific knowledge, but also in increasing a concern that went well beyond scientific and professional circles, and reached NGOs and politicians alike. As a result, after SCALE especially, there was a strong push in the EU to designing and implementing policies. Throughout these processes, the EU frequently used consultative forums with different stakeholders, ranging from WHO to NGOs and industry, to discuss the priorities in both research and policy on children's environmental health. We assess this ongoing participation and cooperation between actors and agencies from the scientific community, from the professional scene, from inter-governmental and non-governmental organisations as a decisive feature of the agenda-setting process and the gradual yet incomplete policy formation and implementation at member state level. The agenda setting went on once the EU identified children's environmental health as a separate entity in the environment and health domain. The participation in the EU and WHO process by professional and non-governmental organisations was crucial to keep the issue on the agenda and to initiate its first institutionalisation: the establishment of CEHAPs at member state level. The European Commission's role was to endorse and strengthen this agenda-setting process by providing additional financial resources, not only for research, but also for the forging of a coalition between scientists and professionals, NGOs and national institutes of public health.

When policy is made on children's environmental health, the effects of the measures need to be evaluated, to see if the genuine goal, the improvement of children's health, is reached. There is an obvious need for assessment and evaluation of the different initiatives like the SCALE process and to learn lessons from that. Attention should be paid to see if policy targeting other factors, such as poverty or other socio-economic factors, is more effective,

[1] The EEHC (installed by WHO and member states) has overseen coordination and follow-up of the outcomes of the environment and health process in the European Region from 1994 to 2010.

and should therefore get a higher priority, or else if tackling both environment and socio-economic factors at the same time is most effective in improving children's health.

Therefore, in retrospect, we regard the agenda-setting of children's environmental health as successful. Its institutionalisation, however, seems only halfway and might stagnate over the foreseeable future. Indicators read as follows. First, and as to its substantive content, children's environmental health agenda did not change much since the Fourth Ministerial Conference in Budapest. The PINCHE project, that furthered both research and policy making by indicating priorities in either domain, was not followed by another children's environmental health related programme or network. The EU commission apparently decided for a more general approach, in which children are no longer treated as a specific target group. Second, and as to its resources, both research and policies in this domain have seen their budgets reduced at EU level, leaving a greater role for member states, yet decreasing the representation and participation of non-governmental organisations in setting the agenda for the next Ministerial Conference. While devolving the issue to member states in itself is acknowledgeable, the EU commission seems increasingly reluctant to stimulate and endorse their efforts, as there is no concrete timing for a next EU Environment and Health Action Plan; the last expired by 2010. DG Environment is even not active on this file anymore. As a result, one can anticipate children's environmental health issues to be no longer among the priorities within public health and research institutes, among scientists and politicians. Over the last 5 years, the issue clearly has lost momentum.

Acknowledgement: the authors wish to thank the following persons for their role in member checking the content of the emergence and development of children's environmental health as a policy issue (in alphabetical order): Martha Berger, Irena Buka, David Gee, Philippe Grandjean, Bruce Lanphear, Peter Pärt, Martha Shimkin.

Funding: Two of the authors were co-ordinators of the EU funded project PINCHE, the Policy Interpretation Network on Children's Health and Environment (EU project number QLK4-2002-02395).

Competing interests: None declared

Ethical approval: Not required

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CHAPTER 3 CHILDREN'S VULNERABILITY AND SUSCEPTIBILITY TO ENVIRONMENTAL STRESSORS

Peter van den Hazel

Submitted

Abstract

The literature on children's susceptibility has grown extensively the last ten years. This article reviews the literature on children's vulnerability and susceptibility. A systematic search was conducted in scientific literature using the Scopus database. The differences in exposure between children and adults are analysed. The differences between children and adults are analysed by toxicokinetic principles as absorption, distribution, metabolism and excretion. The health effects caused by environmental factors transpire differently in children than in adults. Furthermore, the differences between children and adults are analysed by toxicodynamics principles of development, timing or dose-response, including epigenetics and genetic susceptibility. There is still a knowledge gap on children's vulnerability and susceptibility for many compounds. Preventive policies, precautionary approach, more research, and better testing methods in children's environmental health are needed to fill this knowledge gap. Integrated knowledge about complex systems with multiple exposures and knowledge about a range of biological effects in the different developmental windows of time in children, including the foetal period, is needed. Children's environmental health needs to become an adult science within society.

Keywords: Children, environment, health, toxicodynamics, toxicokinetics, vulnerability, susceptibility

Introduction

The position of the child in society has evolved from child labour before the 20th century to a valuable partner in society in the modern, western world. The position of the child in society changed from a pension provider, to be the person as insurance for a better old age of its parents, and later to a symbol of wellbeing on which parents can spend money. In the centuries before 1900 children were considered as little adults with the same physical characteristics as adults. However, children are a heterogeneous group of people with their own qualifications. Children have their own physical entity. Children are totally different from other children in their physical and biological constitution, including their thinking process and their reaction to societal and environmental factors, during all periods in their development towards adulthood.

The scientific literature on children's susceptibility has grown extensively the last ten years. In recent years some descriptive overviews have been published[1-8]. Some of these articles analyse the biochemical, physiological or genetic differences between children and adults[4,5,8]. Economic, social and psychological factors are also influencing the vulnerability and exposure of children. These influencing factors are described in other papers (e. g. Licari[9]). However, there is a limited amount of scientific literature available that analyses the link between children's vulnerability and the policy domain of environmental health. This article gives 1) an overview of the biological, biochemical, physiological or genetic factors of children's vulnerability and susceptibility; 2) arguments to link (lack of) knowledge on children's vulnerability and susceptibility to the development of policies.

This article starts with the definitions of vulnerability and susceptibility, followed by an analysis of children's vulnerability and susceptibility by toxicokinetic and toxicodynamic concepts. Following, the concept of critical periods of development in children is analysed. The article concludes with some thoughts on which direction the knowledge production has to take in order to protect children better from environmental hazards.

Methods

A systematic search was conducted in scientific literature and grey literature, using the Scopus database over the years 1997–2011. The search terms used were 'vulnerability', 'susceptibility', 'sensibility' and 'child(ren)' including environmental health as restricting term. Articles with a focus on economic, social or psychological factors were excluded as were articles on occupational settings. Search terms for exclusion used were 'occupational health', 'socio-economic', 'social factor(s)', 'children and psychology' singular or as combination in keywords. Furthermore, besides scientific articles literature was collected and analysed from reports, books or conference background material, which has been produced as background material to a range of children's environmental health related activities, such as the WHO initiated Ministerial Conferences on Environment and Health, the EU SCALE initiative and EU funded research projects or Thematic Networks. The number of these kind of documents used in this article is 25.

Definitions

The words vulnerability and susceptibility have definitions which are closely related. In this article we use the following descriptions.

Vulnerability, according to several online dictionaries means: the state of being vulnerable or exposed. Somebody's vulnerability is comparative to that of others. The terminology is valid to use in the environment and health field because one can compare between persons with exposure related to location (school, home), time period, behaviour, genetics, phenotypes, dietary deficiency etc.

Children have more time than an adult to develop adverse health effects, due to the fact that they have more years to live. The period of exposure may also be longer. These comparisons are dependent on the personal activity of the person. In children the feature of child behaviour is a very important aspect in considering vulnerability. One important aspect of vulnerability is that it can be changed by circumstances. Vulnerability is about the position or place one person is in. We can say that someone can be manoeuvred into a certain vulnerable position. And a person can leave this position again.

Susceptibility, according to Merriam-Webster online dictionary means the quality or state of being susceptible: the state of being predisposed to, sensitive to, or of lacking the ability to resist some extraneous agent (as a pathogen or drug)[10].

Susceptibility is intrinsic to a person as it is independent of the position someone is in.

For example there is different susceptibility to exposure of the same dose of lead depending on the physiological state which changes with age, nutritional status, etc. Differences in susceptibility include the likelihood, the nature and the amount of the damage produced by exposure to a defined quantity of a toxic agent, and differences in exposure , i.e. the total intake of a toxic agent per unit of body weight (or body surface)[5].

In children one can see different absorption, different metabolism, different distribution and different excretion of compounds that enter or contact a child's body. During different periods of development susceptibility changes several orders of magnitude as different responses are occurring due to some intrinsic mechanisms.

These differences in susceptibility are connected to age-related physiological differences with impact on toxicokinetics and toxicodynamics. This means that children at different age groups may react differently to environmental toxicants. There are also individual differences among children from the same age group. Not every environmental stressor will cause health effects in children differently than in adults.

While in the past the physical differences between children and adults were merely mentioned as a fact, it is only since the last two decades that a more systematic approach prevails in research on the differences between children and adults[5].

In this article three areas of concern are reviewed. First (1), the differences in exposure between children and adults are analysed. Second (2), the differences between children and adults are described according to toxicokinetic principles as absorption, distribution, metabolism and excretion. Third (3), the health effects are analysed according to the toxicodynamics principles of development, timing or dose-response, including epigenetics and genetic susceptibility.

Development stages

A child from conception until adulthood has a continuous spectrum of development. The organ systems develop over different time periods and some organs do so until late in childhood or early adulthood.

The subdivision in development stages in children used for this paper: a) unborn children with periconceptional development (first 2 weeks), embryonic (3 – 7 weeks) and foetal (8 – 38 weeks) stages of development; b) new-born children and infants (younger than one year of age) as the postnatal period; c) toddlers, children between 1 and 3 years of age; d) preschool children, between 3 and 6 years of age; e) school-age children, between 6 and 16 years of age; and adolescents between 10 and 19[11]. Target organs or endpoints of effect to be distinguished in different age groups have been determined at the nervous system, the immune system, the reproductive system, the respiratory system, but also bones, teeth, blood coagulation and oxygen transport[8].

It is known that children have critical periods of development. There are major stages of development from conception to adulthood. This growth ranges from germ cell development, embryonic and foetal development to on-going development during childhood.

1) Different exposure in children

Many articles have analysed the different exposures in children compared to adults. The differences are related to a) different settings of exposure for children; b) unique pathways for children (e.g. breast milk); c) different activities of children; and d) potential time lag between exposure and effect.
Increased air, water and food intake per body weight have been reviewed in a range of publications[5,8]. Different behaviour, including hand-to-mouth activity, object-to-mouth transfer and crawling have also been reviewed extensively[5,8]. The breathing zones of children differ from adults as children inspire air that is closer to flooring, where concentrations of compounds such as radon, pesticides, or mercury are present[12].
A unique pathway of exposure of children is the consumption of breast milk, which reflects to maternal exposure to an array of chemical compounds. Less reviewed are the differences between different age groups of children. Distinct dietary patterns in younger children show differences in food selection and amounts consumed[13]. Another exceptional route of exposure is the take-home exposure when parents or caretakers bring chemicals on clothing or skin into the house[14].

In toxicological reviews some differences in toxicokinetics and toxicodynamics in different age groups from conception to adolescence are studied[15,16].

“Children experience the world differently than adults, meaning that children's exposures to environmental toxicants and their levels of exposure can vary dramatically from those of adults” as stated by Freeman[17].

”Exposure differences are a result of locations where children spend time, the activities in which children indulge, and children's level of personal hygiene. Thus, in identifying how children may be exposed to a chemical and the level of exposure, it is inadequate to simply extrapolate from adult exposure, since children are not "little adults"[17].
“Children older than 12 may have exposures similar to adults -- through their part time jobs cutting grass or working on farms -- in addition to sources of exposure through their play activities”[17].

Some studies are limited to description of exposures to certain age groups. For example the National Human Exposure Assessment Survey (NHEXAS) studies did not include children less than 3 and older than 12; thus no information is available on these crucial subpopulations of children[17].

Another problem is the potential time lag between the relevant periods of exposure during different stages of development and associated outcomes that may be shown at later life stages[18]. This can lead to a cascade of alterations which may only become manifest as structural or functional effects later in life. Developmental effects can show themselves as persistent deficits, developmental delays or transient effects[18].

For example, the carcinogenic polycyclic aromatic hydrocarbons are causing intrauterine growth retardation and low birth weight. The occurrence of diabetes and cardiovascular diseases in middle age is related to exposures occurring around the period of birth. Research has to be developed to look better at the long term effects that can be seen as a cascading effect of previous exposure.

Long-term effects of exposure to chemicals associated with late neurotoxicity are seen in children, but vary depending on a variety of co-exposures, genetic polymorphisms and even characteristics of the social environment[19]. Several authors conclude that other conditions have to exist before a contaminant can produce its effect, which reflects numerous unknown or unmeasured modifying factors[20], or which work in concert to produce health outcomes[21].

2) *Toxicokinetics*

Children's physics are an entity to consider on its own. It is obvious that children's physics are different in body weight, higher ratio of body surface to body weight, and that there is a different size proportion between organs. Children have, compared to their lower body weight, a higher cardiac output, increased blood flow to the brain and reduced blood circulation in the kidneys up to the age of 5 months[22].

There is a whole range of scientific articles and books that make clear that children are different than adults in their consumption of vital sources, such as water, air and food[8,17,23].

"An infant more than doubles its weight in the first four months of life. Young children breathe more rapidly and take in more air, have higher metabolic rates, and have higher proportionate food and liquid intakes than do adults"[13,17]. Some other quotes from the literature:

"When an infant drinks six ounces of formula or breast milk per kilogram of body weight daily, it is equivalent to an adult male drinking 35 cans of soda in a day[12]. The average one-year-old eats two to seven times more grapes, bananas, pears, carrots, and broccoli than an adult does[12]. Because children eat more fruits and vegetables and drink more liquids, potential exposure to toxins such as lead, pesticides, and nitrates is greater"[17].

Proportional intake differs between children themselves in food and nutrition. This interindividual difference may have a greater impact on health than the differences between children and adults.

Additionally, specific toxicokinetic factors have to be taken into consideration when the harm of the conceptus is determined, like the kinetics in the mother, the transfer from the mother to the embryo or foetus via the placenta, and the kinetics in the embryo or foetus itself[3].

On top of these intake disparities there are differences in different age groups in absorption, distribution in the organism, metabolism and elimination[4,12].

Toxicokinetics - Absorption

The absorption in children differs per age group. The duration of exposure to a compound affects the absorption and thus the internal dose. Furthermore, absorption can be influenced by the properties of the chemical compounds, the cell properties or other organisms that are needed. Below the absorption in different tracts is described.

Gastrointestinal tract

Different studies focus on specific routes of uptake. Greater oral absorption has been reported in infants due to greater pinocytic activity of intestinal epithelium prior to closure. Nutritional deficiencies may influence oral absorption, for example low iron or calcium intake increases the absorption of lead[13].

Gastrointestinal absorption changes mainly due to a change in gastric pH in the first few days after birth. The presence of digestive enzymes increases the first half year after birth to adult levels and the intestinal flora appears rapidly after birth. Also bile acid metabolism is not fully developed and thus the absorption of fats and lipid-soluble substances may be affected, leading to impaired fat digestion[4]. But fat in breast milk is 100 % absorbed together with the fat soluble substances like dioxins due to the specific glycoproteins around the fat balls.

The presence of other compounds may increase or decrease the amount of absorbed chemicals. An adult will absorb 10% of ingested lead; a toddler absorbs 50% [25], which is related to the presence of lactose, some proteins, some lipids or vitamin D in case of increase of absorption. There is a relation to high levels of zinc, copper, phosphorus, calcium or iron in case of a decreased lead absorption.

Percutaneous

Children have higher ratios of skin surface area to body weight (roughly double in infancy) than adults and probably experience more intensive contact with their surroundings than adults in non-occupational settings[26]. Furthermore, their skin is more permeable than that of the adult[27].

In preterm children the keratinization is delayed. The skin of premature neonates can be substantially more permeable than that of full-term neonates because of immaturity of the stratum corneum that is still unkeratinised[28,29]. This may lead to a higher vulnerability to exposure of chemical compounds[12]. In contrast, full-term new-borns have a well-developed stratum corneum of the skin[28]. The effect is a reduced barrier function in preterm children. Skin damage and hydration of the skin are other factors to increase the permeability in infants[28].

There are many examples of compounds that lead to adverse effects in children due to early dermal exposure[7]. With respect to benzophenone-3, a chemical sunscreen agent, data by

Jiang raise some concerns regarding the formulation of sunscreen products for specific application to children as it was found to have penetrated human skin to the receptor phase after the 8 hour study period, with up to 0.08 g m^{-2} or 10% of the applied dose penetration[30]. The duration of exposure to the skin is important for children as they wash their hands less often than adults.

Respiratory tract

Respiratory absorption during early life, because of the greater respiratory volume per surface area in young children, may lead to an approximately 2- to 3-fold increase in respiratory tract exposure (per unit surface area) of young children compared with adults[13]. Premature children have even less mature lungs and thus show greater local effect to xenobiotics by inhalation[3]. Differences in uptake in children are driven by blood-air partition coefficient, respiratory rate, cardiac output and systematic extraction, depending on the chemical itself. The blood-air coefficient is dependent on the presence of haemoglobin, lipid in blood, which can vary across different age groups[31].

Transplacental

In the foetus absorption takes place via the placenta, in which different substances can permeate depending on the physico-chemical properties. Compounds of low molecular weight cross the placenta easily[12]. Before birth there is a specific situation: the foetus is exposed via the vena umbilicalis that brings arterial blood from the placenta and this blood is directed immediately to the brain and organs like the pancreas and kidney, via de ductus venosus through the liver and via the open foramen ovale into the aorta. So decontamination in the liver by sulphation takes place after birth.

An immature bile acid metabolism causes lipophilic substances to be only partially absorbed by bottle fed babies[6], while the same substance can be absorbed by breast-fed babies[32]. Compounds can also be absorbed through skin, alveoli and the gastrointestinal tract of the foetus.

The absence of demethylating bacteria in the intestine of the unborn child causes a higher absorption of methyl mercury. This happens until the weaning period in which the bacterial flora changes.

	Obvious difference	Main period in development of difference
Absorption	More skin absorption	Young children (3- 5 days after birth; and longer in premature children
	Surface area to body weight ratio	Decreases from birth to adulthood
	Greater respiratory volume per surface	Young children
	Less alveoli	Increase during first years up to 8 years
	Higher gastric pH	Neonates first few months
	Intestinal absorption	Higher at birth
Distribution	More permeable blood-brain barrier	Neonates
	Less plasma protein binding sites	Neonates –first year
	Water proportion high	Foetus, Neonates
Metabolism	Immature metabolic and renal clearance	Neonates – first two months, especially pre-term neonates
	High metabolism rate	Children between 1 and 5 years
	Increase or reduced activation	Neonates, compound depending
	Absorption glucose, 70% converted to fat	Foetus
	Enzymatic functions (most markedly CYP1A2) more active than in adults	Young children
Excretion	Renal and biliary excretion diminishes	At birth
	Kidneys show functional immaturity	First 6 – 12 months
	Different clearance	Some drugs are cleared fastest by older infants
	Bile elimination is not fully developed	First few months
	Renal clearance	Maximum at 6 months, remains high during childhood
	High ventilation rates per body weight	Young children

Table 1. Main differences in toxicokinetics

Toxicokinetics - Distribution

Chemical-specific factors such as lipid and water solubility, chemical size, the size of the body water and lipid compartments, regional blood flow, the ability of transporters across membranes, and affinity for plasma or tissue proteins mark the distribution into systemic compartments[31]. Neonates generally have higher water and less lipid content in the body, less quantity of plasma protein binding sites and a more permeable blood–brain barrier. The plasma protein binding sites in neonates may be less available for xenobiotic binding than at older ages[16,34]. Total body water varies with an individual's age and amount of muscle mass and body fat. 80%–85% of a premature infant's body weight is attributed to water, while about 70% of a full-term infant's body weight is attributed to water compared to ~ 65% total body weight in male young adults and ~ 52% of total body weight in young female adults[35]. The water content from a 4-month old child starts to be comparable proportionally to that of an adult[3].

These factors tend to increase the volume of distribution for many chemicals in early life[16,34]. This other volume of distribution can lead to lower blood concentrations and longer chemical half-lives in the body. Chemicals are less available to the central compartment for transfer to sites of metabolism (e.g. liver) and elimination (kidney, lung, bile)[31].

The body fat content is low in premature (1%) compared to a full term child (10%), and will increase in the 5 to 7 years of age period. The body fat increases more in females. This increase continues into adulthood[3]. Thus, in girls there might be an increased retention of fat-soluble compounds or the concentration of the compounds is more diluted.

In certain stages of child development there is a smaller distribution volume for fat-soluble compounds than in adults[33]. Water-soluble compounds will find higher water content in the child's body[7] and thus a higher volume of distribution on a body weight basis. The water proportion is highest in the foetus and high in neonates[36]. The concentration of an absorbed water-soluble substance will be lower in the blood serum in neonates than during later development stages in childhood.

The child has a greater blood flow to the brain and other organs than an adult in proportion to body mass. This may lead to a greater storage of chemical compounds in children's organs[37].

The perfusion of the brain is higher in children than in adults. The blood-brain barrier is not yet fully developed in young children until the age of 6 months, and thus a higher intracellular absorption takes place. The barrier matures further during childhood. The transfer of compounds through the blood-brain barrier is greater for lipid-soluble compounds. Different regions of the brain show a different effectiveness of the blood-brain barrier against absorption[38].

The foetus experiences an additional distributional phenomenon by placental transport of chemicals from mother to foetus. The existing knowledge suggests that most chemicals can cross the placenta, but the rates can vary depending upon molecular size, lipophilicity, and serum protein binding[16,34]. Maternal metabolism/clearance factors may lead to lower concentrations in the foetus compared to the mother or sometimes to higher concentrations.

Another child specific distribution of chemicals takes place from maternal blood into breast milk. This distribution is controlled by chemical characteristics, such as lipophilicity, and physiologic changes during lactation[39].

The policy implication is that exposure to water soluble compounds needs to be limited in the first six months of life.

Toxicokinetics -Metabolism

Most chemicals in the body are converted to a variety of metabolites. Most chemical compounds are metabolized in the liver. These compounds are excreted in urine, bile or breath. A variety of data show that young children, foremost in the first 2 months of life, have an immature metabolic and renal clearance. In the foetus most compounds, that are absorbed, have a higher concentration than in the mother because of the limited capacity to metabolize. The metabolism of growing tissues can lead to higher local intracellular absorption. Furthermore, different enzymes play a role in metabolism. The structure of compounds needs to be changed before elimination takes place. If these mechanisms are not yet well developed in neonates this will lead to longer half-life in the plasma. If the foetus metabolizes a compound to a less polar metabolite, this metabolite could be kinetically hindered from crossing back across membranes to be eliminated by the maternal elimination pathways[26]. However, other substances might show reduced activation when they are not formed into more toxic substances. The hepatic metabolic capacity is still minimal at birth, especially in pre-term neonates. The liver enzyme systems reach adult levels at 3- 6 months of age.

A number of metabolic compounds are involved including a variety of cytochrome P 450 (including CYP1A2 and CYP2E1, that are particularly important in toxicant activation), glucuronidation, serum esterases, epoxide hydrolase, and glutathione *S*-transferases (GST), representing a major group of detoxification enzymes[31]. Some foetal enzymes (e.g., CYP3A7, 3A4, 4A1, GST-pi) exist, but these seem to have a different range of specificities from the adult enzymes. The foetus absorbs glucose, of which 70% is converted to fat, if membranes and brain are included as fat. The transition from a low fat diet to a high fat diet takes abruptly place at birth. Glycogen stores have to meet the metabolic needs until triglycerides and lactose from milk take over[40].

The renal function is low in the first weeks to months of life, leading to prolonged half-life of a variety of renally cleared drugs. By 6 months of age this functional state changes, and even for a time, some enzymatic functions (most markedly CYP1A2) appear to become somewhat more active than in adults[16,34,41,42].

In some cases it is not the compound to which the child has been exposed but its metabolite which may cause effects. Studies on inappropriate use of methyl parathion showed elevated levels of metabolites in urine in children less than 3 years of age[24].

Finally, there is low activity of methaemoglobin reductase in infants. Substances, such as nitrite, that form methaemoglobin, are therefore more harmful to infants than adults.

Toxicokinetics - Elimination or excretion

At birth the renal and biliary excretion via the placenta stops due to the collapse of placental circulation. The transplacentally transfer of compounds also stops. The renal clearance will increase to its maximum at about 6 months, being even twice that of the adult. It remains high during childhood. Elimination of xenobiotics shows a varying pattern. Some studies show a fast clearance of morphine in infants compared to new-borns or adults. There are also examples of fast clearance for other drugs like methotrexate or chlorpromazine[43] that show a reduced chemical toxicity in children. Children have rapidly changing clearance with high interpatient variability.

Bile elimination is not fully developed during the first few month of life[6], because glucuronidation capability and other hepatic functions are immature. This can cause delay of excretion of toxic substances.

Exhalation of volatile chemicals may be higher in young children because of high ventilation rates per body weight. Because other clearance pathways are immature the level of volatile chemicals to be exhaled can increase[31].

3) Toxicodynamics

Toxicodynamics is considered as the process of interaction of chemical substances with target sites and the subsequent reactions leading to adverse effects. The dynamic differences in development in children are described by biochemical, molecular, cellular, organ and organism processes at each life stage as response to toxicant exposure. Some authors connect toxicodynamics to organ sensitivity and cytoprotective mechanisms[3].

Many integrated events regulate the normal development of a child. Science has only identified a few critical or limiting processes that lead to significant changes in development and function. A few mechanisms of susceptibility are reviewed in this article. These mechanisms have temporal, dose response and genetic considerations.

Different health effects can be seen during foetal human development. Foetal death, malformation in physical structure or dysfunction in a designed activity can take place during this early developmental phase. The kind of effect is depending on the stressor itself and the gestational age during the exposure. The structural malformations in the early prenatal period have been studied in several papers[7]. These malformations are physical incompleteness of organs or limbs.

Different phases of development can be discerned. These phases are briefly discussed. The periods are compared by some critical developmental features in table 2.

Toxicodynamics - Timing

Germ cell development

Sperm and egg cells begin their development in foetal life. These cells mature until puberty. In the male foetus the germ cells develop in utero. In the female foetus the germ cells undergo mitosis and the first phase of meiosis into primary oocytes. During each stage the germ cells or primary oocytes can become damaged by environmental exposures[3,7,44]. This may result in a reduced fertility later in life or in offspring with congenital health problems (Loeffler, 1999; Silbergeld, 1999 in Altshuler[7]).

	Time period	Main findings
Germ cell development	Pre-conception	Reduced fertility by damage to germ cells
Conception		
Periconceptional development	First 2 weeks	High rate of growth; foetal death by environmental exposure
Embryonic period	3-7 weeks	Most sensitive to exogenous induced malformations in single organs; physical incompleteness of organs or limbs; abnormal formation of disc like placenta
Foetal development	8-38 weeks	Characteristic by tissue differentiation; risk for impaired growth, functional deficiencies; female foetus increased risk for mutation in germ cells (month 4)
Birth		
Perinatal period	39 weeks of pregnancy – 1 week after birth	
Neonatal period	Birth to 1 month	Enzyme systems under development
Weaning period	➢ 6 -8 months	Greater hepatic extraction and shorter chemical half-lives Cortical synapses reach maturity between 6 and 24 months after birth
Childhood	➢ 12 years	Neuron migration, cell proliferation and synapse formation through three years of age. Cellular insulation around nerve fibers, myelination, continues until early adulthood. Myelination of the nervous system continues into adolescence. Different toxicokinetic mechanisms. At birth a baby has about 10 million alveoli, but at age 8 years, a child has 300 million alveoli.
Adolescence	➢ 18 years	Sexual maturation.

Table 2. Phases of development

Periconceptual development (First 2 weeks)

The zygote develops from a single cell to an infant. This phase is characterised by its high rate of growth. This period of development knows a specific set of vulnerabilities to environmental stressors. At this stage environmental exposures usually cause foetal death rather than injury[45]. However, there is also a threshold for causing foetal death, as every pregnant woman is exposed to environmental stressors. The blastocyst implants around day 6. Chemical compounds can accumulate in the secretions within the blastocyst[3]. However, the cells at this stage still show a high degree of potential to differentiate into various kinds of cells.

Embryonic period (3-7 weeks)

During the embryonic period the formation of most major organs is established. The organ development varies by organ system. Most basic structures are formed before week 16 of pregnancy. In this stage environmental exposure can result in major disruption of the structure of the organ. This may result in major physical malformation (congenital anomalies) or in foetal death.
After neurogenesis in this period each neuronal cell continues to mature through a process of migration. Earliest synapses develop during the embryonic period, and by 10 weeks immature synapses are present[31].

For the lung development it is established that cell number, cell type and function of the airways and alveoli can be altered by exposure to different compounds[31].

Foetal development (8-38 weeks)

The functions of organs are developed in the foetal development period while in the embryonic period the structural development primarily existed. Environmental exposures can lead to impaired growth, physiological defects or functional deficiencies. There are different periods of maximal susceptibility for each forming organ. Damaged or lost cells can no longer be replaced and may result in permanent damage. Effects are seen in the central nervous system and reproductive organs, although these effects do not show sometimes until after birth (Dencker, 1998; Rogers, 1996; both in Danish Environmental Protection Agency[3]).
In the nervous system development it is seen that each neuronal cell continues to mature through a process of migration, settling to a specific location. These processes of migration

continue well after birth and continue for 7 months to 2 years after birth. Most anomalies occurring in the nervous system are seen in the early gestational phase. Most known cases are due to exposure to drugs, as far as we know, as these have been studied more extensively than other chemicals.

Similar to lung development during the embryonic period the cell number, cell type and function of the airways and alveoli can be altered by exposure to different compounds[31].

Exposure in this period of development might influence the initiation of haematopoiesis, as it regulates the appearance of cells necessary to sustain immune development. Furthermore, the migration of stem cells and expansion of progenitor cells, and the emergence of the bone marrow might lead to differences in the manifestation of impact. Finally, the formation and innervation of the thymus can be influenced[31].

Some studies show effects in children when they are exposed in utero. The Northern Manhattan study and the Krakow study, both related to prenatal exposure to polycyclic aromatic hydrocarbons have demonstrated multiple adverse effects of prenatal exposures across a gradient of exposure[46].

The Northern Manhattan study showed associations between reduced foetal growth and neurocognitive delay in children prenatally exposed to environmental tobacco smoke, polycyclic aromatic hydrocarbons and pesticides[46].

The Krakow study demonstrated genetic damage - more than 10 fold higher than maternal adducts - in umbilical cord blood after exposure to combustion-generated pollutants from coal burning and traffic[46].

This exposure was linked to decreased foetal growth and asthma symptoms.

Another example is exposure to ethanol that can cause the foetal alcohol syndrome. Ethanol changes the neurotransmitter activity at receptors, which causes disruption in transmission. Finally this leads to brain related disorders[27,47].

Childhood (birth to 19 years of age)

Several systems in the body continue to develop after birth. The nervous system is the best known example, where cellular structures of the brain show neuron migration, cell

proliferation and synapse formation through three years of age. Cellular insulation around nerve fibres, myelination, continues until early adulthood[48]. Klingberg et al. studied myelination in children and adults. It was found that anisotropy in the frontal white matter was significantly lower in children than in adults, suggesting less myelination in children. These results express that maturation of the frontal white matter continues into the second decade of life[49]. Cortical synapses at birth are still immature and the morphological characteristics of maturity are reached between 6 and 24 months after birth[31].
Immune memory is established during early childhood[50], as well as maturation to complete immunocompetence[31]. The maturation of the immune system is rapid during the peri- and postnatal period. It is driven by exposure to antigens from different sources (food, infection, vaccination, chemical compounds).

Brain growth is rapid during the first two years of life. The full number of neurones is present at the perinatal period, but the myelination of the nervous system continues into adolescence. Xenobiotics have a chance to interact with the nervous system development.

Like the nervous system, the respiratory system continues to grow and develop through linear growth. At birth a baby has about 10 million alveoli, but at age 8 years, a child has 300 million alveoli. Certain types of exposures (e.g. second-hand tobacco smoke, particulates and ozone) during these growth periods are known to have adverse effects on both structure and function of the airways[50].

In lung development metabolic and biochemical functions continue to change their process of differentiation and morphogenesis[52]. Growth of the lungs is complete by the end of adolescence.

Physical growth of organ systems continues the total period of childhood. Sexual maturation is an example of clear physiological and hormonal change in children.

Adolescence is marked by physical growth, associated with sexual maturation and rapid increase in muscular strength. Adolescent females grow prior to the onset of menstruation, the growth of male adolescents occurs largely after the onset of puberty[51]. Post pubertal females show a high body fat content, resulting in increased retention of lipid-soluble compounds such as PCBs and dioxins. Furthermore, adolescents have a substantially greater capacity to metabolize compounds than younger children or neonates, by an enzyme activity peak.

Daston et al. stipulate that “Inhalation exposure to substances during critical windows of development may have profound effects that would not be seen if the same exposure were to occur in the adult[31]. Because lung development occurs over the entire prenatal period, exposure effects can have significantly different consequences depending upon whether they occur during the pre- or postnatal period of life. Although our understanding of these changes at this time is extremely limited, one would expect that abnormal developmental changes that occur in the prenatal period because of exposure to a variety of chemicals may have long-term effects persisting into adult life”[31]. In addition, it is known that children have a greater number of years in which the long-term diseases, such as cancer and neurodegenerative disorders caused by toxins can evolve[53]. It has been established that altered lung growth or functional deficits in the lungs are a result from exposure early in organogenesis to neonatal and adolescent developmental time periods[54].

Toxicodynamics - Genetic susceptibility

Gene-environment relationships during foetal development have been studied in drug metabolism enzymes associated with altered susceptibility to toxicant-induced birth defects. The importance of Ah receptor status and teratogenic response to benzo[a] pyrene, that requires metabolic activation by P450 enzymes, has been studied in animal models[55].

Epoxide hydrolase has been linked with susceptibility of offspring to developmental toxicity following maternal exposure to diphenylhydantoin[56]. Besides examples of genetic variations in drug-metabolizing enzymes as genetic susceptibility factors there is also genetic variability in growth factor regulators[57].

A temporal sensitivity in gene-environment interaction is seen with methaemoglobinemia. Children with less functional methaemoglobin reductase are a concern when exposed to nitrate in their formula[26]. Other examples are found in the polymorphism in the paraxonase (Pon1) gene related to the exposure of organophosphate pesticides[26]. Genetic variability in growth factor regulators and homeobox genes has been shown to cause developmental effects[26].

Levit et al. found 49.7% ($p = 0.04$) of the variance in liability to Respiratory Distress Syndrome (RDS) was the result of genetic factors alone. These authors concluded that there is a significant genetic susceptibility to RDS in preterm infants[58].

Toxicodynamics - Epigenetics

Epigenetics refers to processes that alter gene expression while the DNA is not changed. Genes are turned on and off and epigenetic changes can influence that. Epigenetically induced changes in the DNA can result in DNA hypo- or hypermethylation, which cause genes not normally expressed to be expressed, while other genes normally expressed are silenced. Environmental factors like diet or chemicals like PCBs can change DNA epigenetically. An example is the stable epigenetic changes of genes in the baby, that took place during the first trimester of pregnancy caused by the Dutch Hungerwinter from November 1944 - May 1945. These changes resulted in more obesity, diabetes, cardio-vascular disease and cancer. Because development is so fast during embryonic and foetal life, with many genes involved, environmental hazards to the baby in this period are easier to occur. Recently research is investigating epigenetic changes in DNA by chemicals during pregnancy and early postnatal period that cause later obesity (OBELIX)[66]; also a project started on exposure to chemicals during the perinatal period with effects that occur later such as autism and ADHD (project DENAMIC)[67]. Interestingly Mitra and others describe the silencing of the TSGA14 gene caused by both organochlorine pesticides and PCBs perinatally[59].

Discussion

The differences between children and adults are seen in a range of susceptibilities to environmental factors and vulnerabilities to certain exposures. A health effect may occur and manifest itself right at the moment of exposure or later during life at other stages of development or even after completion of the development stages. All the different stages of development qualify as a critical stage as in each period there are environmental stressors that can lead to adverse health effects.

It was concluded already in the 1990s that the combination of susceptibility and the additional opportunity to be exposed to certain environmental stressors can increase health hazards to children[60].

There is a need to identify health effects during the critical periods of development of a child. Techniques to assess health risks for children can be developed using information on how children differ from adults. Almost for each compound a period of potential harmful impact can be indicated. Susceptibility testing needs to be done on a compound by compound basis as organs change from foetal through puberty stages[5]. In addition, the interaction between compounds plays a role. The exposure to mixtures of compounds is an additional complicating factor in judging children's susceptibility in real life. Exposure to environmental agents during these vulnerable periods can cause effects that may be very severe and long-lasting. Knowledge about the windows of vulnerability has to be increased.

The available knowledge should have policy implications. It would benefit children's environmental health to have specific policy measures to prevent exposure to harmful compounds during certain developmental periods. These policy measures can use knowledge which is associated with the following topics: 1) pharmaceutical research, 2) cascading effects, 3) use of thresholds and safety factors, 4) study design, 5) sensitive groups.

Ad 1) There is more knowledge on pharmaceuticals than on environmental compounds. Pharmacokinetics of compounds can differ extensively between children and adults due to physiological differences. Also, the immaturity of enzyme systems and clearance mechanisms are different between children and adults. The extrapolation of adult dosimetry estimates to children is uncertain, especially at early postnatal ages. This uncertainty of extrapolation is even greater for exposure to environmental compounds. While there are few data for environmental toxicants in children, there is a wealth of such data for therapeutic drugs. Research has compared pharmacokinetic parameters between children and adults for many drugs. A comparison of child and adult pharmacokinetics function across a number of cytochrome P450 (CYP) pathways, as well as certain Phase II conjugation reactions and renal elimination has been done. It has been pointed out that in premature and full-term neonates many drugs tend to have 3 to 9 times longer half-life than in adults. The difference disappears by 2–6 months of age. In contrast, beyond this age, half-life can be shorter than in adults for specific drugs and pathways. These lessons learnt from pharmaceuticals could be applied to environmental compounds. Research has to focus more on this relationship between pharmaceuticals and environmental compounds.

The substrates metabolized in the liver by P450 enzymes show even more differences in different age groups. The elimination is slower in infants, but rapid elimination compared to adults was seen in children of 6 months to 12 years of age. These age differences show that not all ages of children are alike, and children in some cases, and at some stages, may be able to eliminate xenobiotics more efficiently than adults.

Ad 2) One effect can lead to another. Animal experiments have shown that the blood brain barrier becomes more permeable after oral administration of pesticides[61]. Such situations could lead to neuronal damage by other toxins that can enter the brain cells or affect other nervous system cells. This could lead to other health effects later in life. These cascading effects can be seen in children as well.

Ad 3) A reason of concern in children's environmental health is the use of thresholds. In science we tend to stick strictly to thresholds as means to build and enforce policy. Literature states that the common used safety factor to protect children may not be adequate for certain chemicals in the early postnatal period[16]. But the examples of lead and mercury have shown that thresholds are not very valid for a long period of time, as scientific knowledge progresses. The last decades policy makers lowered the thresholds for those compounds several times. Thresholds that are based on adult studies should be considered for children. Consequently, there is a need to focus and increase research on multiple low-level environmental contaminants.

Ad 4) In research we have too many false negative results. This is not acceptable in research on children's health, as we need to protect children to avoid adverse health effects later in life. We need to reconsider study design and the use of statistics (e.g. lower significance levels) to prevent false negative results and give more support to the precautionary principle in children's environmental health.

Ad 5) Daston argues that the toxicokinetic perspective helps to identify a specific age group of particular concern by reviewing chemical-specific and age group-specific data. For each age group more research on compound specific data on toxicokinetic mechanisms, like absorption, distribution, metabolism or excretion is needed. This is predominantly needed for premature and full term neonates as they show from birth through the first several months the clearest differences with children in other age groups and with adults[31].

Each age group deserves its own attention. The age group (6 months to 2 years) is important as this group has greater hepatic extraction and shorter chemical half-lives because of larger liver size per body weight[16,34].

The foetus lives in a critical time period as most chemicals cross the placenta. Enzymes present in the placenta or in utero are cause of chemical metabolic activation.

Early detection of exposures early in life provides important information on a potential lifelong impact on health of a person. The characterisation of the relation between health risks and exposures helps to understand better the relationships between multiple environmental factors and complex diseases such as asthma and obesity[62,63].

Besides the importance to look at different age periods it is also important to study different groups of chemicals. It is desirable to study the effects in children by potential neurotoxic compounds because the nervous system has a long period of development until adolescence[65]**.** It is known that 25% of 70,000 commercial chemicals in use in Europe has neurotoxic potential. Only 10% of those have been tested for neurotoxic effects. A smaller percentage of chemicals is tested for its effects on children. There is a big knowledge gap to fill.

A few words are needed to clarify that children are in some cases of exposures better off than adults. The ability to detoxify and excrete toxins differs from adults and this can be sometimes protective for children. The difference is sometimes to children's advantage, but more frequently children are not capable to excrete toxins. In this case they are more vulnerable than adults[17,64].

Conclusions

Bearer summarised back in 1995[12] that children and " their exposures are different, their pathways of absorption are different, their tissue distribution is different, their ability to biotransform and eliminate chemicals is different, and their bodies respond differently to environmental chemicals and radiation". Each of these differences is dependent on the developmental stage of the child.

One can plea for consolidation of our knowledge into policies with current safety measures to protect children. However, a greater scientific effort is warranted to fill the knowledge gaps in order to improve children's environmental health. The motivation to study children's environmental health is to help avoid surprises like those in the past such as DES, Thalidomide or valproic acid.

Public health programs that focus on the most important overall causes of death in society may miss the most frequent causes of death in children or for that matter in foetuses. The focus on overall death rates may hide trends in children's mortality associated with specific causes. The same is true for morbidity trends and causes. There is also the issue of early foetal loss which is badly recorded almost anywhere.

It is not useful to look only at dependency of individual compounds when health effects are evaluated. Children's vulnerability has to be seen in a broad analytical perspective. Associations to vulnerability may vary, depending on modifying factors, which can be host characteristics, co-exposure to other contaminants or social-environmental factors, including stress and cognitive and emotional stimulation[19]. The targets for xenobiotics develop during the embryonic, foetal, neonatal and childhood periods, causing age-dependent differences in effects. Toxicity depends on exposure to a wide range of compounds and the production of toxic intermediates, that is related to the progress of development of enzyme systems, making neonates sometimes to be less vulnerable than older children or adults.

The overall conclusion is that knowledge on children's vulnerability and susceptibility is insufficient. In order to protect children better we have to work on preventive policies, to use precautionary approach, to produce more child specific research, and to use better testing methods in children's environmental health. We need to collect sufficient integrated knowledge about complex systems with multiple exposures and about a range of biological effects in the different developing windows of time in children, including the foetal period.

In order to make some real progress we need to develop integrated policy actions related to research, prevention and societal structure. Children's environmental health needs to become an adult science within society.

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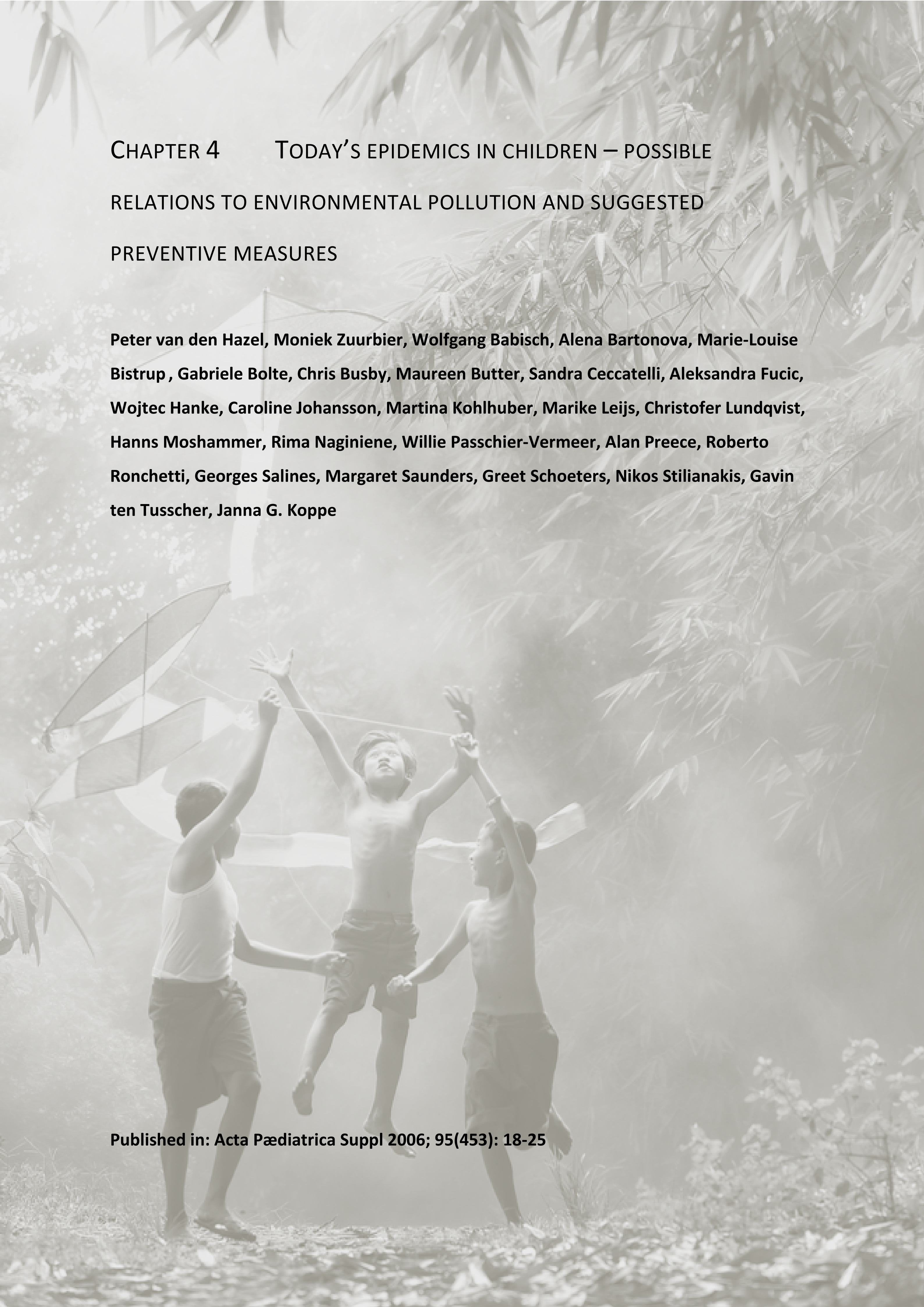

CHAPTER 4 TODAY'S EPIDEMICS IN CHILDREN – POSSIBLE RELATIONS TO ENVIRONMENTAL POLLUTION AND SUGGESTED PREVENTIVE MEASURES

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Published in: Acta Pædiatrica Suppl 2006; 95(453): 18-25

Abstract

Background: Facts and hypotheses on the relationship between some children's diseases or disorders and external stressors during the developmental stage of a child, both prenatally and postnatally are described in literature. In this paper the following changes in patterns and causes of the main childhood illnesses are summarized and recommendations for actions are made.

- Prematurity
- Intra-uterine growth restriction
- Testicular dysgenesis syndrome
- Type I and Type II diabetes
- Asthma, atopy and hay fever
- Autism
- Attention deficit hyperactivity disorder (ADHD)
- Learning disabilities
- Cancer
- Obesity
- Hearing problems

Results: Literature provides a growing amount of information on changing patterns in childhood diseases.

Conclusions: The following recommendations for action are formulated:

- Immediate research on endocrine disrupters in relation to prematurity
- Diabetes: avoid Maillard Compounds in liquid baby food and in food in general: promote breastfeeding
- Asthma: avoid exposure to smoking, the use of chemical household products, dioxin and dioxin-like chemicals, and avoid air pollution with high levels of particulate matter, especially around conception, during pregnancy and in the first years of life
- Autism: more research on incidence and causes
- ADHD and learning disabilities: more research on prevalence and causes. Preventions: 1) preconception counselling to avoid potentially harmful substances; 2) controlling and further lowering levels of polychlorinated biphenyls, lead and methyl mercury

- Cancer: promote breastfeeding, carry out research into effects of foetal exposure to internal fission-product radionuclides
- Obesity: stop smoking in pregnancy, avoid parental obesity, longer night sleep
- Hearing problems: lower noise levels in discothèque s, promote the day-evening-night level to avoid noise (longer night sleep)

Keywords: Children, environment, health, epidemic

Introduction

Health problems in children that are related to environmental contaminants may follow from developmental disturbances in intra-uterine life or in the first years of life. This article describes facts and hypotheses on the relationship between some children's diseases or disorders and external stressors during the developmental stage of a child, both prenatally and postnatally. During growth and development the organs of children may be affected by exposure to harmful environmental stressors. The first trimester of pregnancy is a period of organogenesis. Disturbances due to exposure to agents that damage or control the morphology of developing tissue can for example cause hypospadias and gastroschizis, obesity, or autism. Learning disabilities and attention deficit hyperactivity disorder (ADHD), and trans-sexuality may be caused by interference during the second trimester, prematurity in the second and third trimester and intra-uterine growth retardation and cancer in all three trimesters of pregnancy. Diseases related to autoimmune phenomena such as type I diabetes, and to allergic diseases such as asthma and hay fever might have their roots in pregnancy, but the first year(s) of life are important as well, which also seems to be the case for ADHD. These developmental effects can follow from intrinsic subtle heritable genetic or genomic disturbances or from hormonal or hormone-mimicking exposures.

Socioeconomic factors have an influence on every stage of a child's life. Therefore, socioeconomic disparities have to be considered in the relationship between environmental exposures and children's health. A brief overview of the impact of social inequalities is given in a separate contribution to this supplement, entitled ‘Children’s environmental health: why should socio-economic disparities be considered?’

Prematurity

There has been a rise in prematurity in the last decade. Eight percent of all deliveries are premature, which means about 500 000 in Western Europe each year. Prematurity is an important public health problem with health consequences later in life. Emotional costs for the individual mother and hospital costs for society are high for every case of prematurity.

It is well known that socioeconomic factors can play an important role[1]. A 40% increase in prematurity in the last decade in the north of Belgium (Flanders) cannot be explained by changes in the four most well-known determinants such as multiple pregnancies, obstetric interventions such as early caesarean sections, the use of assisted reproduction techniques, or maternal age[2]. An increase is also seen in many developed countries including France[56], USA[57] and Canada[58]. An effect on the neuro-endocrine axis, resulting in a lower progesterone level, is hypothesized to be a risk factor. This is supported by animal experiments[3]. It is plausible that this increase in prematurity is the female counterpart of the testicular dysgenesis syndrome and may be caused by endocrine disrupting chemicals (EDCs) (see below), or by direct effects of exogenous hormone-like substances such as phthalates during the pregnancy[4]. Prevention of what triggers premature delivery is very important.

To clarify this it is recommended to monitor endocrine disrupting chemicals (EDCs) in pregnant women with a threat of premature delivery and in their mothers (analogous to the DES story). This research should also be carried out in different regions of Europe and these regions must be directly involved in research and hypothesis formulation.

Intra-uterine growth restriction (IUGR)

Intra-uterine growth restriction (IUGR) is a pathological decrease in the rate of foetal growth, resulting in a foetus that does not achieve its intrinsic growth potential[5]. Another definition is all babies with a birth weight below the 10th percentile for gestational age and sex[59]. Many pollutants (including smoking, alcohol, drugs and medicines) used by the mother or accumulated in her body fat can negatively influence growth of the baby. IUGR can contribute to adult diseases such as cardiovascular diseases, diabetes, renal diseases, disorders with high blood pressure, high triglycerides and high cholesterol.

Thus, some of these adult diseases may have a foetal origin[6]. Both abnormal foetal programming and anatomical changes in the foetus can result in disease later in life. Negative effects on blood pressure in later life might also be based (besides effects of an anatomical change in vasculature) on a disturbance of the cortisol/cortison ratio. This ratio may be influenced by the inhibition of 11 beta-hydroxysteroid dehydrogenase type 2 in the placenta by pesticides or organotins resulting in higher cortisol levels in the baby[7,8]. IUGR babies are often born prematurely. In a retrospective study on a group of growth retarded babies with birth weights over 1500 g but under the tenth percentile, in relation to gestational age 35% have an unknown cause of the growth retardation[25].

Studies from the Czech Republic have shown an impact of particulate matter on IUGR in a highly polluted area. Mothers who were exposed to particulate matter (PM10) annual levels above 40 µg/m3 or annual PM2.5 (particles smaller than 2.5 µm) levels above 27 µg/m3 during the first month of gestation had a significantly increased risk of giving birth to a child with IUGR[55]. Studies based on a four-year dataset showed similar results. The risk of IUGR was 1.44 higher (95% CI 1.03-2.02) in the group of mothers exposed to mean PM10 levels between 40 and 50 µg/m3 compared to those exposed to mean PM10 below 40 µg/m3 during the first month of gestation. Levels above 50 µg/m3 increased the risk to 2.14 (95% CI 1.42-3.23)[34]. Further analysis showed a highly significant increase of IUGR with exposure to a range of carcinogenic polycyclic aromatic hydrocarbons (PAHs) above 15 ng/m3. The adjusted relative risks were 1.59 (95% CI 1.06-1.39) for medium levels of carcinogenic PAHs and 2.15 (95% CI 1.27-3.63) for high exposure levels. Interestingly, all these effects were associated with exposure during the first month of gestation. Molecular epidemiology studies suggest involvement of various biological mechanisms affecting birth weight and IUGR. The available data do not allow precise identification of specific pollutants and the effect of the timing of exposure; thus more studies are warranted with specific focus on the carcinogenic PAHs.

Research on the association between IUGR and adult disease is needed. Further prospective studies with long-term follow-up are warranted in this group of babies.

Testicular dysgenesis syndrome

The increases in hypospadias, cryptorchidysm and testicular cancer and the decline in sperm count is hypothesized as part of the testicular dysgenesis syndrome[9,10]. Endocrine disrupting chemicals (EDCs) are blamed for possibly contributing to the increased prevalence of this syndrome during recent decades, together with life-style factors and genetic background. A very high percentage of hypospadias has recently been noted in a population based study from Denmark with a prevalence of 4.6% [11]. Foetal and placental growth impairment seem to share a pathogenetic factor with this abnormality, with an increased level of follicle stimulating hormone three months after birth in the babies with hypospadias which may indicate a shortness of testosterone.

Transsexualism

A combined female and male effect of EDCs on the offspring (possibly in combination with infection) is trans-sexualism. This disease also fits with the concept of endocrine disruption. Recently a rise was reported in Sweden by Olle Söder[12]. In addition, in the offspring of mothers on anticonvulsant drugs (phenobarbital) a significant increase in trans-sexualism has been found[13]. For action, see above under prematurity.

Type I and type II diabetes

In the last three decades there has been an increase in auto-immune diseases such as type I diabetes in young children. The prevalence of type I diabetes is about 1.5 per 1000 children. There is a shift in HLA-type; less HLA type: Dr3, Dr4 and more Dr3 or Dr4 alone. Gillespie suggested that the increase of type I diabetes must be the result of exposure of a genetically susceptible subgroup of the population to an environment that is increasingly conducive to diabetes development: ''The heightened proportion of lower risk haplotypes and decreased median age at onset of the disorder are suggesting an environmental contribution on diabetes development.''[15] Interesting is the hypothesis that air pollution, especially ozone, plays a role in development of type I diabetes, because of oxidative damage to the beta cells in susceptible children[14]. Finland and Sardinia are known to have high prevalences of diabetes.

Type II diabetes in children is rapidly increasing and can be considered a new epidemic[16]. The increase in type II diabetes is assumed to be related to obesity; however, there are indications that type II is also based on an auto-immune phenomenon. Both types of diabetes are aggravated by consumption of Maillard compounds (caramelized sugars and proteins present a.o. in liquid baby formula)[17-19]. Advanced glycated end (AGE) products or Maillard compounds are formed during cooking or container sterilization at 110-120^{o}C during 10-30 min. Chips or French fries, crackers and crisp bread are known to be high in AGEs, as are some liquid baby formulas, due to sterilization. Breastfeeding protects against diabetes. Formula, on the other hand, contains a protein from cows that has been suggested to be involved in the development of type I diabetes. Dietary measures and increased activity can prevent or postpone the development of type II diabetes, see also below under obesity. Breastfeeding must be supported as a means for preventing diabetes development.

Asthma, atopy and hay fever

There is a steep increase in allergic diseases (allergic asthma, hay fever and atopic ermatitis) and atopy in many countries around the world. This is less clear for non-allergic asthma, but it is difficult to separate between the different causes of asthma and often the causes are mixed. In this section mainly the nonallergic mechanisms of asthma are discussed.

A sharp increase in asthma is described in the UK between 1970 and 1990, from 6% to 12%, as well as an increase in hay fever from 12% to 23%. This increase seemed to continue until the beginning of this century. In recent years it has levelled off to a stable but high level. Lung development hampered by intra-uterine growth retardation results in lung dysgenesis, making the baby susceptible to the development of asthma. A good example is given in the recent publication in JAMA by Maureen Hack, who found a 21% prevalence of asthma in children born with birth weights under 1000 g, while the prevalence in Cleveland, Ohio in normal birth weight children is 9%[20]. In several regions of Europe it is also 9%. Data from south-west Germany, however, are around 5%. This is partly explained by the tradition in Germany not to use the word 'asthma'. There is a sharp difference of incidence between Germany and the Netherlands which is probably due to medical diagnosis tradition. There is some levelling off described in Switzerland and Rome, Italy. In Germany the prevalence of hay fever (and the condition atopy) has stabilized at 35%[21,22].

A negative effect on lung development has been described in relation to in-utero exposure to smoking, dioxins[60,61], the use of different chemical household products by the mother[23] or air pollution especially the polycyclic aromatic hydrocarbons (PAHs) and volatile organic compounds (VOCs). Also allergies are described more in hotspots with dioxin pollution, while atopy is related to smoking of the mother[24].

Prevention

A further reduction of exposure to smoking, the use of cleaning products containing synthetic chemicals, to dioxins and dioxin-like chemicals, and avoiding air pollution and VOCs around conception and during pregnancy as well as in the first years of life are important to reduce or at least control the prevalence of asthma.

Autism

An increase in prevalence of autism has been suggested. However, this might at least partly be explained by an increased awareness of autistic symptoms and a shift in diagnosis, and further studies of the incidence of autism are warranted[25]. A UK publication states that a seven- fold increase (0.3 to 2.1/1000) for autism was seen from 1988 to 1999. It has been reported that autism can be related to congenital rubella, as is the case with type I diabetes,

and also to thalidomide when used at day 49 after conception[26]. This indicates that events occurring early in pregnancy can influence the development of the disease. For example, environmental chemicals which may influence the immune system may contribute

to the ontogeny of an autoimmune process in a genetically susceptible foetus, possibly in combination with an infection such as a streptococcal infection. In line with this hypothesis, a higher prevalence of autoimmune diseases has been described in families of autistic children[28].

Research: The CHARGE (Childhood Autism Risks from Genetics and the Environment) study is a large ongoing case-control study of children with autism or developmental delays. A broad array of exposures and physiological factors are investigated to determine whether particular genes or environmental exposures are associated with symptoms (for details see http://beincharge.ucdavis.edu/).

Attention deficit hyperactivity disorder (ADHD)

The prevalence of attention deficit hyperactivity disorder has been suggested to be increasing. The prevalence of ADHD is high: 3-5% at school age of which 30-60% persists into adulthood. In Germany 1.6% of all children use methylphenidate, the most widely used pharmacological agent in ADHD treatment. A doubling of the use of this drug is described in the Netherlands from 1990 to 1995.
The genetic component of the disease is estimated at 80% and some of the genetic factors involved may overlap with genes influencing autism and dyslexia. Gene-environment interactions are investigated, but no conclusive results have been reported yet[29]. Exposure to lead, PCBs, or nicotine during pregnancy are suggested to contribute to or cause the expression of the phenotype[30,31]. Brain abnormalities have been described in fronto-striatal, temporal and cerebellar volume in neuroimaging studies of children with ADHD. Unaffected brothers and sisters show the same cerebral abnormalities, but not the cerebellar abnormalities[32]. The cerebellum develops mainly after birth, and this might explain why a relation with postnatal exposure to manganese in drinking water and in bottle-feeding formulas has been reported.

Learning disabilities

Learning disabilities defined as an IQ lower than 70 are found in about 1-2.5% of children. Lead, methylmercury, PCBs and dioxins are known intrauterine neurotoxicants suggested to cause a poorer cognitive development[25,26]. Co-exposure to more than one neurotoxic substance is thought to be important in this respect[33]. Examples of such 'Multiple Exposure' include PCBs, PBBs and dioxins with methylmercury and/or lead, and the combination of PCBs and dioxins. Other examples are combinations of different pesticides together, or particulate matter and polycyclic aromatic hydrocarbons (PAHs) acting together as in air pollution[34]. Life-style factors such as smoking, alcohol and drugs are other well-known neurotoxicants[25].

Disturbed thyroid hormone metabolism in both the mother in early pregnancy and later in the developing child might have negative effects on cognitive development[35]. PCBs and other chemicals such as dioxins and PBBs, mercury, DDE, nanochlor and hexachlorobenzene can all have negative effects on thyroid hormone metabolism by lowering T3 levels in the mother. In the second half of pregnancy, when the baby starts to produce its own thyroid hormone, inhibited transport of T3 into the neuronal tissue can have negative effects for development[36-38].

Prevention

Learning disabilities and ADHD might in some cases be prevented by good preconception counselling at an individual level. Recommendations include folic acid supplementation, control of the thyroid hormone status, sufficient vitamin A and the use of food high in anti-oxidants such as broccoli, berries, tea, beets, carrots, olive oil and green vegetables and fish (small)[25]. Smoking and drinking should of course be avoided. At the level of government and industry, suggested actions include controlling and further lowering the levels of dioxins, PCBs, and other persistent bioaccumulating toxicants such as brominated flame retardants, musks, alkylphenols and also metals such as lead and mercury.

Cancer

Childhood cancer is rare, affecting about 1 in 10 000 children each year in Europe. In a recent article in the Lancet, Steliarova-Foucher et al. describe a 1.0% incidence increase per year since the 1970s for the last three decades in children (0-14 years) and 1.5% in adolescents. In particular, for infants the increase of 1.6% per year is significantly more than in the other age groups[39]. The most notable cancer in this age group is neuroblastoma[40,41].

A trend of an increase in brain cancer (1.5% increase annually) as has been reported in the USA has not yet been reported in Europe. This could be a result of better diagnostic facilities such as MRI. It is likely however that there is also a real effect which needs to be monitored by the use of the improved differential diagnosis of neurological childhood disease[43]. In the 1-4 years age group there has been a demonstrable increase in acute lymphoid leukaemia (ALL) of unknown aetiology. Most significant is a positive association with higher socioeconomic status (SES)[44]. Since childhood leukaemia rates have been found to be significantly increased near certain types of nuclear plants, exposure to radio-active fission product isotopes has come under suspicion as a cause. It is now universally conceded that exposure of the foetus to external ionizing radiation (e.g. Xrays) causes childhood cancer.

In order to improve prevention, breastfeeding longer than six months confers some protection against acute lymphoid leukaemia and should be encouraged.

Obesity

The recent epidemic in obesity in children is of great concern, because of the development of type II diabetes early in life as well as other problems associated with overweight. Factors during foetal life and life-style factors, such as less physical activity and more foodstuffs rich in saturated fats and sugars are blamed.

There are indications that factors during foetal life may also affect the appetite centre. The set-point of appetite is optimal for bad environmental circumstances but much too tolerant when food is abundantly present. It is known that conscripts conceived during the height of the Dutch Hunger Winter were exposed to malnutrition (mainly protein deficiency) during the first three months in utero. These conscripts were more obese than controls at age 19 years[45]. Also, later on at the age of 50 years, obesity was found to be related to prenatal malnutrition[46]. It is unknown if other causes of intra-uterine growth retardation, such as pesticides or PCBs which interfere with the functioning of metabolizing enzymes in the liver and with lipid metabolism, may be related to obesity later in life. Leptin levels might give an answer in follow-up studies of cohorts studying effects of these pollutants.

The Avon Longitudinal Study of Parents and Children (ALSPAC) includes a long-term, prospective population-based study studying several aspects[23]. Data from the ALSPAC study show a significant relation between parental obesity (a.o.genetic factors), maternal smoking of more than 20 cigarettes a day during pregnancy, birth weight, TV viewing, shorter duration of night time sleep and catch-up growth between birth and two years and childhood obesity. However, childhood obesity has little effect on future economic, educational and social well-being[47,48]. The finding that smoking in pregnancy is related to obesity in childhood can indicate that other compounds causing oxidative stress can have the same effect.

Hearing problems

It has been estimated that approximately 10% of Europeans suffer from hearing loss[54]. Studies have shown that the proportion of young people with hearing impairment and symptoms of tinnitus is high[49-51]. Congenital hearing impairment affects 0.1% of all live- born children, but is 10 times higher in graduates of neonatal intensive care units[52]. Problems with hearing may result from damage in the perinatal period f.i. by bilirubin in preterm babies, or during intra-uterine life when exposed to high levels of PCBs[30].

Because young people have never been exposed to occupational noise, exposure to leisure noise is a likely explanation for the observed notch at 4-6 kHz in the audiograms, which is typical for a noise-induced hearing loss and tinnitus. Noise levels in discothèques, at rock concerts, from personal audio equipment, in entertainments, from toys and firecrackers can be extremely high and damaging to the ear. Hearing damage occurs either due to continuous and repeated noise over a long duration or due to high bursts of noise of short duration (e.g. impulse noise). Based on the risk damaging criterion which was derived from empirical studies in the occupational environment (ISO 1999), it has been estimated that 10-20% of young people may be at risk for noise-induced hearing impairment due to loud music[53].

Prevention: It is recommended that education of young people about the adverse effects of noise must be improved to make them more sensitive to the hearing issue, and to make them change their behaviour when exposed to loud sound sources of various kinds. The risk of hearing impairment due to loud music can be substantially reduced if average noise levels on the dance floor and at rock concerts is limited to at least below 100 dB(A). Nevertheless, even this value imposes a risk for frequent visitors.
The use of portable audio equipment has increased throughout recent years due to digital recording and mass storage devices. Only devices that fulfil the recommendations of maximum sound levels according to EN 50332[62] should be available on the market.

Summary actions

The following actions are recommended:
. Immediate research on endocrine disrupters in relation to prematurity
. Diabetes: avoid Maillard compounds in liquid baby food and in food in general. Promote breastfeeding
. Asthma: avoid exposure to smoking, the use of chemical household products, dioxin and dioxin like chemicals, and avoid air pollution with high levels of particulate matter, especially around conception, during pregnancy and in the first years of life
. Autism: more research on incidence and causes
. ADHD and learning disabilities: more research on prevalence and causes.
Preventions: 1) preconception counselling to avoid potentially harmful substances;
2) controlling and further lowering levels of polychlorinated biphenyls, lead and methyl mercury
- Cancer: promote breastfeeding, carry out research into effects of foetal exposure to internal fission-product radionuclides
- Obesity: stop smoking in pregnancy, avoid parental obesity, longer night sleep
- Hearing problems: lower noise levels in discothèques, promote the day-evening-night level to avoid noise (longer night sleep).

Acknowledgements

The PINCHE project was financed by the EU DG Research as a Thematic Network in the Fifth Framework Programme, Key Action 4: Environment and Health. QLK4-2002-02395. The organization, ECOBABY, helped making the publishing of the supplement possible.

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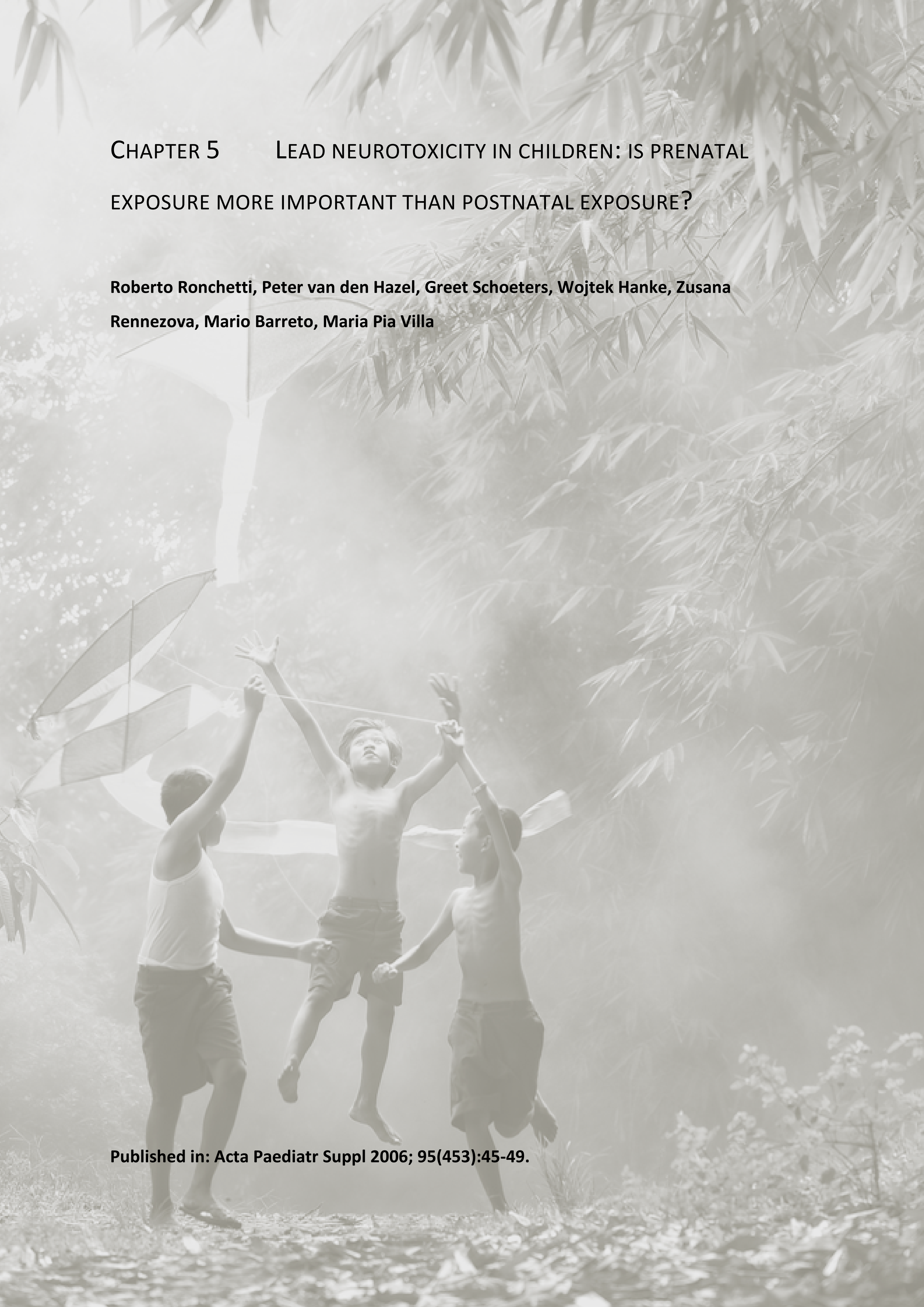

Chapter 5 Lead neurotoxicity in children: is prenatal exposure more important than postnatal exposure?

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Published in: Acta Paediatr Suppl 2006; 95(453):45-49.

Abstract

Numerous studies indicate that low-level lead poisoning causes mild mental retardation and low IQ scores in children. The general mean lead intake in the adult European population corresponds to a reassuring 14% (0.5-56%) of the tolerable daily intake: at this low level of exposure only few children (less than 10%) have blood lead levels (PbB) higher than 10 µg/dl, previously considered the PbB of concern. In more recent years data now suggest that even when 'the lifetime average blood lead concentration' is below 10 µg/dl an inverse association exists with intelligence quotient (IQ) scores. Two-thirds (45-75%) of lead in blood, however, comes from long-term tissue stores and this is especially true for new-born infants and pregnant women. Several data suggest that for lead the main toxic event is prenatal exposure: therefore we should focus our attention on maternal lead stores and whenever possible avoid their mobilization during pregnancy. In this regard we should design appropriate studies to confirm whether dietary supplementations can reduce bone resorption and lead mobilization during pregnancy. The hypothesis that the amount of maternal bone lead stores is the relevant parameter for predicting the level of neurotoxicity of this metal gives some optimism for the future: if we study children whose mothers never underwent high environmental pollution (born after the withdrawal of lead from gasoline) and hence have relatively low bone lead stores we could find that, at the population level, lead has little influence on children IQ scores

Keywords: Children, lead, neurotoxicity, prenatal lead exposure, maternal lead stores

Introduction

Lead exists in the earth's crust, and occurs naturally in the environment through a variety of mechanisms, including volcanic emissions and geochemical weathering. Lead pollution, however, derives mainly from human activities to extract and exploit the metal.

Severe lead exposure in children (blood lead levels around 350 µg/dl) can cause coma, convulsions, and death. At lower levels of exposure numerous studies[1-6] indicate that lead poisoning causes reduced gestational age and weight at birth, impaired growth in children, impaired synthesis of the active metabolite 1,25-(OH)2 vitamin D, impaired haemoglobin synthesis, anaemia, impaired visual and motor functioning, hearing loss, mild mental retardation, low intelligence quotients (IQs) and attention span, reading and learning disabilities, hyperactivity and behavioural problems, antisocial behaviour and delinquency, decreased ability to maintain steady posture, puberty delays, brain, liver, kidney, nerve and stomach damage, both female and male reproductive impairment, and cancer.

Importantly, lead induces its major deleterious effects on health without causing overt signs of toxicity. At the epidemiological level, lead exposure is estimated to account for almost 1% of the global burden of disease: most of its effects involve children of the developing world[7]. In Europe, the World Health Organization (WHO) estimates that nearly 157 000 days of healthy life are lost in children less than four years of age from lead poisoning[8].

What is the 'safe' level of lead exposure in children?

Owing to the reduced use of alkyl leads in petrol and to other interventions in recent decades, blood lead concentrations in children have fallen substantially in a number of European countries (United Kingdom[9], Germany[10], Poland[11]). Lead is also present at low concentrations in most foods. Offal and -molluscs may contain higher levels. The main reason for increased lead intake via foodstuffs is lead contamination during food processing. Over recent decades, thanks to source-related efforts to reduce lead emission and improvements in quality assurance of chemical analysis, the lead level in food has also significantly decreased. Present dietary lead levels are well delineated in SCOOP (2004)[12], a survey reporting that the mean daily lead intake from food and beverages of adult populations from 12 European countries is 0.42 µg/kg bw/day[2]. Assuming a provisional tolerable daily intake (TDI) of 3.6 µg/kg bw/ day, this average lead intake in the adult European population corresponds to a reassuring 14% (0.5-56%) of the TDI[12].

Dietary lead levels are nevertheless less favourable in certain European countries, and in children and subgroups of European adults or children who consume higher quantities of certain foods. In general, the mean blood lead level (PbB) is estimated to be below 5 microgram/dl in Western and between 5 and 10 microgram/dl in Eastern European countries[12]. These general means include children with increased blood lead levels (e.g. > 10 µg/dl) whose prevalence increases significantly when water, soil and dust from the house environment are high and socioeconomic conditions are low. Accordingly, recent studies report that up to 5% of children have blood lead levels > 10 µg/dl in England[13].

We must keep clearly in mind that, notwithstanding the continuous improvement in lead exposure in Europe thanks to the concerted efforts on the part of the regulatory authorities, reducing lead exposure in European children further will inevitably be a costly and challenging task. Are these efforts really necessary or can we be satisfied with what has already been achieved? Even though the level of exposure in Europe is indeed far better today than it was 10-20 years ago, pre-industrial humans had an estimated 100- to 1000-fold lower exposure to lead levels than populations of today[14].

Until recently the most reliable information on the effects of lead exposure came from meta-analysis of studies which assessed an estimated mean decrease in the intelligence quotient (IQ) for exposures greater than this level (loss of 2-3 points for an increase from 10 to 20 µg/dl in PbB[14,15]). Until recently, 10 microgram/dl was therefore considered the 'PbB of concern'. In a recent study, however, using the more meaningful 'lifetime average lead blood concentration' to assess its consequences on IQ, Canfield et al.[4], while confirming a loss of 4.6 points of IQ decrement for each increase in PbB of 10 µg/dl, found a larger effect of a loss of 7.4 IQ points for a PbB change between 0 and 10 µg/dl. These data are consistent with the interpretation that the effects of lead on IQ are proportionally greater at lower lead concentrations and strongly suggest that the relationship between PbB and IQ is non-linear

[2] bw= body weight

with the greatest interval decrements in IQ at PbB less than 10 microgram/dl[4]. From these data we deduce that, for lead, the NOAEL (non-observable adverse effect level) and the LOAEL (lowest observable adverse effect level) are both equal to zero[4]. Hence, there seems to be no threshold below which lead is not toxic to the developing central nervous system[5].

If this is so, then the majority of European children are at risk of losing several IQ points owing to the present level of lead contamination. Lead should therefore still be considered a danger which requires interventions and resources.

Are blood lead levels the best biomarker of lead toxicity?

We report above ample data from the literature showing that blood lead concentrations are inversely and significantly associated with IQs. Even when 'the lifetime average blood lead concentration' is below 10 µg/dl (until recently the 'level of concern'), this inverse association seems to exist, and has become even stronger. These studies, on the basis of the significant and strong correlation between 'sub-clinical' blood lead levels and adjusted IQs, assumed that the blood lead level is the biomarker of the 'internal dose' biologically effective for neurotoxicity.

Some evidence nevertheless suggests otherwise. In the paper by Canfield et al.[4], the plots of blood lead levels and IQ scores as covariate disclose tremendous scatter around the regression lines with low values of the coefficient of correlation, suggesting that children vary in their response to these low levels of exposure[16]. The potential sources of individual variability in the lead-associated neurodevelopmental risk are many, among them gender, genetic polymorphisms involved in lead metabolism and co-exposure to other toxicants.

One explanation focuses on toxicokinetic and toxicodynamic factors. While blood lead levels are largely influenced by concurrent or recent lead exposures it is also true that the blood lead level in general represents only the existing equilibrium between endogenous and exogenous sources of lead. In normal subjects (adults and children) lead leaves the blood to be stored in bone (or other tissues) and continuously re-enters the blood from tissue deposits; this happens under the influence of several physiological or pathological factors and in these movements lead simply mimics the behaviour of calcium.

By measuring the ratio between different lead isotopes in the blood (four different isotopes of lead exist in nature and their ratios vary in different parts of the world) one research group was able to estimate the contribution of lead stored in bones to the actual blood lead concentration in adult women (20-30 years) who emigrated to Australia from Eastern European countries[17]. These studies demonstrated that in normal adult women two-thirds (45-75%) of blood lead comes from long-term tissue stores: bone lead becomes an even more predominant source of PbB when lead exposure from external sources is low.

We therefore conclude that in general ingested lead contributes to the amount of lead in circulating blood by no more than 35%[18]. This is especially true for new-born infants and women during pregnancy. In a study conducted by Gulson et al.[18] in new-borns during the first months of life, the amount of lead coming from maternal milk, from cow's milk and from beikost contributed only 35% to the lead in circulating blood. An interesting finding in these children was that lead excreted in the urine was three times higher than the dietary lead intake. These findings were explained by the rapid bone turnover which takes place in the new-born; the whole skeleton turns over during the first 12 months of life and this causes a large mobilization of bone lead stored during pregnancy.

PbB in infants is mainly the expression of skeletal lead; the dietary contribution to the PbB level is normally of minor importance especially because at that age the intake of dust is negligible and the lead intake/excretion balance is negative.

During pregnancy, starting from the early stages, maternal calcium requirements increase and continue to rise until delivery[19]. A full-term infant accumulates over 30 g of calcium during the gestation period, most of which is assimilated into the foetal skeleton in the third trimester. Maternal calcium needs are maintained by a fall in the serum albumin concentration[20] and increased gastrointestinal absorption of calcium[21,22], but most importantly through increased bone resorption[23,24]. Increased bone resorption during pregnancy facilitates the active transfer of calcium to the foetus but maternal lead follows a transfer pattern similar to that of calcium and without any barrier at the placental level[25]. This is particularly true during the last part of pregnancy and the lactation period when maternal PbB increases by 25-100%; this increase derives from the further mobilization of lead from bones[26].

The various body compartments in which lead is dissolved are in constant dynamic equilibrium; the bidirectional constants of equilibrium linking different compartments can be very high (rapid lead exchange, e.g. between erythrocytes and plasma) or very low (slow exchanges, e.g. between bone and blood), but in general mother and foetus can be considered separate compartments of the same system throughout pregnancy and these compartments remain in equilibrium. It is not surprising, therefore, that when pregnancy ends a match exists between the blood lead concentrations in the mother and child, and between the bone lead concentration in the two organisms[27].

Because blood lead levels in the new-born or child at different ages come under the influence of the child's bone lead stores, they tend to remain high if the mother was highly contaminated and vice versa. These considerations imply that if we measure PbB several times during the first few years of life ('lifetime exposure'), we really measure a variable that is heavily influenced by the child's bone store, a measure that in turn mirrors the mother's bone stores. Hence evidence that lifetime (postnatal) lead exposure is inversely linked to IQs does not, per se, show that the brain damage took place postnatally; lifetime exposure might simply be the proxy for prenatal lead brain exposure.

In conclusion, maternal bone lead concentration determines the amount of the foetal bone lead stores and in parallel the amount of lead deposited in the foetal brain tissue; foetal brain lead could be the variable associated with lead's neurodevelopmental toxicity.

Effects of prenatal lead exposure

Prenatal lead exposure is a major risk factor for impaired foetal and infant development[28-32]; during the early embryonic and foetal stages lead can pass through the placenta to affect the nervous system[33]. Various toxic mechanisms are purported to explain the lead-induced injuries that damage the developing brain when the brain and spinal cord are growing and differentiating[28-32].

Neurodevelopmental events are initiated in the embryo, 'fine-tuned' in the foetus, and elaborated further during the postnatal years into adolescence. It is becoming increasingly apparent that the level of mental acuity (or lack thereof) witnessed in later life is linked to the environments encountered during these formative periods of developmental neurogenesis.

Evidence underlining the importance of early environmental events comes from the results of in vivo studies in adult rats exposed to Pb during the perinatal period[34,35]. In the developing nervous system refinement and stabilization of neuron connections and the fine tuning of synaptic connectivity are dependent on the repetitive activation of certain biochemical signalling events; this process increases the synaptic strength that underlies learning processes in the mature nervous system (long-term potentiation). In a study investigating early lead toxicity, Gilbert et al.[34] propose that the persistent impairment in cortical plasticity found in adult animals after early exposure to lead may result from toxicant-induced perturbations of activity-dependent plasticity during critical periods of nervous system development.

The foregoing observations clearly do not necessarily exclude the possibility of postnatal lead toxicity. Scientific data which allow us to decide whether, at the epidemiological level, prenatal or postnatal lead exposure is the main neurotoxic event, are scarce. The two possibilities are probably not alternative in the sense that both prenatal and postnatal lead exposure could be important in single individuals, according to the modalities (amount, timing, etc.) of lead exposure itself.

From the viewpoint of prevention, however, the two hypotheses suggest completely different actions. If the determinant toxic event is postnatal exposure, we must operate on the environment, with interventions that as we underlined before, are costly, difficult and of uncertain usefulness. If the determinant main toxic event is prenatal exposure we should direct our main attention to the amount of maternal lead stores and if possible avoid mobilizing these stores during pregnancy.

What actions are needed for the prevention of lead neurotoxicity?

The amount of lead bone deposits depends on lifetime exposure. Lead ingested with air, foods or drinking water is initially taken up by erythrocyte-plasma compartments. With time lead is incorporated into various tissues, especially into bones where lead competes with calcium for the formation of hydroxyapatite crystals. In the bones, lead can be retained indefinitely, with a half-life of the order of decades[36]. Lead can be partially mobilized from bones during aging or other conditions (including osteoporosis, fractures, menopause, and pregnancy).

These data underline that the main way to reduce bone lead stores in young women is to reduce lifetime exposure. Notably, the epidemiological data appearing nowadays in the literature refer to women who underwent high exposure before lead was withdrawn from gasoline, in about 1990. If we study the children of mothers who never underwent high environmental pollution and hence with lower bone lead stores, we will presumably find less severe lead-related IQ deficits.

To answer the question whether we can avoid or reduce lead store mobilization during pregnancy we must consider two sets of data. First, we should consider a set of experimental data demonstrating that nutritional and social factors, together with other unrecognized environmental situations, can deeply modify blood lead levels; the fractional absorption of lead from the environment (referred to as external dose) and the mobilization of lead stores (described as internal dose) can be modified by nutritional status. At least four nutritional conditions increase the effects of environmental lead exposures: irregular food intake (i.e. periods of fasting), high fat intake, marginal calcium ingestion, and subtle iron deficiency[37]. The data are nevertheless difficult to interpret because these marginal nutritional conditions are more common among subpopulations at greater risk of environmental exposure to lead.

Secondly, starting from the notion that fasting and nutritional deficits modify PbB and Pb distribution, studies have been conducted to assess whether a maternal diet rich in calcium could significantly reduce the mobilization of the maternal lead bone stores during pregnancy and lactation. In their study investigating patterns and determinants of blood lead during pregnancy, Hertz-Picciotto et al.[38] reported that higher calcium intake was inversely associated with blood lead levels in the latter half of pregnancy. Also, the paper by Janakiraman et al.[39] documented that dietary calcium supplementations decreased bone resorption in the last trimester of pregnancy. A recent trial of Téllez-Rojo et al.[40] found that during pregnancy plasma lead levels were inversely related to dietary calcium intake; yet only recently has the idea that dietary supplementation can reduce bone resorption and lead mobilization during pregnancy received due attention. Moreover, calcium could be only one of the many candidate substances (iron, vitamin D, phosphates and probably many more), which could be used in various combinations to attain the maximum result.

Conclusions

Despite the progressive abatement of lead in the environment, concern continues over lead-engendered IQ impairment in children.

The 'no lower threshold' notion for this toxic substance forces us to engage in costly efforts aimed at reducing lead exposure levels in children to near zero. Because this is an almost impossible task we should pessimistically envisage that the toxic effects of lead on health will never be overcome.

Conversely, if maternal bone lead storage is indeed responsible for lead-related brain damage in children, then we should focus our efforts on limiting lead mobilization during pregnancy. In the meantime, when women born after the environmental fall in lead in the past 15-20 years become mothers, early lead neurotoxicity in Europe will on its own account almost disappear.

Acknowledgements

The PINCHE project was financed by the EU DG Research as a Thematic Network in the Fifth Framework Programme, Key Action 4: Environment and Health. QLK4-2002-02395.
The organization, ECOBABY, helped making the publishing of the supplement possible.

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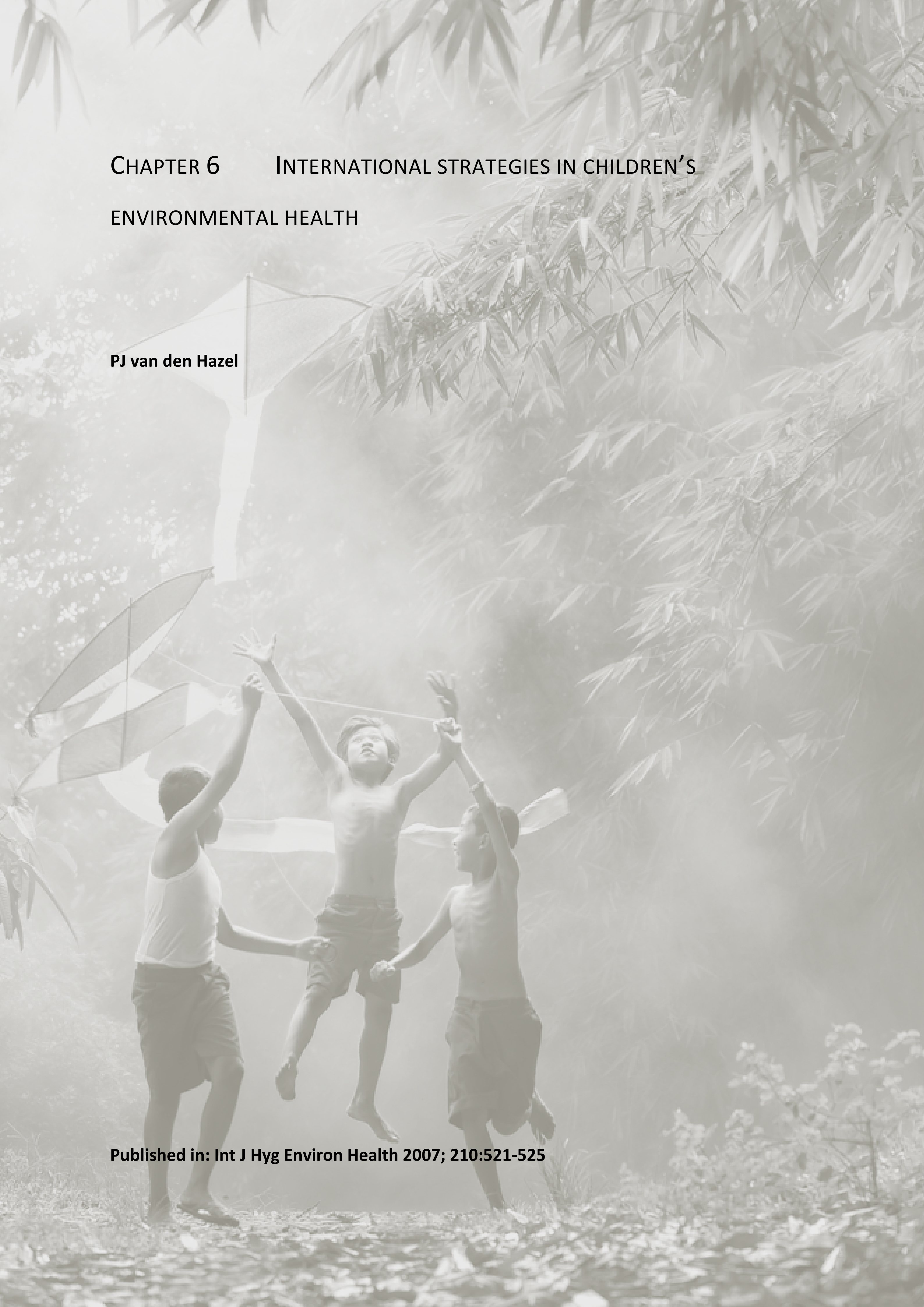

CHAPTER 6 INTERNATIONAL STRATEGIES IN CHILDREN'S ENVIRONMENTAL HEALTH

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Published in: Int J Hyg Environ Health 2007; 210:521-525

Abstract

In recent years the fact that children need to be protected against environmental stressors has been widely accepted by decision- and policy-makers. However, there is not yet a good or unified strategy to improve children's health by improving their environment. The Policy Interpretation Network on Children's Health and Environment (PINCHE) network suggested a range of recommendations to support the development of a strategy on children's environmental health on different levels of authority: international, national, regional, and local. There clearly are indicated bottlenecks in the thematic network approach. Three main challenges for success have been identified; first is data comparability. PINCHE identified the need for standardisation of environmental assessments, classification of childhood respiratory diseases and symptoms, and a format for defining diagnostic groups and presentation of data. Second, data accessibility must be addressed. Accessibility of the scientific data to the general public, including health professionals and policy makers, is important and requires translation that is often lacking. Third there is a requirement to harmonise definitions and methods to ensure that scientists and authorities speak the same language. Obstacles are the subsidiarity principle, fragmentation of available knowledge or lack of expertise and purpose at various levels, the lack of political commitment or input and economic issues.

Keywords: Children, Environment, Health, Policy, Capacity building, Education

Introduction

The UN Millennium declaration is quite clear on the protection of children. It states: ''we must spare no effort to free all our children and grandchildren from the threat of living on a planet irredeemably spoilt by human activities''. At the World Summit on Sustainable Development in Johannesburg the declaration said: ''conclusions listed environmental health measures to protect the child in areas of water, energy, health and agriculture''[1]. In addition, the European Commission recognised that scientific results can lead to not only more research, but also to new policies. The European Commission put their ideas on protecting children in a strategy document in 2003[2]. This strategy plan indicated the priority areas of children's environmental health in Europe. It was followed by an action plan[3] as the next step in the process of the European Union to protect children's environmental health. The World Health Organisation produced at the same time a Children's Environment Health Action Plan for Europe (CEHAPE) for the Ministerial Conference in Budapest[4]. These planning activities reflected a political will to improve the situation. Besides the policy field within the scientific community, the science–policy interface in the field of children's environmental health has recently gained more attention[5-8]. In parallel, the scientific community realised that they had to pay attention to the translation of their scientific results for policy makers.

The scientific community founded a consortium of 30 organisations in 14 countries of the EU and two countries outside the EU to form a network of organisations working on children's environmental health. The network was called Policy Interpretation Network on Children's Health and Environment (PINCHE)[9]. The participants consisted of different kinds of organisations including universities, research institutes, intergovernmental organisations, nongovernmental organisations, industry, and consumer groups. The European Commission funded this network within the Fifth Framework Programme.

The objective of the PINCHE-project was to create a widely supported basis for public health policy related to improving children's environmental health in Europe as well as to establish regulatory mechanisms to achieve that goal. The network's policy recommendations are based on results from scientific research.

This paper describes the need for the development of a strategy to deal with children's environmental health on different levels of authority and in different communities and disciplines.

Problem

In recent years the fact that children need to be protected against environmental stressors has been widely accepted by decision- and policy-makers. However, there is not yet a good or unified strategy to improve children's health by improving their environment.

There are more than 163 million children in Europe under the age of 19 years. More than 35 million children are in the age group of 0–4 years, which is a vulnerable period in life. It is generally accepted that children's exposure, metabolism, susceptibility, life expectancy and political standing differ from those of adults. Literature describes different windows of susceptibility in childhood in which children can be affected. But even preconception exposure and in-utero exposure to a range of environmental stressors can cause health effects. Different child specific activities and child settings complete the picture of the relation between children's hazards and health effects. In modern times the nvironmental risks have changed as compared to those of the past. The unsafe use of chemicals, inadequate toxic waste management, and environmental degradation of the residential areas are some of the examples of modern environmental risks to children. Additional threats will be seen in the near future, such as global climate change, ozone layer depletion, radiation and contamination by persistent organic pollutants. The increased knowledge on these issues is reflected in some of the recent reports by the World Health Organisation[10], 2004), the European Commission[2] and scientific reports such as those from the PINCHE network[9,11].

Actions

The PINCHE network proposed a range of recommendations to support the development of a strategy on children's environmental health on different levels of authority: international, national, regional and local. Some of these recommendations will be discussed in this paper.

It concerns the recommendations dealing with education, data use, capacity building and training as they are relevant for applying a general strategy on improving children's environmental health.

Education and awareness raising

In line with the whole set of recommendations on an educational level on chemical, biological and physical hazards in the PINCHE reports[9,11], it is foreseen that recommendations on educational programmes will be fitted according to specific hazards in certain settings or locations. The on-going awareness of authorities at different levels about the advantages of making data and information available to the general public needs to be translated into practical mechanisms to do so. The confrontation between aiming at short term political solutions and the long term process of behaviour change through health promotion and education should be solved. This can be done partly by local investment of health education seminars and local expert workshops for dissemination of vital health information.

The relation between health and environment needs to be better incorporated in all kinds of training and education.

Data availability and accessibility

Several organisations and meetings related to children's health and environment have stated recommendations to improve the use of data to underpin the production of sound policies. The access to reliable scientific data is often difficult to achieve. Also in the PINCHE project access to the studies under EU funding was in many cases difficult to accomplish. In most cases this was due to the fact that the outcomes of projects are used for dissemination via scientific journals. These journals have a delay of publication, which can run over 1 or 2 years. Scientists and their funding organisations should be aware of this delay-effect and strive for other, quicker ways of publishing results.

Access to medical and environmental hazards records is essential for the monitoring of the health status of populations and for research on the causes and mechanisms of childhood carcinogens, neurotoxicants, respiratory health hazards, noise and other themes. Concerns about data protection and confidentiality may impede monitoring and research. Formal guidelines on interpretation and implementation of current legislation, taking account of the needs of public health research in general and childhood environmental health research in particular are needed at EU level.

Dissemination of data on daily impact on children by environmental hazards is needed to (public) health professionals, policy makers and the general public. Refraining from spreading the data causes delay in addressing emerging problems.

The EU requires a certain level of systematic approach to the interpretation of research results. It is a challenge to develop such an approach.

Progress regarding protection of children will only be possible if scientists and authorities speak the same language. To reach this goal, a harmonisation of definitions and methods used is mandatory. This includes (working) definitions of neurodevelopmental disorders, epidemiological collectives and methods used, biomonitoring matrices, and biomonitoring parameters.

There is a need for harmonisation of data. Cancer data are sometimes presented in terms of their primary site, e.g., breast cancer, lung cancer, and colon cancer. While this is broadly satisfactory for most adult onset cancers, which are mainly carcinomas, it is inappropriate for cancers in children in whom carcinomas are rare. All data on cancer in children and young people should be presented mainly in terms of morphology, as is already done in some existing cancer registries. It is important for comparing results on an international basis that a standard format for defining diagnostic groups and the presentation of data is adopted.

Data accessibility should be improved to enable public health authorities to do research on small numbers of cases within a population. For example, data for cancer cluster research should be available at a level of approximately 500 adult cases or persons in a distinct region instead of a large geographical scale. The EU needs to formalise existing regulations or implement new ones to enable health authorities or their scientific representatives to use data on a small scale to study potential clusters of environmental diseases or cancer without violating ethical issues or privacy rules.

Capacity building and training

Several regions in Europe are lacking the expertise in the field to cope with environmental and health problems. The medical profession is lacking specific knowledge on children's vulnerability in relation to environmental hazards. It is also lacking the expertise to judge the potential health effects when children are exposed to environmental stressors. In the policymaking profession there is no clear view on which discipline should be questioned. Training has been seen as a possible improvement to integrate the input from different disciplines. But training should not only be directed to paediatricians, general practitioners, and nurses, but also to school teachers, journalists, lawyers, industrial key players, policy advisors and policy makers at local, regional and national levels.

Discussion

The development of a strategy on children's environmental health takes place at different levels of authority. At each level there are similar problems in developing such a strategy.

The development of an EU-wide strategy to achieve a better children's environmental health quality is met by a variety of barriers. Different categories of barriers can be discussed: the subsidiarity principle, fragmentation of available knowledge or lack of expertise and purpose at various levels, the political commitment/input and economic issues.

The subsidiarity principle is one item among the barriers that prevent children's environmental health quality from reaching the EU policy agenda. This principle states that policy action will be taken at the EU level only when it would be more effective than action taken at a national, regional or local level. This principle is common for the EU regulatory decision making on, for example, indoor environmental quality. The subsidiarity principle ensures that member states make their own policies and further in this way decentralisation. Many countries rely on different ministries when making strategies or setting the policy agenda in children's environmental health. The subsidiarity principle makes the problem even greater for the EU to provide guidance and expertise in countries where national or local policies have not been developed.

The development of strategies or setting the policy agenda knows a second barrier. The fragmentation in knowledge, expertise, interests, disciplines and responsibilities[12] hinders the policies to be developed in children's environmental health. At the level of scientific input, there is fragmentation of expertise in science, environmental knowledge and health expertise at different levels of disciplines. The health and environment field covers such unrelated topics as air quality, radiation, water quality, noise, and health effects, each with its own experts.

The expertise needed to address children's environmental health is scattered among a range of research disciplines. The fragmentation of knowledge makes it difficult to form a knowledge base that is essential to set an agenda for policy making.

At the receiver end of policies there is a fragmentation of interests. The stakeholders in the environment and health field are similar to those for children's environmental health or for that matter for stakeholders for any vulnerable part of the population. These stakeholders do not encompass with the consequences of their interests for other fields in health or environment. Besides, the different stakeholders have specific level (national or local) or field (health or environment) interests at heart, making a European approach difficult. Health interests are often neglected in a market traditionally pushed by economy.

At the producer end of policies, and thus the level of regulatory authorities and policy makers, there is fragmentation of responsibilities. The lack of clarity in responsibility in the political arena makes it difficult to find a stakeholder who will push children's environmental health up the political agenda. There is more than one department responsible for the topic of children's environmental health at both the EU and the member state level. In many countries for example, the departments of health, housing, public health, environment, education and trade are responsible for policies related to children's welfare. It takes time for the responsible decision makers to pursue the subject, and to coordinate the various views and responsibilities.

Since fragmentation is faced at all policy levels (local, national and EU), much deliberation and coordination is needed to reach the EU policy-making agenda.

A third barrier to an integrated EU approach to children's environmental health is the economic factor. An integrated EU approach may invite over-regulation on an area in which individuals' economic wishes and possibilities would not align with the regulated goal of a child friendly environment. A complicating factor is that children are not capable to speak for themselves in designing the ideal environment for them. Individuals judge and accommodate their environment often based on cost- rather than health-based decisions.

Conclusion

The results of PINCHE indicate bottlenecks in the thematic network approach. Three main challenges for success have been identified. First is data comparability[3]. PINCHE identified the need for standardisation of: (1) environmental assessments, including estimates of ETS exposure, of indoor and outdoor air quality and of dietary (including breast feeding) and exercise habits and practices; (2) classification of childhood respiratory diseases and symptoms; and (3) a format for defining diagnostic groups and presentation of data. Furthermore, the importance of morphological data on cancer in children and young people was recognised.

Second, data accessibility must be addressed[3]. Although the internet is a powerful tool for rapid access of information and data, publication of scientific data usually lags 1–2 years after completion of a study. The subsequent step, accessibility of the scientific data to the general public, including health professionals and policy makers, is even more crucial and requires a translation that is often lacking. Finally, there is a requirement to harmonise definitions and methods to ensure that scientists and authorities speak the same language[3]. This is crucial to a viable science-policy interface. As with all networks, there is the inherent threat of becoming ''self-protective''. A closed network becomes self-persistent, thereby remaining too small and having limited research translated into policy recommendations. Networks should remain open, but integration should not expand too widely, as that may also lead to a weakened identity and reduced impact. The challenge is to find the balance.

To overcome the barriers for a sound development of a lasting strategy on children's environmental health a few actions need to be undertaken by the European Commission and the member states: they need to provide guidance on building policies in relation to national policies and regulations. A strong support to increase knowledge, capacity and trans-disciplinary cooperation is called for. Finally, the economic factor of children's environmental health needs to be made transparent by showing the benefits and costs of acting or not-acting in prevention of children's ill health effects due to environmental hazards.

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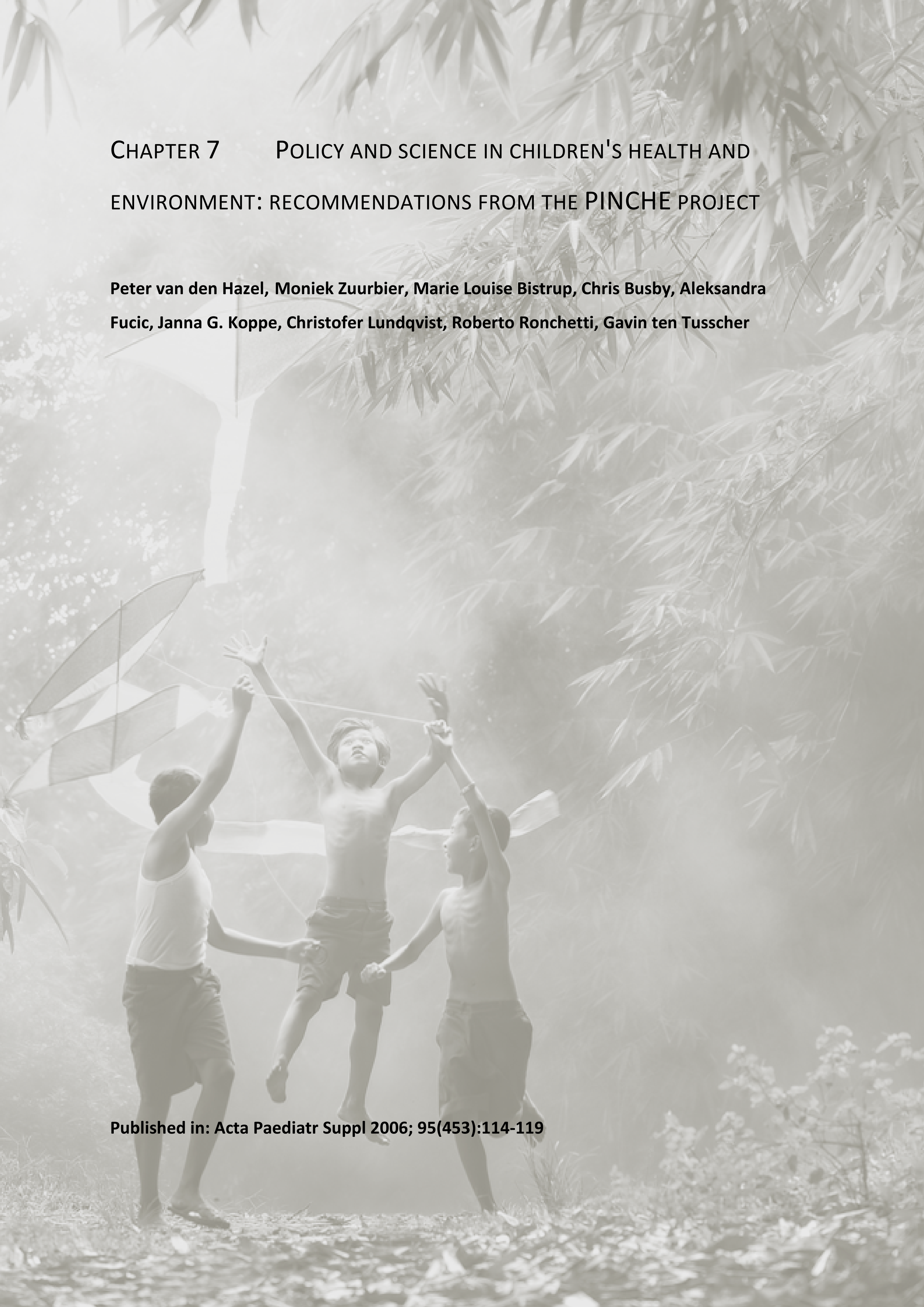

Chapter 7 Policy and science in children's health and environment: recommendations from the PINCHE project

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Published in: Acta Paediatr Suppl 2006; 95(453):114-119

Abstract

Background: Policy recommendations result from the discussions and analysis of the present situation in environment and health. Such analysis was performed in PINCHE. This led to recommendations based on the scientific literature. In the field of children's environmental health the policy process will follow more or less fixed rules, but this process is still at an early level of development. The link between science and policy still faces many challenges. Scientific assessment of environmental risk must recognize and tackle the problems of data sets, variability of human and environmental systems, the range, spatial and temporal diffusion of potential health effects and many biases and confounding factors.

Results: The PINCHE network recommends a general improvement of the supporting scientific fields in environment and health. Assessments from epidemiology or toxicology should play a key role in influencing science-policy decisions in programmes that are intended to inform the public policy process. Scientific committees at a local level could play a role. The relation between health and environment needs to be better incorporated in training and education. There is a need for harmonization of data production and use. The priorities in PINCHE focus on the most important issues. A classification of low, medium or high priority for action was used to describe a range of different environmental stressors.

Conclusions: PINCHE provided recommendations to reduce exposure for children. Exposure reduction is not always linked to improved health in the short term, but it will reduce the body burden of accumulating chemicals in children. A strategic choice is reduction of exposure of children to compounds by changing production techniques or by increasing the distance of child specific settings to sources. The contribution of all players in the production, distribution and use of scientific knowledge in the field of children's environmental health is necessary.

Keywords: Children, environment, public health, policy, science

Introduction

We define a policy recommendation as a proposed action in relation to a described risk factor in a specific situation which is intended to minimize or prevent unwanted effects of the risk factor. In addition and more generally, we include policy proposals intended to promote health, or actions to support and promote health and healthy environments. A policy proposal may have to be adapted to a specific situation; for example, depending on who should implement the policy, the level of the policy and the characteristics of the policy.

This article presents the main outline of policy recommendations resulting from the discussions and analysis of the present situation which were performed in PINCHE. Some recommendations are relevant for the European Commission or for the European Parliament. Some recommendations confirm the conclusions that were drawn in the process of developing the EU Environment and Health Action Plan[1,2]. Other recommendations are related to the work of Member States. These recommendations target ministers and policy makers in the ministries responsible for the environment, health or education. Finally, recommendations at a third level are related to regional or local authorities or municipalities. Regional differences and variation in environmental impact of stressors might have to be reflected in how policy is actually implemented.

These recommendations are presented in the PINCHE reports and are based on the scientific literature that was evaluated in the PINCHE project.

Policy objectives

Historically, the development both on content and organizational level of scientific information into policy has taken place to some extent in the area of environmental problems. This has lead to some institutionalizing of this field with clear roles for different stakeholders that apply the rules according to regulations, environmental policy programmes and laws. However, such a development has not been very clear in the field of environmental health.

We note that many major concerns about children's environmental health as expressed in many different international conventions or ministerial declarations have not yet been institutionalized. What do we mean by the term 'institutionalizing'? The concept of institutionalization is one of the central concepts in social and political science. It is defined as a process where values, norms and social activities are reflected in institutions. These institutions make a steady, collective pattern of rules and acquisition of data sources and information according to which, through the actions of the institution, societal players must (or in the best case, should) act accordingly.

In each social area policy will develop into a systematic statutory (i.e. legally binding) and inevitable system involving problem definitions and solutions with fixed patterns of interaction between different stakeholders and the development of policy processes according to more or less fixed rules.

In the field of children's environmental health this institutionalization has not yet taken place. The phase of naming the problems, of identifying the priorities in society and the building of a framework according to which the problems can be handled, are still at an early level of development.

Scientific objectives

The role of science as a guide beacon for policy making has become more complicated over the last few decades. From a linear relationship between knowledge and policy, the science-policy interface has become very complex. The increasing complexity of scientific knowledge goes hand in hand with the increasing risks in environmental health. The dependency of policy makers and citizens on the expertise of scientists is even more complicated by the lack of direct sensory perception of environmental health risks. The sensory perception of smoke from a stack, the noise of traffic and the visible pollution of soil are partly replaced by invisible, odourless, soundless pollution such as ionizing and non-ionizing radiation, low dose food contamination or fine particles in the air. This change disturbs the relation between science and policy. Humans have evolved to deal with evolutionary stresses, mostly visible, or if not visible, available through hundreds of years of observation of causes and effects and therefore accessible to the parents of children and for which warnings can be given. The rapid technological developments in the last 200 years have upset this process. Parents can no longer keep their children from harm since they cannot see or sense the threats. Nor can policymakers. Specialized equipment and knowledge are required. Furthermore, the social impacts of environmental health risks are not uniformly distributed among the non-scientific population or stakeholders. The universal apprehension in the public's mind of their children as potential victims has increased civil unrest about environmental health problems.

In addition, we see that other non-scientific stakeholders are also involved in the production of scientific knowledge. Not only universities, but also consultancies and advisory boards or research institutes produce scientific knowledge. At the side of the public there is increase of interest from different stakeholders. Not only national authorities, but also consumer groups, patients, industrial groups or environment and health organizations are using scientific knowledge. These stakeholders might use the scientific information for their own policy setting agenda.

The structural uncertainties of the scientific results put the science-policy relationship even under more stress[7].

In conclusion, the role of science is part of a complex system leading to policies.

Methods to connect science and policy

The literature has many models of science and its relation to policy. Policy process factors depend on the stage of the policy cycle, the make-up of the policy network, the nature of the issues involved (amenable to regulation or embedded systemic risk), the political climate and also increasingly the role of NGO stakeholders, the media and the general public. These Policy and Science in children's health and environment models are supportive in understanding how science can contribute in making policies.

There is more attention on translating scientific results into policies. However, there are some challenges in the science-policy interface. Scientific knowledge of environmental risk should ideally consist of a coherent body of codified, enlightened, objective, expert knowledge. It would be located in a relatively unified community subject to peer review and would be prepared to speak truth to power. There would be empirical reductive and deductive testing of hypotheses and inductive modelling of risk events, and the outcome for science advice to policy would be based on scientific views of experimentation, theory falsification, verification, replication, consistency and predictability. Empirical observation would be supplemented by controlled experiments. Indirect estimation would take place through extrapolation from analogous circumstances or exposure and chemical group characteristics. Estimating risk through statistical probability should be emphasised and applying 'no regret' policy should be the characteristic approach.

However, this ideal has to be tempered by pragmatism in the real world. Scientific assessment of environmental risk must recognize and tackle the imprecise nature of some core data sets, the dynamic nature and variability of human and environmental systems, the range, spatial and temporal diffusion of potential health effects, the complexity of many of the phenomena under investigation and especially the many biases and confounding factors.

Further problems that need to be solved include resolving the relationship between direct epidemiological study results and mechanistic effects based on laboratory animals, cell-culture or theoretical work. Furthermore, the relative limitations of epidemiology must be conceded, such as the statistical power problem for low prevalences, the cost and time required for prospective epidemiology and, again, especially the role of judgement in research scoping assumptions, determining the applicability of evidence and interpreting that evidence[3].

All these considerations demonstrate that ultimately, even in an ideal system, there must be concessions to uncertainty and some way of dealing with this, for example by using the precautionary principle. For theoretical approaches there are similar uncertainties; there is parameter uncertainty, model uncertainty and systemic uncertainty. The science-policy interface has to deal with these difficulties. The EU and other authorities have to deal with such a difficult field.

PINCHE recommendations

Research on exposure assessment, epidemiology and toxicology

The PINCHE network recommended a general improvement of the supporting scientific fields in environment and health.

However, more unconventionally PINCHE examined the process itself, looking behind the decisions themselves, at the process itself and came to various significantly novel conclusions. PINCHE concluded that the interface between science and public health policy and the important role that scientific assessments play in this interface are important issues and challenges. It seems obvious to give assessment primacy in programmes that are at the interface between science and public policy. It does not necessarily mean that exposure assessments or assessments from epidemiology or toxicology should be the primary focus of such programmes, but rather that they should play the key role in influencing science-policy decisions in programmes that are intended to inform the public policy process.

In this regard, PINCHE has recognized and cited evidence in its WP6 report that the acquisition of and handling of scientific environmental health data may be culturally biased by the needs of the institution handling the data and making representations about its meaning. This is the key area of argument in the case of science and policy. For example, the UK 'mad cow disease' science-policy interface was later shown to be both wrong (children died) and biased by the exclusion of independent scientists from the policy advice committee. The example studied in PINCHE was the transposition of the science of trichloroethylene carcinogenicity[4-6] into policy, and in this case independent examination of the process showed clearly the alarming uncertainty introduced by the various scientific players and organizations involved, who were from industry, academia and governments and were pulling in different directions through different interpretations of the same data.

PINCHE, for this reason, developed a recommendation that scientific advice committees on specific exposure questions be set up at the beginning as discursive or oppositional committees, with institutional funding to include independent scientists to examine issues of environmental health. Reports of these committees' discussions would include all sides of issues where there is some argument as to the health consequences of policies involving these substances or processes. It would then be for the policy makers to decide on the safety of the process that was being suggested or the exposure that was being investigated. Thus, the many stages in the science policy sequence would be available for examination if later anything went wrong. This is PINCHE's main recommendation in this area.

In line with this, PINCHE believed that there should be some method implemented such that retrospective epidemiological analysis can be easily accomplished; the simple recommendation was to 'flag' the medical records of children living near environmental pollution hotspots, so we can see who have been exposed when, at a later stage in life, they show health effects. This discussion should deal with the ethical issues as well as with the practical side of such registrations.

Traditionally, research data from adult humans or animals have been used as a basis for development of policies. In risk assessment children have usually not been included. The special vulnerabilities in some hazards and children's specific exposure patterns have not been considered adequately. It is recommended to include children specifically in risk assessments if these are part of the science policy process. In this process the limitations of the role of interpretation of scientific data should be made clear.

Education and awareness raising

There is a whole set of recommendations on an educational level on chemical, biological and physical hazards. It is foreseen that recommendations on educational programmes will be fitted according to specific hazards in certain settings or locations. The ongoing awareness at different levels of authorities on the advantages of making data and information available to the general public needs to be translated into practical mechanisms to achieve this. The confrontation between striving for short term political solutions, and the long term process of behaviour change through health promotion and education, should be solved. This can be done partly by local investment of health education seminars and local expert workshops for dissemination of vital health information.

The relation between health and environment needs to be better incorporated in all kinds of training and education.

Data availability and accessibility

Several organizations and meetings related to children's health and environment have stated recommendations to improve the use of data to underpin policies. The access to reliable scientific data is often difficult to achieve. Also, in the PINCHE project, access to the studies under EU funding was in many cases difficult to accomplish. In most cases this was due to the fact that the outcomes of projects are used for dissemination via scientific journals. These journals have a delay of publication which can run over one or two years. Scientists and their funding organizations should be aware of this delay effect and strive for other, quicker ways of publications of results.

Access to medical and environmental hazards records is essential for monitoring of the health status of populations and for research on the causes and mechanisms of childhood carcinogens, neurotoxicants, respiratory health hazards, noise and other themes. Concerns about data protection and confidentiality may be impeding monitoring and research.

Formal guidelines on interpretation and implementation of current legislation, taking account of the needs of public health research in general and childhood environmental health research in particular, are needed at EU level.

Dissemination of data on daily impact on children by environmental hazards is needed by (public) health professionals, policy makers and the general public. Refraining from spreading the data causes delay in addressing emerging problems.

The EU requires a certain level of systematic approach to the interpretation of research results. It is a challenge to develop such an approach.

Progress regarding protection of children will only be possible if scientists and authorities speak the same language. To reach this goal a harmonization of definitions and methods used is mandatory. This includes (working) definitions of neurodevelopmental disorders, epidemiological collectives and methods used, biomonitoring matrices, and biomonitoring parameters.

There is a need for harmonization of data. Cancer data are usually presented in terms of their primary site, e.g. breast cancer, lung cancer, and colon cancer. While this is broadly satisfactory for most adult onset cancers, which are mainly carcinomas, it is inappropriate for cancers in children in whom carcinomas are rare. Data on cancers in children and young people should be presented mainly in terms of morphology. It is important for comparing results on an international basis that a standard format for defining diagnostic groups and presentation of data is adopted.

Data accessibility should be improved to facilitate research on small numbers within a population. Data for cluster research should be available at a level of approximately 500 adult persons in the population.
Formal guidelines on interpretation and implementation of current legislation and on ethical issues are needed at EU level.

Capacity building and training

Several regions in Europe are lacking the expertise in the field of coping with environment and health problems. The medical profession lacks specific knowledge on children's vulnerability in relation to policy and science in children's health and environment environmental hazards. However, training should not only direct paediatricians, general practitioners, and nurses, but also school teachers, journalists, lawyers, industrial key players, policy advisers and policy makers at local, regional and national level.

The establishing of Paediatric Environmental Speciality Units, such as in the USA and Spain, could serve as an example of building capacity in a group of important stakeholders.

Compounds per theme air pollutants, noise, carcinogens and neurotoxicants

A challenge in PINCHE was to identify the environmental stressors with the highest priority for action. The priorities in PINCHE are attempting to focus on the most important issues. It was not always possible to reach unanimously the same qualification for prioritizing the recommendations. For communications purposes a classification of low, medium or high priority was used. The level of proof for the contribution by some compounds to the burden of disease was one of the factors which influenced the priority setting. There was common agreement that all of the issues discussed were important. The discussion was more about the timing of taking action or the amount of urgency to deal with certain problems. Thus, there are children's environmental health problems that might receive higher priority in the near future. The partners in PINCHE sometimes had different priorities for brominated flame retardants, lead, PCBs, dioxins, ionizing radiation and some of the noise sources, such as discothèques.

There was immediate agreement on giving high priorities to the reduction of exposure to outdoor air pollutants and environmental tobacco smoke. For the heavy metals, the halogenated compounds (dioxins, PCBs, brominated flame retardants) and ionizing radiation there were different opinions on whether exposures to these stressors should be rated medium or high.

PINCHE concludes that reducing exposure to most of the air pollutants related to motor vehicle transport, including benzene, diesel engine emissions, nitrogen oxides and particulate matter, has the highest priority in protecting children's environment and health. Exposure to these outdoor air pollutants is high in most areas of Europe and causes serious health effects. Reducing exposure to environmental tobacco smoke, a fully preventable exposure, also has high priority because of high exposure and serious health effects.

The priority of reducing allergic symptoms is considered to be medium to high, because allergens are ubiquitous and millions of children in Europe are sensitized to allergens. Exposure of sensitized children to allergens greatly affects their daily performance.

PINCHE further concludes that reduction of exposure to ozone, another outdoor air pollutant, has medium priority. It is of specific importance for a susceptible group of children, those with asthma, in relation to outdoor activities. Reducing exposure to polycyclic aromatic hydrocarbons, which mainly originate from motor vehicle emissions and smoking, has medium priority; it can negatively influence the development of the foetus. Furthermore, exposure to the metals arsenic, lead, cadmium and mercury has a medium to high priority for action. Exposure to these metals has decreased, but some sources or settings still cause enough exposure to produce severe health effects.

Indoor exposure to mould, radon, formaldehyde and other volatile organic compounds (which also occurs outdoors, but indoor concentrations can reach especially high levels) also has medium priority for action. For each of these stressors, situations can be identified in which children can be exposed to high concentrations. Relevant indoor levels can cause adverse health effects.

Exposure to PCBs and dioxins has decreased but is now stabilizing, and current exposure levels can still cause some health effects; the priority is therefore medium. The concentration of brominated flame retardants required to produce health effects is not known, but concern is raised because of their toxic similarities to some persistent organic pollutants and their abundance. In addition, the levels of brominated flame retardants have increased rapidly in recent decades. The priority is medium, based on the precautionary principle, since more research is required.

Reducing exposure to noise at schools and from road traffic as well as 'voluntary' exposure to noise from personal audio players and to noise in discothèques also has medium priority. This exposure can lead to cognitive and auditory effects.

Reducing exposure to ionizing radiation from human-made sources has a medium priority, because this exposure might lead to additional cases of cancer, but the beneficial effects of therapy and diagnostics might outweigh the harm of these sources. Furthermore, reducing exposure to solar radiation has medium priority.

Reducing exposure is very important because of the relationship with skin cancer. Especially acute sunburn should be prevented. Nevertheless, the vitamin D produced through exposure to sunlight is important, and a shortage of sunlight should therefore be avoided as well.

Finally, reducing exposure to pesticides is rated to have medium priority. This is because of the major differences in the use of pesticides, and thus children's exposure to pesticides, in different regions in Europe. Exposure to pesticides in countries with pesticide intensive farming (often small-scale farming) may be high because, for example, the parents take pesticides home with them on their clothes, and this exposure may cause negative health effects in children.

Based upon the information available, the other risk factors have all been rated to have a low priority. It must be noted, however, that near certain hotspots or in certain regions some of these compounds can have a high priority.

Discussion

The role of PINCHE and its results can be viewed against the different types of scientific knowledge that are important to discern in relation to the policy field - monitoring, direct policy advice, strategic knowledge and policy evaluation.

Monitoring is a method which is applied in the phase of policy implementation. The method is meant to judge and care for the progress of the implementation process. In addition, it provides insight into the consequences of the on-going policies and its efficiency. In the field of children's environmental health there is a lack of monitoring. The PINCHE recommendations point at the development of monitoring systems which will include environment and health indicators in Europe. The scientific community is currently developing such systems. It would be promising to make links to the clinical monitoring systems in order to look for trends of new emerging diseases in children.

The direct policy advice deals with the relation between environmental stressors and children's health. PINCHE provided for a range of environmental stressors recommendations to reduce exposure for children. Even when exposure reduction is not always linked to improved health in the short term, it will at least reduce the body burden of accumulating chemicals in children. The EU and WHO have stated in several reports that exposure reduction is a way to comply with precautionary principle to avoid diseases in children. PINCHE underlines this approach by prioritizing some compounds to which children are exposed.

Strategic knowledge is used to improve health in the long term. There are strategic choices to reduce exposure of children to compounds by changing production techniques or by increasing the distance of child-specific settings to sources, such as highways or industrial sites. The scientific knowledge needs to be strong to stand in the political arena when long term changes are needed.

Policy evaluation is a tool to check the efficiency and effectiveness of implemented policies. This includes the evaluation of the process of reaching the goals of certain policies.

The contribution of all players in the production, distribution and use of scientific knowledge in the field of children's environmental health is necessary. PINCHE had such cooperation. That PINCHE reached consensus for most of the recommendations strengthens the results of the project. Radiation and some industrial bulk compounds were topics which lost some power owing to the fact that the scientific results were not all pointing in the same direction or not yet conclusive enough. In those cases it is recommended to carry out more research and avoid extra unnecessary exposure according to the precautionary principle.

The interaction between chemicals and multiple exposure is an issue that needs to be researched more, as there might be unknown effects and children might be more susceptible in situations of multiple exposure.

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CHAPTER 8 THE ENVIRONMENTAL HEALTH OF CHILDREN: PRIORITIES IN EUROPE

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Published in: International Journal of Occupational Medicine and Environmental Health 2007; 21(3):291-307

Abstract

Objectives: To evaluate existing research on the environmental health of children and provide a prioritised list of risk factors and policy recommendations for action, the Policy Interpretation Network on Children's Health and Environment (PINCHE) was set up within EU FP5 (QLK4-2002-02395). The project focused on air pollutants, carcinogens, neurotoxicants and noise. PINCHE was a multidisciplinary and multinational network of representatives from science, industry, NGOs, and consumer and patient organisations in Europe.

Materials and methods: A literature search was performed using the Pubmed, Embase and Toxline databases. The quality of the gathered articles was assessed and their information and relevance was interpreted within a systematic framework. Information related to exposure, epidemiology, and toxicology was analysed separately and then a risk evaluation of particular environmental factors was made. Socioeconomic factors were specifically taken into account. The results were compiled, and considering the present regulatory situation, policy recommendations for action were made. Finally, the risk factors and policy recommendations were prioritised through a process of discussion between all the partners.

Results and conclusions: PINCHE concluded that outdoor air pollutants (especially traffic-related), environmental tobacco smoke, allergens, and mercury were high priorities with an urgent need for action. Brominated flame retardants, lead, PCBs and dioxins, ionising and solar radiation, and some noise sources were classified as being of medium priority. Some toxins were given low priority, based on few exposed children, relatively mild health effects or an improving situation due to past policy measures. We recognise the shortcomings of such a prioritisation and, though some measures are more urgent than others, emphasise that ideally all policy measures should be carried out without delay for all toxins. This priority list must be continuously revised, the precautionary principle should be central to all decisions, and the focus should be on safe exposure levels for children.

Keywords: Child, Environmental health, Air pollution, Carcinogens, Noise, Neurotoxicology

Introduction

The Policy Interpretation Network on Children's Health and Environment (PINCHE) was a network set up and funded by the EU for three years (from January 2003 until January 2006) to focus on the relationship between children's health and the environment. The main objective of PINCHE was to provide policy recommendations with the aim of protecting children's health and environment based on published scientific research. The backbone of PINCHE was the recognition that children are more susceptible to some environmental factors than adults, while most legislation is based on data for adults.

PINCHE's aim was to identify the environmental risk factors to which children are susceptible or have an increased risk of exposure and where special protective or preventive measures are required. It focused on the interpretation of existing scientific results to provide decision-makers, environmental health professionals and other stakeholders with information relevant for developing policy. In the final step, PINCHE prioritised recommendations for action to improve the environment of children in Europe[1].

The project focused on four themes:
Among indoor and outdoor air pollutants, nitrogen dioxide, particulate matter, ozone, environmental tobacco smoke, moulds and allergens were considered. Under the neurotoxicity theme, PINCHE focused on polychlorinated biphenyls (PCBs), dioxins, brominated flame retardants, pesticides, volatile organic compounds and heavy metals. In the third theme on noise, both involuntary and voluntary noise exposure in children's settings was studied. The carcinogenic compounds analysed were those listed on the IARC 1 and IARC 2a lists (Table 1)[2]. Some compounds on these lists were excluded because exposure was not considered relevant for children in Europe. The chosen themes were among those also prioritised by the European Commission and the World Health Organization[3,4]. Environmental stressors that are possibly hazardous to children's health but were not studied in PINCHE include electromagnetic fields, endocrine disruptors (other than PCBs, dioxins, pesticides and brominated flame retardants), phthalates and carcinogens classified by IARC as group 2b carcinogens.

Group	Classification	Definition (simplified)
1	Carcinogenic agent	There is sufficient evidence of carcinogenicity in humans
2a	Agents probably carcinogenic to humans	There is limited evidence of carcinogenicity in humans, but sufficient evidence of carcinogenicity in experimental animals
2b	Agents possibly carcinogenic to humans	There is limited evidence of carcinogenicity in humans, and less than sufficient evidence of carcinogenicity in experimental animals.
3	Agents unclassifiable as to carcinogenicity in humans	There is inadequate evidence of carcinogenicity in humans, and inadequate or limited in experimental animals.
4	Agent probably not carcinogenic to humans	There is evidence suggesting a lack of carcinogenicity in humans and in experimental animals.

Table 1. Classification of carcinogenic agents as defined by the International Agency of Research on Cancer (IARC)

PINCHE was a multidisciplinary and multinational network of representatives from science, industry, NGOs, and consumer and patient organisations in Europe. Researchers such as epidemiologists and toxicologists, public health administrators, policy scientists and representatives of patient organisations, industry and non-governmental organisations within environment and health were partners in PINCHE. The broad spectrum of stakeholders that contributed to the project is a strength of PINCHE because its results are based on discussions from a variety of perspectives, even though it proved to be difficult to reach consensus on all recommendations. The scientific results were evaluated in seven work packages: on exposure assessment; epidemiology; toxicology; risk and health impact assessment; socioeconomic factors; science–policy interface; and the work package final analysis. At the end of the project, work package 7 was the forum that created the priority list of the policy recommendations discussed in the present article. PINCHE reviews of health risks due to children's exposure to environmental risk factors have been published elsewhere[1].

Methods

Children were defined by PINCHE as "human beings below the age of eighteen". Research on exposure and effects from conception to birth were included in the analyses, and in some instances, preconception exposure was also taken into consideration. We analysed existing evidence on the impact of environmental risk factors on children's health, from studies supported by the European Union and from international publications. Relevant EU studies funded under the Fourth and Fifth Framework Programme were collected using the databases of the EU Directorate General on Research and on Health & Consumer Protection. International scientific literature was searched by using the literature databases, Pubmed, Embase and Toxline. The search focused on reviews and studies published in the last five years (1998–2003). Papers were sought that either specifically comprised data on children or on children as a sub-group; where appropriate, complementary publications were added to the database.

An evaluation system was developed to extract the important information from the studies which was entered on an evaluation form. The quality of the evaluated studies was assessed using quality criteria regarding the methods used and the handling and reporting of biases. The evaluation used a systematic framework to interpret the data and answer the following questions:

- Exposure: the routes and sources and levels of exposure in the regions of Europe.

- Epidemiology: what health effects were found in children exposed to the environmental stressor? How strong were the relations found?

- Toxicology: what were the health effects found in toxicological studies? What was the mechanism of effect? Were children more susceptible than adults?

The information from the interpretation framework formed the basis for analysing the information from the research results and - later on - for prioritisation.

The criteria used for setting priorities for action regarding the environmental risk factors were:

- the number of children exposed and the dose;
- the nature of adverse health effects and the likelihood that these health effects will occur at the current exposure levels;
- the extent to which children are more susceptible than adults;
- the extent to which children are more exposed than adults; and
- the regulatory measures already in place as well as probable future developments in exposure patterns.

These criteria were not defined quantitatively but were used as qualitative guidelines by the PINCHE members for the process of prioritisation. When there were some indications of irreversible or severe adverse health effects but a lack of confirmatory scientific evidence, we applied the precautionary principle and recommended action.

Results

Literature collection

Out of 219 publications that were found to be related to outdoor and indoor air pollutants and children, 120 references were evaluated and summarised using the evaluation form; 99 publications were either not applicable to children's respiratory health, or were extensive reviews which were taken into account as a whole rather than being summarised. On neurotoxicity, 252 articles were identified, mainly non-review articles. Of these, 201 articles were evaluated using the evaluation form. The remainder were not considered because they were irrelevant. For the noise theme, 222 relevant references were identified. Only 30 articles were evaluated using the evaluation form, because most partners working on noise preferred writing the results directly, without the additional step of systematic evaluation of the literature. For the carcinogenicity theme, 324 articles of relevance were identified and 167 references were evaluated. The remaining articles were either not related to children's health specifically or were not considered relevant for the current European situation We were unable to collect the results from some (EU-funded) projects, either because the projects were still ongoing or because the results were not available yet.

Transport-related air pollutants

Children are exposed to nitrogen dioxide, ozone, particulate matter, benzene and diesel engine exhaust. Exposures are higher in urban areas, because of intense traffic, except for ozone: ozone levels are higher in rural areas[5]. Exposure to benzene is related to acute myeloid leukaemia and probably also to other subtypes of leukaemia[6]. Children are not known to be more susceptible to benzene, but their intake is relatively higher than that of adults.

Exposure to nitrogen dioxide, particulate matter and diesel engine exhaust is highly correlated. Many children in Europe are exposed to high levels of these pollutants. The European Environment Agency (EEA) reports NO_2 levels up to several 100 µg/m³ (hourly mean)[5] and emphasises that the annual EU limit value (40 µg/m3) is often exceeded at sites of heavy traffic, and also at some urban background sites. Children are more susceptible than adults to developing NO_2-related health effects. Effects of NO_2 in children are asthma symptoms[7], altered lung function[8], and respiratory symptoms[9]. It is not clear to what extent the observed effects are caused by NO_2 itself, by secondary pollutants formed from NOx (ozone, secondary nitrate particles), or by the mixture of pollutants from combustion sources (especially vehicular traffic) for which NO_2 only serves as a proxy.

Particulate matter (PM) is an important environmental air pollutant in terms of health effects. Annual mean levels of PM10 (particulate matter with a diameter size smaller than 10 µm) range between 20 and 40 µg/m³, but in some years and in some places, the current (annual mean) limit value of 40 µg/m³ of PM10 is exceeded[5,9]. The limit value for the daily mean (50 µg/m³) is frequently exceeded in many (mostly) urban settings. Maximal daily means reach even several hundred µg/m³. Children are more susceptible to PM than healthy middle-aged adults. PM exposure is related to neonatal mortality, respiratory effects in children, hospitalisation and school absenteeism[9,10].

Exposure to sulphur dioxide has declined considerably since the 1980s. This exposure is associated with increased upper and lower respiratory tract symptoms in children and some studies suggest an association with decreased birth weight[9,11].

Ozone

Ozone is the main ingredient of summer smog. Ozone concentrations in Europe regularly reach levels that can affect respiratory health, especially for children. The health effects of ozone exposure seem to be greater in asthmatic children and in children who are exercising or playing outside more often when ozone levels are high[12].

Environmental Tobacco Smoke

All children are exposed to environmental tobacco smoke (ETS) to some extent. An estimated 40% of children in Europe are exposed in their homes by one or two parents smoking[13]. About 20–30% of women actively smoke during pregnancy. Children, especially when exposed perinatally, are very vulnerable to environmental tobacco smoke. The mean birth weight of foetuses exposed to maternal smoke is reduced by about 250 grams, and the mean birth weight of foetuses exposed to maternal passive smoking is reduced by 25 to 100 grams[14]. Infants of lower birth weight and gestational age are at increased risk for neonatal mortality and morbidity. The risk of Sudden Infant Death Syndrome (SIDS) in children of smoking mothers is almost twice as high as of non-smoking mothers[15]. Postnatal ETS exposure due to parental smoking is associated with: 60% increase in the risk of lower respiratory tract infections, 24–40% increased risk of chronic respiratory symptoms and 21% increased risk of asthma[16]. There is increasing evidence that ETS exposure is linked to intellectual impairment[17]. ETS is also carcinogenic: polycyclic aromatic hydrocarbons and nitrosamines, two compounds of ETS, may play major roles in genotoxicity (induction of DNA damage).

Allergens

The number of children sensitised to allergens is increasing. Exposure to allergens can induce symptoms in persons already sensitised, and exposure can cause sensitisation, mainly in young children. It has been assumed that exposure to allergens early in life would reduce the incidence of respiratory allergies, but this is currently debated. Air pollution increases susceptibility to allergic reactions in sensitised individuals[18,19]. Sensitised children should be sheltered from exposure to allergens or pollutants. Exposure can be reduced, for instance by taking the pollen season into consideration in planning holidays or by the encasing of mattresses and bedding material.

Endotoxins

Endotoxins are toxic molecules derived from the outer cell wall of gram-negative bacteria. They are present in varying amounts in most indoor environments, particularly where domestic animals are present. Endotoxins are associated with induction of airway inflammation, reversible bronchoconstriction, wheezing and asthma exacerbations[20]. On the other hand, exposure to endotoxins has also been suggested to protect against allergic sensitisation[21,22]. This discussion is ongoing at present.

Moulds

Moulds are ubiquitous in the outdoor environment and can enter the home not only through doorways and windows, but also by ventilation and air conditioning systems. Most moulds proliferate in moist environments. The problem of indoor moulds has increased during recent decades because of the development of more well insulated houses. The association between dampness and moulds and the prevalence of wheeze and cough has been confirmed in several studies with odds ratios in the range of 1.5–3.5[23]. The dampness that promotes mould growth also encourages infestation with house dust mites or insects[24]. Mould growth could thus also be a marker for other causes of illness.

Cleaning products and chlorination by-products

Several cleaning products are classified as irritants to lung, skin, and eyes. The most hazardous cleaning products are already no longer used. Sodium hypochlorite is the main ingredient in household (chlorine) bleach, the most common cleaner accidentally swallowed by children. Ammonia can be found in some cleaning products. Ammonia fumes are very irritating to the eyes, nose and airways. When sodium hypochlorite is mixed with ammonia or acid-based cleaners (including vinegar), it releases highly toxic gases: chlorine and chloramines. Short-term exposure to chloramine gas may cause mild asthmatic symptoms or more serious respiratory problems. Because hypochlorite products carry mandatory warning labels, such exposures are limited to accidents or the results of deliberate misuse. Therefore, children's exposure to cleaning products is not likely to cause acute health effects frequently in the future. However, chronic exposure may increase the risk of asthma symptoms[25].

Chlorination by-products are produced when the disinfectant chlorine reacts with organic matter in tap water or swimming pool water. Some of the chlorination by-products are carcinogenic[26]. Whether chronic exposure by drinking chlorinated tap water might lead to bladder or colon cancer has not been resolved. Drinking of chlorinated tap water has been associated with adverse reproductive outcomes: low birth weight (LBW), small for gestational age (SGA) infants, preterm delivery, spontaneous abortions, stillbirth and birth defects[27]. However, these risks are small compared to the risks resulting from drinking water that has not been disinfected. In a recent study, regular attendance at indoor chlorinated pools was found to be associated with the risk of developing asthma in atopic children[28]. The risk seems to be greater for children and especially babies who are more susceptible and who attend small pools which are shallow, hot and polluted.

Formaldehyde

Formaldehyde, one of the most ubiquitous indoor air contaminants, is found in cigarette smoke and is released from building material. Some epidemiological studies connect formaldehyde exposure, even at low concentrations, with an increased risk of asthma[29,30]. Formaldehyde has been classified as a group 1 carcinogen by IARC. It can, in concentrations found in occupational settings, cause nasopharyngeal cancer and is also suspected to cause leukaemia[31]. All children are exposed to formaldehyde with usually higher concentrations found indoors than outdoors. Although a measurable increased cancer risk has only been observed in occupational settings with comparably much higher exposure, several studies have found an association between indoor formaldehyde exposure and respiratory health in children. Especially, asthmatic children are likely to develop respiratory symptoms because of their exposure.

Volatile organic compounds

Volatile organic compounds (VOCs), mainly used as solvents, in fuels, and as dry cleaning agents, inhibit the functioning of the central nervous system.

IARC has determined that trichloroethylene, tetrachloroethylene, and vinyl chloride are probably carcinogenic to humans (group 2A)[32]. Exposure to tetrachloroethylene can be high near dry-cleaning plants, but apart from that, the levels are generally low. Children's exposure to trichloroethylene and vinylchloride is also low.

Pesticides

In several countries, an increased risk of spontaneous abortion has been found among women in agricultural occupations and among gardeners who spray pesticides[33-36]. The following pesticides have been linked to a decreased fecundability ratio amongst Finnish greenhouse workers: cynazine, carbamates, pyrethroids, benzimidazoles, thiocarbamate and organophosphates[37]. A change in the sex ratio (more girls being born) has been found in children of pesticide applicators exposed to chlorophenoxy herbicides, dibromochloropropane (DBCP) and organochlorine pesticides[38]. Increased rates of birth defects have been described in agricultural areas with heavy use of chlorophenoxy-herbicides[39], pyridil derivatives[40], phosphine fumigants[36] and the herbicide glyphosate[36]. Women exposed to pyrethroids have a higher risk of giving birth to children that are small-for-gestational-age (SGA)[41]. In children, many of the cancers associated with pesticides, such as leukaemia, soft-tissue sarcoma, and Hodgkin's disease, are the same cancers that are repeatedly associated with pesticide exposure among adults, suggesting that a role for pesticides and cancer among children is highly plausible[42].

Children are exposed to pesticides in food, water, breast milk and contaminated soil. In addition, pesticides can be ingested, inhaled or absorbed through the skin. In an EU monitoring study in Sweden in 2003, two out of 101 samples from foods specifically for infants or young children had residue levels exceeding the Minimum Risk Levels (MRLs)[43]. There is evidence that children, especially the foetus and neonates, are more susceptible to pesticide toxicity. This evidence is supported by similar findings in neonates of other species[44] and may be partly due to lower levels of detoxifying enzyme systems[45].

Organohalogen compounds

Even under current exposure levels, dioxins and dioxin-like polychlorinated biphenyls pose a health threat mostly to the developing foetus (via in utero exposure) and new-borns (via breast milk). Effects on cognitive and behavioural development, on bone marrow, on growth and reproductive development are most probably persistent. Toxic effects on thyroid metabolism detected at birth, and liver function abnormalities are no longer seen at 2 and 8 years of age[46]. Nowadays, the levels in breast milk are 50% lower in western European countries than in 1990, thanks to reduction policies. This lowering has not been as effective for PCBs, although their production was banned in 1977. However, the advantages of breast feeding outweigh in most cases the pollutant-related disadvantages. A Tolerable Daily Intake (TDI) for dioxins and dioxin-like PCBs of 1 to 4 pg I-TEQ per kg bw/day was recommended for dioxins by the World Health Organisation in 1998[47]. Current mean intake of dioxins in European countries is within this range of TDI levels. However, it should be noted that the WHO's ultimate goal is to reduce human intake levels below 1 pg TEQ per kg bw/day.

The class of polybrominated flame retardants studied in PINCHE is the group of polybrominated diphenyl ethers (PBDEs). The widespread and rapidly increasing use of PBDEs, their persistence, and structural similarities to PCBs have raised concern about their effects on human health[48]. Children are exposed to PBDEs through diet, mainly through fish, meat and milk. Limited data are available on human health effects in adult populations, and these data are mainly from occupational exposure studies. Exposure to penta- and octa-BDE, two congeners of PBDE, lead to learning impairment and impaired motor behaviour in rodents[49,50]. Exposure to penta-, octa- and also deca-BDE has effects on thyroid homeostasis in animals[48,50].

The EU has banned the production and use of penta- and octa-BDE since 2004, however, exposure will continue during the next few decades. Data on exposure and toxicity regarding deca-BDE are scarce. Therefore, based upon current scientific evidence, health effects cannot be linked to human exposure to deca-BDEs[51].

Metals

Chronic exposure to arsenic-contaminated water has been associated with skin cancer, cutaneous lesions, peripheral vascular diseases, abdominal pain, diarrhoea and nausea[52,53]. Arsenic compounds are classified by IARC as carcinogenic to humans (IARC group 1). Increased exposure has been associated with adverse pregnancy outcomes (stillbirths and miscarriages). Several million European children may be exposed to drinking water in which the limits of 10 µg/l are exceeded. In some areas near industrial sites, exposure through soil (hand-mouth behaviour), dust, and home-grown food might be above the maximum permissible oral intake level as set by the US EPA or by FAO. Based on current levels of arsenic in the air, it is expected that the present exposure of children in Europe will induce hundreds of cancers later in life[54].

Cadmium is a known human carcinogen, IARC group 1; it induces cancer upon inhalation[55]. Chronic exposure is associated with health effects such as impaired kidney function and osteoporosis. This has been observed at current levels of exposure in some countries[55]. Children's urinary cadmium levels have been associated with immune response modification[56]. Experimental animal studies suggest that cadmium exposure early in life may induce neurotoxic and behavioural effects[57]. Emission of cadmium has been reduced by 40% between 1990 and 1999[58]. Children are exposed to cadmium mainly through food and through inhalation of environmental tobacco smoke. Children in eastern Europe and children living near copper smelters are exposed to higher cadmium levels. A few percent of children in Europe have a cadmium intake that exceeds the tolerable daily intake (TDI)[59].

For chromium (VI) compounds as well as for nickel (both classified by IARC as group 1 substances) the cancer risks for children were evaluated as being low at current child exposure levels[60-62].

A link has been suggested between inhaled manganese and the central nervous system and cognitive problems, reduced fertility and pulmonary effects[63,64]. However, insufficient manganese intake can also lead to adverse health effects[65].

Lead poisoning in children causes reduced birth weight, anaemia, impaired motor functioning, hearing loss, reduction in IQ, behavioural problems, puberty delays, cancer, and damage to brain, liver and kidney[66,67]. Currently, 10 µg/dl is the blood lead level (PbB) above which there is concern for health; however, recent data suggest that there is no threshold below which lead is not toxic to the developing central nervous system. Many studies address the cognitive effects of lead in children. A decrease of 2–3 points in IQ with an increase from 10 to 20 µg/dl PbB was found in a meta-analysis[68]. Recent studies confirmed a decrement of 4.6 points of IQ for each 10 µg/dl increase of PbB but found a larger effect of a loss of 7.4 IQ points for a PbB change between 0 and 10 µg/dl[69].

Because of interventions such as the ban of leaded petrol, blood lead concentrations in children have fallen substantially in most European countries[70,71]. The majority of children in Europe are, however, still exposed to lead, mainly via food and air. Lead in paint is the major source of lead in older homes. Lead is also present in tap water from household plumbing systems containing lead. Also tobacco and tobacco smoke contain lead. Soil lead from leaded gasoline and pulverised lead-based paint is a source of human exposure which might be more important as a source than intact lead-based paint[68]. Infants are also exposed to lead through maternal milk. A pooled analysis of 12 studies confirms that lead-contaminated house dust is now the major source of lead exposure for children[68]. Indoor floor dust accounts for approximately 50% of a young child's total lead intake. Mean blood levels are below 5 µg/dl in western Europe and between 5 and 10 µg/dl in eastern Europe. Up to 5% of English children have blood lead levels exceeding 10 µg/dl[72].

Mercury and its compounds are highly toxic. High doses can be fatal to humans, but even relatively low doses can have serious adverse neurodevelopmental impacts, and can be linked to harmful effects on the cardiovascular, immune and reproductive systems[73,74]. Methylmercury passes both the placental barrier and the blood-brain barrier, inhibiting cognitive development even before birth. Two large-scale longitudinal cohort studies were performed at the Faroe Islands and the Seychelles. The Faroe Islands study showed several neuropsychological deficits to be associated with methyl mercury levels in cord blood[75,76]. No detectable adverse effects were found in relation to methyl mercury levels in maternal hair grown during pregnancy in the Seychelles study[74,77]. The difference has been explained by the fact that in the Seychelles, exposures were entirely from nearly daily fish consumption, while in the Faroe Islands, exposure was mainly attributable to episodic consumption of pilot whale. Pilot whales have much higher levels of mercury than typical ocean fish and also contain other contaminants such as PCBs.

Exposure to methylmercury mostly occurs via consumption of fish and seafood. Most people in the coastal areas of the Mediterranean countries and around 1–5% of the population in central and northern Europe ingest amounts close to the reference dose of 0.1 µg/kg bw/day. Children are more exposed than adults, because of relatively higher food intake, and nursing infants are more exposed because of exposure through breast milk[78].

Other carcinogens

Asbestos, beryllium, coal tar pitches and ethylene oxide are IARC 1 compounds, indicating that these compounds are proven to be carcinogenic to humans. Children's exposure to these compounds is generally very low in Europe. Acrylamide, 1,3-butadiene, n-nitrosodimethylamine and n-nitrosodiethylamine are IARC 2a compounds, meaning that these compounds are probably carcinogenic to humans. For children, the levels of exposure to these carcinogens are very low as well.

Polycyclic aromatic hydrocarbons (PAHs) as a group are considered to be proven human carcinogens, associated with the induction of lung cancer by inhalation[79]. No direct evidence exists regarding lung carcinogenicity of PAHs in children, or in adults after exposure during childhood. However, childhood exposure to ETS (of which PAHs are one of many carcinogenic components) has been linked with increased lung cancer risk later in life[80]. Children are exposed via inhalation of PAHs (also present in tobacco smoke), via consumption of PAH-containing foods (mainly grilled or smoked meat and fish) and via ingestion of PAH-contaminated soil and household dust[79]. Intrauterine growth restriction (IUGR) and low birth weight (LBW) were observed at PAH concentrations higher than 15 ng/m^3, the concentrations encountered in highly polluted urban areas in Europe[81]. There appears to be a downward trend in outdoor air PAH concentrations as a result of interventions.

Noise

From the international literature and extended reviews performed on noise in relation to children's health[82-84] it can be concluded that children are more susceptible to acquiring noise-induced hearing impairment. Exposure to transport noise can lead to annoyance, stress responses, cognitive impairment and possibly cardiovascular problems. Exposure to noise in schools is related to deficits in reading and recognition memory[85,86]. Cognitive impairment related to aircraft noise exposure may be reversible if exposure is terminated, as seen in the Munich airport studies[87].

Leisure noise is a hazard to hearing in young people, both children and adolescents. Many young people are exposed to high noise levels by using personal audio players, such as MP3 players, and by visiting discothèques. Also toys and firecrackers can produce very high noise exposure levels transiently. Prolonged exposure to loud music may lead to permanent hearing threshold shift, and to temporary as well as permanent tinnitus (ringing in the ear)[88]. Studies of noise exposure in neonatal intensive care units have shown that noise levels can reach high levels in incubators, but these levels do not often occur, and exposure has only been proven to be related to sleep disturbance, not to other health effects[84].

Solar radiation

Exposure to solar radiation is inevitable and necessary for vitamin D production. The main adverse effects on health are due to the high-energy ultraviolet radiation (UV). UV intensity has been increasing since 1980 due to destruction of the stratospheric ozone layer. Exposure to UV and solar radiation during childhood may cause skin cancer in childhood or adulthood. It has been suggested that exposure to solar radiation during childhood contributes more to developing skin cancer than similar exposure during adulthood[89]. Over 90% of non-melanoma cancers can be attributed to exposure to UV-B while UV-A may be a cause of malignant melanoma[89]. UV exposure may be associated with non-Hodgkin's lymphoma[90]. On the other hand, exposure to UV results in synthesis of vitamin D, and vitamin D may lead to decreased risk of non-Hodgkin's lymphoma[91]. UV exposure can cause eye damage including retinal damage, snow blindness and in the long term cataract. Exposure to solar radiation depends on the latitude where children live and their behaviour. Susceptibility of children to the carcinogenic effects of solar radiation depends on the skin type.

Ionising radiation

Ionising radiation includes exposure from natural and man-made radiation sources which may be *external,* such as X-rays and gamma rays, or *internal,* due to the ingestion or inhalation of radioactive substances. Ionising radiation is genotoxic and carcinogenic, without a dose threshold. Radon is a naturally occurring radioactive gas. It makes up about half the total annual exposure of humans to radiation. Long-term exposure to radon is associated with lung cancer in adults[92].

The foetus is at particular risk from thyroid and bone-seeking isotopes. There is high cell-turnover during childhood, and the processes associated with cell division are well known to be more radiosensitive. Background radiation probably accounts for 10% of all childhood and adult cancers. Because background radiation is difficult to reduce, the main focus should be on avoiding additional exposure and unnecessary increases in exposure. Radon is a special case because intervention is possible.

Conclusion

Based upon the information on health effects and exposure, and using the criteria mentioned above in a qualitative manner, PINCHE ranked the priorities for the reviewed environmental risk factors into high, medium and low. The priority ranking was prepared realising the shortcomings of such a qualitative approach and was not intended as an exclusive or final list. It should be seen rather as an indication of PINCHE's prioritisation for action. All actions suggested need to be done and under ideal circumstances all should be done immediately.

High priority

Reducing exposure to nitrogen dioxide, particulate matter and diesel engine exhaust has a high priority, because children's susceptibility is high for most symptoms, and because exposure of children in Europe to these air pollutants is very high, leading to respiratory effects and neonatal mortality. Also exposure reduction of benzene has a high priority, because exposures in urban areas are often high, leading to additional cases of cancer. Reducing children's exposure to environmental tobacco smoke is of high priority, because children are more susceptible than adults, most children are exposed and exposure is associated with many severe health effects. Exposure reduction of allergens is given a high priority, because many children experience allergic symptoms. Reduction of exposure to mercury in Europe still has a high priority. Many children are exposed to mercury levels that are shown to be associated with serious health effects.

Medium priority

PINCHE concludes that exposure reduction of ozone is of medium priority. In children, health effects of exposure to ozone can be severe, but the formation of ozone can not easily be changed by policy measures. Also exposure reduction of moulds is of medium priority, because exposure to mould, or associated types of exposure, leads to respiratory symptoms. Exposure reduction of pesticides has a medium priority in general, but this priority differs greatly between European regions. In the North-West of Europe exposure is low, but in Central and Eastern Europe, children's exposure to pesticides is higher because of a higher pesticide use and because of a small-scale farming that brings children into closer contact with pesticides. There is a high priority to reduce exposure in those areas. The priority for reducing exposure to formaldehyde is medium. Many children are exposed to formaldehyde at levels that cause respiratory health effects. Reduction of exposure to polychlorinated biphenyls (PCBs) and dioxins is of medium priority, because exposure levels have decreased, but children are susceptible and the health effects demonstrated at current exposure levels are serious. Although no health effects are expected at current exposure levels to polybrominated biphenylethers (PBDEs), their priority level is medium, because of the lack of toxicity data and because the levels in the environment are rapidly increasing. Similarities with other organohalogens regarding possible toxic mechanisms and the long persistency of these substances also suggest concern. PINCHE recommends continuation of monitoring studies and toxicity studies on deca-BDEs and other BDEs.

PINCHE further concludes that reducing exposure to transport noise, noise in schools, noise in discothèques and noise from personal audio players has a medium priority. Many children are exposed, children are more susceptible to develop some health effects, and exposure can lead to various serious health effects. Arsenic has a medium priority, because in some parts of Europe, mainly in Eastern Europe, children and pregnant women are exposed to levels causing adverse pregnancy outcomes and other health effects. Also the priority for cadmium is medium, because some children in Europe are exposed to high levels, leading to several health effects. Even though current lead exposure can still lead to severe adverse health effects, PINCHE rates the priority of lead reduction as medium, because most sources of lead have been regulated. Exposure to solar and UV radiation is of medium priority: exposure may lead to skin cancer, but exposure is also necessary for vitamin D production. More research on the amount of UV radiation necessary for vitamin D production is necessary. Exposure reduction to ionising radiation, including radon, is concluded to be of medium priority. Ionising radiation is suspected to cause a substantial part of all cancers, but mainly through natural background radiation that cannot be changed. Radiation from man-made sources could be reduced, but the health benefits of medical use of radiation should be acknowledged. Reduction of radon concentrations indoors is possible, though effective measures can be costly. Because of the consistent evidence that exposure to atmospheric polycyclic aromatic hydrocarbons (PAHs) at current levels may cause increased risks of cancer and intrauterine growth retardation, reduction of PAHs is of medium priority.

Low priority

Reduction of exposure to sulphur dioxide is of low priority, because current exposures are low due to policy measures taken in the past. Exposure reduction of endotoxins is of low priority, because respiratory effects may occur, but exposure may also lead to fewer allergies.

Some of the PINCHE partners who specialised in noise were of the opinion that exposure from fire crackers and toys is very important, because the noise levels can cause instant and non-reversible hearing impairment, but the majority concluded that although these exposures are very intense, they are infrequent, and therefore, may have less impact on auditory health than other sources of prolonged noise exposure.

The priority of reducing exposure to cleaning products is low, because of the small health effects associated with the cleaning products currently in use. The priority for reducing exposure to chlorination by-products is low, because disinfection of water is necessary, and because the health effects caused by chlorination by-products are not clear. Exposure reduction to tetrachloroethylene, trichloroethylene and vinylchloride is of low priority, because exposure levels are low and the cancer risk is very low. Expo sure reduction of chromium and nickel has a low priority, because the cancer risk is low at current exposure levels in children. Because manganese is a micronutrient and because health effects at current exposures are small, the priority for reducing manganese exposure is concluded to be low. The carcinogens such as asbestos, beryllium, coal tar pitches, ethylene oxide, acrylamide, 1,3-butadiene, n-nitrosodimethylamine and n-nitrosodiethylamine are given a low priority, because children's exposure is very low, and therefore the risk of developing cancer due to these exposures is also very low.

The results of the prioritisation and the arguments used for classification are summarised in tables 2, 3, and 4.

Studied factors	**Argument for classification**
Nitrogendioxide, particulate matter, diesel engine exhaust	Children are more susceptible to the majority of the symptoms caused by these pollutants. Current exposure to these pollutants is high in Europe and leads to many respiratory effects
Benzene	Many children are exposed to high levels and there is a strong causal relationship with cancer
Environmental Tobacco Smoke	Many children are exposed and exposure is associated with many health effects
Allergens	Many children experience allergic symptoms and the societal impact is great
Mercury	Many children are exposed to levels that are shown to be associated with serious health effects

Table 2. Factors with high priority

Studied factors	Argument for classification
Ozone	Ozone leads to respiratory effects, but the formation of ozone cannot (easily) be changed
Mould	Exposure to mould (or associated types of exposure) leads to respiratory problems
Pesticides	Exposure is low in Northern Europe, but children's exposure may be higher in other regions because of higher pesticide use (due to small-scale farming and domestic use) and this exposure may cause health effects
Volatile Organic Compounds (VOCs)	Exposure occurs in different settings, and this can lead to some irritation and nervous system effects
Formaldehyde	Formaldehyde exposure is ubiquitous because of its widespread use. There are situations in which it leads to respiratory effects
Dioxins and Polychlorinated Biphenyls (PCBs)	Even though exposure levels have been decreasing, the health effects demonstrated at these levels are potentially serious
Brominated flame retardants	Although there are no health effects expected at current low levels, toxicity data are lacking and levels are increasing rapidly. Because of their persistence and their similarity to polychlorinated biphenyls (PCBs) concern has been raised about the effects on human health. Their priority may change in the future when more toxicity data are available
Noise in discothèques and from personal audio devices	Adolescents are exposed to high noise levels, which can lead to hearing impairment, including tinnitus
Transport noise and noise in schools	Many children are exposed to levels that may lead to adverse effects, mainly on cognition
Arsenic	Children and pregnant women are exposed to levels causing health effects, but only in some parts of Europe
Cadmium	Some children in Europe are exposed to levels that may cause health

	effects
Lead	Most sources of lead exposure have been regulated, but lead is still a problem in some places and is associated with severe health effects
Solar radiation	Exposure can lead to skin cancer, but vitamin D production is important as well. Research should be encouraged on the amount of solar radiation necessary for vitamin D production
Ionising radiation	Ionising radiation is suspected to be responsible for a substantial part of all cancers, but mainly from background levels that cannot be changed. Human-made (internal) exposure may cause additional cancer, but beneficial effects of medical radiation therapy should also be taken into account
Radon	Radon is associated with lung cancer. Exposure in dwellings can be reduced, though effective measures can be costly
Polycyclic Aromatic Hydrocarbons (PAHs)	Current exposure to PAHs may lead to lower birth weight and intrauterine growth retardation. The exposure levels are associated with a small risk of cancer

Table 3. Factors with medium priority

Studied factors	**Argument for classification**
Sulphur dioxide (SO_2)	Current exposure levels are low due to policy measures taken in the past
Endotoxins	Respiratory effects from exposure are not clear and early exposure may benefit health
Cleaning products	Children’s exposure is not suspected to lead to severe health effects
Chlorination by-products	Disinfection of water is necessary and health risks of exposure to chlorination by-products from drinking water or from pool water

	are not clear
Noise from toys and firecrackers	Although the exposure level can be high and can occur at a very young age, extreme exposure does not occur often
Noise in neonatal intensive care units	Exposure has only been proven to be related to sleep disturbance and not to other health effects
Chromium VI	Children's exposure is low
Nickel	Environmental exposure causes a very low cancer risk
Manganese	Exposure is low and manganese is a nutrient
Beryllium	Children's exposure is very low

Table 4. Factors with low priority

Discussion

The different stakeholders of PINCHE, mainly scientists, NGOs and industry, coming from different areas in Europe, did not reach consensus on whether or not it was feasible or even desirable to assess the priorities for environmental health of children in Europe. Once that issue was settled, determining the priorities for such a broad range of exposure factors proved to be difficult because no one had extended knowledge on all of these exposure factors, because the health effects related to the different exposure factors are very different and therefore difficult to compare, and also because priorities differ from region to region. Nevertheless, a priority list has been created, using the qualitative criteria mentioned, because it was felt that informing the EU and member states on relative priorities is necessary to focus EU policy on the stressors that should be targeted first. Although priorities in some regions of Europe may differ from this list, the list provides an overview of which environmental hazards we see as being the most immediately threatening to children's health in Europe. There has recently been a publication which uses the WHO "burden of disease" principle to evaluate the burden of disease attributable to selected environmental factors on children[93]. This publication also concludes that there is an urgent need to reduce children's exposure to certain environmental factors such as air pollution.

However, no attempt is made to prioritise these factors against others as has been done in PINCHE.

We feel that the present overview of environmental risk factors and the urgency of preventing negative effects on children's health caused by those risk factors represent important information for the policy makers of the European Union as well as for its Member States.

PINCHE's partners agreed to give high priority to the reduction of exposure to outdoor air pollutants and environmental tobacco smoke. The main discussion within the group concerned the priority setting for the brominated flame retardants, lead, PCBs, dioxins, allergens, pesticides, ionising radiation and some of the noise sources.

PCBs, dioxins, lead, pesticides and ionising radiation clearly all have severe effects on children at present exposure levels. However, some policy measures are already in place and exposure levels are declining or are expected to decline in the future. For this reason, their priority was set as medium.

The priority setting for pesticides was based on the literature related to pesticides used in agriculture. There is, however, an increase in the use of pesticides in home and gardening applications in Europe, which might lead to reconsideration of the medium priority.

For polybrominated biphenyls, the discussion was based on the use of the precautionary principle in the present situation of an expected rapid increase of these substances in the environment, versus the lack of sufficient data demonstrating a clear direct toxic effect. Priority was set as medium.

For noise, there was a difference of opinion regarding the effects of short exposures to high intensity noise versus long-term effects of lower level noise from various sources. Also here, a medium priority level was chosen.

Allergens were discussed as well, because exposure to allergens is very difficult to change outdoors, but also because the measures aimed at reducing allergen exposures indoors are often not effective. Because many children are sensitised to allergens and because allergic symptoms can also be reduced by improving outdoor air quality, their priority was rated as high.

It should be made clear that exposure factors that were rated with a 'low' priority, for example many carcinogens to which children's exposure is low, should not be considered as causing no harm to children's health. It means that, at present, exposure reduction of these compounds is of lower priority than that of the other compounds. However, exposure reduction should be carried out in hotspots, and in cases where exposure reduction is relatively easy to achieve, it should certainly be done.

In PINCHE, many environmental health hazards were studied, but this did not include exposure to all the potentially harmful environmental agents for children. The risk factors not studied in PINCHE were, for example, non-ionising radiation, phthalates and some endocrine disrupting chemicals. Because of this, and because exposure of children may change and more evidence on health effects may be found, the priority list should be revised when new information becomes available. The precautionary principle should apply under all circumstances and safe levels for children should be the target.

Acknowledgements

PINCHE was financed by Directorate-General (DG) Research of the European Commission within the Fifth Framework Programme for research, technological development and demonstration activities in the Quality of Life and Management of Living Resources (LIFE) Programme Key Action 4: Environment and Health (QLK4-2002-02395).

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CHAPTER 9 THE CHALLENGE OF SOCIAL NETWORKING IN THE FIELD OF ENVIRONMENT AND HEALTH

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Published in: van den Hazel et al. Environmental Health 2012, 11(Suppl 1): S15

Abstract

Background: The fields of environment and health are both interdisciplinary and trans-disciplinary, and until recently had little engagement in social networking designed to cross disciplinary boundaries. The EU FP6 project HENVINET aimed to establish integrated social network and networking facilities for multiple stakeholders in environment and health. The underlying assumption is that increased social networking across disciplines and sectors will enhance the quality of both problem knowledge and problem solving, by facilitating interactions. Inter and trans-disciplinary networks are considered useful for this purpose. This does not mean that such networks are easily organized, as openness to such cooperation and exchange is often difficult to ascertain.

Methods: Different methods may enhance network building. Using a mixed method approach, a diversity of actions were used in order to investigate the main research question: which kind of social networking activities and structures can best support the objective of enhanced inter- and transdisciplinary cooperation and exchange in the fields of environment and health. HENVINET applied interviews, a role playing session, a personal response system, a stakeholder workshop and a social networking portal as part of the process of building an interdisciplinary and transdisciplinary network.

Results: The interviews provided support for the specification of requirements for an interdisciplinary and transdisciplinary network. The role playing session, the personal response system and the stakeholder workshop were assessed as useful tools in forming such network, by increasing the awareness by different disciplines of other's positions. The social networking portal was particularly useful in delivering knowledge, but the role of the scientist in social networking is not yet clear.

Conclusions: The main challenge in the field of environment and health is not so much a lack of scientific problem knowledge, but rather the ability to effectively communicate, share and use available knowledge for policy making. Structured social network facilities can be useful by policy makers to engage with the research community. It is beneficial for scientists to be able to integrate the perspective of policy makers in the research agenda, and to assist in co-production of policy-relevant information. A diversity of methods need to be applied for network building: according to the fit-for-purpose-principle. It is useful to know which

combination of methods and in which time frame produces the best results. Networking projects such as HENVINET are created not only for the benefit of the network itself, but also because the applying of the different methods is a learning tool for future network building. Finally, it is clear that the importance of specialized professionals in enabling effective communication between different groups should not be underestimated.

Background

The lack of a structured and integrated international network encompassing the entire field of stakeholders in the domains of environment and health is apparent. Furthermore, there is no common platform for interaction between policy makers, scientists and other societal representatives. The European Commission requested the organisation and structuring of networking activities between a diversity of actors in the field of environment and health in the HENVINET (Health and Environment Network) project, an FP6 project funded by DG Research. The core concept is that by facilitating interactions between professionals across disciplines and specialisations, an interdisciplinary and trans-disciplinary social network could lead to an enhanced problem solving potential. Inter- and transdisciplinary networks are frequently considered as a useful means of enhancing communication and cooperation between different actors in order to raise the problem solving potential of both science and policy makers. However, such networks are not easily organized, as openness to such cooperation and exchange is often lacking[1].

The aim of this study is to analyse which network building actions are most efficient. Questions arising in this respect include how could the diverse actors in environment and health learn from each other, listen to each other, and find ways to cooperate and exchange knowledge? HENVINET investigated the complex relationship between disciplines, and how the actors could open up to networking in order to enhance the possibilities for solving problems, exchange of knowledge on good practice and understanding each other's role. The main question is what kind of social networking activities and structures can be most supportive in delivering enhanced inter- and transdisciplinary cooperation and exchange?

The main objective of HENVINET was to establish an inter- and transdisciplinary network of professionals active in different disciplines and at different levels including local, regional, national or international. Sub-objectives were related to 1) the expectations of a network, 2) the most relevant policies to be addressed by a network, 3) the structure, organisation and provision of knowledge to be used by a trans-disciplinary network and, 4) the practical issues related to dissemination and outreach to potential stakeholders. The first, third and fourth sub-objectives are addressed in this paper, formulated into the following questions:

1) What gap can an inter- and transdisciplinary network of different professionals fill in integrating the domains of environment and health? (*What is the need?)*

2) How can the production and exchange of knowledge be organized and improved by means of an inter- and transdisciplinary network? (*What are the organizational aspects of a network?*)

3) How can an inter- or trans-disciplinary network be positioned in such a way that it serves the needs of a substantial portion of the experts, including policy makers and other actors? (*How can it reach out?*)

4) What are the results or outcomes of the different methods of creating an inter- or trans-disciplinary network, and how can lessons be drawn for future network building activities? (*What did we learn from different applied methods?*).

In this study experimentation with a diversity of actions took place in order to investigate the main research question: what kind of social networking activities, actions and structures can be most supportive in reaching the objective of enhanced inter- and transdisciplinary cooperation and exchange in the fields of environment and health.

As with most EU-funded projects the starting point for network building in HENVINET was focused on traditional communication, specifically dissemination of the work undertaken in the project; traditional in the sense of a one-way communication from experts to target audience. At the start of the project the aims and research methods of the consortium were defined and the publications to be prepared for the EU for dissemination purposes identified. In addition, information on the project was promoted via the HENVINET project website (http://henvinet.nilu.no), which was progressively developed. Newsletters, website, leaflets were some of the traditional tools used for project dissemination. The actual use of this information material by the broad range of stakeholders was largely unknown. The website statistics did not provide any definitive information on the usage of the scientific information provided. The experience of the authors from previous EU projects was that the outputs of research projects often fail to survive for long after the end of the project. There are no mechanisms in place in EU research projects to maintain project collaborators in a network, either formally or informally, after the end of EU contract funding.

Methods

HENVINET promoted a number of activities in order to facilitate experiment, and to meet the stated goals to develop understanding between diverse actors in order to improve the process of trans-disciplinary communication via networking.

Stakeholder Interviews

HENVINET conducted interviews with a diversity of actors to identify the needs of policy makers and other stakeholders for information from the scientific community. In particular, interviews were conducted to obtain inputs from a diversity of stakeholders concerned with the construction of an inter- and transdisciplinary network in the fields of environment and health.

Respondees

Candidates for interviews were proposed by the HENVINET consortium (scientists, policy experts, and some advocacy stakeholder groups), and a range of experts from both the environment or (public) health fields were engaged. The HENVINET partners prepared a list of policy experts located at regional, national and inter-governmental organisation levels, which all had some connection with environment and health. The potential interviewees were contacted by telephone by members of the consortium, an appointment was made for a personal interview, and in a few cases where the distance between the partner and the interviewee was great e.g. Argentina, a telephone interview was held. All interviewees received the questions by email in advance, and the answers to the questions were compiled in English.

Networking portal

Evidence from other EU projects indicated that networks, consisting of a diversity of disciplines in environment and health, are difficult to maintain[1,2], and accordingly a novel approach was sought. Different actions to secure actor involvement, both within and outside the consortium, were considered, ranging from classical approaches to knowledge exchange using reports to establish a social network. HENVINET examined the option of establishing a virtual network of actors from different disciplines, and decided to pursue this option by building an internet based network portal, to provide a structural tool for inter- and trans-disciplinary networking. A virtual network facilitates communication amongst a large group of different actors, and can be viewed as a means of providing a dynamic for social networking. There is little known about the long term effects of virtual social networks, and most existing networks are used for building professional contacts (such as Linkedin) or to exchange information on any given topic. Social interdisciplinary networks with the aim of supporting the policy process were not identified in the literature.

A role play session

Role Playing Games (RPG) are used as Information and Communication Technology (ICT) tools that aim to provide support for educational activities, and for analysis and support for negotiation processes[3]. RPG aim at providing participants with improved knowledge of a given case or situation, reproducing part of the complexity of any issue in order to assist scientific and/or stakeholders understanding. From analysis to support, RPG are involved either collectively or individually in various negotiation processes. The design of RPG is not standardized, therefore they should be used as a tool based on an empirical approach, and should address awareness of behavioural patterns through the specification of roles and rules, as well as learning about the behaviour and viewpoints of players[3]. Barreteau states: "RPG aim at simulating complex systems such as those that are at stake in negotiation processes. These simulations are based on the background assumption that it is useful to control part of this complexity in order to (i) better grasp the consequences of the controlled part and (ii) make the other part react to the situation proposed by the controlled part"[3].

To the best of our knowledge, the network building capacity of role play has not been reported in the literature.

Voting session

A Personal Response System (PRS) is a form of technology that permits an audience to reply to questions or statements individually by selecting an answer on a hand-held wireless transmitter. The answers are collected by receivers connected to a computer. Computer software aggregates the responses, and the results are projected on a large screen using a standard beamer and software.

The PRS is very easy to use and offers a method of active engagement. Some research has found that it has a very significant effect on students' performance in lectures, stimulating their interest and concentration[4] and creating greater engagement and broader participation[5].

Furthermore, it increases the audience's enjoyment of lectures, and it has proved to be an excellent method of encouraging active learning. There is no data about the role of PRS in building trans-disciplinary networks, and this technique has not been used in the field of environment and health before.

Stakeholder workshop

HENVINET conducted a workshop for stakeholders including policy professionals working on the theme of climate change in cities (for an extensive report on this workshop see[6]). The European Commission (EC) White Paper "Adapting to climate change: Towards a European Framework for Action"[7], for example as a frame of reference, considers the necessary adaptation responses of the EU and the member states in defining a framework for action in response to climate change, including human health. A workshop is a common forum to bring actors from different fields together.

Results

Stakeholder interviews

The geographic origin of interviewees was 74% from Europe and 26% from outside Europe. The period of the interviews was between July 2007 and April 2008, and a total number of 23 interviews were performed.

At the commencement of the interviews the purpose of building a network within the HENVINET project was explained, and subsequent questions related to the establishment of this network included: ‘Do you have comments, suggestions, and concerns about the HENVINET network? What do you expect from HENVINET?’ To these open questions four different key word response options were provided which related to a role or expectation from the network including: information, cooperation, dissemination and policy.

The key word information was mentioned by most of the interviewees (n=23). In addition, the interviewees had more suggestions for what kind of information is needed or how this should be presented. These included information as review of research, stimulation of empirical multidisciplinary research, collection of data (showing associations between environmental factors and human health), provision of access to data- bases, access to information at the local level, identification of knowledge gaps, and finally gathering information from other research fields.

Cooperation between a diversity of actors was mentioned by interviewees as an opportunity for a network to maximise the distribution of the available results. Interviewees also stressed that the European dimension provides added value with the respect to distribution, such that results could be disseminated internationally. Interviewees emphasised the need for extension of the network to include other, new stakeholders, if it intends to maintain its growth in the future. As stated by one interviewee: ‘the challenge is not the lack of information and research results, but we are not able to make knowledge available for decision making.’

The role of the network in respect of dissemination was identified by interviewees as a role interacting with different actors, but more specifically it is viewed as an opportunity to secure gain closer collaboration between policy makers and researchers. This role is identified as critical in the responses of the interviewees, confirming the need for an integrated approach, the formation of a network, and we ensuring the trans-disciplinary approach of the portal.

A specific role for the portal was identified in the translation of scientific information to vulnerable groups. Interviewees suggested that this could be done in a practical way with leaflets targeted at schools, hospitals or public authorities. The interviewees were clear about the need for a network in the field of environment and health, and although a challenge was identified in remaining fully up-to-date in the dynamic field of health and environment, this might be assisted by involving as many experts as possible in order to keep the information up to date. This recommendation links to the role of an intermediary, and the different roles Jeffrey[8] identifies for cross-disciplinary research. The intermediary is accepted by all parties on grounds of the mediator's integrity and good will. Jeffrey states that "the disciplinary groups need to believe that the intermediary is a credible and competent individual, and that he or she has the best interests of the project as a whole at heart"[8]. The intermediary is an effective communicator and experienced in operating intellectually in more than one disciplinary area.

The third research question dealt with the positioning of a network to fulfil the needs of a substantial portion of the experts. A first step was identified, by the interviewees, with regard to the policy field, namely the need to make a distinction between different groups of decision makers, and the view that the network should address the science-policy interface by providing clear and concrete policy recommendations, relevant to the different groups of decision makers.

Indeed several distinct strands of opinion can be identified in the responses of interviewees. There is a group that want the network to heighten the awareness of policy makers with respect to the effects on health of environmental factors. This group suggests that we need products that can be used by politicians to improve access to information.

Another group wants the communication improved between researchers and decision makers. This includes an increased awareness of researchers about their own objectives, their own interests and that of policy makers. A suggestion was also made that the network should develop the concept of the scientist for global responsibility.

Another strand of responses identifies the need for experts who can act at the interface between research and policy to influence policy making. The misleading and prevalent model in which knowledge flows from the scientist that produces, to the policy maker that consumes is according to this group of interviewees, an incorrect interpretation. When policy makers do not respond to scientific inputs one might identify a communication problem, but equally policy makers may have their own strategic requirements supporting selective use of scientific information. Therefore, as indicated by several interviewees, the network has to consider the construction of a robust and enduring structure by early engagement with stakeholders.

Finally, most interviewees identified the difficulties in building a network between the scientific and policy community. The starting point is that simple policies do not exist, and one measure is never the solution, so a plan consisting of a series of measures is necessary, as many factors are involved in the management of any environmental - health effect relationship. In this respect a notable suggestion was that the research community has to play a role in the development of integrated health policies.

Based on the interviews with different stakeholders, most of them working in the policy making field, a concept emerged focused on the establishment of a social, virtual network as a platform for communication between different stakeholders. This was seen as a possible way to position an inter- or trans-disciplinary network linking experts in the field of environment and health. In conclusion, the interviewees confirmed the need for an inter- or trans-disciplinary network.

Networking portal

HENVINET developed a social, virtual network portal for a trans-disciplinary group of individuals working in the health and environment domain at http://www.henvinet.eu. The aim was to develop a parallel communication between scientists and policy experts, and also between scientists themselves, and between policy experts. This does not, however, mean that the communication is only limited to the scientific and policy communities. Other actors were also invited to participate and become a part of this virtual network. Up-to-date knowledge on the selected themes of HENVINET was made available via the portal, and current social networking tools, comparable to Facebook or Linkedin, were installed. Individuals registered for the portal, created a personal profile, and indicated their interests in specific topics and their own speciality. Automated notifications of new information uploaded on the website were installed, and several thematic discussion groups were formed.

The fourth research question dealt with the outcome of the different methods applied and the lessons which could be defined. The portal is relatively new, but some initial results are already available.

The structure of the portal is comprehensive, including functionalities concerning making new contacts, viewing related events, and discussing trans-disciplinary topics of interest[9,10]. The framework of the portal was sufficiently broad in scope to address and assemble content for the various sub-themes of the health and environment field, for example the HENVINET project topics of: cancer, neurodevelopmental disorders, asthma and allergy, endocrine disrupting effects, climate change and health, and nanoparticles. Other example topics addressed included: noise pollution, bio-monitoring, children's health, and transport induced air pollution.

Whilst the design and structure of the portal is robust, overall participation within the networking portal during the project period was low. The quality of the content within the various thematic groups and topics was considered satisfactory, but the amount and diversity of content available was less satisfactory. These results suggest that whilst a functioning platform was offered to enhance social networking great, a gap or some blocking mechanism existed which prevented the virtual network from being effectively established and becoming sustainable.

A role playing session

HENVINET conducted a role play session at one of the project annual meetings (April 2009). The role play format was inspired by experience with the development and use of role play previously developed within the field of environment and health[11,12]: where by a balance needs to be found between respect for the complexity of environment and health issues which the role play aims to discover and discuss, and the reality that the role play should not be too difficult to perform by the participants in order to fulfil its social learning capacity. In order to make the role play easier to perform but also sufficiently illustrative of the complexity of reality, the discussion agenda was narrowed to one simple question. At the same time the diversity of actors involved in the discussion aimed to create the potential for the discussion to mirror the complexity of environment and health. The aim was, so to speak, to conceal the complexity of the situation behind the different social perspectives on what could be viewed, at first sight, as a simple issue.

The participants had to play roles, in small groups of two to four persons, representing stakeholders from different organisations such as national authorities, scientific organisations (as consultants), industry, public health authorities and NGOs. The topic of the role play was a discussion on the meaning of a policy brief on the environment and health risks of a pollutant: the role play discussion by a diversity of actors aimed to provide the authorities with advice on measures to be taken regarding the pollutant, based on the expert advice in the policy brief. The aim of the role play was on the one hand to test how a stakeholder discussion on such a policy brief evolved, and on the other hand to introduce stakeholder involvement to the participating experts. It thus aimed to perform a learning experience in different respects.

At the beginning the participating scientists were sceptical about the usefulness of such a session. Two moderators introduced the topic and the structure of the RPG. The roles were distributed among the participants of the session. These roles were randomly distributed. The roles were allocated to five different groups: local government, local residents, industry, non-governmental organisations, and public health authorities. The diversity in roles aimed to ensure that the complexity of the issues under discussion would be highlighted by the different perspectives and stakeholders. The moderators provided role-information at the start of the session. Most participants could use their own experience and knowledge to fit their role. First a plenary exchange of views was provided by the different role groups. In two rounds the issue at stake was debated and in plenary sessions views were exchanged. After the role play the outcomes were presented at a plenary session of HENVINET in order to inform experts not present at the role play about its findings.

The participants were free to choose a view or opinion on the issue. Each role was represented by three to four persons. Each group was then requested to present two arguments in favour of their view. The next step was a plenary exchange of views. Already during the first round it was clear that the industry group was in opposition to most other role-groups, for example the NGOs. The moderators on occasion stimulated the discussion in the role-group by feeding them with additional information to develop discussion. Two rounds of argument and discussion followed in which the other role-groups defined their position. Finally, a plenary discussion about advice to local government actors was scheduled. After this the role play group discussion and evaluation took place. In this session the participants learnt from each other the lessons that emerged, and how each group supported its own arguments. The subgroups easily adopted the stereotype role of the stakeholder they represented. Industry was defensive, NGOs greatly opposing industry views, experts requesting more research, and local authorities waiting for a decision. In the evaluation it was stated that the views of different social perspectives were most valuable.

The scientists performing the role of the NGO discovered how simple it was to use their own scientific knowledge to attack the polluter, the industrial representative. While the national authority representatives found it hard not to allow their scientific knowledge to prevail over the other issues they had to address including economic and social issues. The public health authorities were easily manoeuvred into the position of defending the general public's interest and health, although internally they had difficulties in agreeing the level of scientific proof. As a result they became less interesting partners for both the national authorities and the NGOs. Finally, the industrial representatives became defensive and deployed all available arguments concerning lack of scientific certainty to avoid any responsibility or claims of harm done.

Voting session

Using PRS, the participants at the HENVINET Final Event were asked to participate at an interactive voting session in order to review feedback concerning the HENVINET portal and to develop suggestions for further deployment and development. Areas addressed at this session involving 53 participants included: analysis of stakeholders; needs of the participating stakeholders; involvement of stakeholders in network activities; science-policy interface.

The participants were mainly represented by researchers (44%), providers of public information on Environment and Health (17%), risk assessors (15%) and those related to the policy field (15%).

The majority of voters considered the most important feature of the HENVINET portal to be the provision of scientifically sound information provided by experts in the user's field of interest. Detailed issues such as user friendliness or the value of an automatic system for notifying new items on the portal appeared to be less important.

Questions arose about the most important and desirable factors in the development of policy advice, and 50% of the participants agreed that the traditional evidence based culture is in need of critical discussion and innovation. Only a small number of voters favoured the view that scientific information, as presented during the conference, should continue to be used by policy makers for decision making. The full results are reported in[13].

Stakeholder Workshop

The HENVINET workshop on integrated urban management - climate change and health impacts addressed a prime goal identified by the White Paper[7] concerning: integration of climate change adaptation and health within policy frameworks at both local and EU levels.

The workshop deployed the backcasting approach as a form of expert analysis, building on the experience and expertise of a multidisciplinary group of experts in response to the complexity of many issues. This complexity is identified in the risks associated with climate change adaptation and mitigation measures proposed at the urban level, and the associated uncertainties regarding outcomes in respect of human health, quality-of-life, and economic vitality. The methods and reasoning for this approach are fully explained in Keune et al.[6]. Presentations were given on behalf of the cities of Bristol, Prague, Bologna, Ancona, Tilburg, and Frankfurt, and it is evident that the cities are using a wide range of integrated management strategies in response to a range of environmental topics based on the varying geographical and historical conditions of each city.

A first observation arising from the HENVINET workshop, but similar to that seen in other workshops, is that the participants from organisations outside the project consortium are already active in the topic. Most of these stakeholders are seeking additional knowledge, want to exchange ideas with colleagues to increase the quality of their own policy making, or want to confirm their proposed policies.

A common message resulting from the city presentations was the need for caution in adopting strategies from cities with different structures i.e. most strategies are customised to the specific region they were developed for, and it may be inappropriate to simply export these strategies to new areas with locally differentiated requirements.

The backcasting exercise was based on an agreed common target statement for the year 2030 – the statement stresses the importance of a healthy population and cooperation towards this goal. The numerous opportunities and barriers to the attainment of this goal were discussed, in which many of the issues included factors such as economics, communication, public engagement, policy specifics, and local alliances. A major recurring issue, much discussed when developing common targets, concerned the lack of knowledge regarding the connection between climate change and specific health effects. There is sufficient knowledge to realize some actions, but this could become a bottleneck in the future when more concrete measures need to be implemented.

The workshop was appreciated by all participants, and can be seen as a valuable exercise for cities in sharing their experience in formulating integrated management approaches addressing climate change and health issues. It is hoped that a permanent expert group can evolve from these workshops to provide a bridge between science and policy for enhanced collaboration between health and environment.

Discussion

With regard to network building, activities used in HENVINET may be identified as a form of action research. They were used as drivers to produce practice-relevant results in building a network consisting of a diversity of actors. The ambition was to enable scientists, policy makers and other actors to interact and co-operate by involving them in the various activities. Participation in these activities aimed to enhance the understanding of each other's position in the process of policy making.

Social scientists supported the process of network building. The activities were established by an interdisciplinary group of actors from HENVINET, including (social) scientists, medical doctors, veterinarians, statisticians, epidemiologists, public health professionals, policy makers and other professionals. These activities were undertaken to enhance awareness by the participants of each other's role in the environment and health policy making process. The relevance of such a mixed methods approach has been described[14], elsewhere, and the context in which the network building was defined was interdisciplinary triangulation, where several disciplines are used to inform the research process[15].

Since the EU FP5 programme network activities[16] have been developed within Coordination Action projects, and thematic networks, as a new form of research project. However, all these networks have been scientifically oriented and had difficulties in engaging

with policy related issues. Some networks produced reports on stakeholder analysis (e.g. AIRNET, NoMiracle, INTARESE) but all projects had difficulties in establishing stable connections to policy makers. No continuous network with a trans-disciplinary character was established.

One positive effect from these networks has been the establishment of more frequent contact between the scientific community and the multinational knowledge and data oriented organisations, most of them funded by the EU or the World Health Organisation, including the Joint Research Centre (JRC), European Environment Agency (EEA), and International Agency for Research on Cancer (IARC). These contacts have been useful in the exchange of knowledge, discussion on setting priorities in environment and health, understanding the interface with policy development at the EU-level, as well as awareness of the scientific impact on society and the social impact of non-action (e.g. EEA report: Late Lessons from Early Warnings[17]). So far a structured participation of representatives from the policy field has been rare, but there are a few exceptions. Policy makers participated as consortium members in an EU-funded project on Good Practice in exposure reduction options in the field of transport and health; and in the field of indoor environment and health[18]. National government policy makers contributed in the analysis of good practice, and inputs on analysis and feasibility of the implementation of measures was a useful contribution, which was widely disseminated across Europe. However, there were also some more negative aspects. One issue was the failure to use or promote innovative measures, and the presumed difficulty of 'selling' some examples at the political level blocked the implementation of certain measures. Furthermore, some conservatism in complying with the fixed set of rules and regulations of the political system prevailed, and there was a lack of organisational opportunity to act and to obtain internal financial support from the project consortium.

In addition, there is no discussion about the available knowledge or the quantity or quality of results from research in the field of health and environment. This is confirmed by the views of the policy experts interviewed, although the sharing of knowledge and transfer to actors in other disciplines or other fields of work is less common.

All of this may reflect the fact that there is some reluctance within the scientific community in participating in the science-policy interface, as it appears to be a focus for "stiff competition". Dabelko[19] stated: "An information glut is flooding everyone who can influence public policy. The competition for eyes and ears is stiffer than ever. And many academics who are reluctant to stray beyond the narrow bands of disciplinary journals take that competition as confirmation that we should let policymakers find us, not the other way around"[19]. The application of some actions in HENVINET, such as the role playing session and the workshop with policy makers, opened the interaction between scientists and policy experts. It can be argued that the topic of the workshop, climate change and health, remains at the stage of scientific fact finding and thus might be more open for interaction.

However, time is also needed for building a trans-disciplinary network. At the start of HENVINET scientists did not see the need to provide policymakers with information. The attitude was passive. The project leaders had to shift this attitude towards a more active one by finding the right activities and structure to enhance cooperation between disciplines. The results of the different actions demonstrate that the various exercises and presentations during the project to encourage network building have altered this passive stance of the various health and environment experts. For example, placing the scientist in the role of industry or local authority radically changed the position of some participants in the role playing session. Dabelko explains this situation well, "But if scientists don't engage in policy discussions and make our work more widely available, then we lose the ability to complain about policy decisions. And we miss genuine opportunities to share our insights. And a range of so-called "experts," whether from industry or advocacy, will engage whether we do or not. Scientists (…) need to be part of these policy debates. Otherwise we cede the ground, I think, needlessly”[19].

Interviews, role playing session, voting system and stakeholder workshop

This paper has discussed a number of activities to stimulate and facilitate the interaction between policy makers, scientists and other actors from civil society and industry. It has been concluded that the institutionalisation of this interaction is not easy. A first threshold is the fact that within this project consortium members were present who were very sceptical about cooperation across disciplines. Most likely this will be a starting point for other networks as well. Different activities were undertaken to increase awareness among the scientific partners within the consortium. The role playing game proved to be a successful action.

The role play session illustrated the usefulness of stakeholder involvement in procedures that aim to provide policy advice based in scientific expertise. The social complexity of environment and health issues was clearly illustrated during the role play, indicating the added value for policy makers to be informed not only about scientific aspects of environment and health issues, but also about social aspects from a diversity of actor perspectives. The role play moreover was able to convince most of the participating experts of the usefulness of stakeholder involvement. One of the more sceptical experts in the end became one of the main defenders, and as a spokesman for the group vigorously presented the benefits both of the role play and stakeholder involvement to the non participating experts from HENVINET.

Moreover some participating experts indicated that the use of a method like the role play would have been beneficial to their perception of their involvement in the HENVINET project development, as it gave them the opportunity to better express their opinion in an interactive and cooperative manner.

The voting session provided ideas about ten different issues. Such a session could be applied as a tool to illustrate different opinions, points of interest and linkages between stakeholders from different fields of expertise. The formulation of questions or statements has to be carefully considered. Discussion regarding the votes proved to be an easy way to collect additional arguments around the questions.

The application of a PRS was received very positively by the participants. Quick feedback on the questions presented and the subsequent discussion was considered useful. The system can be used to bring the opinions of a trans-disciplinary network to the table in a rapid and participatory way, and the different disciplines can contribute without any feeling of being in the minority.

The stakeholder workshop was used to bring together the scientific community and the policy community. The sharing of information about the knowledge required, and also about success in the implementation of policy measures, stimulated desire among the participants of the workshop for further contact. From the acknowledgement of shared problems a small ad hoc network was formed. The role of intermediary was undertaken by HENVINET. Such a role should be defined to build a bridge between scientific and policy communities in a trans-disciplinary stakeholder workshop. These actions as well as the network portal, the role of intermediary institutes, organisations or group of individuals should be further investigated. It was believed by experts interviewed, and also mentioned during the PRS session, that this role is crucial for the survival of a trans-disciplinary network. This role could be compared to what Jeffrey calls the intermediary role[8].

In any stakeholder workshop one has to consider that there are some limitations to its success. Most of these limitations have to do with lack of communication between the expert, the non-expert stakeholders and the policy regulators. A human obstacle is that some people do not change their minds, which may be a failure attributed to the project actors. The lessons learnt from risk communication are that there has to be trust in the intermediary, besides the quality of the scientific knowledge used. A regulatory obstacle may be that local politics can conflict with national/international regulations.

A practical reason can be financial: the resources are needed right now in order to achieve the goals, but are not available; and politically: it may be more acceptable to invest in the domains where there are the most visible problems, while it might be less effective to solve these. These same arguments are also true for the success or failure of the network portal.

Networking portal

The action considered being more influential and most durable of those applied in HENVINET was the creation of a networking portal. The networking portal has the potential to be an effective tool to facilitate the sharing of knowledge and communication between stakeholders. The drawback of the networking portal is that each contributing part in such a network waits for the initiative of another actor (for example to supply content), and that success depends on the actions of a few leading stakeholders in the network. Furthermore, there are many other hurdles related to these types of networks: differences in the basic knowledge of actors, the different perceptions and perspectives of policy relevance, gaps in communication or communication language, dependency on funds, and the uncertainty of scientific knowledge. The benefits of a network of trans-disciplinary nature include: building of alliances with the private sector and civil society; building of new ways of communicating messages for the public. Stern et al. state that "the participation of both scientists and non-scientists is necessary for careful consideration of the implications of decision rules"[20,21] and therefore in contributing to the formation of policy measures.

The network portal provides a supportive structure for inter- and transdisciplinary cooperation, but such a platform needs continuous participation in order for it to become an active network. It has been proposed that skilled intermediaries are useful players to help policy makers engage with the research community. The example of the professionals in organisations like EEA, IARC and JRC are the given as intermediaries at the European level. At a more national, regional or urban levels these kinds of intermediaries are less available or even absent. While stakeholders from the policy field indicated in interviews that a trans-disciplinary network on health and environment would be a useful addition in this domain, they did not give clear answers on how to fill the role of intermediaries who could interact between the science and policy domains.

Social networking portals, role play, stakeholder workshops or a Personal Response System applications are means to bring the different stakeholders together. They were applied here partly to get input on the required structure of the proposed network.

The HENVINET experience demonstrated that the networking portal is a tool suitable for disseminating knowledge, but it will never be the sole source for information- rather a complementary tool for policy makers. The networking function enables stakeholders across disciplines and domains to find the experts, but it does not provide policy makers with the insight to engage with the research community in a way which connects with scientific thinking. Therefore it can be concluded that the role of intermediaries is in essence not replaced by the portal.

Conclusion

The answers to the research question concerning the needs of an inter- or trans-disciplinary network was provided by the interviews. The role of a network in dissemination was identified as an interacting role with different actors, but even more specifically to secure a closer collaboration between policy makers and researchers. This role is clearly specified in the responses of the interviewees and confirms the need for an integrated approach and the formation of a network.

HENVINET developed a social networking portal to enable stakeholders across disciplines and domains to find the experts, but it did not provide policy makers with the insight to engage with the research community in a way which connects with scientific thinking. Therefore it can be concluded that the role of intermediaries is in essence not replaced by the portal. The other applied tools provided insight in other domain’s thinking and acting, but do not have a role in the positioning of a network.

Several methods to form an inter- or trans-disciplinary network were applied. These methods, a role playing session, a personal response system and a stakeholder workshop were successful in increasing awareness among scientific partners about their role towards the policy domain. As supporting activity these methods can be used in building new networks. None of these methods can be used as the sole method to form a network.

The concept of the integration of science and policy within the environment and health fields using social networking principles has been outlined. This endeavour was envisioned at the beginning to be a purely scientific quest. It was anticipated that with the right group of professionals within the project consortium, the bridge to policy experts with regard to policy priorities for example, would naturally follow. In building bridges towards policy interpretation though, the limitations of a purely scientific undertaking were clearly demonstrated. Due to the many uncertainties and limited specialized knowledge, no scientist or group of scientists stepped outside their own niche and dared to use their knowledge to initiate discussions or to answer difficult questions about relevance. Similar conclusions have been drawn from other projects. One example of this is provided by a project involving a working group of scientists, governmental experts and policy representatives, mostly involved in the work of the Flemish Centre for Environment and Health, where they prepared an action-plan for the interpretation and use of policy for human biomonitoring data[14,22].

Participatory and dialogue based processes are available to combine scientific or practical expertise with policy and decision making. The main benefit of the different actions undertaken by HENVINET was to bring together people from different disciplines and domains.

The participation by different actors in the actions brought scientists and policy experts closer together. The combination of actions was productive at the moment of performance. It is not clear what the longer lasting effects of these actions will secure. The social networking portal is a transparent tool with a lot of potential, but the role of the scientists in a social portal is not yet clear. This lack of clarity is a major threshold for scientists to overcome in order to fully participate.

The policy expert is open to interdisciplinary activities, seeks transparency in problem identification based in integrative problem description and wants a clear knowledge transfer. These are essential ingredients for building a constructive and sustainable network of multiple stakeholders. The different actions provided by HENVINET contributed to these ingredients, but only for a short period. The social networking portal aimed to contribute to sustainable and continuing network building. It is yet too early to conclude if the social portal will be successful in contributing to building a transdisciplinary network in the field of environment and health.

Acknowledgements

The work has been funded by the EU FP6 coordination action HENVINET, contract no GOCE-CT-2006-037019. The text was prepared also with contribution from Research Council of Norway, grant no 205652.

The authors would like to acknowledge the HENVINET consortium for their participation in the role play scenario, and their input in the development of the social networking portal. The authors would like to thank the participants of the HENVINET conference in Brussels in April 2010 for their contribution to the voting session. The authors would also like to sincerely thank the participants of the stakeholder workshop in Brussels in February 2010.

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CHAPTER 10 CONCLUSIONS AND DISCUSSION

Introduction

This thesis focuses on knowledge about children's environmental health and analyses the role that knowledge plays in policy development. Various aspects are considered. First, the rise of the children's environmental health domain during the last two decades in Europe. Secondly, a validation of the knowledge in this field. Thirdly, an assessment of its relevance to policy making by providing recommendations on its use by policy makers, and fourthly an analysis of how this knowledge is used through networking between scientists, policy makers and other stakeholders. The following questions have been central in this thesis.

- Which mechanisms and actors have played a role in the agenda setting of children's environmental health during the last two decades in Europe?
- How has the children's environmental health domain developed in the last two decades?
- How did the validation of knowledge in the children's environmental health field contribute to the development of this field?
- How did making the knowledge in the field of children's environmental health relevant contribute to this field's development?
- How did the utilisation of knowledge in the children's environmental health field contribute to the development of this field?

Conclusion

Agenda setting of children's environmental health

The analysis in Chapter 2 (Article: *Children in European environmental health policy: the emergence and development of a policy issue*) clearly shows that international discourses on the production of knowledge about children have been strong drivers in the development of a children's environmental health agenda. The mechanisms underlying these newly emerging discourses about children´s environmental health and its institutionalisation process were studied through a historical analysis of the last two decades. One obstacle was that environmental health problems in children were not identified for a long time. Furthermore, most studies did not provide conclusions that could be used in policy making. The lack of specific knowledge about children and the complexity of knowledge are two key features of the obstacle to producing new policies. In the period 2000-2010 many new studies were conducted on children’s environmental health.

The WHO and NGOs have played an important role in in the domain of environmental health with regard to the scientific development and incentives for research production. These stakeholders have produced extensive compilations of knowledge about children that resulted in 1) the scientific community's growing interest in the topic; 2) insight in the vulnerability of children in a growing number of environmental incidents; and 3) insight in the effects of environmental stressors on children at low dose exposure. This shift in knowledge production paved the way to making the knowledge available to policy makers and was one of the mechanisms that played a role in the agenda setting of children’s environmental health. The EU's role with regard to policy development was important in the rise of children´s environmental health on the policy agenda in the period 2001-2010.

The historical analysis revealed that international and European initiatives (SCALE, CEHAPE, FP5, Ministerial Conferences on Environment and Health) for research and policy making were strong drivers that triggered the development of a children´s environmental health arrangement. These initiatives had strong implications for the agenda setting as they interfered with shifts in the science-policy interface: 1) a shift towards more co-production of knowledge as hypothesised in Post-Normal science; 2) a reconsideration of the role of knowledge as unquestioned source of legitimacy for policy arguments; 3) more legitimacy for the participation of transdisciplinary stakeholders in governance.

It is concluded that these mechanisms had an impact on the following steps: knowledge validation, making knowledge relevant and the utilisation of knowledge in children’s environmental health domain.

Knowledge validation

The EU and the WHO have commissioned the scientific community to validate knowledge about children’s environmental health and to observe the strength and relevance of scientific evidence. These organisations provided the resources needed to increase the knowledge validation after the Third Ministerial Conference in 1999.

The PINCHE thematic network validated results from studies related to more than 30 environmental stressors and the exposure of children to these. In addition, gaps in knowledge and barriers in research on children's environmental health were identified. The results of reviewed studies in PINCHE were scrutinised for their specific value to protect children. Tools such as risk evaluation, risk assessment and risk communication were validated for their use in the field of children's environmental health. A considerable amount of knowledge was compiled.

Four key discursive changes in knowledge validation have been observed that contributed to the epistemological development of children's environmental health:

1) The increased recognition of the value of knowledge specifically related to children. Institutions, such as the US Environmental Protection Agency, acknowledged that there was a gap in knowledge about children's environmental health; this has been highlighted in Chapter 2;

2) The recognition of children's vulnerability in relation to environmental stressors. A discursive shift was observed within environmental health from research on adults only to research on vulnerable groups, and most explicitly children. This result is shown in Chapter 3 based on an article about children's vulnerability;

3) The need to widen the knowledge base in children's environmental health. In Chapter 4 the importance of prominent health effects and diseases in children in relation to environmental pollution is provided. New emerging diseases, insight in chronic childhood diseases related to environmental exposure, and the missing role of several scientific disciplines in the knowledge production process were acknowledged. Chapter 5 gives the results of a study with a specific example of the effects on children from exposure to lead as an environmental stressor, showing the limitation of knowledge to protect children;

4) The increased recognition that different scientists and disciplines had a dissimilar perception of the health effects caused by environmental stressors (e.g., endocrine disruptors, childhood carcinogens).

The efforts by the WHO and the EU can be regarded as drivers which, through the four discursive changes, resulted in validated knowledge that could be made relevant for policy makers.

The conclusion is that knowledge validation positively contributed to the development of the children's environmental health domain. Children have become an entity on the environmental health policy agenda in Europe since 1999.

Making knowledge relevant

The PINCHE consortium has played a strong role in compiling a lot of validated knowledge. The specific request of the European Commission was to make the available and validated knowledge relevant to policy makers. The political will was there to interpret the knowledge for the benefit of children.

Four major discourses are seen in making the available knowledge relevant for policy makers at the European level. These discourses are described in Chapter 6 (Article: International strategies in children's environmental health) and Chapter 8 (Article: The environmental health of children: priorities in Europe).

1) The involvement of specialised stakeholders, such as politicians, paediatricians, environmental scientists and NGO representatives, in the discussion on children's position in the environmental health field;

2) The integration of relevant policy fields. The developments of the SCALE initiative, the Environmental Health Action Plan for Europe (EHAPE) and the Children's Environment and Health Action Plan for Europe (CEHAPE) were instrumental in making the knowledge relevant by integrating different policy fields. These discursive developments have allowed the children's environmental health field to evolve from a multidisciplinary into an interdisciplinary, and even transdisciplinary field;

3) The distinction of children as a vulnerable target group in society and their participation at international governance level. The fact that research has shown that children are vulnerable to environmental stressors in a different sense than adults has played a major role in making the available knowledge relevant. Children are increasingly seen as a

vulnerable group in society and hence incorporated in international policy making. PINCHE has produced a prioritisation of children's environmental health issues to ameliorate the quality process and the urgency of policy making in this new field;

4) The emergence of new organisational structures in environmental health with a focus on children. Different stakeholders have developed new organisations (NGOs), platforms (transdisciplinary symposia, meetings), new tools (pre-natal screening, risk communication) and methodologies (proposed norms for children, adjusted risk assessment for children, childhood cancer registries); these structures improved the interaction between science, politics, and society and made the children's environmental health knowledge relevant for policy makers to use.

In summary, the window of opportunity where scientific knowledge, political interest and advocacy activities of multi-stakeholders came together was established at the end of last century. Different stakeholders entered the arena and directed their attention on children's health and well being in relation to their environment. All of these stakeholders, partly new ones, brought new knowledge from their own disciplines, but also new questions to the table.

The conclusion is that the validated knowledge has been made relevant for policy makers at the international level. As we will see in the next section the EU used the knowledge as input for the implementation of research programmes under FP6. Member states used the results of the validation of knowledge for the Children's Environment and Health Action Plans.

Knowledge utilisation

The PINCHE and HENVINET projects analysed how knowledge about environment and health has been used. Three key issues can be discerned in the utilisation of knowledge that influenced the development of the children's environmental health field: 1) resources at different levels of governance; 2) development of strategies; and 3) networking. These issues have been analysed in Chapter 7.

Ad 1) Resources

The resources in children's environmental health are found in the scientific community and a limited group of NGOs and (inter)governmental organisations. The main resources are the people working in the field of children's environmental health and research funding. The WHO Regional Office for Europe and later the European Commission have been providing resources for steps towards knowledge utilisation (e.g. training, workshops) and initial steps towards the institutionalisation of children's environmental health. The increasing amount of knowledge, its validation and its framing by PINCHE was used by the European Commission to further the research agenda on children's environmental health (6th Framework Programme). In the EU's 6th Framework Programme the research agenda was set on identified priorities in children's environmental health. This resulted in a growing number of scientists working on child-related research.

The EU provided resources for the development of policy making in the field of children's environmental health. The then European Commissioner for the Environment Margot Wallström encouraged the process of policy making and the further support of research in this field. At different levels of governance resources were allocated to the children's environmental health policy domain. The policy agenda on children's environmental health was strong until the Fifth Ministerial Conference in 2010, when the decision was taken to broaden the scope to other vulnerable groups. Also resources from the EU allocated for research on children's environmental health stopped in 2007 at the beginning of the 7th Framework Programme.

Ad 2) Development of strategies

The agenda setting developed once the EU identified children's environmental health as a separate entity in the environmental health domain. But there has not been a prevailing strategy within the EU on how to help any Member State or the WHO to make rapid progress towards the institutionalisation of children's environmental health. The strategy, both on research and policy, was directed towards international development of children's environmental health. The only strategy to bring the children's environmental health arrangement from an international to a national level came from the WHO Regional Office for Europe. The WHO came with the idea that each European Member State had to produce a Children's Environmental Health Action Plan (CEHAP). In most countries this has been a one-off action. No institutionalised body has been established in the children's environmental health domain to develop strategies for policy making at EU or national level. Consequently, a national or international overarching strategy on environment and health, with a focus on children, which is explicitly integrated in all policy fields, is lacking. Some singular issue strategies (for example to protect children from air pollution) have been developed at the international level, but they have not been consistent or widely adopted at national or local governance levels.

Ad 3) Networking

The discourse of children's environmental health has led to transdisciplinary cooperation between actors. This has been described in Chapter 9. The formation of CEHAP committees in member states and the organisation of many conferences that focused on children's environmental health all reflect an involvement of stakeholders. This involvement is also seen in different forms of networks. Some interdisciplinary networks, but also transdisciplinary networks, have been established. The scientific community has collected, validated and translated the knowledge about children's environmental health into policy recommendations as shown in this thesis. Nevertheless, the analysis has also provided insights into some shortcomings of the cooperation between the scientific community and the policy domain at different governance levels. Some support structures for networking, such as the Consultative Forum of combined EU Directorates, have been abandoned. Consequently, networking activities are dispersed and fragmented when it comes to the application of knowledge.

In summary, the knowledge utilisation furthered the children's environmental health domain in relation to policy development until 2010 and for research development until 2007 at the start of the 7th Framework Programme. The lack of strategies and the lack of support for networks have been hindering the utilisation of the available knowledge in the children's environmental health field.

Discussion

As stated, the central aim of this thesis is to assess the extent to which knowledge production, knowledge validation, making knowledge relevant and knowledge utilisation have contributed to discursive changes, which in turn, have affected the institutionalisation process of children's environmental health arrangements. The discussion below focuses on some issues of children's environmental health as a new science-and-policy domain. Knowledge has contributed to the quick rise of the children's environmental health domain since the late 1990s. The reflection on children's environmental health elicits the question as to whether this new domain is here to stay as a policy domain.

The discussion of the potential institutionalisation brings forward the discursive changes on the following issues: 1) resources for knowledge development for policy making; 2) stakeholder involvement and networking; 3) regulatory processes; 4) science-policy interface; 5) problem ownership; and 6) effectiveness and political commitment.

Ad 1) Resources for knowledge development for policy making

Over the last two decades, scientific knowledge about the relation between environment and health has increased. DG Environment and DG Research of the European Commission, the European Environment Agency and the WHO have invested a lot of resources in the production of new knowledge and the validation of existing knowledge. Because of these increased resources, especially in children's health, a lot of transdisciplinary work could been done by scientists, policy makers, and NGOs. To ensure that the results of this work were used to underpin concrete policy actions, the EU developed the Environment and Health Action Plan. While this plan can be considered as a transdisciplinary effort to make use of the knowledge at an international level, there has been resistance at national level encouraging knowledge development for policy making in children's environmental health. National Environment and Health Action plans do not wholeheartedly incorporate children's environmental health issues. This could be because member states have to deal with many different environmental problems at a national, regional or local level and have been given a higher political priority. Consequently, resources at national, regional or local level to develop policies on the children's environmental health domain remain limited.

Since the start of the 7th Framework Programme in 2007 resources for research have decreased. The member states did not ask for additional research on children's environmental health. However, the scientific community was still looking for funds to continue research in the children's environmental health field. For example, there is a need for child-specific knowledge in toxicology due to the growing number of new chemical compounds. This knowledge is needed to protect young or even unborn children from health effects due to exposure to environmental stressors during their development.

Ad 2) Stakeholder involvement and networking

The window of opportunity to build the children's environmental health agenda was opened by the concurrent involvement of the scientific community, NGOs and governmental bodies from the Third Ministerial conference onwards (1999). The rise of children's environmental health on the policy agenda has been a clear recognition of children as a vulnerable group in society. The role of societal groups has become more influential, especially while the European Commission continued with the SCALE process and its Environment and Health Action Plan (EHAP). Children even have participated as stakeholders at the Ministerial Conference in Budapest (2003). After the Third Ministerial Conference (1999) many NGOs were supported by member states to do work on children's environmental health.

However, these developments, which originated from the EU, occurred in a short period between 2002 and 2010. No institution has been created to support the continuation of children's participation or any other stakeholder in the policy arrangement on children's environmental health. Additionally, stakeholders from the scientific, societal or NGO communities have been partly involved in the decision-making process. Their involvement declined after the last Ministerial Conference in Parma in 2010 and followed the decrease in resources from the EU since 2007. Furthermore, stakeholders are increasingly excluded from the decision-making process at an international level due to financial and political constraints. For the same constraining reasons, it is difficult for stakeholders, representing local actors or patient groups, to collaborate with the scientific community. The gap between the science community, working on children's environmental health, and the policy domain has been widening again since the Parma Conference (2010). However, stakeholders should be part of transdisciplinary networks in order to enhance the communication and cooperation to increase the problem-solving potential of scientists, society and policy makers. These stakeholders could play the role of boundary workers to bridge the gap between science, society and policy. Moreover, the participation of multiple stakeholders can increase the quality of the decision-making process. However, as mentioned, these stakeholders as boundary workers to bridge the gap between science, society and policy in the field of children's environmental health are missing. The power of those transdisciplinary experts in children’s environmental health is limited because they are not supported by strong institutes and they lack resources. There is a gap between the stakeholder’s specific expertise and the broad approach of institutes working in environmental health. Additionally, the direct stakeholders, in this case the children, are not represented themselves.

Ad 3) Regulatory processes

Besides problems related to the tier of governance, there are problems associated with regulatory processes. Policy makers at EU, WHO or Member State levels are bound by norms and standards that fit longstanding policies. These norms are mainly developed to protect the health of the general population, but are of limited value to children as they are based on studies of adult populations. However, it is difficult to maintain a parallel set of policies for children’s environmental health based on children's norms and standards that explicitly consider children’s vulnerability during certain periods of their life, as there is a large variation in exposure to environmental stressors and their effects during different periods of a child's life.

The legislative, regulatory and policy frameworks within the environmental health field have been slow to develop. This could be due to the ambiguity of the terminology used in the field and the lack of integrative strategies. It might also be due to the difficulty in translating the knowledge about complex environmental health problems into policies. Policy makers are used to thinking in terms of clear-cut risk assessment methodologies that use a fixed set of norms and standards. The lack and complexity of knowledge prevents policy makers from taking another approach on children’s environmental health. Hence policies on environment and health tend to be developed and implemented in separate and isolated ways.

Ad 4) Science policy interface

The science policy interface at an international level has become visible and established in CEHAPs. However, this is not the case at regional or local level. Policy makers at regional or local levels find it difficult to use the knowledge about children's environmental health when dealing with local problems. The reasons for this seem to be:

a) Lack of access to validated knowledge. Many policy makers are not connected to the scientific community or to transdisciplinary networks related to environmental health issues. Knowledge from other sectors, such as economy, transportation, agriculture, infrastructure or energy, is hardly used for specific integrative policies in the children's environmental health domain;

b) Available knowledge is not suitable to use for regional or local problems. The results of many epidemiological studies are related to large populations of children. It is difficult to downscale these results to measures that protect children at a local scale;

c) Children's environmental health problems are not recognised. Except in the case of disasters, regional and local policy makers tend to see environmental health problems as abstract, distant problems that should be dealt with at a national or international level. PINCHE analysed environmental hazards to children. This analysis showed that for many compounds, reducing environmental health exposures has greater health benefits in children than in adults. However, this insight has not led to an increased use of this knowledge for policy making;

d) Furthermore, the children's environmental health arrangement has been politically polarised. Some are calling for precautionary "child-centred" risk evaluations and regulatory policies. For example the release of the EPA's revised cancer risk assessment guidelines was delayed due to pressure from some advocates to change its focus to children's risk assessment. In contrast, other advocates argued that regulatory practices were already adequate enough to protect children from environmental exposures, and thus they opposed more stringent regulation.

Policy makers have reached an international consensus on the need for specific children's environmental health policies between the Third (1999) and Fifth (2010) Ministerial

Conferences. Since then policy makers have altered their focus to other, competing policy issues such as terrorism, migration etc. Different disciplines that were linked to this new domain of children's environmental health have been asking for institutional support from the authorities, yet no supportive infrastructure has been established.

The available funds for research and the agenda setting at lower administrative levels have not been realised. Also research funds at a European level have been allocated to newer fields of interest. As mentioned before, this happened for the policy domain after the last Ministerial Environment and Health Conference in Parma in 2010 and for research with the start of the 7th Framework Programme (2007). Part of the scientific community has therefore moved on to other topics.

Nevertheless, the PINCHE work has provided insight in the children's environmental health issues that have been important enough to be addressed by both science and policy. Different topics have been identified as relevant to policy making. These topics have been qualified as being scientifically valid and policy relevant, and this scientific knowledge has been translated into policy recommendations. These recommendations have been used for the research agenda setting of the European Commission as well as for other organisations. However, not all the recommendations of the PINCHE project have been used. There are still issues to address the improvement of children's health that has not been followed up by authorities. For the reasons highlighted above, specific regulation on environmental stressors to protect children has not been developed.

Ad 5) Problem ownership

Another phenomenon seen in the environmental health field is the shift from problems from one domain to another. At many governance levels the domains of health and environment are allocated to different political responsibility levels and it is unclear whether environmental health policy making belongs to the health or the environment policy domain. These are organisational problems in the environment and health domain. In addition, transdisciplinary experts in children's environmental health have had difficulties in making the child-related problems relevant to policy makers, as no large children's environmental health incidents have occurred. Historical analysis shows that incidents and disasters had a great impact on making an emerging field relevant for policy makers.

Furthermore, the EU has broadened the focus from children to other vulnerable groups in society. Therefore by shifting their focus and by diminishing allocated funds the EU has hindered the development of the children's environmental health domain. The political ownership of children's environmental health problems remains indecisive. As children cannot speak for themselves, and society has the plight to take care of the weak groups, someone should take up the responsibility for this policy domain.

Ad 6) Effectiveness and political commitment

An effective children's environmental health arrangement would be able to meet environmental health objectives to reduce environmental health risks for children. Political commitment for children's environmental health at a global and European level (WHO, EU) dates back to 1997. However, at a national or local level no explicit commitment has been given to children's related environmental health issues. This has partly been explained under ad 4. Furthermore, concrete long-term and medium-term children's environmental health objectives or a vision are lacking at these governance levels. There are a few national exceptions, such as Denmark. One reason for this lack of effectiveness is that downscaling of scientific knowledge to a local or regional level is complicated. The problems at a local level ask for more practical solutions. Politicians prioritise short-term problems. Another reason is that it is challenging to take knowledge utilisation into account as well as the different perspectives and values which stem from different policy fields. This could be because sectoral policy objectives do not match integrated children's environmental health policies.

In addition, over the last few years a reduction of resources for the implementation of results of research on children's environmental health is occurring at EU and WHO level. The regional office of the WHO in Rome, which specialised in children's environmental health, was closed in 2010. Over the last five years, since 2007, DG Research has not funded research in the field of children's environmental health. Many countries did not continue to fund the establishment of new CEHAPs after the one they made between the Fourth (2003) and Fifth (2010) Ministerial Conferences.

In conclusion: is 'children's environmental health' institutionalised?

Children's environmental health is certainly on the agenda of many organisations or stakeholders, ranging from public authorities to politicians, and from local advocacy groups to scientific organisations. At a global level politicians at the highest administrative level have pledged to protect children from hazards in their environment. This has been endorsed in numerous declarations and adopted by many other organisations. The scientific community has supported the children's environmental health issue by providing the necessary knowledge base. The scientific community in Europe has provided this knowledge base with financial support mainly from the EU and human resources support from the WHO.

At the same time, several activities have been launched in Europe to prepare the policy community for policy making on children's environmental health. Initiatives such as SCALE, and the Environment and Health Action Plan are clear examples thereof. These activities have resulted in the establishment of children's environmental health action plans at national level in most European countries. This all happened between 1999 and 2010. So far, so good.

The discussion shows that in order to institutionalise children's environmental health, this new domain had to be further elaborated. These international activities had to be transferred from an international to a (sub)national level to integrate children's environmental health with policies on issues such as the environment, health, transport, spatial planning and so forth. Besides the integration with other policy domains, the step from large-scale policies to smaller scale, more practical policies had to be made to institutionalise children's environmental health. However, the process of integration and downscaling has not been established in Europe since the last Ministerial Conference in 2010. The institutionalisation process has slowed down.

The scientific community has not been able to raise sufficient funding to continue the growth of research on children's environmental health. The knowledge production on children's environmental health has decreased since the 7th Framework Programme that started in 2007. The knowledge validation and knowledge utilisation of children's environmental health have not been advanced. The results of studies are no longer translated into child-specific policies. The political commitment shifted to other scientific domains, which have more economic interests. Authorities have not been able to transfer the policies of the international plans (CEHAPS, SCALE) into national, regional and local level plans.

The summarising conclusion is that, since the SCALE process and the development of Children's Environmental Health Action Plans in member states the field of children's environmental health has been institutionalised in terms of research and advocacy at an international level. But there is no clear indication that children's environmental health has been institutionalised in the policy domain at national, regional or local administrative levels. The integration of children's environmental health objectives in other environment or health policy domains is still far away.

Recommendations

The previous section suggested discussion points on how the institutionalisation of children's environmental health was hindered. After a thorough analysis of the children's environmental health arrangement I have considered which recommendations could improve the institutionalisation process. The recommendations to further the institutionalisation of children's environmental health encompass both substantive and organisational aspects.

The substantive recommendations are:

- The knowledge production on children's environmental health needs to be further enhanced. In the EU Horizon 2020 Programme, mechanisms should be included to ensure a child-specific focus in many research topics. The review process of research proposals should be conducted by international teams of experts, providing them with the responsibility to focus on innovation and child protection issues.
- Knowledge production needs to focus on children's vulnerability and how it is distributed in various geographical and social settings. This unequal distribution partly depends on society's social and political capacity to organise a strategic response. There are several factors impinging upon that social and political capacity.

The economic and technological resources are amongst the most decisive factors. These resources are unequally distributed around the regions in Europe. Knowledge may be endorsed within the scientific community, but can still be unused in society if it is not robust enough to mobilise that society, including policy makers and politicians, to take action. Therefore, the resources to identify problems or to perceive the effects need to increase.

- The co-production of knowledge in a transdisciplinary manner; It is recommended that such transdisciplinary tools, e.g. thematic networks, are used more often to generate research results which are supported by multidisciplinary groups in the research community and by stakeholders from societal groups, NGOs and policy makers. The role of public health is important to bring the medical and societal aspects of knowledge to the policy makers.
- A framework should be put in place that incorporates the problem identification, the knowledge collection, validation and application, and finally the mobilisation of stakeholders to have research validated to its full capacity in children's environmental health.
- The integration of knowledge in children's environmental health policies into adjacent policy domains needs to be supported;
- The definition of child-specific environmental health indicators. The development and use of such indicators will support standard setting, intervention and evaluation studies in order to optimise children's environmental health policies at different governance levels.

The organisational recommendations are:

- The increase of transdisciplinary networks; networks between scientists and policy makers are needed to find support for maintaining children's environmental health as a research field and to strengthen the institutionalisation of children's environmental health as an emerging policy domain.
- The increase of children's participation in networks;
- The establishment of environment and health institutes, inspired by the model of the EEA or ECDC; an international or national platform including the transdisciplinary

participation of stakeholders would benefit the children's environmental health arrangement;

- Lessons should be learnt from the joint activities of the EU and the WHO at an international level between 1999 (Ministerial Environment and Health Conference in London) and the last conference in Parma in 2010. This cooperation was capable to bring the science and policy fields together on the children's environmental health domain.

Reflection and methodology

When I started working on this thesis, I encountered a broad range of topics within research on children's environmental health in a European setting. The initial idea for the thesis was to show the collection and validation of knowledge and what the relevant knowledge was on children's environmental health. It seemed obvious that from these studies policy recommendations on children's environmental health were easy to extract. But most studies on children's environmental health did not include any policy recommendations. These studies were initially done from a mere scientific perspective.

I therefore decided to gain an understanding of what was going on in this new domain labelled as children's environmental health, at both research and policy levels. The PINCHE project dealt with a broad range of topics that were analysed by an international consortium of researchers and policy makers. The aim was to look at the available information and to make links to policy making. However, the data to make recommendations to the policy domain were not so easy to interpret. So during the process of the PINCHE project and the writing of this thesis I shifted my research questions to different phases of the science-policy interface.

The research questions have been adjusted throughout an iterative process of data collection, analysis, theoretical framing, interpretation and finding some common ground for this interpretive qualitative research.

I touched upon different concepts of the science-policy interface. In the knowledge production and knowledge validation phase of the PINCHE project we used mainly epidemiology and toxicology concepts. Concepts from sociology of science were used for the relevance making of the knowledge. Concepts from policy science were applied on the knowledge utilisation and agenda-setting phase of my thesis.

This interdisciplinary journey was needed to cross the bridge from scientific data to the utilisation of knowledge in the domain of children's environmental health. I experienced this as difficult because of my unfamiliarity with the fields of sociology of science and policy analysis. These approaches have helped to combine different phases of the PINCHE and HENVINET project and to make a link between the different articles in this thesis. Due to this iterative way of working on this thesis different methods for analysis have been used.

The mechanisms behind the agenda setting in Europe have been made clear from the document analysis. This analysis has used most available documents related to the international discourses on children's environmental health and was aided by the author attending several of the international meetings where the agenda setting actually took place. The actual performance of the different methods in networking has provided strength for the validity of the results within the HENVINET project. Although several methods described here are being applied in other EU-funded research projects where different stakeholders are participating, the method in this thesis has to be considered as a practical example.

The thread through this thesis is not based on fundamental science but is instead practice-oriented. My work in the PINCHE and HENVINET projects therefore relate to my personal scientific journey. The acquired knowledge about the science-policy bridge (from knowledge production to policy making via knowledge validation, making knowledge relevant and knowledge utilisation) is useful for application in other transdisciplinary work. This knowledge can be used for enhancement of new policy domains.

SAMENVATTING

Dit proefschrift beschrijft de kennis over de milieugerelateerde gezondheid van kinderen en analyseert de rol die kennis in de ontwikkeling van beleid op dit gebied speelt. Verschillende aspecten worden beschouwd. Ten eerste, de opkomst van het domein 'kinderen, milieu en gezondheid' tijdens de laatste twee decennia in Europa; ten tweede een validatie van de kennis in dit veld; ten derde een beoordeling van de relevantie van deze kennis voor de beleidsvorming door beleidsmakers bij het verstrekken van aanbevelingen; en ten vierde een analyse over hoe deze kennis door middel van netwerken van wetenschappers, beleidsmakers en andere belanghebbenden wordt gebruikt.

Doelstellingen

Dit proefschrift heeft vier doelstellingen:

1) analyse van de opkomst van het domein 'kinderen, milieu en gezondheid' tijdens de laatste twee decennia in Europa;
2) het schatten van de validatie van kennis op dit gebied;
3) het schatten van de relevantie van deze kennis voor beleidsvorming door het verstrekken van aanbevelingen over het gebruik ervan door beleidsmakers;
4) analyse van verschillende soorten netwerkondersteuning die gebruik van kennis voor beleidsmakers ondersteunen.

Onderzoeksvragen

Het onderzoek in dit proefschrift heeft een sterk praktische inslag. Het onderzoek is uitgevoerd in antwoord op een verzoek van de Europese Commissie ter ondersteuning van haar aanstaande onderzoeksprogramma's. De volgende vragen staan centraal in dit proefschrift.

1) Welke mechanismen en actoren hebben een rol gespeeld in het kader van de agendering van milieugerelateerde gezondheid van kinderen tijdens de laatste twee decennia in Europa?
2) Hoe heeft het domein 'kinderen, milieu en gezondheid' zich in de laatste twee decennia ontwikkeld?

3) Hoe heeft de validatie van kennis op het terrein van milieugerelateerde gezondheid van kinderen bijgedragen aan de ontwikkeling van dit gebied?
4) Hoe heeft het relevant maken van kennis op het gebied van milieugerelateerde gezondheid van kinderen bijgedragen tot de ontwikkeling van dit gebied?
5) Hoe heeft het gebruik van kennis op het terrein van milieugerelateerde gezondheid van kinderen bijgedragen aan de ontwikkeling van dit gebied?

In de volgende secties worden de belangrijkste conclusies van dit proefschrift gepresenteerd. De vaststelling van de agenda milieu en gezondheid op het gebied van kinderen binnen Europees beleid is geanalyseerd aan de hand van de rol van belanghebbenden en de verspreiding van wetenschappelijke kennis. De analyse van de agendasetting en het strategische gedrag van de betrokken actoren is gebaseerd op het barrièremodel van Bachrach en het stroommodel van Kingdon. De conferenties "milieu en gezondheid" van de Wereldgezondheidsorganisatie worden beschouwd als het begin van de Europese agendasetting. De beschikbaarheid van wetenschappelijke informatie en het smeden van een coalitie van actoren en instanties uit verschillende organisaties heeft agendavorming versterkt. Wetenschappelijke kennis is gebruikt om verder onderzoek en beleid te onderschrijven en legitimeren. Deze kennis is verder gebruikt binnen de politieke arena voor besluitvorming in het domein 'milieugerelateerde gezondheid van kinderen'.
Het EU-SCALE initiatief gaf een sterke impuls aan het verder uitdenken en uitvoeren van beleid. Kinderen kregen een vaste plek op de agenda van de ministeriële conferenties "milieu en gezondheid". Complexiteit en onzekerheid bij minder wetenschappelijk onderbouwde kwesties binnen de relatie milieu-gezondheid bij kinderen hebben de institutionalisering belemmerd. Terwijl de agendasetting van milieugerelateerde gezondheid van kinderen als een succes wordt gezien, lijkt de institutionalisering halverwege gestagneerd en in de nabije toekomst opnieuw te kunnen stagneren. Er zijn sterke redenen om te kijken naar de positie van kinderen in het domein milieu en gezondheid. De kwetsbaarheid van kinderen is één van die redenen.

De kwetsbaarheid en gevoeligheid van kinderen voor milieustressoren zijn geanalyseerd. De verschillen tussen kinderen en volwassenen zijn geanalyseerd volgens toxicokinetische beginselen als absorptie, distributie, metabolisme en excretie. De door milieufactoren veroorzaakte gezondheidseffecten komen anders tot uiting bij kinderen dan bij volwassenen.

Verder zijn de verschillen tussen kinderen en volwassenen geanalyseerd volgens toxicodynamische beginselen van de ontwikkeling, de timing of de dosis-respons relatie, met inbegrip van epigenetische en genetische gevoeligheid. Er bestaat nog steeds een kenniskloof op het gebied van kwetsbaarheid en gevoeligheid van kinderen voor veel chemische verbindingen. Preventiebeleid, voorzorgprincipes, meer onderzoek en betere testmethoden op het gebied van milieugerelateerde gezondheid van kinderen zijn nodig om dit kennisgat te vullen. Geïntegreerde kennis over complexe systemen met meerdere blootstellingen en kennis over een scala van biologische effecten in de verschillende stadia van ontwikkeling bij kinderen, met inbegrip van de foetale periode, is nodig.

De resultaten van PINCHE worden gepresenteerd als onderdeel van de validatie van de kennis in dit proefschrift. PINCHE was een multidisciplinair en multinationaal netwerk van vertegenwoordigers van de wetenschap, industrie, NGO's, en consumenten- en patiëntenorganisaties in Europa. Het PINCHE project richtte zich op luchtverontreinigende, kankerverwekkende en neurotoxische stoffen, en geluidsoverlast.

Het belang van de voornaamste gezondheidseffecten en ziekten bij kinderen door milieuvervuiling wordt beaamd door veranderingen in het verloop en de oorzaken van de belangrijkste kinderziekten. We zien veranderingen in het beeld van gezondheidseffecten bij prematuriteit, intra-uteriene groeibeperking, testiculaire dysgenesie syndroom, type I en type II diabetes, astma, atopie en hooikoorts, autisme, attention deficit hyperactivity disorder (ADHD), leermoeilijkheden, kanker, obesitas en gehoorproblemen.

Een concreet voorbeeld van kennisvalidatie is de studie over effecten bij kinderen ten gevolge van blootstelling aan lood. Uit talrijke studies blijkt dat loodvergiftiging al bij lage dosis een milde mentale retardatie en lage IQ-scores bij kinderen kan veroorzaken. Verschillende onderzoeksresultaten suggereren dat prenatale blootstelling voor lood een belangrijke blootstelling is. We moeten onze aandacht schenken aan loodopslag bij moeders en waar mogelijk voorkomen dat tijdens de zwangerschap die loodopslag gemobiliseerd wordt. Passende studies moeten uitgevoerd worden om te bevestigen of dieetsupplementen de botresorptie en de loodmobilisatie tijdens de zwangerschap kunnen verminderen. De hypothese dat de loodopslag in de botten van moeders de relevante parameter is voor het voorspellen van de mate van neurotoxiciteit van dit metaal geeft enig optimisme voor de toekomst. Uit studies van kinderen (geboren na het verwijderen van lood uit benzine) waarvan de moeders geen hoge loodbelasting hebben en een relatief lage loodopslag hebben, zouden we kunnen verwachten dat lood weinig invloed meer heeft op de IQ-scores van kinderen.

De ontwikkeling van een strategie op het gebied ‘kinderen, milieu en gezondheid’ voor verschillende bestuursniveaus (internationale, nationale, regionale en lokale overheden) heeft als doel het relevant maken van kennis. In de afgelopen jaren is het feit dat kinderen moeten worden beschermd tegen milieustressoren algemeen aanvaard door beleidsmakers. Er is echter geen goede uniforme strategie ter verbetering van de gezondheid van kinderen door verbetering van hun milieu. Het PINCHE netwerk stelde een reeks aanbevelingen op ter ondersteuning van de ontwikkeling van een strategie op het gebied ‘kinderen, milieu en gezondheid’ voor verschillende bestuursniveaus. Er zijn duidelijke knelpunten bij een thematisch netwerk. Er zijn drie belangrijke uitdagingen voor het behalen van succes vastgesteld: 1) vergelijkbaarheid van data: PINCHE heeft gewezen op de noodzaak voor standaardisatie van milieueffectbeoordelingen, voor een classificatie van respiratoire ziekten en symptomen bij kinderen en een indeling van diagnostische groepen en voor een toegankelijke presentatie van onderzoeksgegevens; 2) data toegankelijkheid moet worden aangepakt:toegankelijkheid van de wetenschappelijke gegevens voor het grote publiek, met inbegrip van professionals in de gezondheidszorg en beleidsmakers, is belangrijk en vergt vertaling van wetenschap naar beleid die vaak ontbreekt; 3) er is een noodzaak om definities en methoden te harmoniseren zodat wetenschappers en autoriteiten dezelfde taal spreken. Obstakels zijn het subsidiariteitsbeginsel, de versnippering van de beschikbare kennis of het gebrek aan expertise en einddoelen op verschillende niveaus, het gebrek aan politiek draagvlak of economische kwesties.

Het PINCHE project heeft wetenschappelijke gegevens verzameld op het gebied van milieugerelateerde gezondheid van kinderen. Deze gegevens zijn gevalideerd en vertaald in beleidsaanbevelingen (kennisrelevantie). Aanbevelingen voor het beleid komen voort uit discussies binnen het project en uit de analyse van de huidige situatie op het gebied van milieu en gezondheid. Op het gebied van milieugerelateerde gezondheid van kinderen volgt het beleidsproces min of meer vaste regels, maar dit proces is nog steeds in een vroeg stadium van ontwikkeling. De link tussen wetenschap en beleid staat nog voor vele uitdagingen. Wetenschappelijke beoordeling van milieurisico's moet de problemen van datasets overwinnen, zoals de variabiliteit binnen mens en milieusystemen, het bereik van ruimtelijke en temporele verspreiding van potentiële effecten op de gezondheid en vele soorten bias en verstorende factoren.

PINCHE raadt aan een algemene verbetering te realiseren van de ondersteunende wetenschappelijke velden in het domein van milieu en volksgezondheid. Evaluaties van kennis, gegenereerd met epidemiologie of toxicologie, moeten een sleutelrol spelen bij het beïnvloeden van besluitvorming op het snijvlak van wetenschap en beleid, vooral bij programma's die bedoeld zijn voor het algemeen belang. Wetenschappelijke commissies op lokaal niveau kunnen een rol spelen. De relatie tussen gezondheid en milieu moet beter worden opgenomen in training en opleiding. Er is behoefte aan harmonisatie van productie van kennisdata en gebruik daarvan. De prioriteiten van PINCHE richten zich op de belangrijkste kwesties. Een classificatie van lage, gemiddelde of hoge prioriteit om actie te ondernemen is toegepast op een aantal verschillende milieustressoren.

PINCHE stelde aanbevelingen op om blootstelling voor kinderen te beperken. Vermindering van de blootstelling is niet altijd verbonden met een verbeterde gezondheid op korte termijn, maar het zal de totale lichaambelasting via accumulatie van chemische stoffen bij kinderen verminderen. Het is een strategische keuze om de blootstelling van kinderen aan verbindingen te verminderen door productietechnieken te wijzigen of door het verhogen van de afstand van kinderen tot specifieke bronnen. De bijdrage van alle betrokkenen in de productie, distributie en gebruik van de wetenschappelijke kennis op het gebied van milieugerelateerde gezondheid van kinderen is noodzakelijk.

Resultaten van de activiteiten van de PINCHE leidden tot een lijst van prioriteiten op het gebied van milieugerelateerde gezondheid van kinderen, die vervolgens zijn gebruikt als input voor aanvullende beleidsmaatregelen van de EU. Dit heeft betrekking op het gebruik van kennis. Evaluatie van lopend onderzoek op het gebied van milieugerelateerde gezondheid van kinderen zorgt voor een prioriteitenlijst van risicofactoren en beleidsaanbevelingen voor actie.

Informatie met betrekking tot blootstelling, epidemiologie en toxicologie is afzonderlijk geanalyseerd, en vervolgens is een risico-evaluatie van bepaalde milieufactoren gemaakt.

Sociaaleconomische factoren zijn specifiek in aanmerking genomen. De resultaten werden opgesteld, en gezien de huidige wettelijke situatie zijn beleidsaanbevelingen voor maatregelen opgesteld. Tot slot is er prioriteit gegeven aan risicofactoren en beleidsaanbevelingen op basis van discussie tussen alle partners. De conclusie binnen PINCHE was dat voor verontreinigende stoffen in de buitenlucht (vooral verkeersgerelateerde verontreiniging), secundaire tabaksrook, allergenen en kwik met de hoogste prioriteit actie ondernomen moet worden.

Gebromeerde brandvertragers, lood, PCB's en dioxines, ioniserende en zonnestraling en sommige lawaaibronnen werden geclassificeerd als gemiddelde prioriteit. Sommige toxines kregen lage prioriteit, op basis van het kleine aantal blootgestelde kinderen, relatief milde gezondheidseffecten of een verbeterende situatie die toegeschreven kon worden aan toegepaste beleidsmaatregelen. De tekortkomingen van het stellen van dergelijke prioriteiten is bekend en hoewel sommige maatregelen dringender dan anderen zijn, wordt benadrukt dat idealiter alle beleidsmaatregelen moeten worden uitgevoerd voor alle toxines. Deze prioriteitenlijst moet voortdurend worden herzien, het voorzorgsbeginsel moet centraal zijn bij alle beslissingen, en de nadruk moet liggen op veilige blootstellingniveaus voor kinderen.

Dit proefschrift onderzocht de praktische mogelijkheden om wetenschap en beleid samen te brengen in een netwerk, rekening houdend met opties om te communiceren met het gehele veld van belanghebbenden op het terrein van milieu en gezondheid. Praktische methoden zijn gebruikt om de werking van trans- en multidisciplinaire netwerken te verkennen. De resultaten van netwerken tussen wetenschappers en beleidsmakers vloeien voort uit een door de EU gefinancierd project HENVINET, een follow-up project van PINCHE. De rol van netwerken en andere hulpmiddelen bij de ondersteuning van de interface tussen wetenschap en beleid, ter versterking van een nieuw beleidsdomein (gebruik van kennis), zijn afhankelijk van de antwoorden op vragen die betrekking hebben op de behoeften, de inhoud, de structuur en de verspreiding van een netwerk van professionals.

De samenvattende conclusie luidt dat, sinds SCALE en de ontwikkeling van ‘kinderen, milieu en gezondheid’ actieplannen in de lidstaten van de EU, het gebied van milieugerelateerde gezondheid van kinderen geïnstitutionaliseerd is op het gebied van onderzoek en belangenbehartiging op internationaal niveau. Er is echter geen duidelijke aanwijzing dat het domein ‘milieugerelateerde gezondheid van kinderen’ als beleid op nationaal, regionaal of lokaal niveau is geïnstitutionaliseerd. De integratie van doelen op het gebied van kinderen, milieu en gezondheid in andere beleidsdomeinen binnen milieu of gezondheid is nog ver weg.

SUMMARY

This thesis focuses on knowledge about children's environmental health and analyses the role that knowledge plays in policy development. Various aspects are considered. First, the rise of the children's environmental health domain during the last two decades in Europe, secondly a validation of the knowledge in this field, thirdly an assessment of its relevance to policy making by providing recommendations on its use by policy makers, and fourthly an analysis of how this knowledge is used through networking between scientists, policy makers and other stakeholders.

Objectives

This thesis has four objectives:

5) to analyse the rise of the children's environmental health domain during the last two decades in Europe;
6) to assess the validation of knowledge in this field;
7) to assess the relevance of this knowledge to policy making by providing recommendations on its use by policy makers;
8) to analyse how networking techniques support the provision of knowledge to policy makers and their utilisation of this knowledge.

Research questions

The research performed and reported on in this thesis has a strong practical focus. It was work performed in response to a request by the European Commission in support of its upcoming research programmes. The following questions are central in this thesis.

3) Which mechanisms and actors have played a role in the agenda setting of children's environmental health during the last two decades in Europe?
4) How has the children's environmental health domain developed in the last two decades?
    - How did the validation of knowledge in the children's environmental health field contribute to the development of this field?
    - How did making the knowledge in the field of children's environmental health relevant contribute to this field's development?

- How did the utilisation of knowledge in the children's environmental health field contribute to the development of this field?

The following sections present the main conclusions of this thesis.

The agenda setting of children's environmental health in the European policy field is analysed by its role of stakeholders and the spread of knowledge. The analysis of the agenda setting processes and the strategic behaviour of actors involved is based on the barrier model by Bachrach and the policy streams approach of Kingdon. The WHO Environment and Health conferences are considered as the start of the European agenda setting process. The availability of scientific information and the forging of a coalition of actors and agencies from different spheres increased the agenda formation. Scientific knowledge was used to endorse and legitimise further research and policy claims, and managed to successfully transfer it to political arenas and translate it into decision making in a new domain of children's environmental health. The EU-SCALE initiative gave a strong push to designing and implementing policies. Children got a fixed spot on the agenda of Ministerial Conferences on Environment and Health. Complexity and uncertainty that goes with less obvious issues of the environment-health relation in children hindered the institutionalisation.
While the agenda-setting of children's environmental health is seen as successful, its institutionalisation seems only halfway and might stagnate over the foreseeable future. There are strong reasons to look at children's position in the environment and health domain. Children's vulnerability is one reason.

Children's vulnerability and sensitivity to environmental stressors are characterized by analysis. The differences between children and adults are analysed by toxicokinetic principles as absorption, distribution, metabolism and excretion. The health effects caused by environmental factors transpire differently in children than in adults. Furthermore, the differences between children and adults are analysed by toxicodynamics principles of development, timing or dose-response, including epigenetics and genetic susceptibility. There is still a knowledge gap on children's vulnerability and susceptibility for many compounds. Preventive policies, precautionary approach, more research, and better testing methods in children's environmental health are needed to fill this knowledge gap. Integrated knowledge about complex systems with multiple exposures and knowledge about a range of biological effects in the different developmental windows of time in children, including the foetal period, is needed.

The results of the Policy Interpretation Network on Children's Health and Environment (PINCHE) as a research intervention in the children's environmental health domain are presented as part of the knowledge validation in this thesis. PINCHE was a multidisciplinary and multinational network of representatives from science, industry, NGOs, and consumer and patient organisations in Europe. The PINCHE project focused on air pollutants, carcinogens, neurotoxicants and noise.

The importance of prominent health effects and diseases in children in relation to environmental pollution are reflected by changes in patterns and causes of the main childhood illnesses. Prematurity, intra-uterine growth restriction, testicular dysgenesis syndrome, type I and type II diabetes, asthma, atopy and hay fever, autism, attention deficit hyperactivity disorder (ADHD), learning disabilities, cancer, obesity and hearing problems show changing patterns in effect.

A specific example on knowledge validation is the study of the effects on children from exposure to lead as an environmental stressor. Numerous studies indicate that low-level lead poisoning causes mild mental retardation and low IQ scores in children. Several data suggest that for lead the main toxic event is due to prenatal exposure: therefore we should focus our attention on maternal lead stores and whenever possible avoid their mobilization during pregnancy. In this regard we should design appropriate studies to confirm whether dietary supplementations can reduce bone resorption and lead mobilization during pregnancy. The hypothesis that the amount of maternal bone lead stores is the relevant parameter for predicting the level of neurotoxicity of this metal gives some optimism for the future: if we study children whose mothers never underwent high environmental pollution (born after the withdrawal of lead from gasoline) and hence have relatively low bone lead stores we could find that, at the population level, lead has little influence on children IQ scores.

The development of a strategy on children's environmental health at different levels of governance: international, national, regional, and local relates to making knowledge relevant. In recent years the fact that children need to be protected against environmental stressors has been widely accepted by decision- and policy-makers. However, there is not yet a good or unified strategy to improve children's health by improving their environment. The Policy Interpretation Network on Children's Health and Environment (PINCHE) network suggested a range of recommendations to support the development of a strategy on children's environmental health on different levels of authority: international, national, regional, and local. There clearly are indicated bottlenecks in the thematic network approach. Three main challenges for success have been identified: 1) data comparability. PINCHE identified the need for standardisation of environmental assessments, classification of childhood respiratory diseases and symptoms, and a format for defining diagnostic groups and presentation of data; 2) data accessibility must be addressed. Accessibility of the scientific data to the general public, including health professionals and policy makers, is important and requires translation that is often lacking; 3) there is a requirement to harmonise definitions and methods to ensure that scientists and authorities speak the same language. Obstacles are the subsidiarity principle, fragmentation of available knowledge or lack of expertise and purpose at various levels, the lack of political commitment or input and economic issues.

The PINCHE project has collected scientific data on children's environmental health, has validated these data and translated these into policy recommendations (knowledge relevance). Policy recommendations result from the discussions and analysis of the present situation in environment and health. In the field of children's environmental health the policy process will follow more or less fixed rules, but this process is still at an early level of development. The link between science and policy still faces many challenges. Scientific assessment of environmental risk must recognize and tackle the problems of data sets, variability of human and environmental systems, the range, spatial and temporal diffusion of potential health effects and many biases and confounding factors. The PINCHE network recommends a general improvement of the supporting scientific fields in environment and health. Assessments from epidemiology or toxicology should play a key role in influencing science-policy decisions in programmes that are intended to inform the public policy process. Scientific committees at a local level could play a role. The relation between health and environment needs to be better incorporated in training and education. There is a need for harmonization of data production and use. The priorities in PINCHE focus on the most important issues. A classification of low, medium or high priority for action is used to describe a range of different environmental stressors.

PINCHE provided recommendations to reduce exposure for children. Exposure reduction is not always linked to improved health in the short term, but it will reduce the body burden of accumulating chemicals in children. A strategic choice is reduction of exposure of children to compounds by changing production techniques or by increasing the distance of child specific settings to sources. The contribution of all players in the production, distribution and use of scientific knowledge in the field of children's environmental health is necessary.

Results of the PINCHE activities led to identified priorities on children's environmental health that are used as input for additional EU policy actions. This relates to the knowledge utilisation. Evaluation of existing research on the environmental health of children provides a prioritised list of risk factors and policy recommendations for action.

Information related to exposure, epidemiology, and toxicology was analysed separately and then a risk evaluation of particular environmental factors was made. Socioeconomic factors were specifically taken into account. The results were compiled, and considering the present regulatory situation, policy recommendations for action were made. Finally, the risk factors and policy recommendations were prioritised through a process of discussion between all the partners. PINCHE concluded that outdoor air pollutants (especially traffic-related), environmental tobacco smoke, allergens, and mercury were high priorities with an urgent need for action. Brominated flame retardants, lead, PCBs and dioxins, ionising and solar radiation, and some noise sources were classified as being of medium priority. Some toxins were given low priority, based on a small number of exposed children, relatively mild health effects or an improving situation due to past policy measures. The shortcomings of such a prioritisation are realised and, though some measures are more urgent than others, it is emphasised that ideally all policy measures should be carried out without delay for all toxins. This priority list must be continuously revised, the precautionary principle should be central to all decisions, and the focus should be on safe exposure levels for children.

This thesis explores the practical possibilities for bringing science and policy together in a network, taking on board the options to communicate to the entire field of stakeholders in environmental health. Practical methods have been used to explore the functioning of transand multidisciplinary networking. The results of network building activities between scientists and policy makers arise from an EU-funded project HENVINET, which serves as a follow-up of PINCHE. The role of networks and other tools in supporting the science-policy interface to strengthen a new policy domain (knowledge utilisation) are depending on the answers to questions that relate to the needs, content, structure and dissemination of a network of professionals.

The summarising conclusion is that, since the SCALE process and the development of Children's Environmental Health Action Plans in member states the field of children's environmental health has been institutionalised in terms of research and advocacy at an international level. But there is no clear indication that children's environmental health has been institutionalised in the policy domain at national, regional or local administrative levels. The integration of children's environmental health objectives in other environment or health policy domains is still far away.

DANKWOORD - WORD OF THANKS

Kinderen hebben het recht op een schone en gezonde leefomgeving. Kinderen zijn kwetsbaar. Kinderen hebben geen keuze in welke omgeving ze opgroeien. Kinderen moeten beschermd worden. Kinderen die het niet hebben gered zijn mijn inspiratie geweest voor het schrijven van dit proefschrift. Aan het eind van de jaren negentig van de vorige eeuw heb ik met een aantal collega's een internationale conferentie georganiseerd op het gebied van kinderen, gezondheid en milieu. Veel personen van verschillende disciplines afkomstig van een reeks organisaties kwamen daar op af. De dag voor de conferentie hebben we met verschillende partners het "International Network on Children's Health, Environment and Safety" (INCHES) opgericht. Inspirerende mensen van onder andere de Wereldgezondheidsorganisatie, het Amerikaanse 'Environment Protection Agency', het Canadian Institute of Child Health, het 'European Environment Agency', het 'Childwatch International', het 'Children's Environmental Health Network' uit de Verenigde Staten, maakten deel uit van die oprichting. Het onderwerp liet me niet meer los.

Eindelijk of nu al? Als ik de dankwoorden lees van andere proefschriften dan is er meestal sprake van verzuchting dat het ploeteren voorbij is. Ik vroeg me af of ik dat gevoel ook heb? Eigenlijk moet ik bekennen dat dat niet zo is. Misschien omdat het schrijven van dit proefschrift is voortgekomen uit het dagelijkse werk bij de GGD Gelderland-Midden en de andere GGD'en in de regio Oost Nederland. Ik heb dan ook steeds geprobeerd de dagelijkse praktijk van de medische milieukunde mee te nemen in alle activiteiten die rechtstreeks of zijdelings te maken hadden met dit proefschrift. Dat bracht iets vanzelfsprekends in het werken aan dit proefschrift. Niet dat het vanzelf ging. Verre van dat. Het begrijpen van andere vakgebieden zoals dat van milieubeleidswetenschappen is een grote uitdaging geweest. Natuurlijk dank ik alle personen met wie het mogelijk was om deel te nemen aan verschillende Europese projecten: Wolfgang Babisch, Alena Bartonova, Marie-Louise Bistrup, Gabriele Bolte, Chris Busby, Maureen Butter, Sandra Ceccatelli, Aleksandra Fucic, Wojtec Hanke, Caroline Johansson, Martina Kohlhuber, Nanny Koppe, Hans Keune, Marike Leijs, David Ludlow, Christofer Lundqvist, Hanns Moshammer, Rima Naginiene, Willie Passchier-Vermeer, Alan Preece, Scott Randall, Roberto Ronchetti, Georges Salines, Margaret Saunders, Greet Schoeters, Stephen Stansfeld, Nikos Stilianakis, Gavin ten Tusscher, Aileen Yang, Moniek Zuurbier.

Als externe promovendus is de afstand naar de universiteit wel groter. Het vasthouden van de wetenschappelijke waarden is lastiger als je dagelijks in de praktijk werkzaam bent. Maar gesprekken met mijn promotoren Pieter Leroy en Koos van der Velden waren altijd nuttig, inspirerend en stimulerend. Bovendien waren deze gesprekken open en behelsden ze meer dan het onderwerp van het proefschrift. Heren, dank!

Verder dank aan Mark van Bruggen, Bernard Groot en Henk Jans voor hun suggesties om meer te redeneren in de tekst en minder sprongen te maken. Er waren natuurlijk ook meerdere collega's die belangstelling toonden als mijn proefschrift ter sprake kwam. Daarvoor mijn dank, ook al was het soms lastig uit te leggen waar ik nou precies mee bezig was.

Hetzelfde geldt voor mijn familie en vrienden. In het bijzonder wil ik mijn ski-club vrienden bedanken die altijd nieuwsgierig zijn gebleven naar mijn werk. De ski-club bestaat net zolang als ik aan mijn proefschrift heb gewerkt dus hebben deze vrienden het hele proces meegemaakt. Het liefst hadden ze een rijtje stellingen samen met mij gemaakt. Maar dat is geen vereiste aan de Radboud Universiteit. Toch wel aardig onze favoriete stelling te noemen die op de short-list stond.

- Wintersport met acht mannen kan de beste stellingen voor een proefschrift naar boven brengen; deze zijn niet altijd geschikt voor publicatie.

Heren bedankt: Ferdy, Han, Henk, Jaap, Ronald, Terco en Theo.

Ik heb weinig veldwerk met andere onderzoekers gedaan en het feit dat ik een externe promovendus was maakte dat ik geen collega’s op de universiteit had. Het onderzoek heeft niet op de universiteit plaatsgevonden maar grotendeels bij de GGD in Arnhem of in andere steden van Europa. Het schrijven van een proefschrift is daarom soms een eenzame bezigheid. Achteraf best wel bijzonder als je aan een universiteit promoveert en daar zo weinig bent geweest. Het laat zien dat wetenschap op meerdere plekken in de maatschappij leeft.

The work of this thesis is based on the work done in several EU funded projects. It was a privilege for me to be able to work in these projects. Each project has been an inspiring and challenging experience. The opportunity to meet people all across Europe and learn about their lives and work has been very inspiring.

I would like to thank the co-authors of the articles published in this thesis. Most of them are well respected scientists who dearly contributed to different projects in Europe. For a list of most of my co-workers in the PINCHE project I would like to refer to the names on the previous page. I am honoured to be able to consider quite a few of you as friends now. Thanks for the cooperation and friendship.

Special thanks to Nanny Koppe, Cathey Falvo, Margaret Saunders and Hans Keune for reading through articles or chapters more than I expected them to do. A word of thanks for inspiration to keep on working and encouragement to Kristine Sorensen who follows the same route as extraneous PhD of writing a thesis. Thanks to all those persons who provided information on which articles are based. Then there are all those persons who were so important in feeding me on the topic of children's environmental health. They were either cooperating in the scientific work or in the NGO activities that I did in the International Society of Doctors for the Environment (ISDE), the International Network on Children's Health, Environment and Safety (INCHES), the Nederlandse Vereniging voor Medische Milieukunde (NVMM), the Health and Environment Alliance (HEAL): Stephan Böse-O'Reilly, Rima Naginiene, Karen Hopfl-Harris, Cathey Falvo, Lilian Corra, Roberto Romizi, Ernesto Burgio, Wim Zwart Voorspuij, Hanns Moshammer, Marie-Louise Bistrup, Gonnie Jongmans, Henk Jans, Anne Stauffer, Génon Jensen, the staff and experts at the World Health Organisation (Jenny Pronczuk, Leda Nemer, Elaine Price, Roberto Bertollini, Giorgio Tamburlini), JRC, EEA (David Gee, Dorota Jarosinska), UNEP (Maaike Jansen), UNICEF, the EU Commission (Environment, Research, Sanco). A word of thanks to Margot Wällstrom, former EU Commissioner for the Environment, to give children a voice in Europe through the programmes and research you made possible. I would like to thank Martha Berger, Irena Buka, David Gee, Philippe Grandjean, Bruce Lanphear, Peter Pärt, Martha Shimkin for their input in the chapter on the agenda setting.

Thanks to my colleagues at the Public Health Services Gelderland-Midden for bearing with me if I was away again abroad: Chris, Harma, Ingrid, Joris, Klaartje, Moniek, Manon, Mayke,

Rik, Simone, Thea, Vivian and all those who were at the office during the period of writing my thesis.

Then there are those who read parts of the introduction or closing chapter to filter most of my English language flaws: Colin Butler, Margaret Saunders and the professionals at Radboud in'to Languages.

Thanks to the members of the Doctoral Thesis Committee, Prof. Dr. Ilse Loots, Prof. Dr. Ernst von Mühlendahl and Prof. Dr. Ad Ragas for reading my thesis and your judgement.

The inspiring meetings with my supervisors Pieter Leroy and Koos van der Velden were always very useful and stimulating. I enjoyed the clear, professional and energising feedback. Furthermore, the conversations we had were open and reached out to other issues than the mere topic of the thesis. Gentlemen, thanks for being my supervisors!

At the end of a word of thanks for those you expect a word of thanks: my family. Right so! Very special thanks to my loved ones for letting me spend all those hours behind the computer. For your support and love, Willy! For your love and support my children: Ailsa, Céline and Ewoud. Children are always an inspiration, especially your own children. My wish is that some of the thoughts of this thesis may benefit the children of my children.

Peter van den Hazel, July 2013

CURRICULUM VITAE

Peter Jan van den Hazel was born on January 21st 1954 in Amsterdam in the Netherlands.

Education

Gymnasium (Cartesius Lyceum, Amsterdam) Diploma 1972;

Medical Doctor, University of Amsterdam, 1982;

General Practitioner, degree University of Amsterdam, 1985;

MPH: degree in Environmental Medicine, Dutch Institute of Preventive Medicine (TNO- PG), 1986–1989. Registered since 1989;

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Since 1986 he has worked as a Physician specialised in Social Medicine and Environmental Health as subspecialty for several Municipal Health Services in Gelderland, the Netherlands. Daily practice consists of consulting in a broad range of environmental health issues. Since 1993 he has been a consultant for and partner in the Bureau Medische Milieukunde (Bureau of Environmental Medicine (BMM)). He is the past President of the International Society of Doctors for the Environment, ISDE, (2001-2003). Peter van den Hazel is the Co-founder and Chair of the board of the International Network on Children's Health, Environment and Safety (INCHES). Since 2004 he acted as co-chair for the Healthy Environments for Children Alliance (secretariat at WHO). Since 2005 he is President of the EUPHA section Environment Related Diseases and council member of European Public Health Association (EUPHA). Since 2007 Peter van den Hazel is Member of the Committee "Signalling Health and Environment" of the National Health Council. Since 2012 he acts as President of the NGO Health and Environment Alliance (HEAL) based in Brussels. He successfully worked to ensure children's environmental health was an issue taken up at the World Summit for Children and the World Summit on Sustainable Development in 2003. Since 2002 he has been coordinator for several EU-funded projects: PINCHE (Policy Interpretation Network on Children's Health and Environment), CHEST (Children's Health, Environment and Safety Training), PRONET (Pollution Reduction Options Network), PHEEDUNET (Public Health Environment Education Network), Climate TRAP and TOP (Training of Professionals).

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This thesis focuses on knowledge about children's environmental health and analyses the role that knowledge plays in policy development. Various aspects are considered. First, the rise of the children's environmental health domain during the last two decades in Europe, secondly a validation of the knowledge in this field, thirdly an assessment of its relevance to policy making by providing recommendations on its use by policy makers, and fourthly an analysis of how this knowledge is used through networking between scientists, policy makers and other stakeholders.

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