Clinical Environmental Medicine

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SUMMARY

Introduction: Clinical environmental medicine deals with environmental effects on human health in individual patients. Patients seek medical advice for problems of many different kinds that may be due to environmental exposures; such exposures must be considered carefully along with other potential causes. An environmental medical assessment should include thorough medical history-taking and physical examination, the formulation of a differential diagnosis, and (whenever indicated) human biomonitoring, site inspections, and ambient monitoring.

Methods: This review of clinically relevant environment-related health disturbances is based on a selective evaluation of the pertinent literature and of own experiences.

Results: Overall, relevant environmental exposures can be identified in up to 15% of patients who attribute their health complaints to environmental factors. (Clinical disorders are more common and more severe in these patients.) 40% to 75% are found to suffer from other physical and/or emotional conditions without any specific environmental aspect, i.e., without any apparent or verifiable exposure.

Discussion: Despite the relative rarity of verifiable environmentally related health disturbances, these must be clearly identified and delimited to avoid further harmful exposures. Environmental medical counseling should include risk assessment and behavior recommendations for all patients who attribute their medical problems to their environment. Physicians performing specific environmental-medical diagnostic procedures must be aware of their limitations in order to avoid performing tests whose results have no therapeutic consequences and are thus of no help to either the physician or the patient.

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Key words: environmental medicine, environmental pollution, monitoring, consultation, multiple chemical sensitivity

Environmental factors are increasingly being viewed as (contributory) causes of a great variety of health problems, e.g., diseases of the nervous system, airways, or skin, allergies, malignancies, other functional disturbances, non-specific malaise, and anxiety or panic states (1, e1). Clinical environmental medicine is thus confronted by many and varied problems with regard to the effects of environmental influences on individual health.

The most important reasons for the ever-widening discussion of the role of environmental influences in illness are as follows:

- The growing number and amount of physical and chemical factors whose long-term effects on human health have not been sufficiently established
- Public discussion of proved and potential health risks arising from environmental pollution
- The resulting perception of a threat from environmental hazards
- Therefore, the tendency to connect ill health with environmental factors.

All this necessitates painstaking assessment of potential environmental pollutants and other competing explanations for illness and malaise. Against this background, this article reviews adequate current diagnostic practices for clinically relevant environmentally related health problems. Furthermore, selected environmental medicine syndromes or constellations of symptoms are discussed in light of current knowledge.

Methods

Standard diagnostic procedures and evaluation strategies were examined in light of a selective analysis of the pertinent literature. The authors also drew on their own long experience of research and clinical practice.

On the basis of the findings, recommendations were then formulated with regard to procedures for investigation of environmental medicine problems and evaluation of the results of environmental medicine examinations.

Investigation procedure

The complexity of history-taking in environmental medicine is shown by the questions listed in box 1 (2). A standardized questionnaire should be used (3).

Subsequent specific diagnostic procedures are based on the patient's symptoms and the possible environmental factors involved (tables 1 and 2, figure) (e2).

The variety of possible environmental scenarios and
Box 1

Core questions in an environmental medicine inquiry (from 6, 17)

Where? (site of exposure)
Household (interior), household (surrounding area), kindergarten/school, vehicle (interior), workplace, etc.

What? (agents)
Allergens, amalgam, asbestos/artificial mineral fibers, dioxins/furans, dust, electromagnetic fields, formaldehyde, fumes/gas/smoke, indoor air quality, metals/heavy metals, molds, noise, odors, ozone, PCB, plant protection products/pesticides, radioactivity, solvents, UV irradiation, wood preservatives, etc.

How? (media, pathway)
Air (indoors), air (outdoors), foodstuffs, soil, water (bathing), water (drinking), other media

Human biomonitoring

Human biomonitoring measures the concentrations of harmful substances in bodily fluids and tissues (10). The indication for human biomonitoring is decided on the basis of information provided by the patient, previous findings, if any, and the findings of a site inspection. Human biomonitoring can also help to convince the patient of a differential-diagnostic explanation of his/her symptoms and prevent or terminate “doctor hopping.”

Because the results can be influenced by many different factors, the planning, execution, and analysis of human biomonitoring must be preceded by careful consideration of quality assurance and evaluability (box 2) (11, e4). One study of 99 patients showed that about 20% of the preliminary tests in human biomonitoring investigations were made in unsuitable media (box 3) (e5).

The mere demonstration of the presence of a substance, however, cannot be equated with a toxic effect or disease. For example, pentachlorophenol (PCP), which was used in Germany up to the end of the 1980s, is still regularly demonstrated in the course of human biomonitoring. Nevertheless, it can be classified as a health risk only in those individuals in whom toxicologically established threshold values are exceeded.

Ideally the human toxicological relevance of the results should be classified by means of the human biomonitoring values HBM-I and HBM-II (12). If the HBM-I value is found to be exceeded, a follow-up examination and possibly a search for the source of contamination are indicated. No immediate danger to health is assumed. If the HBM-II value is exceeded, however, urgent steps must be taken to identify the source and reduce or end the exposure. Details on derivation of the HBM values can be found in box 2.

If toxicologically derived thresholds other than the HBM values, such as the German BAT value (biological tolerance value for occupational exposures) or reference values, are used for evaluation, the physician should check for what population and following what toxicological concept they were derived. Examples of population groups are employees, men, women, children, or representative samples of the general population.
### TABLE 1

**Most frequently encountered problems in environmental medicine practice (17): single noxae**

<table>
<thead>
<tr>
<th>Problem</th>
<th>Relevant substance(s)</th>
<th>Routes/sources of uptake</th>
<th>Environmental medicine anamnesis, physical findings</th>
<th>Indication for laboratory tests</th>
<th>Laboratory test evaluation criteria</th>
<th>Environmental medicine relevance/evaluation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Amalgam intoxication</strong></td>
<td>Mercury</td>
<td>Food and drink, dental fillings, ambient air</td>
<td>Number and condition of amalgam fillings</td>
<td>Not in those with fillings, only at patient’s express request</td>
<td>Mercury in urine/HBM values (e10) not indicated: — Saliva — Chewing gum test — DMPS test — Hair analyses</td>
<td>— Patients with fillings still attain toxicological concentrations — Connections with various non-specific symptoms and chronic illnesses are not confirmed (17)</td>
</tr>
<tr>
<td><strong>Amalgam allergy</strong></td>
<td>Mercury</td>
<td>Contact allergy</td>
<td>Local mucosal lesions, particularly whitish tartar</td>
<td>Symptoms in proximity to fillings</td>
<td>Epicutaneous test plus clinical findings</td>
<td>— Lichenoid reaction (1:10 000) and proven clinically relevant allergy (type IV) — Removal of fillings indicated</td>
</tr>
<tr>
<td><strong>Acrodyinia (Feer’s disease, pink disease)</strong></td>
<td>Mercury</td>
<td>Ingestion (calomel, worm powder, tooth powder) or cutaneous uptake (bleaching creams)</td>
<td>Neurological, mental, dermatological symptoms esp. in young children</td>
<td>Symptoms and/or current exposure</td>
<td>Mercury in urine/HBM values (e10)</td>
<td>— Risk group, e.g., migrants using relevant foreign preparations — No evidence of amalgam-related health problems (e11)</td>
</tr>
<tr>
<td><strong>Lead poisoning</strong></td>
<td>Inorganic lead</td>
<td>Consumer products, household dust</td>
<td>Pallor, weakness, vacation souvenirs (e.g., pottery), alternative therapies (ayurveda), paints: white lead</td>
<td>Anemia</td>
<td>Lead in blood/HBM values</td>
<td>— Case reports on pottery, alternative medicine known</td>
</tr>
<tr>
<td><strong>Liver cirrhosis in infants</strong></td>
<td>Copper</td>
<td>Drinking water</td>
<td>Age of house/age of water supply system</td>
<td>—</td>
<td>Stagnant drinking water/TrinkWV values</td>
<td>— At low doses, developmental and neurological disorders possible esp. in children — Preventive measures at higher concentrations: removal of source</td>
</tr>
<tr>
<td><strong>Cancers</strong></td>
<td>PCB</td>
<td>Food and drink, ubiquitous in environmental media; joint sealants etc. in interiors</td>
<td>Preparation of baby foods with soft, acidic well water supplied via copper pipes</td>
<td>Current exposure and unexplained cirrhosis</td>
<td>Drinking water/TrinkWV values</td>
<td>— UBA study (e12) — Few children affected, reasonable but unconfirmed suspicion of drinking water related cirrhosis; sufferers all did not consume water from public supply</td>
</tr>
<tr>
<td><strong>Wood preservative syndrome</strong></td>
<td>PCP</td>
<td>Indoor air, treated wood products</td>
<td>—</td>
<td>If current indoor source demonstrated</td>
<td>PCP in urine/HBM values</td>
<td>— Connections with non-specific symptoms and chronic illnesses not proven — Preventive measures: renovation if HBM-I value exceeded and indoor source confirmed</td>
</tr>
<tr>
<td><strong>Neural lesions</strong></td>
<td>Pyrethroids and other biocidal agents</td>
<td>Indoor pest control, textiles, foodstuffs</td>
<td>Acute after pest control measures: mucosal irritation, rarely perioral tingling</td>
<td>Symptoms and current exposure</td>
<td>For example pyrethroid metabolites in urine/HBM values</td>
<td>Preventive reduction of exposure</td>
</tr>
<tr>
<td><strong>Lung cancer</strong></td>
<td>Radon</td>
<td>Geographical differences</td>
<td>Gneiss-granite area (see also radon atlas (24), construction method)</td>
<td>Preventive, at patient’s justified request</td>
<td>Precise information only via radon measurement (dosimetry)</td>
<td>— Second most frequent cause of lung cancer in Germany — Reduction of exposure as preventive measure (e15) — Observation of legal requirements for indoor air in apartments (e16)</td>
</tr>
</tbody>
</table>

**Note:**
- DMPS, (RS)-2,3-dimercaptopropane-1-sulfonate; HBM, human biomonitoring; PCB, poly-chlorinated biphenyls; PCP, pentachlorophenol; TrinkWV, Trinkwasserverordnung (German Drinking Water Ordinance); UBA, Umweltbundesamt (German Federal Environment Agency).
Toxicological concepts consider whether healthy persons have suffered occupational exposure for a limited period of time or whether healthy and particularly sensitive individuals have experienced lifelong exposure. Since physicians inexperienced in environmental medicine may find it difficult to determine which is the case, it is recommended to engage the help of experts, e.g., a more experienced colleague or the local environmental medicine service.

According to the current state of knowledge in environmental medicine, investigations of susceptibility monitoring, e.g., on genetic sequence variations (polymorphisms) of enzyme systems that metabolize foreign substances (13) or lymphocyte transformation tests (LTT) for demonstration of allergic reactions to environmental agents (14), are not applicable to the evaluation of individual health complaints. The findings on genetic polymorphisms yield no further-reaching information, and the informative power of the LTT is inadequate as yet.

**Site inspection and environmental monitoring**

The source and precise nature of the harmful substance can be identified by a site inspection and environmental monitoring. In most cases, the patient’s private space, his/her household and the immediate surroundings are investigated and analyses in environmental media (environmental monitoring) are performed if appropriate.

Physicians inexperienced in environmental medicine will have difficulty carrying out environmental monitoring. For example, a university environmental medicine service evaluated the preliminary findings in 99 patients. The physicians who first treated these patients requested a total of 545 single-substance analyses, but their colleagues in the environmental medicine service considered only 62 (11%) of these analyses necessary (c5).

The physician who has grounds to suspect that a patient is being harmed by environmental factors should recommend investigation by qualified personnel, followed by joint evaluation of the findings with an expert.
Diagnostic procedure and treatment options in environmental medicine (after Wiesmüller 2002 [18] and Herr et al. [e18]). Principal diagnoses explain all of the patient's symptoms, while secondary diagnoses explain only some of the symptoms. DD, differential diagnosis

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**Quality assurance in HBM**
- Who performed/should perform the measurements?
- What was/should be measured?
- When was/should it be measured?
- Where was/should it be measured?
- Why was/should it be measured?
- How was/should it be measured?
- How can the findings be interpreted?

**Meaning of the HBM values**

**At low concentrations:**
- Impairment of health: currently considered harmless
- Action required: none

**At concentrations above the HBM-I value (alert level):**
- Impairment of health: cannot be excluded with sufficient confidence
  - Action required: – Check the values (analysis, time course)
  - Search for specific sources
  - Where appropriate, reduction of burden (if attainable at reasonable cost)

**At concentrations above the HBM-II value (intervention/action level):**
- Impairment of health: possible
  - Action required: – Environmental medicine counseling
  - Urgent measures to reduce the burden

Suitably qualified staff can be contacted via regional health offices, regional offices for environmental protection, or regional university environmental medicine services and helplines.

The findings of interior environmental monitoring should be evaluated in light of the recommendations of the ad hoc committee of the Interior Air Hygiene Commission (IRK, Innerraumlufthygienekommission) of the German Federal Health Office and the Interior Air Subcommittee of the Environmental Hygiene Committee of the Joint Working Group of the State Health Authorities (AOLG, Arbeitsgemeinschaft der Obersten Landesgesundheitsbehörden) (15). Particularly for the concentrations of volatile organic compounds there is an evaluation scheme based on a cumulative index of total volatile organic compounds (TVOC) (16). This enables preliminary estimation of the exposure in daily clinical practice.

Analyses of water, soil, air and foodstuffs may be the responsibility of the environmental or health authorities. It is thus advisable to contact the authorities, e.g., the local Health Office, in advance. Environmental monitoring is not generally covered by health insurance. Unless the above-mentioned authorities are responsible, the patient him-/herself must bear the costs of the environmental medicine inspection of the household and of the environmental monitoring (17).

**Counseling on the relation of symptoms to environmental factors**

According to data from university environmental medicine institutes and public environmental medicine services, the proportion of patients with symptoms caused by environmental factors varies from 0% to 15% (table 1). In contrast, environmental medicine physicians not attached to such institutions report figures ranging from 36% to 45% (1, 4). It should be noted that these publications related to case series. One possible reason for the discrepancy might be that clearly environment-related health problems are diagnosed by independent physicians, while more complex cases are concentrated at university facilities. Another feasible explanation is that the budget difficulties experienced by non-hospital physicians prevent them performing the exhaustive differential diagnostic work-up required for environment-related disorders.

Risk communication, oriented on the patient’s anxieties and subjective illness models, represents a particular challenge for the environmental medicine practitioner (16). Environmental medicine counseling includes recommendations and suggestions that can often be made before detailed investigation of the individual case. This embraces, for example, advice on the risks from amalgam in dental fillings, radiation from cell phones and masts, and fine-particle air pollution. Also included is explanation of the scope and limitations of investigations, together with their suitability and utility, and of their consequences (figure, tables 1 and 2) (18).

Should it emerge during the process of diagnosis that the patient’s symptoms are due to chemical substances or products (17), the physician is legally obliged to make a report to the Poison and Product
There are no comparable data for Germany. The consequences of SBS are estimated at US$ 10 to 70 million working days, and loss of productivity (22).

In the USA, for example, the economic impact of SBS has appreciably negative consequences on the economy. In Germany, a project “ProKlimA,” started in 1994, showed that 30% to 40% of employees report non-specific health complaints involving especially the eyes, the respiratory tract, the skin, and the central nervous system. The most widespread and most frequently used classification of SBS is that published in 1998 by Mølhave (20), reproduced in box 4.

In environmental medicine there are various syndromes or constellations of symptoms that describe patients' complaints but whose causes are inconsistently and inadequately explained. Examples are multiple chemical sensitivity (MCS), electrosensitivity (ES), and sick building syndrome (SBS). Under conditions of general daily population exposure, the supposed environment-associated health disorders are observed only in isolated cases. Reliable German data on the occurrence of these symptom complexes are almost non-existent. A representative, population-based survey on MCS conducted by the Allensbach polling institute in 2032 adults in Germany revealed a frequency of 9% for self-reported MCS (sMCS) and 0.5% for MCS diagnosed by a physician (19). SBS is described in more detail in the next section, while table 1 gives some information on the other syndromes and constellations of symptoms.

**Sick building syndrome**

The term "sick building syndrome" is employed when people using a particular building report non-specific health complaints involving especially the eyes, the respiratory tract, the skin, and the central nervous system. The most widespread and most frequently used classification of SBS is that published in 1998 by Mølhave (20), reproduced in box 4. Physical, chemical, biological, personal, and psychosocial factors may all have a causative role. SBS can be assumed to comprise a multifactorial event in which various simultaneously occurring factors combine in different ways to result in the syndrome.

In the absence of a binding definition and of representative epidemiological studies, there are no reliable figures on the prevalence of SBS. A preliminary study in 613 people carried out in the framework of the joint project "ProKlimA," started in Germany in 1994, showed that 30% to 40% of employees report non-specific malaise (e8). Petrovitch estimated that at least 1 million people in Germany had SBS of some degree (e9).

It must be assumed that the loss of productivity arising from SBS has appreciably negative consequences on the economy. In the USA, for example, the economic consequences of SBS are estimated at US$ 10 to 70 billion for commercial buildings (21). This is made up of the costs of medical care, absence from work (150 million working days), and loss of productivity (22). There are no comparable data for Germany.

Important data were yielded by the German ProKlimA study, which enabled the evaluation of environmental factors in buildings in the context of SBS through a comprehensive workplace-related survey of exposure. This study showed by means of multiple logistic regression analyses that the occurrence of SBS symptoms (self-reported sensory and physical symptoms, non-specific malaise) are associated in particular with the characteristics of those interviewed (gender, age, allergic diseases) and of their work (work requirements, job satisfaction). Only in a few isolated cases in the sample population did typical interior environmental influences such as room air quality and indoor climate have a measurable effect on the symptoms. Personal views and expectations of people using the room, however, were
The symptoms most frequently reported by users of buildings where SBS is suspected can be classified in the following five categories:

- Irritation of eyes, nose, and/or throat
- Skin irritation
- Symptoms associated with the nervous system
- Non-specific hypersensitivity
- Sensations of smell and taste

The symptoms occur only in a particular building.

**Conflict of interest statement**

Prof. Nowak and Prof. Herr have participated in studies that benefited from external funding via the Robert Koch Institute and have received fees for lectures. The remaining authors declare that no conflict of interest exists according to the guidelines of the International Committee of Medical Journal Editors.

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