Environmental health risks –

Aktionsprogramm
Umwelt und Gesundheit

Action Programme
Environment and Health

what are the differences between children and adults?

Umwelt Bundes Amt

Für Mensch und Umwelt

This review is a contribution to the Action Programme Environment and Health and its public relations activities. Expenses for printing have been covered by the Federal Environmental Agency (Umweltbundesamt).

Published by

Umweltbundesamt
Federal Environmental Agency
Postfach 33 00 22
D-14191 Berlin
Germany
Internet: www.umweltbundesamt.de

with the collaboration of:

Bundesinstitut für Risikobewertung
Federal Institute for Risk Assessment
Postfach 330013
D-14191 Berlin
Germany
Internet: www.bfr.bund.de

Bundesamt für Strahlenschutz
Federal Office for Radiation Protection
Postfach 10 01 49
D-38201 Salzgitter
Germany
Internet: www.bfs.de

Robert Koch Institute
Postfach 650261
D-13302 Berlin
Germany
Internet: www.rki.de

Editors

Part I: Dr. med. Wolfgang Straff, Department of Environmental Hygiene, Federal Environmental Agency

Part II: Prof. Dr. med. Ursula Gundert-Remy, Federal Institute for Risk Assessment

Status: May 2004

Translator

Chris Charlesworth

Photography

Dr. med. Axel Hahn

This review is available free of charge from the publishing institutions mentioned above or from the Office of the Action Programme Environment and Health, Federal Environmental Agency:
Geschäftsstelle zum Aktionsprogramm Umwelt und Gesundheit (APUG) im Umweltbundesamt, Corrensplatz 1
D-14195 Berlin, Germany
It has also been published on the internet (www.apug.de and www.umweltbundesamt.de) as a PDF document that can be downloaded.

Table of contents

Part I: What are the differences between children and adults?

Part II: The use of child-specific safety factors when deriving limit values

1. Introduction

Society places a high value on protecting children. For that reason, the demand is repeatedly made that children's particular vulnerability be given special consideration when evaluating environment-related health risks and deriving limit values. Current regulatory practice often attempts to do this in a relatively schematic way, in the form of safety factors. An intraspecies factor ("uncertainty factor") of up to 10, used to take particularly vulnerable groups into account, also covers children. In addition to this intraspecies factor, soil protection legislation contains a number of provisions designed to protect children from certain genotoxic carcinogens, as a rule specifying a "default factor" of 10 [BMJ, 1999]. The same approach is also used to determine intervention values as set out in the German Drinking Water Ordinance (TrinkwV 2001) [Dieter and Henseling, 2003]. Due to the fact that children's respiratory minute volume per kg of body weight is roughly twice that of adults, the Commission on indoor air hygiene at the German Federal Environmental Agency (German acronym: UBA) introduced an additional factor of 2 when deriving guide values in order to take children into account [IRK, 1996].

Publications on this topic by various institutions (e.g. the report published in 2002 by the WHO/EEA "Children's health and environment: A review of evidence") put forward the theory that generally speaking children are particularly vulnerable to a broad range of environmental noxae [EEA and WHO, 2002].

However, this general statement is a vast simplification. It does not take into account that when referring to children we are actually looking at an inhomogeneous group whose susceptibility can vary throughout their developmental stages, even when the same noxa is under consideration.

The reasons for the differences are connected both with the age-related behaviour of children which determines exposure (e.g. infants and toddlers crawling and ingesting dirt), and with age-related physiological differences in susceptibility that impact on toxicokinetics and toxicodynamics. For example, we know that the different stages of organ development [Schneider et al., 2002] lead to particular "windows of susceptibility" [EEA and WHO, 2002].

The interaction of factors of this kind affects the specific sensitivity of an individual at a particular stage of development, so that children of different age groups may react with differing sensitivity to certain toxicants and may even be less sensitive than adults. There may also be differences in sensitivity from one individual to another due to a genetic disposition, and this applies equally to children and adults.

In order to adequately take into account the particular conditions related to the different stages of development, it is therefore useful to divide children into different age groups: unborn children (in the embryonic and foetal stages of development), newborn babies and infants (<1 year), toddlers (1-3 years), preschool children (3-6 years), school-age children (6-16 years) and adolescents (16-18 years). However, it is important to bear in mind that particular behaviour patterns, uptake pathways and developmental stages last for different lengths of time in different individuals so that it is not always possible to draw distinct lines between the age groups. For certain noxae it might also be sensible to apply a different division of age groups like performed in case of radiation protection (see part II, table 1).

This paper compares possible specific health risks to children with those to adults. It analyses both non-substance specific, general criteria (such as differences in exposure) that can lead to differences in susceptibility and the substance-specific influences of particular toxicants relevant in terms of environmental medicine, for which particularly good toxicological characteristics and information on harm to children's health are available. This is the case, for example, with lead and methylmercury. An important basis for this overview was provided by the research project carried out as part of APUG (German acronym for Action Programme Environment and Health) entitled "Taking children into account as a particular risk group when deriving health-related environmental standards" (project no: 201 61 215, Schneider et al., 2002).

2. Exposure

Different patterns of activity and behaviour in the different age groups have a significant influence on children's exposure to pollutants in or from the environment. For that reason, children cannot be regarded as a homogeneous group; rather, they are exposed to particular harmful substances to differing degrees throughout their developmental years.

2.1 Exposure in the embryonic and foetal period

Exposure of the embryo is considered to be particularly significant due to the rapid cell division and differentiation that takes place during this stage of development. Intrauterine exposure can occur through the placenta, which is permeable in some cases to toxic substances with a small molecular weight, such as carbon monoxide, ethanol, or lipophile substances such as polycyclic aromatic hydrocarbons (PAHs). Some substances that are significant in terms of environmental medicine, such as lead and methylmercury, which are toxicologically well characterised, can penetrate the placenta barrier. For example, a study in Greenland found higher concentrations of methylmercury in the umbilical blood than in the mothers' blood [Hansen et al., 1990]. Components of tobacco smoke can also cross the placenta barrier. It is also possible for substances that have been stored in the mother's fatty tissue, such as polychlorinated biphenyls (PCBs), to be mobilised during pregnancy and passed on to the embryo or foetus [EEA and WHO, 2002].

Other harmful influences may occur directly, i.e. independently of the placenta as a protective (filter) organ, through ionising radiation and electromagnetic fields [EEA and WHO, 2002]. That kind of exposure of the mother, like impacts on the mother caused by noise or heat, can also indirectly have a detrimental effect on the embryo or foetus, i.e. by harming the mother's health.

2.2 Exposure during the neonate period and infancy

The living conditions and behaviour patterns characteristic of newborn babies and infants have a significant influence on their absorption of harmful substances through oral or dermal contact, or inhalation [U.S. EPA, 2000].

2.2.1 Oral exposure

Breast-fed infants can absorb fat-soluble contaminants such as PCBs or dioxin congeners through their mother's milk [Neubert, 1994]. Their exposure to these substances during the breast-feeding period can be considerably higher than that of adults [BMU, 2002]. During this time there may also be a mobilisation of lipophile substances from the mother's fatty tissue and lead from her bones causing additional exposure of the infant via the breast milk [Gulson et al., 2003]. Methylmercury may also be transmitted through breast milk. [EEA and WHO, 2002]. Despite these problems, it is still recommended that babies up to the age of 6 months should be fed breast milk only, because the positive effects of breast-feeding far outweigh any possible negative effects [Tietze, 1997].

The infant may also be exposed to contaminants when industrial products based on cow's milk are used as a replacement for breast milk. The concentrations may vary depending on where the milk was produced. However, it is generally assumed that, since milk from many different places of origin is now mixed together in dairies, the exposure of individual cows is no longer significant [Neubert, 1994]. The dioxin concentration in cow's milk is considerably lower than in human milk. Today, more attention is paid to the allergizing effect of cow's milk with regard to the problem of atopic genesis [Neubert, 1994; Oranje et al., 2002]. There is a fundamental risk with industrially produced baby food of contamination through microbial or chemical impurities.

Drinking water may contain substances such as fluoride, lead, copper, nitrate and pesticides. Infants who are no longer being breast-fed take in around five times as much drinking water as adults in relation to body weight. However, the limit values for these substances stipulated in the Drinking Water Ordinance (TrinkwV) take this into account.

Through mouthing activities, babies can also take in substances from their surroundings to a certain extent. Exposure to harmful substances is also possible from toys, in particular articles such as dummies. An example is the release of phthalates from soft PVC [Schneider et al., 2002].

2.2.2 Dermal exposure

For many substances, a far higher dermal absorption is assumed for children, particularly newborn babies, due to the greater permeability of the skin and the greater surface area of skin in relation to body weight [Plunkett et al., 1992; EEA and WHO, 2002]. Creams or wet-wipes used particularly for newborn babies and infants may contribute to a higher exposure to the substances contained in these products, in particular under occlusive conditions (e.g. if nappies are worn at the same time which can create an area that is virtually airtight) [Schneider et al., 2002]. Components such as perfumes and preservatives are relevant here.

2.2.3 Exposure by inhalation

Newborn babies and infants spend most of the time indoors where they may be exposed to tobacco smoke, emissions from building materials and furnishings, and pesticides through inhalation. In some areas there may also be a possibility of exposure to radon. Outdoors, high ozone concentrations in summer may lead to increased exposure because, for example, when babies are crying or kicking in their prams their respiratory minute volume is higher.

2.3 Exposure during the toddler stage

2.3.1 Oral exposure

Generally, bottle or breast-feeding stops at the age of one or two years, and throughout the toddler stage the child increasingly eats a range of food similar to that of adults.

Children's calorie intake in relation to body weight is between twice and four times that of adults. Exposure to pesticides or heavy metals occurs at this age due to cereals, fruit or vegetables. However, the main source of any possible exposure remains cow's milk, since toddlers continue to consume it in greater amounts than adults. Due to the animal fats contained in dairy products, the exposure of toddlers to (fat-soluble) organic substances is higher than for adults.

Through the intake of house dust via hand to mouth contact, substances such as phthalates, heavy metals and pesticides can be taken into the body. Stroking pets can also lead to pesticide contamination if the animals have been treated with pesticides.

Depending on children's individual behaviour, playing outdoors can also lead to exposure to harmful substances – for example, via contaminated sand in the sandpit. Heavy metals may play a role here [Nielsen et al., 2001]. Also, substances that are formed during the combustion of hydrocarbons and released into the atmosphere [Heinemeyer and Gundert-Remy, 2002] may subsequently be deposited on the sand.

Children can be poisoned by accidentally ingesting household products containing harmful substances, such as cleaning agents. With some substances, such as lamp oils, there is a danger that the vomiting caused by irritation of the mucous membranes will lead to aspiration into the lungs, which is the actual hazard in cases of this kind [Hahn, 2002].

2.3.2 Dermal exposure

If children come into contact with household products, cosmetics, crayons or finger-paints containing harmful substances dermal exposure can occur, also through soil sticking to their skin when playing outdoors. [Schneider et al., 2002]. Children crawling and playing on the floor may also absorb lipophile substances through house dust such as pesticides from carpets or pets (that have been externally treated with pesticides) [Heinemeyer and Gundert-Remy, 2002].

2.3.3 Exposure by inhalation

From this age on, the increase in outdoor activities means that pollutants such as nitrogen oxides, ozone and PAHs become more significant. Due to their small stature, children may be exposed to higher concentrations of vehicle exhaust gases because they breathe closer to the source of the exposure [EEA and WHO, 2002]. The parents' use of household products, paints and varnishes containing toxins, as well as the use of coloured pens not suitable for children, means that not only the dermal exposure mentioned is possible, but also exposure by inhalation. There is also a possibility of inhaling toxins from contaminated soil.

2.4 Exposure of preschool children and older children/adolescents

2.4.1 Oral exposure

With increasing age, children's food consumption becomes more like that of adults, both in terms of quality and quantity. The higher amounts of fruit and vegetables and fruit juices can lead to an exposure to pesticides that is higher than for adults [EEA and WHO, 2002]. Weighed against this is the fact that ingestion of harmful substances due to mouthing (cf. 2.2.1) gradually decreases with age.

2.4.2 Dermal exposure

The change in clothing habits of older children can bring about an increase in dermal exposure, particularly when textiles containing harmful substances are worn next to the skin. However, there is no longer the intensive contact with nappies, which can lead to increased absorption from the components from skin care creams and ointments under occlusive conditions. The greater amount of time spent outdoors, which for children is more likely to be at midday than it is for adults, also means increased exposure to UV radiation.

2.4.3 Exposure by inhalation

On the way to kindergarten or school, children may breathe in car exhaust gases, causing exposure to nitrogen oxides, fine dusts, PAHs, VOCs (volatile organic compounds) and carbon monoxide (cf. 2.3.3). For children taking part in sports activities at school or in their free time increased ozone exposure is possible in summer if there is strong solar radiation. Playing outside also means that an exposure to NO_2, fine dusts and a series of organic compounds is possible. There is a possibility of exposure to heavy metals by inhalation as well as oral and dermal exposure (e.g. when playing on slag heaps consisting of spoil containing heavy metals).

3. Toxicokinetics

Toxicokinetic differences by comparison with adults must be given particular consideration in the foetal period, and for newborn babies and infants. General differences are lower body weight, higher relative weight of liver, higher ratio of body surface area to body weight, different lung anatomy and – in each case in relationship to the lower body weight – higher cardiac output, increased blood flow to the brain and reduced blood circulation in the kidneys up to the age of 5 months [Schneider et al., 2002]. In the course of its development, the child's organism by comparison with adults has, in certain phases, a greater relative distribution volume for water-soluble substances and a smaller one for fat-soluble substances [de Zwart et al., 2002].

3.1 Absorption

In the foetal period, absorption takes place diaplacentally, with the permeability of the placenta differing greatly for different substances – depending on their physico-chemical properties.

Following birth, different substances are absorbed with differing efficiency through the gastrointestinal tract. The extent of the absorption depends on a number of factors.

Before a child is a few months old, lipophile substances such as DDT, dioxins and PCBs cannot be fully absorbed due to immature bile acid metabolism [de Zwart et al., 2002]. Nevertheless, breast-fed babies can absorb considerable amounts of dioxins and store them in the fatty tissue [Kreuzer et al., 1997].

Some toxins ingested with food, such as lead and methylmercury, for which there has been particularly good toxicological research, are absorbed significantly better by children than by adults, especially in the early stages of childhood development [EEA and WHO, 2002; Plunkett et al., 1992]. In children, only 60% or less lead is deposited in bones (by contrast with 90% in adults) and is therefore present in the child's organism in higher organ concentrations [Kojda, 2002]. If there are not yet any demethylating bacteria in the intestine, there is higher absorption of methylmercury. After weaning, the change in the bacterial colonisation in the intestine makes demethylation of the organic mercury possible, causing absorption to be lowered [EEA and WHO, 2002].

3.1.1 Conditions for absorption by inhalation

Absorption by inhalation is relatively higher than in adults due to the fact that the respiratory minute volume per kg of body weight is on average twice as high, given a comparable concentration of a toxin in the inspired air [Schneider et al., 2002]. The bronchial tree is not yet as finely structured as in adults, and furthermore there are fewer alveoli and they are smaller, which has an effect on the absolute alveolar surface area. Relating the quotients from the respiratory minute volume and alveolar surface area to body weight, various authors using different models have concluded that the relative respiratory minute volume in children calculated in this way is considerably greater than in adults [Snodgrass, 2001; cf. Heinemeyer and Gundert-Remy, 2002]. This would mean that an exposure by inhalation to toxins in children leads to greater absorption than in adults. It is difficult to make a quantitative estimate of absorption by inhalation because we do not have sufficient knowledge of the exact structural and physiological conditions of the child's lungs. There is thus a significant need for existing models to be underpinned by experimental evidence.

There are scarcely no data available on actual absorption via the lungs in children, particularly of environmental pollutants. Most evaluations prefer to err on the side of caution and assume complete absorption.

3.1.2 Dermal absorption

Generally speaking, substances such as pesticides [Nau, 1994] that have a high lipid solubility are very well absorbed. Differences in the thickness, degree of hydration, and cornification influence the skin's absorption capacity (cf. also 2.2.2). However, basic physiological differences in absorption characteristics exist only during the first week of life [Nielsen et al., 2001].

3.2 Distribution in the organism

During certain phases of development, the child's organism has a smaller distribution volume for fat-soluble substances than that of adults [Nielsen et al., 2001]. This means that substances such as PCBs, dioxins or pesticides can temporarily be present in higher blood and organ concentrations. It is difficult to quantify the distribution volume for fat-soluble substances in the individual phases of development, since the build up of fatty tissue during the growth phase is a dynamic process, in which the different quality of the fat plays a role (more structural fat for heat regulation in children; more storage fat in adults).

By contrast, the higher water content of the child's body means that the distribution volume is relatively higher for water-soluble substances. This difference is particularly marked in neonates in whom water accounts for 75% of body mass. This proportion is even higher in foetuses [Rascher and Kruse, 2003]. Thus, given the same dose per kg of body weight, the concentration of a water-soluble substance in the blood serum is lower in neonates than later in life. The higher metabolism of different tissues due to growth (cf. 3.3) can lead to higher local intracellular absorption, which must be seen as problematic, in particular in tissues with a high cell division rate. This is also the case for the brain, due to the fact that the blood brain barrier is not fully developed until the age of 6 months. Furthermore, the organ perfusion rate for the brain is higher than in adults. In animal experiments it was also demonstrated that the blood brain barrier can become more permeable when pesticides are administered orally [Gupta et al., 1999]. If this is also true in humans, in the case of exposure to pesticides there would also be the possibility of further additional neuronal damage caused by other toxins, in particular in children (combination effect).

Up to the age of one, the protein bonding of foreign substances is lower than in adults. In addition, up to the age of 2-3 years the plasma has a lower protein content. The plasma concentration drops as a result of this, while the tissue concentration increases, including the concentration at the possible place of effect [Röper and Lauven, 1999].

3.3 Metabolism

Biotransformation enzymes are an important component in the metabolism of foreign substance, which in many cases is species-specific. They change the structure of endogenous and exogenous substances to enable them to be eliminated. Two phases are distinguished in the reactions mediated by these enzymes: phase-I reactions lead to a change in the structure of a molecule (metabolization); phase-II reactions bring about a conjugation with other molecules making it possible for them to be excreted through the kidneys and thus eliminated from the organism. The fact that phase-I (and II) reactions are not as developed in neonates leads on the one hand to a longer half-life of foreign substances in the plasma but on the other hand to reduced activation (toxification) of some toxic substances.

By contrast, children between one and five years old have a higher metabolic capacity. That means that at this age children can convert and eliminate toxic substances more quickly than adults. However, if the metabolization produces a substance that is equally or even more toxic, children might – at least theoretically – be at greater risk [Heinemeyer and Gundert-Remy, 2002; Schneider et al., 2002].

The low activity of methaemoglobin reductase in infants makes them significantly more susceptible than adults to substances such as nitrite that form methaemoglobin (cf. 4.8).

3.4 Elimination

The functional immaturity of the kidneys (lower glomerular filtration rate and tubular secretion) in the first 6-12 months results in a longer half-life in the plasma for certain substances [Nau, 1994].

Elimination of substances in the bile is not yet fully developed during the infant's first few months of life [de Zwart et al., 2002], which can also delay the elimination of foreign substances.

On the other hand, a model calculation has shown that the elimination half-life of lipophile substances such as dioxin (TCDD) is lower in children than adults and rises with age (approx. 4 months for newborn babies and approx. 10 years for 40-60 year olds [Kreuzer et al., 1997]).

4. Toxicodynamics

A child will not necessarily suffer a negative influence on its health or development each time it comes into contact with a toxicologically problematic substance, either because the dose required to cause harmful effects is not reached due to low concentration or because the duration of the exposure is too short, or because the metabolization of the substance does not lead to toxification. On the other hand, there are allergological, immunological and possibly other mechanisms we are not yet able to classify in which the dose-effect relationship cannot easily be described.

Effects can occur in children because their exposure to the noxae in question is higher than in adults. However, effects may also occur because certain "windows of susceptibility" exist, which cause a higher sensitivity during a particular developmental stage.

In the case of harmful influences during pregnancy, the child is not usually subject to a higher exposure than the mother. At certain times, the rapidly developing organism shows a higher sensitivity, which means that concentrations that cause no problem to the mother could have an effect on the child. In particular during the toddler stage, effects increasingly come to the fore that are caused by a higher exposure.

Since a toxicodynamic effect is more likely to be substance-specific, we shall describe here a number of examples. However, for reasons of clarity, it will be necessary to examine not only toxicodynamic, but also toxicokinetic, aspects.

4.1 The multiple effects of tobacco smoke

Active smoking on the part of the mother during pregnancy is associated with babies being born smaller and with a lower birth weight, and with higher probability of premature labour and miscarriage. A higher infant mortality rate has also been reported [EEA and WHO, 2002]. It is probable that both toxicodynamic and toxicokinetic mechanisms play a role in the consequences of the mother smoking tobacco (e.g. reduced blood circulation in the placenta).

The exposure of the infant to passive smoke increases the risk of SIDS, or "sudden infant death syndrome," [EEA and WHO, 2002] as well as the incidence of bronchial hyperreactivity, bronchitis and pneumonia. Pre-existing asthma in older children is likely to be aggravated. A higher rate of inflammation of the middle ear and a positive relationship to necessary adenoidectomies and tonsillectomies were also reported. There also seem to be a connection with the occurrence of delayed mental and social development [EEA and WHO, 2002].

4.2 Carcinogenicity

The higher cell division rate of all organ systems in children makes a greater influence on carcinogenesis in children conceivable, in particular if the carcinogenic substances or their carcinogenic metabolites impact over longer periods of time. For certain genotoxic carcinogens a number of different animal experiments suggest a higher susceptibility of the juvenile by comparison with the adult organism, whereas for non-genotoxic carcinogens there are no indications for this [Schneider et al., 2001].

To date, it has not been possible to establish an unequivocal connection between ionising radiation in low doses and the incidence of childhood leukaemia [EEA and WHO, 2002]. There are, however, connections between intrauterine exposure to X-rays and the occurrence of leukaemia and other cancers [EEA and WHO, 2002]. Furthermore, the development of skin tumours such as spinaliomas and basaliomas in older people is connected with the cumulative total of UV exposure, in other words also with exposure in childhood and adolescence. In the case of melanomas there are thought to be connections with UV exposure, particularly during childhood. While associations were found in epidemiological studies, no connection was established in case-control studies [Whiteman et al., 2001].

4.3 Neurotoxic effects

It is known that certain substances (lead, mercury) have a greater influence on the brain of the foetus, infant or child than on the brain of an adult; for other substances (PCBs) there are indications that this is the case.

Reasons for the greater sensitivity of the infant brain include the increase in the number of neurons up to the first year after birth, the intensive synaptogenesis that occurs up to age 2 [Heinemeyer and Gundert-Remy, 2002], and the myelination of axons that continues in spurts postnatally into early adulthood.

For certain compounds, including dioxins and PCBs, there are indications that the brain development of exposed children might be influenced via their influence on thyroid function [EEA and WHO, 2002].

4.3.1 Pesticides

Animal experiments have shown that the brain is particularly sensitive to exposure to a number of pesticides such as DDT, chlorpyrifos, pyrethroids, paraquat and organophosphates [Eriksson, 1997]. Since organophosphates inhibit the enzyme acetylcholinesterase, which is necessary both for the function and the development of the nervous system, children must be seen as particularly vulnerable.

4.3.2 Lead

After exposure, lead is deposited in the bones and brain. The neurotoxic damage depends on the age of the child and manifests in persistent, possibly irreversible, intelligence defects and psychomotor deficits [Human Biomonitoring Commission, 1996]. Toddlers are considered to be particularly vulnerable [Wilhelm and Ewers, 1993]. It has not been possible to find a threshold value for the neurotoxic effects of lead [Wilhelm and Ewers, 1993]. Recent studies have come to the conclusion that intelligent deficits can occur even at a blood concentration less than 100 µg/l [e.g. Canfield et al., 2003], although at these low concentrations the extent of the deficit is considered to be so low that no influence on school or post-school development is to be expected [Human Biomonitoring Commission, 1996].

Other effects in the low-dose range, such as growth impairments or subtle adverse effects on kidney function in children, are being discussed, although the data situation is still patchy [Wilhelm, 1999]. Anaemia in children as a result of a lead-induced haemoglobin synthesis disorder occurs at a concentration of 200 µg/l or more, which in effect no longer occurs in Germany [Wilhelm, 1999].

4.3.3 Mercury

Methylmercury has pronounced effects on the central nervous system, in particular if exposure is prenatal. The sensitivity of the foetus to methylmercury is 3-4 times as high as in adults [Wilhelm, 1999]. High intrauterine exposure can result in cerebral palsy and epilepsy. Even low concentrations (including in postnatal exposure) that are not accompanied by clinically clear-cut symptoms can lead to neuropsychological deficits [EEA and WHO, 2002]. These toxic effects of mercury are often connected with consumption of contaminated sea fish, if this makes up a major part of the mother’s daily diet, since it often contains high concentrations of organic mercury (methylmercury) [EEA and WHO, 2002].

The most common source of exposure to inorganic mercury is amalgam fillings and can therefore be considered negligible for younger children at least, whose teeth have few fillings. Better prevention of tooth decay could help to further reduce or prevent this exposure.

4.3.4 Polychlorinated biphenyls (PCBs)

The main problem connected with the chronically increased levels of PCB caused by the ubiquitous occurrence of this group of substances in the environment (particularly in high-fat foods of animal origin) [Human Biomonitoring Commission, 1999] is prenatal exposure, which can lead to neurological deficits and behavioural disorders [Helbich, 1999].

Postnatal exposure of an infant via breast milk must also be seen as a possible risk because effects on neurological development are also being discussed [Walkowiak et al., 2001].

4.4 Influences on the reproductive system

4.4.1 Cadmium

In animal experiments testicular atrophy was noticed in adult rats following exposure to cadmium. Changes of that kind did not occur in newborn or 2-week old rats [Wong and Klaassen, 1980]. This might also suggest that children are less vulnerable, an indication of the fact that windows of susceptibility do not necessarily apply exclusively to children.

4.4.2 Organohalogen compounds

Chlorinated insecticides can imitate hormones and thus have an influence on the differentiation of organs and tissues. An oestrogenic effect was demonstrated for DDT, dieldrin, toxaphene, chlordane and endosulfan [EEA and WHO, 2002]. Following accidentally high exposure to dioxin, men were found to have significantly lower testosterone levels and higher gonadotropin levels [Egeland et al., 1994].

A change in the sex ratio in favour of female births as a result of exposure to pesticides and dioxin following accidents or extreme cases of exposure at the workplace has been discussed, in particular when the fathers were younger than 19 at the time when the child was conceived [James, 1995; Mocarelli, 2000].

4.5 Effects on teeth and bones

Prolonged intake of large amounts of fluoride can lead to dental fluorosis in children in the phase when tooth enamel is forming. There is no cause for concern in that connection up to a concentration of up to 1 mg/l drinking water. In Germany such high concentrations in drinking water do not occur. An advantage of higher fluoride intake is the protection against caries it provides.

4.6 Effects on the immune system

Epidemiological studies have demonstrated an increase in allergies, particularly in childhood, that manifest for example as atopic eczema or bronchial asthma [Behrendt et al., 1999; EEA and WHO, 2002]. Anthropogenic causes, such as a change in living conditions in indoor environments (mould and house dust allergens) [EEA and WHO, 2002], and also a partially increasing or qualitative change in outdoor air pollution caused by road traffic are being discussed [EEA and WHO, 2002]. In Eastern European countries allergies were not observed as frequently, despite high levels of pollutant emissions [ISAAC Steering Committee, 1998].

4.7 Effects on the kidneys

Children absorb cadmium better (30-40%) than adults (10-15%). In the long term this jeopardises health due to cadmium's accumulative properties [Wilhelm et al., 1999]. High cadmium exposure can favour the progression of a kidney malfunction, in particular in connection with age-related physiological factors [Wilhelm et al., 1999]. Thus cadmium's accumulation properties do not primarily impair children's health during childhood. However, cadmium exposure in childhood can have more severe effects on adult health than exposure in later adulthood.

4.8 Effects on oxygen transport

Due to the reduced activity of methaemoglobin reductase, substances that form methaemoglobin can cause cyanosis in infants. This is the case with raised nitrate concentrations in drinking water. However, this has been taken into account in Germany by the limit value currently in force [Dieter, 1999].

5. Noise

At present it is not unequivocally clear whether children are more vulnerable to noise than adults. They have less control over their immediate environment than adults do and their leisure activities often involve loud sound sources [Bistrup et al., 2001].

An increased risk of exposure can arise from the fact that some kinds of noise pollution are not avoided due to a lack of knowledge about the adverse effects. Examples of this include playing with noisy toys. Findings on the long-term effects on health of chronic noise pollution are available for adults. If the noise exposure begins in childhood it can be expected that the effects will be more severe than if they do not begin until later. Thus, as far as noise is concerned, application of the “precautionary principle” to health protection is of particular importance with regard to children.

The most serious forms of health impairment include damage to hearing and tinnitus as a result of exposure to excessive noise. Damage to hearing is irreversible and can be caused both by acute forms of excessive exposure (e.g. toy guns, a blow to the ear, loud bangs, fireworks) and acute long-term exposure (e.g. frequent use of noisy toys close to the ear, squeaky toy animals, engines, noisy hobbies, listening to music through earphones, music in discotheques and at concerts) [Maassen et al., 2001; Wissenschaftlicher Beirat der Bundesärztekammer, 1999; Zenner et al., 1999].

Furthermore, noise can affect the endocrine system of both children and adults and cause high blood pressure [Babisch, 2000; Evans und Lepore, 1993; Evans et al. 2001]. However, the results of investigations in this area are not entirely unequivocal, which is why it is uncertain whether children should be seen as a high-risk group. However, in principle the effects of noise do apply to children as well as adults.

Noise causes irritable reactions and sleep disorders. Studies have shown that children as well as adults are disturbed by noise, even though they enjoying making noise themselves [Lercher et al., 2000]. The effects of exposure to noise must always be seen in relation to the activity being carried out at the time. Noise during sleep or studying has a different effect from noise during play. When sleeping, children may demonstrate greater “noise resistance” by comparison with adults, in other words they are less likely to be woken by it [Maschke and Hecht, 2000]. Since children go to bed earlier than adults, particular attention should be paid to disturbance by environmental noise in the evening. Since sleep, particularly REM sleep, plays a role in restoring and consolidating the memory, adverse effects on cognitive performance can be expected in children suffering from disturbed sleep [Bistrup et al., 2001].

Studies have unequivocally demonstrated that the cognitive performance of children in schools affected by noise pollution (aircraft noise) is poorer than that of children not exposed to noise of this kind [Haines et al. 2001; Hygge et al, 2002]. The effects seem to be reversible if the noise pollution is eliminated. The acoustic conditions in schools and kindergartens are often not favourable to efficient and non-aggressive learning.

7. Ionising and non-ionising radiation

6.1 Ionising radiation

The risk of malignant diseases such as leukaemia and cancer being triggered by ionising radiation increases with the dose of radiation and also depends on age at the time of exposure. According to the last report on the effects of atomic radiation published in 2000 by the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR), it can be assumed that the risk of cancer associated with ionising radiation is twice as high for children as for adults [UNSCEAR, 2000]. In the recommendations of the International Commission on Radiological Protection (ICRP) published in 1991, it is assumed for the purpose of radiation protection measures that the risk to children from radiation is twice to three times as high as the risk to adults [ICRP, 1991]. This is upheld by the data on the survivors of the atomic bomb from Hiroshima and Nagasaki when determining the radiation risk for the different age groups. The data indicate that the radiation-related risk of leukaemia to children under 10 by comparison with the average across all age groups is as much as a factor of 3.5 higher [Shimizu et al, 1998].

With regard to radiation exposure from natural sources, the radioactive gas radon is of particular importance. With great regional differences that depend on the geology of an area, radon can contribute significantly to the radiation exposure of children, adolescents and adults in the home and other indoor spaces (including kindergartens and schools).

Exposure to radiation for medical diagnostic purposes makes a considerable contribution to the overall exposure of children and adolescents. Here attention should be paid to the medical indication so that unjustified multiple examinations can be avoided or alternative diagnostic procedures used where possible. The radiation exposure of each radiological application should be kept to the minimum required for diagnosis, taking into consideration the proportions of the child’s body.

6.2 UV radiation

The sun is the most significant source of UV radiation in terms of exposure of the population. Excessive UV exposure can have acute effects, such as sunburn, and long-term effects such as premature aging of the skin, skin cancer or weakening of the immune system.

In this connection, children are considered to be particularly at risk. Firstly, babies' skin is thinner than adults' skin and their immune system is not yet fully developed. Special care should be taken to protect children from sunburn of any kind, since their frequency in childhood goes along with a higher risk of skin cancer [Dulon et al., 2002]. Frequent occurrences of sunburn during childhood can increase the formation of moles [Dulon et al., 2002], a risk factor for the occurrence of a malignant melanoma much later in life. Since children like to spend time outdoors, it is estimated that they acquire around three-quarters of their lifetime UV dose before the age of twenty [Greinert et al., 2003].

UV light acts on the skin to convert cholesterol to vitamin D. A vitamin D deficiency can cause rickets in children, and osteomalacia and osteoporosis in adults. As a rule, insufficient supply of vitamin D or vitamin D precursors in the diet is responsible for vitamin D deficiencies, not insufficient sunlight.

6.3 Electromagnetic fields (EMF)

The question of whether young children and adolescents are particularly sensitive to electromagnetic fields has not been scientifically clarified. However, it is conceivable that electromagnetic fields influence development during the period in which the immune system and the nervous system are not fully developed. Two further Questions are also under discussion: whether the fact that children's heads are proportionately smaller means that the electromagnetic fields can penetrate to deeper, and possibly more critical, areas of the brain than in adults, and whether the properties of the tissue in a child's head might lead to a comparatively higher specific absorption rate.

Currently, there is only a small amount of data, some of it conflicting, on these working hypotheses [Gandhi et al. 1996; Schönborn et al. 1998]. The fact that the majority of children today are exposed to mobile phone fields for a considerably longer time span than today's adults must be seen as problematic. This could lead to minimal effects that have not yet been identified. Accumulating over time they could therefore represent an unrecognised health risk.

7. Socio-economic factors

The economic and social situation of the family has a clear effect on the living conditions, lifestyle, and dietary patterns of children. For example, in many cases poor social conditions are linked to higher exposure to pollutants in children. An important factor is parental smoking, particularly if this occurs in the home and in the presence of the children. The social environment also has an influence on the smoking behaviour of the children and adolescents themselves. Since intellectual development is also significantly promoted by stimulation from the home environment, mixed effects often occur under unfavourable socio-economic conditions consisting of lack of stimulation and the effects of harmful substances. It is then no longer possible to attribute clear causality to findings.

However, a higher standard of living is not necessarily exclusively linked with positive effects on health. For example, the rise in atopic eczema mentioned in 4.6 was observed particularly in higher social classes [EEA and WHO, 2002].

8. Conclusions

Throughout the course of their development, children go through different stages of specific exposure and vulnerability to environmental influences. Due to the heterogeneous nature of the influences – with regard to the individual age groups and individual substances – and the reaction mechanisms of the organism, it is not possible to give a general answer to the question whether children are particularly susceptible to harmful influences from the environment.

Due to many of the specific characteristics and behaviour patterns described, children are in fact subject to higher exposure than adults. However, generalisations should not be made on this basis: children are more exposed than adults to certain harmful substances in the environment only in particular phases of their development.

In different developmental stages, children may be more sensitive, but also less sensitive than adults to environmental pollutants occurring individually or in combination. Above and beyond physiological differences, economic and social factors also have an important influence on the exposure and also on the overall effect on the infant organism [Mielck and Heinrich, 2002].

Children have been taken into account as a group in need of special protection in various areas of regulatory toxicology. With regard to the uncertainty factors mentioned at the beginning of this paper, which are commonly used to derive guide or limit values, evidence is currently not sufficient to prove that children generally need more protection from environmental pollutants than already exists, in the form of introducing further uncertainty factors. An intraspecies factor of 10 also seems generally appropriate for ensuring that individual differences are adequately taken into account for the most vulnerable age group.

However, in cases in which certain toxicants have proved to be particularly harmful to children and this has not been sufficiently taken into account by the current procedure for deriving guide and limit values, additional precautions may be necessary. Here the prevalence of a particular characteristic (e.g. greater growth, earlier puberty) or childhood illness should be taken into account as a particular susceptibility factor for a particular toxicant. Since, for example, the prevalence of allergic asthma in children is on the increase, additional protection from factors that favour this increase might be necessary (e.g. ozone, fine dust).

Further research into the endocrinological and especially neuroendocrinological effects of environmental pollutants and the further intensive study of the constantly changing environment with regard to the effect on children at each developmental stage is necessary. Here attention should not focus solely on the classical dose-effect relationship but, in view of the increasing significance of allergies, should also be directed to immunological connections. The framework programme “Children's Environment and Health Action Plan for Europe (CEHAPE),” run by the WHO’s Regional Office for Europe, also emphasises the necessity of research into and prevention of asthma and allergies [WHO, 2003].

In order to gain insight into the environment-related health risks to children, it is necessary to conduct continuous health-related environmental studies and environment-related health studies in children like the currently performed “National Health Interview and Examination Survey for Children and Adolescents” [Kurth et al., 2002; Schulz et al., 2002]. For more Information see www.kiggs.de.

In practice, it should not be generally assumed that environmental influences have a greater effect on health in children than in adults. In many respects, the data situation is still patchy, so that further observation and analysis of the effects of environmental factors on children’s health is an important instrument on the way to long-term environmental and health protection for our society. General guide and limit values should always aim at protecting the most vulnerable group.

9. Bibliography Part I

1. Babisch, W.: Traffic noise and cardiovascular disease: epidemiological review and synthesis. Noise and Health 2, 9-32, 2000

2. Bistrup, M.L., Hygge, S., Keiding, L., Passchier-Vermeer, W.: Health effects of noise on children - and perception of risk of noise. National Institute of Public Health, Copenhagen. 2001

3. BMJ - Bundesministerium für Justiz (eds.): Bekanntmachung über Methoden und Maßstäbe für die Ableitung der Prüf- und Maßnahmenwerte nach der Bundes-Bodenschutz- und Altlastenverordnung (BbodSchV) vom 18. Juni 1999. Bundesanzeiger, 161a, 1999, 15

4. Behrendt, H., Gfesser, M., Ring, J.: Allergien. In: Umweltmedizin. Edited by V. Mersch-Sundermann. Stuttgart: Georg Thieme-Verlag 1999, 455

5. BMU - Bundesministerium für Umwelt, Naturschutz und Reaktorsicherheit: DIOXINE aus Deutschland - ed. 4. Bericht der Bund/Länder-Arbeitsgruppe Dioxine (4th report of the Government/Länder working group on dioxins), Berlin, ISBN-3-00-009326-5, 2002

6. Canfield, R.L., Henderson, C.R. Jr., Cory-Slechta, D.A., Cox, C., Jusko , T.A., Lanphear, B.P.: Intellectual impairment in children with blood lead concentrations below 10 microg per deciliter. N Engl J Med. 348, 2003, 1517-1526

7. Dieter, H.H.: Trinkwasser. In: Umweltmedizin. Edited by V. Mersch-Sundermann. Stuttgart: Georg Thieme-Verlag 1999, 333-349

8. Dieter, H.H., Henseling, M.: Kommentar zur Empfehlung: Maßnahmewerte (MW) für Stoffe im Trinkwasser während befristeter Grenzwert-Überschreitungen gem.§ 9 Abs. 6-8 TrinkwV 2001 , Bundesgesundhbl 46, 2003, 701 - 706

9. de Zwart, L.L., Haenen, H.E.M.G., Versantvoort, C.H.M., Sips A.J.A.M.: Pharmacokinetics of ingested xenobiotics in children: A comparison with adults. RIVM report 623860011/2002, Bilthoven NL, 2002

10. Dulon, M., Weichenthal, M., Blettner, M., Breitbart, M., Hetzer, M., Greinert, R., Baumgardt-Elms, C., Breitbart, E.W.: Sun exposure and number of nevi in 5- to 6-year-old European children. J Clin Epidemiol 55, 2002, 1075-1081

11. Egeland, G.M., Sweeney, M.H., Fingerhut, M.A., Wille, K.K., Schnorr, T.M., Halperin, W.E.: Total serum testosterone and gonadotropins in workers exposed to dioxin. Am J Epidemiol 139, 1994, 272-278

12. European Environment Agency, WHO Regional Office for Europe: Children’s health and environment: A review of evidence. EEA, Environmental issue report 29, Copenhagen 2002

13. Eriksson, P.: Developmental neurotoxicity of environmental agents in the neonate. Neurotoxicology 18, 1997, 719–726

14. Evans, G.W., Lepore, S.J.: Nonauditory effects of noise on children: A critical review. Children's environments 10, 31-51, 1993

15. Evans, G.W., Lercher, P., Meis, M., Ising, H., Kofler, W.W.: Community noise exposure and stress in children. J. Acoust. Soc. Am. 109, 1023-1027, 2001

16. Gandhi, O.P., Lazzi, G., Furse, C.: Electromagnetic absorption in the human head and neck for mobile telephones at 835 and 1900 MHz. IEEE Transactions on Microwave Theory and Tech. 44, 1996, 1884-1897

17. Greinert, R., Volkmer, B., Wende, A., Voss, S., Breitbart, E.W.: Prevention of skin cancer. Necessity, implementation and success. Hautarzt 54, 2003, 1152-1163

18. Gulson, B.L., Mizon, K.J., Korsch, M.J., Palmer J.M., Donnelly J.B.: Mobilization of lead from human bone tissue during pregnancy and lactation - a summary of long-term research. Sci Total Environ. 303, 2003, 79-104

19. Gupta, A., Agarwal, R., Shukla, G.S.: Functional impairment of blood-brain barrier following pesticide exposure during early development in rats. Human and Experimental Toxicology 18, 1999, 174-179

20. Human Biomonitoring Commission at the German Federal Environmental Agency: Stoffmonographie Blei - Referenz- und Human-Biomonitoring-Werte (HBM). Bekanntmachung des Instituts für Wasser-, Boden- und Lufthygiene des Umweltbundesamtes, Bundesgesundhbl 39, 1996, 236-241

21. Human Biomonitoring Commission at the German Federal Environmental Agency: PCB - Referenzwerte für Blut. Bekanntmachung des Instituts für Wasser-, Boden- und Lufthygiene des Umweltbundesamtes, Bundesgesundhbl 42, 1999, 511-521

22. Hansen, J.C., Tarp, U. and Bohn, J.: Prenatal exposure to methylmercury among greenlandic polar Inuits. Arch Environ Health, 45, 1990, 355–358.

23. Hahn, A., Michalak, H., Begemann, K., Preußner, K., Engler, A., Rüdiger, T., Heinemeyer, G., Gundert-Remy, U.: Ärztliche Mitteilungen bei Vergiftungen nach §16e Chemikaliengesetz 2002. Report by the "Zentrale Erfassungsstelle für Vergiftungen, gefährliche Stoffe und Zubereitungen, Umweltmedizin" im Bundesinstitut für Risikobewertung für das Jahr 2002. Edited by: BfR-Pressestelle. Available online at: http://www.bgvv.de/cms/detail.php?template=internet_de_index_js (as of: 2004)

24. Haines, M.M., Stansfeld, S.A., Job, R.F.S., Berglund, B., Head, J.: A follow-up study of effects of chronic aircraft noise exposure on child stress responses and cognition. International Journal of Epidemiology 30, 839-845, 2001

25. Heinemeyer, G., Gundert-Remy, U.: Exposition von Kindern gegenüber Pflanzenschutzmitteln. Final report of an R&D project commissioned by the German Federal Environment Agency (FKZ: 201 61 218/01); Edited by: Bundesinstitut für gesundheitlichen Verbraucherschutz und Veterinärmedizin, Berlin 2002

26. Helbich, H.M.: Polychlorierte Biphenyle. In: Umweltmedizin. Edited by V. Mersch-Sundermann. Stuttgart: Georg Thieme-Verlag 1999, 215-217

27. Hygge, S., Evans, G.W., Bullinger, M.: A prospective study of some effects of aircraft noise on cognitive performance in schoolchildren. Psychological Science 13, 469-474, 2002

28. ICRP-60, publications by the International Commission on Radiological Protection (ICRP), publication no. 60, German version published by the Bundesamt für Strahlenschutz der Bundesrepublik Deutschland. Stuttgart, Jena, New York, G. Fischer Verlag, 1993

29. IRK/AGLMB: Richtwerte für die Innenraumluft: Basisschema. Bundesgesundhbl 39, 1996, 422-426

30. ISAAC Steering Committee: Worldwide variations in the prevalence of asthma symptoms: The International Study of Asthma and Allergies in Childhood (ISAAC). Eur Resp J 12, 1998, 315–335

31. James, W.H.: Offspring sex ratio as an indicator of reproductive hazards associated with pesticides. Occup Environ Med 52, 1995, 429-430.

32. Kojda, G. (Hrsg): Kapitel 18.4 Metalle und Metalloide. In: Pharmakologie/Toxikologie systematisch. Bremen: Uni-Med-Verlag, 2002, 826

33. Kreuzer P.E., Csanady G.A., Baur C., Kessler, W., Papke, O., Greim, H., Filser, J.G.: 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) and congeners in infants. Arch Toxicol 71, 1997, 383-400

34. Kurth, B.M., Bergmann, K.E., Holling, H., Kahl, H., Kamtsiuris, P., Thefeld, W.: The National Child and Adolescent Health Survey. Gesundheitswesen 64, 2002, 3-11

35. Lercher, P., Brauchle, G., Kofler, W., Widman, U., Meis, M.: The assessment of noise annoyance in schoolchildren and their mothers. In: InterNoise 2000. The 29th International Congress and Exhibition on Noise Control Engineering, Nice, 2000

36. Maassen, M., Babisch, W., Bachmann, K.D., Ising, H., Lehnert, G., Plath, P., Plinkert, P., Rebentisch, E., Schuschke, G., Spreng, M., Stange, G., Struwe, V., Zenner, H.P.: Ear damage caused by leisure noise. Noise and Health 4, 2001, 1-16

37. Maschke, C., Hecht, K.: Lärmexposition und Gesundheit bei Kindern und Jugendlichen. Grundlagen und Forschungsergebnisse. In: M. Schwenk, S. Jovanovic, R. Schulz (eds.): Freizeitlärm und Gesundheit. Landesgesundheitsamt Baden-Württemberg, Stuttgart, Umed Info 11, 7-49, 2000

38. Mielck A., Heinrich J.: Social inequalities and distribution of the environmental burden among the population (environmental justice). Gesundheitswesen 64, 2002, 405-416

39. Mocarelli, P., Gerthoux, P.M., Ferrari, E., Patterson, D.G. Jr., Kieszak, S.M., Brambilla, P., Vincoli, N., Signorini, S., Tramacere,P., Carreri, V., Sampson, E.J., Turner, W.E., Needham, L.L.: Paternal concentrations of dioxin and sex ratio of offspring. Lancet, 355, 2000, 1858-1863

40. Nau, H.: Toxikokinetik. In: Toxikologie. Edited by: H. Marquardt und S.G. Schäfer. Mannheim; Leipzig; Wien; Zürich: BI-Wissenschaftsverlag 1994, 61

41. Neubert, B.: Reproduktion und Entwicklung. In: Toxikologie. Edited by: H. Marquardt und S.G. Schäfer. Mannheim; Leipzig; Wien; Zürich: BI-Wissenschaftsverlag 1994, 342-343

42. Nielsen, E., Thorup, I., Schnipper, A., Hass, U., Meyer, O., Ladefoged, O., Larsen, J.C., Ostergaard, G., Larsen, P.B.: Children and the unborn child. Exposure and susceptibility to chemical substances – an evaluation Danish Environmental Protection Agency. Environmental Project No. 589, Miljöprojekt, 2001

43. Oranje, A.P., Wolkerstorfer, A., de Waard-van der Spek F.B.: Natural course of cow's milk allergy in childhood atopic eczema/dermatitis syndrome. Ann Allergy Asthma Immunol 89, 2002, 52-55

44. Plunkett, L.M., Turnball, D., Rodricks, J.V.: Differences between adults and children affecting exposure assessment. In : Guzelian et al., 1992, 79-94

45. Rascher, W., Kruse, K.: Wasser und Mineralhaushalt. In: Pädiatrie, Grundlagen und Praxis. Edited by: Lentze, Schaub, Schulte, Spranger: Springerverlag 2003, 233

46. Röper, A., Lauven, P.M.: Pharmakokinetik bei Neugeborenen und Säuglingen. Anästhesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie 34, 1999, 616-625

47. Schneider, K., Gerdes, H., Hassauer, M., Oltmanns, J., Schulze, J.: Berücksichtigung der Risikogruppe Kind bei der Ableitung gesundheitsbezogener Umweltstandards. Final report of an R&D project commissioned by the German Federal Environment Agency (FKZ: 201 61 215); Forschungs- und Beratungsinstitut Gefahrstoffe GmbH (FoBiG), Freiburg, September 2002

48. Schneider, K.: Zur Frage von Unterschieden in der Empfindlichkeit von Kindern gegenüber krebserzeugenden Stoffen im Vergleich zu Erwachsenen. In: Eikmann, Heinrich, Heinzow, Konietzka: Gefährdungsabschätzung von Umweltschadstoffen. Edited by: Umweltbundesamt Berlin, Erich Schmidt Verlag Berlin, 1999, 5th supplement 10/01

49. Schönborn, F., Burkhardt, M., Kuster, N.: Differences in energy absorption between heads of adults and children in the near field of sources. Health Physics 74, 1998, 160-168

50. Shimizu, Y., Kato, H., Schull, W.J.: Life Span Study Reports 11. Part 2. Cancer Mortality in the Years 1950 –1985 Based on the Recently Revised Doses (DS 86). Radiation Effects Research Foundation, Hiroshima. RERF-TR, 5–88, 1988

51. Snodgrass, W.R.: Children versus adults: Differences and similarities in response to environmental pollutants and chemical poisons. Open presentation on: Workshop on exposure of children to substances used as ingredients in pesticides. Berlin, 27-29.09.2001

52. Schulz, C., Becker, K., Seiwert, M.: The Child Environment Survey. Gesundheitswesen 64, 2002, 69-79

53. Tietze, K.W.: Stillempfehlungen der Nationalen Stillkommission Deutschlands. PerinatalMedizin 9, 1997, 65-66

54. UNSCEAR (United Nations Scientific Committee on the Effects of Atomic Radiation): 2000 Report, Sources and Effects of Ionizing Radiation, Vol. II: Effects. United Nations, New York, 2000

55. U.S. Environmental Protection Agency (EPA): Summary Report of the Technical Workshop on Issues Associated with Considering Developmental Changes in Behavior and Anatomy when Assessing Exposure to Children. Risk Assessment Forum. EPA/630/R-00/005, Washington, Dezember 2000

56. Walkowiak, J., Wiener, J.A., Fastabend, A., Heinzow, B., Kramer, U., Schmidt, E., Steingruber, H.J., Wundram, S., Winneke, G.: Environmental exposure to polychlorinated biphenyls and quality of the home environment: effects on psychodevelopment in early childhood. Lancet 358, 2001, 1602-1607

57. Whiteman, D.C., Whiteman, C.A., Green, A.C.: Childhood sun exposure as a risk factor for melanoma: a systematic review of epidemiologic studies. Cancer Causes Control 12, 2001, 69-82

58. World Health Organization (WHO), Regional Office for Europe: Children's environment and health action plan for Europe (CEHAPE). Available online at: http://www.euro.who.int/eprise/main/WHO/Progs/BUD/resolutions/20030328_2 (as of: 2003)

59. Wilhelm, M.: Metalle und Metalloide. In: Umweltmedizin. Edited by: V. Mersch-Sundermann. Stuttgart: Georg Thieme-Verlag 1999, 153-161

60. Wilhelm, M., Ewers, U.: VI-3 Metalle/Blei. In: Handbuch der Umweltmedizin. Edited by: H.-E. Wichmann, H.-W. Schlipköter und G. Fülgraff. Landsberg/Lech: ecomed Verlagsgesellschaft mbH 1992, 1st supplement. 6/93

61. Wissenschaftlicher Beirat der Bundesärztekammer: Gehörschäden durch Lärmbelastungen in der Freizeit. Deutsches Ärzteblatt 96, A-1081-1084, 1999

62. Wong, K., Klaassen, C.: Age difference in the susceptibility to cadmium-induced testicular damage in rats. Toxicology and Applied Pharmacology 55, 1980, 456-466

63. Zenner, H.P., Struwe, V., Schuschke, G., Spreng, M., Stange, G., Plath, P., Babisch, W., Rebentisch, E., Plinkert, P., Bachmann, K.D., Ising, H., Lehnert, G.: Gehörschäden durch Freizeitlärm. HNO 47, 236-248, 1999

Attention should also be drawn to the "Mini-Monograph" on Assessing Risk in Children, published in Environmental Health Perspectives (Volume 112, No. 2), February 2004

10. Abbreviations and acronyms

DDT	Dichloro-diphenyl-trichloroethane
PCB	Polychlorinated biphenyls
PAH	Polycyclic aromatic hydrocarbons
PVC	Polyvinyl chloride
VOC	Volatile organic compounds
SIDS	Sudden infant death syndrome
TCDD	2,3,7,8-tetrachlorodibenzo-p-dioxin
TrinkwV	Trinkwasserverordnung (German Drinking Water Ordinance)

Part II: The use of child-specific safety factors when deriving limit values

Introduction:

When deriving limit values for harmful substances in the environmental media or food, and when evaluating chemicals using the "margin of safety" approach (MOS approach, 22), the usual procedure is to take the dose ascertained in animal experiments as being without adverse effect (NOAEL) and use standard factors to adjust it to the human situation. A factor of 10 is conventionally used for the differences between animals and humans and a further factor of 10 is then applied to allow for the variability between individuals in the population (14,15,16). In a number of national and international evaluation guidelines, children are mentioned as a particularly vulnerable group requiring special consideration (22).

A number of works, particularly in recent years, have systematically compiled available information about the special vulnerability of children (see Part I). The following factors are relevant when setting limit values:

1. Higher intake

1.1. Exposure by inhalation: the fact that infants and children have a relatively higher respiratory minute volume means that the same concentration in the ambient air (indoor and outdoor air) will produce a higher inhaled dose relative to body weight and consequently a higher internal concentration. The higher concentration can cause a more pronounced effect than in adults.

1.2. Dietary intake: at certain ages, children's consumption of particular food, such as milk, is significantly higher than that of adults, relative to body weight. Infants and toddlers also consume a very different range of food than adults.

2. A child's elimination mechanisms are not fully developed before the age of six months. Thus, the same dose relative to body weight cannot be eliminated at the same rate as later in life. Particularly in the case of repeated exposure, the reduced rate of elimination means that the same intake relative to body weight leads to a higher internal concentration and consequently to the possibility of a more pronounced effect.

3. With certain effects there is greater susceptibility of the tissue in the early years of life (e.g. sensitivity to radiation or to the neurotoxic effect of lead). In these cases, the same internal dose will also lead to a more pronounced effect.

4. In addition, it is also important when deriving limit values to take into account that, by comparison with adults, children have age-related behaviour patterns that may lead to higher external exposure. An example of this would be children crawling on the floor and ingesting house dust.

Specific consideration also applies for radiation. Because children spend a considerable amount of their time outdoors playing, they are exposed to the sun for longer time periods compared to adults.

<u>Institutions consulted:</u>
As part of the APUG project "Vulnerability of children to harmful substances," a questionnaire was sent to the institutions involved in APUG (Federal Office for Radiation Protection (BfS), Federal Institute for Risk Assessment (BfR), Robert Koch Institute (RKI), Federal Environmental Agency (UBA)), requesting details on how children are taken into consideration when deriving limit values.

Summary:

In virtually all areas in which limit values are set for the environmental media, for radiation exposure levels and for food, the specific characteristics of children are taken into account (Table 1).

Generally speaking, a special analysis of the exposure situation, the available findings and known physiological peculiarities, which takes infants and children into account, is carried out to ensure that limit values are set appropriately.

In the field of indoor air, a default approach has been chosen and an additional safety factor of 2 is used to take the special situation of children into consideration. The justification for this is the age-related higher respiratory minute volume per kg of body weight.

A default approach is also used for genotoxic carcinogens. The additional factor of 10 is based on an analysis of studies on the occurrence of cancer that point to the increased susceptibility of animals exposed in experiments to genotoxic carcinogens at an early age by comparison with animals exposed at a later age.

For pesticides, indications of embryo-foetal toxicity and interference with post-natal development have led to an additional factor of up to 10 being incorporated into limit values. This special factor is also used in cases where the data situation on toxicity in the developmental phase is patchy.

A Directive of the European Commission (20) prohibits the use of a number of named pesticides on agricultural produce destined for use in the production of infant formulae and follow-on formulae.

Another Commission Directive (19) sets maximum levels of residues of a number of pesticides for processed cereal-based foods and baby foods for infants and young children that are significantly below the values applicable to adult food. The Commission has also passed a Regulation (24) setting levels for aflatoxin and ochratoxin for infants and young children that are markedly lower than those for adults.

In Table 2 the specific intraspecies assessment factors for the different regulatory areas are given with explanation.

Table 1: Taking into account neonates and children when deriving limit values (as of: 2004)

Agency	Limit value	Population groups taken into account	Are children taken into account?	Calculation basis	Reason
Federal Office for Radiation Protection (BfS)	Physical (radiotoxic) noxae: emissions and immissions: air	All groups, including infants and toddlers, assuming that exposure is very different in certain groups of the population	Yes	Age-specific lifestyle patterns and physiological factors; age- and radionuclide-specific dose- and dose rate coefficient	Statistical surveys and conservative assumptions, scientific consensus
	Radiation protection: Internal dosimetry; Radiation Protection Regulation 1. Primary limit values (dose limit values) and deriving from these 2. Secondary limit values (e.g. limit value for total annual activity)	1. Primary limit values: a) Individuals exposed in the workplace b) Individuals in the population 2. Secondary limit values	Yes, for 2	Nuclide-specific, age-related dose coefficient Age group: - 3 months, 1 year, 5 years, 10 years, 15 years - Embryo, foetus Age-related kinetics of the nuclide may be taken into account (ICRP, 13 – 18)	
	Non-ionising radiation: UV radiation Microwaves	UV radiation: children given special consideration Microwave limit value: children given special consideration as a particularly vulnerable population group	Yes	UV radiation: separate recommendation on protection for children due to the greater sensitivity of children's skin and longer life expectancy (significant for stochastic risks)	

Agency	Limit value	Population groups taken into account	Are children taken into account?	Calculation basis	Reason
Federal Environmental Agency (UBA)	Commission on indoor air/working party of the supreme health agencies of the *Länder*: guide values for indoor air (1, 13)	All groups, including infants and toddlers	Yes	General factor of 2	Higher respiratory minute volume
	Human Biomonitoring Commission: reference values for contaminants (12)	All groups, including infants and toddlers	Yes, depending on the data situation	Data situation on substances taken into account	Specific reference value for children
	Drinking water (5, 6, 11)	All groups, including infants and toddlers	Yes, depending on the data situation	Data situation on substances taken into account, exposure taken into account	
	Trigger and action values as set out in Article 8 of the Federal Soil Protection Act: excluding genotoxic carcinogens (2, 3, 4, 9, 10)	All groups, including infants and toddlers	Yes, depending on the data situation	Data situation on substances taken into account, exposure taken into account	
	Trigger and action values as set out in Article 8 of the Federal Soil Protection Act: genotoxic carcinogens (3)	All groups, including infants and toddlers	Yes	Additional factor of 10	US EPA (23)

Agency	Limit value	Population groups taken into account	Are children taken into account?	Calculation basis	Reason
Federal Institute for Risk Assessment (BfR)	Establishment of maximum levels of pesticide residues (7, 8, 17, 18, 21, 25)	All groups, including infants and toddlers	Yes, depending on the data situation	Data situation on substances taken into account: additional factor of up to 10 if there are indications of interference with post-natal development, embryo-foetal toxicity in animal experiments, or if data is patchy. Exposure taken into account	Specific vulnerability Specific dietary patterns (e.g. dairy products) Higher food intake/kg of body weight
	Contaminants in food: ADI/PTWI (14, 15)	All groups, including infants and toddlers	Yes, depending on the data situation	Data situation on substances taken into account, exposure taken into account	Specific vulnerability
	Special regulations on infant formulae and follow-on formulae			Ban on certain pesticides (20)	
	Processed cereal-based foods and baby foods for infants and young children			Lowering the levels of certain pesticides (19)	
	Aflatoxins and ochratoxin A			Lowering the levels (24)	

Table 2: Intraspecies assessment factor in different regulatory areas

Limit values	Intraspecies factor	Additional factor (default factor) for children in all cases	Reason	Additional factor in certain justified cases	Overall intraspecies factor
Indoor air (Ad-hoc working group of the Commission on indoor air hygiene at the German Federal Environmental Agency)	10	2	Higher respiratory minute volume		20
Drinking water	10			Effect profile of the substance, possible higher exposure due to the higher volume of intake	Possibly > 10
Soil protection Trigger and action values as set out in Article 8 of the Federal Soil Protection Act	10	10 for genotoxic carcinogens	References in the literature for certain substances	Higher exposure possible due to specific play behaviour (e.g. sandpit)	Possibly >100
AEGL values (USA/Germany) (Acute Exposure Guideline Levels in case of accidental release)	10				10
ADI	10			Higher exposure possible due to specific dietary patterns	Possibly > 10
ADI	10			In individual cases, effect- and chemical-specific additional factor	Possibly >10
Maximum residue levels for pesticides	10			Higher exposure possible due to specific dietary patterns	Possibly > 10

Bibliography, Part II

1. AGLMB (Arbeitsgemeinschaft der leitenden Medizinalbeamten der Länder). Standards zur Expositionsabschätzung. 1995, Hrsg.: Behörde für Arbeit Gesundheit und Soziales, Hamburg.
2. Bachmann G, Oltmanns J, Konietzka R, Schneider K. Berechnung von Prüfwerte zur Bewertung von Altlasten. Grundwerk XII/99. 1999. Hrsg. Umweltbundesamt. Erich Schmidt Verlag. Berlin
3. Bekanntmachung über Methoden und Maßstäbe für die Ableitung der Prüf- und Maßnahmenwerte nach der Bundes-Bodenschutz- und Altlastenverordnung (BBodsch V). Bundesanzeiger, 1999, 161a
4. Bundes-Bodenschutz- und Altlastenverordnung. Bundesgesetzblatt I, 1999. 36: 1554
5. Dieter HH. Ableitung von Grenzwerten (Umweltstandards) – Wasser.1999. In: Handbuch der Umweltmedizin. Hrsg. Wichmann H-E, Schlipköter H-W und Fülgraff G. Ecomed Verlagsgesellschaft mbH. Landsberg/Lech Kap. II-1.3.5.
6. Dieter H H, Henseling M Kommentar zur Empfehlung: Maßnahmewerte (MW) für Stoffe im Trinkwasser während befristeter Grenzwert-Überschreitungen gem. § 9 Abs. 6-8 TrinkwV 2001. Bundesgesundheitsbl – Gesundheitsforsch – Gesundheitsschutz 2003, 46: 701-706.
7. FAO/WHO. Principles governing consumer safety in relation to pesticide residues. FAO Plant Production and Protection Division Report No PL/1961/11. 1962 WHO Technical Report Series, no. 240. WHO, Geneva: 5
8. FAO Pesticide residues in food – 2002. Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues. Rome Italy. 16-25 September 2002
9. Gefährdungsabschätzung von Umweltstoffen. Ergänzbares Handbuch toxikologischer Basisdaten und ihrer Bewertung. Kennziffer B 010. Grundwerk. 1999. Eickmann , Heinrich, Heinzow, Konietzka (eds.). Erich Schmidt Verlag. Berlin
10. Gefährdungsabschätzung von Umweltstoffen. Ergänzbares Handbuch toxikologischer Basisdaten und ihrer Bewertung. Kennziffer B 100. Supplement. 2001. Eickmann , Heinrich, Heinzow, Konietzka (eds.). Erich Schmidt Verlag. Berlin
11. Grohmann A, Hässelbarth U, Schwerdtfeger G (eds.). Die Trinkwasserverordnung. Einführung und Erläuterungen für Wasserversorgungsunternehmen und Überwachungsbehörden. 2003. Erich Schmidt Verlag. Berlin
12. Human Biomonitoring Commission at the German Federal Environmental Agency. Konzept der Referenz- und Human-Biomonitoring-Werte (HBM) in der Umweltmedizin. Berichte. 1996 Bundesgesundheitsblatt 39: 221-224
13. ICRP International Commission on Radiological Protection. Age-dependent Doses to Members of the Public from Intake of Radionuclides: Part 1. ICRP Publication 56. Annals of the ICRP 20 (2), 1989
14. ICRP International Commission on Radiological Protection. Age-dependent Doses to Members of the Public from Intake of Radionuclides: Part 2, Ingestion Dose Coeficients. ICRP Publication 67. Annals of the ICRP 23 (3/4), 1993
15. ICRP International Commission on Radiological Protection. Age-dependent Doses to Members of the Public from Intake of Radionuclides: Part 3, Ingestion Dose Coefficients. ICRP Publication 69. Annals of the ICRP 25 (1), 1995
16. ICRP International Commission on Radiological Protection. Age-dependent Doses to Members of the Public from Intake of Radionuclides: Part 4, Inhalation Dose Coefficients. ICRP Publication 71. Annals of the ICRP 25 (3-4), 1995
17. ICRP International Commission on Radiological Protection. Age-dependent Doses to Members of the Public from Intake of Radionuclides: Part 5, Compilation of ingestion and inhalation dose coefficients. ICRP Publication 72. Annals of the ICRP 26 (1), 1996
18. ICRP International Commission on Radiological Protection. Doses to the Embryo and Fetus from Intakes of Radionuclides by the Mother. ICRP Publication 88. Annals of the ICRP 31 (1-3), 2001
19. IRK (Innenraumkommission/AGLMB). Richtwerte für die Innenraumluft: Basisschema. Bundesgesundheitsblatt 1996, 39: 422-426

20. IPCS. Principles for the safety assessment of food additives and contaminants in food. 1987. Environmental health Criteria 70. Geneva, World Health Organization, International Programme on Chemical Safety

21. IPCS. Assessing human health risks of chemicals: derivation of guidance values for health-based exposure limits. 1994. Environmental health Criteria 170. Geneva, World Health Organization, International Programme on Chemical Safety

22. IPCS. Principles for the assessment of risks to human health from exposure to chemicals. 1999. Environmental health Criteria 210. Geneva, World Health Organization, International Programme on Chemical Safety

23. Krewski D, Wargo J, Riszek R. Risks of dietary exposure to pesticides in infants and children. 1991. In: Mac Donalld I (ed.) Monitoring dietary intakes. Springer, Berlin. pp. 75-89

24. PSD. Data Requirements Handbook 23705/01. 2001. Chapter 5: Residues. 3. Guidance on the Estimation of Dietary Intakes of Pesticide Residues. PSD, York, UK

25. Commission Directive 2003/13/EC of 10 February 2003 amending Directive 96/5/EC on processed cereal-based foods and baby foods for infants and young children

26. Commission Directive 2003/14/EC of 10 February 2003 amending Directive 91/321/EEC on infant formulae and follow-on formulae

27. Schilter B, Renwick AG, Huggett AC. Limits for pesticides residues in infant foods: a safety-based proposal. 1996. Regul Toxicol Pharmacol 24: 126-140

28. TGD (Technical Guidance Document) on the Assessment of Chemicals supporting Directive 93/67/EEC and Directive 1488/94/EC (2003). European Chemicals Bureau, Ispra, Italy

29. US EPA Adjusting for Youth, Update Cancer Risk Guidelines. Environmental Health Perspectives 2003, 111: A708-A710

30. Commission Regulation (EC) No 683/2004 of 13 April 2004 amending Regulation (EC) No 466/2001 as regards aflatoxins and ochratoxin A in foods for infants and young children

31. WHO. Principles for the toxicological assessment of pesticide residues in food. Environmental Health Criteria 104. 1990. WHO, Geneva

Aktionsprogramm
Umwelt und Gesundheit

Action Programme Environment and Health

Bundesamt für Strahlenschutz

Umwelt Bundes Amt
Für Mensch und Umwelt

BfR
Risiken erkennen – Gesundheit schützen

ROBERT KOCH INSTITUT

This review is a contribution to the Action Programme Environment and Health and its public relations activities. It has been produced using recycling paper.