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Expert report on total toxic exposure in industrialized countries from the perspective of environmental medicine

The relationship between dose and effect(s) is more or less well understood for a large number of individual substances. The combined effects of several substances, however, can only be roughly estimated, and even that is possible only for the combined impact of no more than two or three substances acting simultaneously.

As regards total toxic exposure of the population at large in the industrialized nations, however, we have to assume that there are dozens, possibly up to hundreds, of different pollutants with varying, below-threshold effects. The experience of environmental medicine in recent years indicates that an association exists between this toxic exposure and the rise of certain health disorders.

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The history of environmental medicine

Environtnental medicine as a discipline in its own right is historically rooted in several specialized fields. Already in the 19th century, the study of workplace conditions led to early insights regarding the connection between testicular cancer seen in chimney sweeps and their workplace exposure to soot, and - at a later point - the quartz-dust silicosis suffered by miners and stonemasons. Since then, the list of occupational diseases for which a toxicological explanation could be found has continued to grow.

Another starting point for environmental medicine was the observation of health damage caused by radioactive rays which claimed many victims among the pioneers in this area of research. The smog episodes which occurred in London in the 1950s and resulted in thousands of deaths in excess of the normal mortality rate, also contributed to rising interest in environmental medicine.

In the United States, environmental medicine developed independent theoretical foundations, with physicians such as Randolph and Kailin who established the field of clinical ecology. They studied the effects of household chemicals, pesticides and food additives on human health. In the 1960s, the first indications were found that certain individuals may be sensitive to pollutants (e.g., DDT) at a level which is below the average exposure of the population at large. These decades of experience created a crucial lead in expertise in the U.S. which resulted, among other things, in the official recognition of multiple chemical sensitivity as a disease - which was not the case in the German-speaking countries in Europe.

Environmental medicine thus deals with many different issues, with most research being conducted by interdisciplinary teams involving scientists from the fields of epidemiology, occupational medicine, toxicology, allergy research, immunology, neurophysiology, statistics, information processing, pulmology, pediatrics, environmental psychology, laboratory medicine, pollutant analysis and many others.

Contrary to the U.S., where medical care for patients with environment-related disorders is also well established, the main public-health focus of environmental medicine in Europe is risk evaluation with respect to exposure to pollutants. In this context, the traditional approach of occupational medicine has long prevented a clear view of the relationships between pollutant exposures that are recognized as relevant in environmental medicine and damage to human health. The relationship remained obscure because risk evaluations were initially carried out with a view to those dose-related effects which were regarded as significant in the workplace, the dose-effect relationships established in

occupational medicine were applied unchanged to the risks involved in environmentally relevant - i.e., significantly lower general pollutant exposures.

lt seemed inconceivable that, for example, a mere 10% of the tolerated workplace exposure to a given pollutant could result in adverse health effects in everyday life. To gain useful insights into the relationship between pollutant exposure and human health disorders, a new question had to be asked and answered. This was:

What are the most easily disturbed body functions which may affected even by low-level exposure?

For most pollutants, such as lead, it was assumed that adverse effects (blood count changes, nerve disorders) will occur only if a certain threshold of toxicity is exceeded. Research into the heavy metal lead, where the above crucial question was first raised, marks the beginning of a new era of environmental medicine.

Risk evaluation from the perspective of environmental medicine

An interdisciplinary research team was asked in the U.S. in the 1970s to find the target organ which is most vulnerable to lead. The purpose of the study was to prove that adverse health effects may occur below the threshold limit of 70 µg lead/dl blood which was then in place for industrial workers. The research team concluded that the developing brains of children would probably be more vulnerable than individual nerves of adults, given that children's organs not only have to fulfill their proper functions, but are undergoing development at the same time.

As the neurotoxicity of lead was well established, the young brain was selected as target organ. lt was known that cognitive functions and socially adjusted behavior require an extremely well-coordinated integration of partial functions. These functions were studied in detail and examined for correlation with lead exposure in infancy.

Needleman published the results of this first preliminary study in 1979. Children with blood lead levels of 30 to 50 µg/dl had a lowered average IQ when compared to others from similar socio-economic backgrounds whose blood lead levels were lower (Needleman, 1979). These effects can be shown even for lower lead levels, as the results of later studies indicated. Blood lead levels of 7 to 10 µg/dl - measured immediately after birth - may be enough to affect the sensoric and motor development of an infant (Bellinger, 1986).

Follow-up studies showed that children with higher lead exposure had persistent reading skill deficits and had a greater risk of dropping out of high school. In addition, they were more likely to engage in violent behavior as adults, with the resulting increased risk of delinquency.

The blood lead level of the newborn infant is identical with that of the child's mother (Tsuchiya, 1984). In a survey of Swiss women, the mean level was about 9 µg/dI, with levels of more than 11 µg/dl in one quarter of those examined (Rickenbach, 1987).

As neuropsychologic disorders - e. g., affecting behavior and learning abilities - have been observed in children whose neonatal blood lead level was about 10 µg/dl and above, we have to assume that a substantial proportion of children in the industrialized world have suffered health damage as a result of lead exposure. The situation improved only after the introduction of unleaded gasoline.

The above-cited studies not only indicated that ubiquitous lead pollution had an effect even at exposure levels far below those found in industrial workplace situations. They also suggested rather convincingly that other complex functions of the human body may be just as easily irritated, and that not only lead, but other widely dispersed substances may also be to blame.

Specifically where children were concerned, one could no longer rule out the possibility that the ubiquitous average exposure to heavy metals, plant protectives, wood preservatives, formaldehyde, and many other industrially produced substances would result in adverse effects on the development

and functions of organ systems. Apart from the nervous system, there are other highly complex systems and processes of the human body which rely on well-coordinated molecular information transfer, including the immune system, reproductive functions and fetal development.

An early result which points in this direction involves reproductive ability and was reported by R. C. Dougherty. In a study involving 132 healthy students, he found a correlation between reduced sperm counts and exposure to halogenated hydrocarbons (Dougherty, 1980). He concluded that, among the analyzed substances (PCPS, PCBS, hexachlorobenzene, tri- and tetrachlorophenol, hexachloronaphtalene and DDT), polychlorinated biphenyls were mainly responsible for the reduction of sperm counts.

Environmental medicine studies in Brixlegg, Austria

After year-long reports on environmental pollution caused by a copper mill in the vicinity of Brixlegg in westem Austria, 1 was asked by the local government to conduct epidemiological studies in the area in cooperation with the pediatric clinic and the department of biostatistics of the University of Innsbruck (Rhomberg, 1990).

In 1988, when the three-part survey was planned, the major components of local pollution were above-average Ievels of dioxins, heavy metals, sulfur dioxide, nitrogen oxides and dust. There were reports on individual workers who had to be treated for lead-related health disorders many years previously. Dioxin levels of more than 20 times the average were found in a farmer who drank the milk of his cows which grazed for many years in an area directly adjacent to the copper mill premises. According to the toxicology expert Mr. Schlatter from Zurich, Switzerland, however, this level constituted only one fourth of the dose required to produce poisoning symptoms.

Apart from these few individual cases, however, there was no evidence of pollutant exposure at a toxicologically relevant level. The dioxin levels found in the breast milk of women who bought milk from the above-mentioned farmer were in the upper segment of the mean value distribution of dioxin levels found in a survey in Germany.

After this preliminary research, we agreed in the planning group that, apart from effects on the respiratory system of school children, health effects could be expected only from the combined impact of all pollutants (total toxic exposure) and only in target functions whose high vulnerability could be inferred from the results of earlier environmental medicine research - which were still scarce at the time. We therefore included the immune system and intrauterine development in our research work.

Our survey, which included 1,600 school-age children, found a correlation between air pollution and a reduction of pulmonary function, especially in the smaller respiratory passages, as well as an association with the incidence of respiratory tract symptoms and allergies. In addition, our group was the first worldwide to discover that prolonged summer ozone episodes can give rise to chronic respiratory tract effects (Schmitzberger, 1992).

We analyzed hair samples of some 100 school children to determine their heavy metal exposure, and studied cellular and humoral immune function parameters. In localities with polluted air, the children's heavy metal levels were substantially higher than in non-polluted areas. However, all exposure levels were well below the limit above which manifest clinical signs of poisoning have to be expected. We found only one child with a blood lead level of more than 10 µg/dl.

We did find, however, statistical correlations which pointed to a connection between living in the polluted zone and changes in immune system parameters. The same connection showed up in the statistical correlation between individual exposure to heavy metals and immune system parameters, such as elevated levels of immunoglobulin E or changes in the helper/suppressor cell ratio (Rhomberg, 1994).

For an examination of development *in utero* we surveyed the files on more than 2,300 births in the region over the previous 10 years. We found a trend towards lower birth weight and a significant average reduction of circumference of newborns' heads by 0.8 cm in tie most heavily polluted area.

Similar results had been reported some time earlier in a study conducted in an industrial region in Norway (Hansteen, 1987).

Reproductive disorders

Professor Gerhard at the infertility clinic in Heidelberg, Germany, began in 1988 to examine her infertile woman patients for exposure to heavy metals (cadmium, mercury, lead) and halogenated hydrocarbons (wood preservatives and plant protectives) (Gerhard. 1992). She found clear evidence of a connection between the measured pollutant levels and health disorders which led her to conclude that *women with hormonal disorders and/or certain fertility disorders should be examined for pollutant exposure before hormone treatment is siarted.* She was able to increase her cure rate significantly through therapies aimed at the elimination of pollutants from the body.

In the industrialized world, the number of couples who remain childless (despite wanting children) has nearly doubled from 8% to 15%, with a significantly greater share of those affected living in urban than in rural areas. According to one study, the infertility rate of women between 20 and 24 years increased from 4% to 1l% over a period of 17 years. A decline in sperm density, motility of sperm cells, and the proportion of morphologically intact sperm cells has been observed in healthy men for the past 50 years (Spechter, 1997).

Where hormone treatment fails, in-vitro fertilization (IVF) is increasingly used to fulfill couples' desire for children. In the context of the debate in Austria about whether or not the cost of IVF should be covered by the health insurance system, 1 was interested in finding out about the potential effectiveness of environmental medicine services, such as pollutant analysis and pollutant-eliminating treatment. Responding to my query to this effect, Professor Gerhard - who has probably the widest experience in the field - stated that *about half of the couples involved could do without IVF* (Gerhard, 1999).

The new pediatric morbidity

The combination of children's exposure to new chemical agents on the one hand, and the successes of vaccination campaigns and antibiotics treatment on the other hand, have dramatically changed the distribution of health disorders in the industrialized nations in the 20th century. Apart from the increasing fertility disorders seen in young adults, the incidence of environment-related conditions has increased especially in children.

The Children's Environmental Health Network (CEHN) is a national project which was launched in the United States to promote a healthy environment and protect children and fetuses against environmental hazards. The network also collects data on the increase of environment-related disorders in children.

It found that asthma mortality among children has doubled over the last decade (Landrigan, 1999). In big American cities such as New York, Chicago, Los Angeles and others, asthma has become the single most important cause for hospital admissions of children.

Regarding infant mortality, a recent study found an association between post-neonatal infant mortality, including sudden infant death syndrome (SIDS), and elevated particulate air pollution (Woodruff, 1997).

According to the data of the American cancer monitoring program, the incidence of acute lymphatic leukemias increased by 27% between 1973 and 1990. Between 1973 and 1994, the incidence of brain tumors in childhood rose by 40%, and that of Wilms' tumors by 46%. The incidence of testicular cancer in young men (ages 20 to 39) rose by 68% between 1973 and 1994 (De Vesa, 1995).

There is mounting , evidence that environmental pollutants may adversely affect health by causing defects in the transfer of hormonal signals. Some of the suspected substances are used as pesticides, others have industrial applications or are contained in plastics (e.g., phthalates in PVC). Embryos, fetuses, and infants seem to be particularly at risk from the impact of substances which affect the hormonal functions (Longnecker, 1997).

Substances that affect hormonal functions may be to blame for the rising incidence of testicular cancer in the last two decades (De Vesa, 1995), as well as for the doubling of the number of hypospadias - malformations of the urethra - seen in newborn boys (Paulozzi, 1997). A Potential association between these substances and the increasingly early onset of puberty is also being discussed (Herman-Giddens, 1997).

With funding from the European Commission, a study was recently conducted in the Netherlands on the impact of environmental PCB and dioxin pollution on early childhood development. Among the industrialized nations, the Netherlands and Belgium are the two countries with the highest levels of dioxin in human breast milk (Wassermann, 1997). The results of the study, which was started in 1990, were published last year (Patandin, 1999).

It was reported that a clear connection exists in the healthy Dutch population between perinatal environmental PCB/dioxin pollution and retarded body growth. The development of the neurovegetative system is associated with behavioral disorders and changes in the immune and endocrine systems. Some of these undesired effects can be demonstrated until pre-school age (e.g. immunological effects), whereas others become apparent in pre-school age for the first time (poorer cognitive function, less focussed attention, withdrawn, depressive behavior).

The research team recommended an extension of the study to cover school-age children and especially the puberty phase in order to gain insights into neurological behavior patterns and fertility.

Conclusions

The last decade has brought mounting evidence which indicates that the working hypothesis of environmental medicine - that pollutants, once absorbed by the body, can disturb information processes on the bio-molecular level, and may therefore cause irritations especially of those body functions which have the highest need of well-coordinated information transfer - is indeed correct. These functions and systems are the central nervous system, the immune system, the reproductive processes and intrauterine development. Some of the mechanisms involved have been toxicologically analyzed, such as the enzyme-blocking effect of heavy metals, or the irritation of cell-surface receptors by hormonally effective substances. Other cause-effect mechanisms are still completely unclear.

lt is evident that regulatory policies concerning the use of chemicals in the industrialized nations have so far been unable to ensure the protection of human health. Children are those who suffer most in the current situation - but also young couples who cannot have children.

Experts involved in environmental medicine research all over the world are calling for more funds to expand the current body of scientific knowledge in the field. In a paper on *International cooperation of environmental protection organizations,* the managing director of the Switzerland-based International Society of Doctors for the Environment (ISDE), Gaudenz Silberschmidt, suggested that the coming decade should be dedicated not only to further research in the field of environmental medicine, but also to committed work for the implementation of the knowledge gathered until now. Past cooperation efforts, which included a joint press conference with WWF and Greenpeace at the 1996 Climate Conference and participation in the preparatory work for the. June 1999 conference of health and environmental affairs ministers in London should be continued and expanded.

Innsbruck, 25 June 1999 Dr. Klaus Rhomberg

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