ORIGINAL ARTICLE

Unnecessary Investigations in Environmental Medicine

A Retrospective Cohort Study

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SUMMARY

Background: Patients in environmental medicine often want a thorough diagnostic evaluation of nonspecific symptoms. Unconventional testing, as well as conventional testing for indications other than the established ones, can lead to false diagnoses and, in turn, to substantial emotional, social, and financial harm. The goal of this single-center study was to assess inappropriate diagnostic testing among the patients of a specialized university outpatient clinic for environmental medicine.

Methods: The charts of 653 consecutive outpatients seen in the institute and outpatient clinic of occupational, social, and environmental medicine in Erlangen from 2010 to 2015 were evaluated, and inappropriate diagnostic tests were assessed.

Results: 9% of the patients had received at least one inappropriate diagnostic test. The most common one was an inappropriate heavy-metal test (26%), followed by an inappropriately ordered hair analysis (15%) and biomonitoring in the blood or urine with an erroneous choice of the testing matrix or an erroneous interpretation of the findings (15%). Biomonitoring performed by us did not confirm the suspected environmental diagnosis in any case. Laboratory values exceeding the normal limits were rarer among these patients than in the patients for whom we considered biomonitoring to be indicated without any pretesting.

Conclusion: An appreciable number of patients in environmental medicine were subjected to inappropriate diagnostic testing. When this happens, proper testing often needs to be done thereafter in order to confirm or refute the findings. This phenomenon should be more thoroughly assessed and quantified.

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One of the tasks of the physician is to explain the role and importance of the wide variety of medical tests that may be recommended to any given patient. Particularly in the field of environmental medicine, patients often demand investigations to determine the cause of unspecific symptoms (1) or bring previous findings with them to the first consultation. In accordance with the obligation to “first, do no harm,” patients must be protected from a detrimental excess of medical procedures; this is termed “quaternary prevention” (2, 3). Together with painstaking documentation of the patient's history, the correct choice and conduct of diagnostic tests is crucial (1, 4, 5). Use of unvalidated methods or faulty interpretation of findings may lead to incorrect diagnoses and superfluous treatments, and in our experience can have damaging mental, social, and financial consequences for patients (4, 6–8). We therefore decided to find out which of the diagnostic investigations previously carried out in patients who consulted us had been inappropriate (i.e., scientifically unjustified) and how often such unnecessary procedures had been performed.

Methods

We evaluated the records of all 653 patients who attended the outpatient clinic of the Institute of Occupational, Social, and Environmental Medicine of the Friedrich Alexander University of Erlangen between September 2010 and December 2015. All of these patients had been referred by physicians in private practice. In many cases the patients' problems could not be classified as purely occupational, social, or environmental, and two or all three fields were involved. For this reason, no attempt was made to divide the sample into environmental, occupational, and social subgroups. No occupational medicine screening and no assessments of occupational fitness were carried out in our outpatient clinic in these patients.

We inspected the patients' records for previous inappropriate investigations. Diagnostic procedures were classified as inappropriate if they were unconventional, i.e., not scientifically established, or conventional but used outside the established indications. Classification of the methods was based on publications of the Robert Koch Institute, statements issued

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TABLE 1

Interpretation of the HBM categories of the German Federal Environment Agency (adapted from [9])

Category	Evaluation	Action
Measured value <HBM-I	Harmless according to current knowledge	No action needed
HBM-I<measured value <HBM-II	Adverse health effects not excluded with sufficient certainty	<ul style="list-style-type: none"> – Check measurements – Investigate specific sources of exposure – if applicable and justifiable in terms of effort/cost, reduce exposure
Measured value >HBM-II	Adverse health effects possible	<ul style="list-style-type: none"> – Management by environmental medicine specialists – Urgent action to reduce exposure

HBM, Human biomonitoring

by medical societies or commissions, and other scientific publications.

Every patient's age, sex, insurance status, and employment status were ascertained. Employment status was classified as employed, unemployed, unfit for work, retired, or other/unknown. The employed group contained those engaged in paid work. Those with jobs but currently unfit for work were assigned to a separate group because their work incapacity was often a long-term situation. Furthermore, we documented how often we had ordered biomonitoring during the course of outpatient consultations, i.e., quantitative investigation of xenobiotics or their metabolites in samples (usually of blood or urine) from patients, and whether any reference levels or thresholds were found to have been exceeded. The criterion for a given substance was, if available, the reference value for background exposure

of the general population from the environmental survey of the German Federal Environment Agency. The reference value is the 95th percentile of all concentrations of a xenobiotic or metabolite of a xenobiotic from a representative sample of the general population or a population group (9). If no reference value was available for a given substance, we took the reference values for biological substances of the German Research Foundation's Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area. These reference values for biological substances describe the "background exposure to [a] substance at a particular time in a reference population comprising persons of working age with no occupational exposure to the substance" (10) and are defined, in analogy to the reference values laid down by the Human Biomonitoring Commission of the German Federal Environment Agency, by the 95th percentile of the concentration of the substance or metabolite. Neither the reference values of the Human Biomonitoring Commission nor the reference values for biological substances take any account of possible effects on health. Exceeding these values by no means implies a health hazard (9).

Moreover, we looked for cases where threshold values were exceeded. Threshold values, in contrast to reference values, have toxicological significance. Primarily the HBM-I and HBM-II threshold values published by the Human Biomonitoring Commission were used (9) (Table 1).

The patients in whom inappropriate diagnostic investigations had been performed were compared with the remaining patients in the cohort, referred to hereinafter as the comparison group. Statistical analyses were carried out using SPSS Statistics 23 with Fisher's exact test to determine differences. We did not set an α level (significance level) with Bonferroni correction; the p values presented are descriptive.

Furthermore, we carried out a systematic survey of the available literature using the PubMed database and the search engine Google (google.de for German, google.com for English). We searched for a total of 23 terms. Only publications in German or English were included. If any of these referred to further relevant texts, those too were inspected.

Results

We identified nine categories of inappropriate investigations that according to the present state of knowledge (11–36) had no or only little relevance to the patient's symptoms. These procedures had been used in 57 (9%) of the 653 patients in the cohort. In some cases two or more such investigations had been carried out in the same patient, yielding a total of 65 procedures in 57 patients. Repeated use of the same procedure in the same patient was not documented owing to the frequent lack of precision in the medical records. Table 2 shows the types of investigations and how often they were used.

Some of the investigations have scientifically established uses but are often applied inappropriately. Box 1

TABLE 2

The inappropriate investigations used in patients of the cohort

Procedure	Proportion of total
Investigation with aid of DMPA/DMSA mobilization (11–15)	26% (n = 17 of 65)
Biomonitoring in blood/urine with incorrect choice of investigation matrix or incorrect evaluation	15% (n = 10 of 65)
Inappropriate use of hair analysis (16–22)	15% (n = 10 of 65)
Arrival at a diagnosis that is not justified either by the patient's exposure or by the symptoms	14% (n = 9 of 65)
Inappropriate use of lymphocyte transformation test (LTT) (23–25)	11% (n = 7 of 65)
Inappropriate use of saliva analysis (17, 26, 27, 37)	8% (n = 5 of 65)
Bioresonance (28–31)	6% (n = 4 of 65)
Applied kinesiology (22, 32–35)	3% (n = 2 of 65)
Pendulum divination (22, 36)	2% (n = 1 of 65)

DMPA, Dimercaptopropanesulfonic acid; DMSA, dimercaptosuccinic acid

gives an overview of the indications and limitations of these techniques. New findings and technical advances may modify the indications. Our statements regarding indications and inappropriate use (*Box 1*) are based on the current state of knowledge.

There are no scientifically recognized indications for bioresonance, applied kinesiology, or pendulum divination (22, 28–36).

Bioresonance techniques are based on the premise that human beings and also potential allergens radiate an ultra-fine spectrum of oscillations that cannot be detected using conventional physical means of measurement. The “resonance pattern” is assessed with the aid of a sensor (28). In accordance with the guidelines of the Joint Federal Committee on Investigation and Treatment Techniques in Private Practice (*Gemeinsamer Bundesausschuss zu Untersuchungs- und Behandlungsmethoden der vertragsärztlichen Versorgung*), bioresonance is not covered by health insurance (29).

Applied kinesiology assesses the reaction of a muscle to manual pressure exerted by the investigator while the patient is touching, for example, a suspected allergen (32).

There are various techniques of pendulum divination. For example, the investigator may concentrate on the question concerned while suspending an unrestrained pendulum. The meanings of the various possible movements of the pendulum are determined in advance (22, 36).

In the course of consultation in the outpatient clinic, validated biomonitoring to confirm a suspected diagnosis was found to be indicated in 70% (40/57) of the patients with previous inappropriate investigations and in 26% (157/596) of those in the comparison group. Reference values were exceeded in only 13% (5/40) of patients in the inappropriate investigations group, and in no case were health-related threshold values exceeded. In the comparison group reference values were exceeded around twice as often, i.e., in 26% of patients ($p = 0.093$) (*Table 3*), and in two cases, both associated with occupational exposure, threshold values were exceeded.

The two groups had comparable age structures (median: 48 years in the inappropriate investigations group versus 46 years in the comparison group; upper quartile: 56 versus 54 years; lower quartile: 37 versus 35 years). The proportion of women was higher in the inappropriate investigations group (60% versus 43%, $p = 0.025$). Among patients with previous inappropriate diagnostic procedures the proportion with private health insurance was 25%, against only 13% in the comparison group ($p = 0.025$).

With regard to employment status, the most obvious features were the lower proportion of patients in employment (47.4% versus 72.1%, $p = 0.0002$) and the higher rates of work incapacity (10.5% versus 3.0%, $p = 0.013$) and unemployment (15.8% versus 4.2%, $p = 0.001$) in the inappropriate investigations group. The proportion of patients who had retired from work was slightly higher (10.5% versus 6.0%; $p = 0.250$), and there was hardly any difference between the groups in the proportion of patients whose employment status was other/unknown (15.8% versus 14.6%; $p = 0.844$).

BOX 1

Inappropriate use of scientifically established procedures in the patients of the cohort

Heavy metal diagnosis after DMPA/DMSA mobilization (11–15)

● Principle:

The chelating agents DMPA and DMSA form stable complexes with various heavy metals; these complexes are excreted predominantly via the kidneys in the urine.

● Indication:

- Treatment of intoxications that have been confirmed clinically and by lab tests, particularly acute intoxications (e.g., lead poisoning)

● No indication for diagnostic application:

- No improvement of the correlation between previous metal exposure and measured values after mobilization
- No validated reference values

● Adverse effects:

- Increased elimination of the essential minerals zinc and copper, allergic reaction, nausea and vomiting

Hair analysis (16–22)

● Applications:

- Forensic/historical/epidemiological questions
- Proof of recreational drug or medication intake
- Late stage of poisoning, if the hazardous substance (e.g., arsenic, thallium) is no longer detectable in other media (semiquantitative evidence)
- Exposure to methylmercury: not the procedure of choice

● Insufficient validity:

- Quantitative documentation of individual exposure (e.g., to metals)

Specific lymphocyte transformation test (LTT) (23–25)

● Principle:

- Detection of cellular sensitization by measurement of the proliferation of memory cells on addition of the suspected allergen

● Applications:

- Detection of allergic reaction to medication and sensitization to beryllium: recommended without reservation
- Detection of contact allergy to nickel: recommended with reservations in the presence of an environmental medicine indication

● No indication:

- Detection of allergic or toxic reactions to other hazardous substances in the environment

Saliva analysis (17, 26, 27, 37–39)

● Principle:

- Collection with or without stimulation

● Applications:

- For example, cotinine determination to quantify exposure to tobacco smoke, monitoring of certain medical drugs

● Insufficient validity:

- Use as matrix for biomonitoring in environmental and occupational medicine problematic for various reasons, e.g., methodological difficulties (complex physiology of saliva formation and transfer of substances into the saliva, variable resorption in the gastrointestinal tract)
- Not suitable for quantification of mercury uptake from amalgam fillings

DMPA, Dimercaptopropanesulfonic acid; DMSA, dimercaptosuccinic acid

TABLE 3

Comparison of the patients with and without inappropriate investigations: biomonitoring, employment status, age, sex, and type of health insurance

	Patients with inappropriate investigations	Comparison group	p value*
Biomonitoring in framework of outpatient consultation			
Biomonitoring ordered	70% (n = 40 of 57)	26% (n = 157 of 596)	<0.0001
Reference value exceeded	13% (n = 5 of 40)	26% (n = 41 of 157)	0.093
Employment status			
Employed	47.4% (n = 27 of 57)	72.1% (n = 430 of 596)	0.0002
Unfit for work	10.5% (n = 6 of 57)	3.0% (n = 18 of 596)	0.013
Unemployed	15.8% (n = 9 of 57)	4.2% (n = 25 of 596)	0.001
Retired	10.5% (n = 6 of 57)	6.0% (n = 36 of 596)	0.250
Other/unknown	15.8% (n = 9 of 57)	14.6% (n = 87 of 596)	0.844
Age			
Median	48 years	46 years	
Upper quartile	56 years	54 years	
Lower quartile	37 years	35 years	
Sex			
Female patients	60% (n = 34 of 57)	43% (n = 258 of 596)	0.025
Health insurance			
Patients with private insurance	25% (n = 14 of 57)	13% (n = 77 of 596)	0.025

*Fisher's exact test

The systematic literature search for information on the application of unconventional diagnostic techniques identified 2456 publications, of which seven contained data on the frequency of such methods. The essential contents of these studies are shown in *Table 4*.

Furthermore, statements on unconventional diagnostic procedures issued by leading institutions in Germany and other countries also yield information regarding the use of these methods (*Table 5*).

The report of the Committee on Education, Research, and Technology Assessment of the Parliament of the Federal Republic of Germany notes that some patients turn to unconventional procedures because of a frequent lack of reliable findings in the field of environmental medicine (e17). In Germany a dedicated committee of the Robert Koch Institute, the Committee on Methods and Quality Assurance in Environmental Medicine, has been set up to prepare statements and expert opinions on this topic (13).

Numerous publications mention that the use of unconventional methods is widespread without providing numerical data (e.g., 12, 13, e6, e18–e23). For example, the Italian researcher de Luca notes that ever-growing numbers of patients in many countries are being sub-

jected to the uncontrolled application of diagnostic and therapeutic procedures that have neither been adequately validated nor shown to be safe and clinically efficacious (e24).

Discussion

Before any diagnostic method is used in patients, its validity, reproducibility, analytic accuracy, sensitivity, and specificity, among other characteristics, should be tested and evaluated (5).

The inappropriate investigations described above were retrospectively identified in the cohort of patients seen in our outpatient clinic. It is highly likely that not all patients report all the diagnostic procedures they have resorted to in the past. Techniques far beyond the bounds of scientific medical practice may have been mentioned less often than unconventional application of verified scientific methods. Overall, the number of patients who used inappropriate investigations is probably higher than presented here. Given that not all of the patients cared for by alternative medical therapists also consult qualified university-based physicians, it can be assumed that such methods are actually applied far more often in patients with suspected environment-related illnesses.

The systematic literature survey showed that the data on the frequency of inappropriate diagnostic procedures and their consequences for patients and for healthcare and social services are sparse. Unconventional means of diagnosis were documented more often in the environmental medicine clinic of the Hesse Center for Clinical Environmental Medicine at Giessen University Hospital than in our cohort. In view of the small case numbers, percentages may vary widely; nevertheless, both here and in the Giessen publications, results are reported in percentages for the sake of comprehensibility. Furthermore, the patient populations were not identical in composition, in that our outpatient clinic covers occupational and social medicine as well as environmental medicine. Presumably the collectives in the four surveys carried out in the Giessen environmental medicine clinic overlapped.

Although biomonitoring had to be carried out more frequently in patients with a history of inappropriate investigations, to exclude exposure or just to reassure the patient, reference values were exceeded much less often than among patients in whom physicians from our hospital ordered biomonitoring without regard to previous findings. In the latter group, biomonitoring was indicated on the basis of a history of exposure or symptoms. It cannot be completely excluded that exposure decreased between the time of the previous diagnostic procedures and our investigation and that this explains the lower number of cases where reference values were exceeded and the lack of findings exceeding threshold values in patients who underwent biomonitoring in our outpatient clinic. However, the

TABLE 4

Data on the frequency with which unconventional or unconventionally applied investigations have been used in other environmental medicine facilities

Country, year, institution, collective (where known)	Results
Germany, 2002 Environmental medicine clinic of the Hesse Center for Clinical Environmental Medicine, Giessen; patients (40)	"A study including 99 patients showed that circa 20% of the previous human biomonitoring procedures were carried out in inappropriate media"
Germany, 2003 Environmental medicine clinic of the Hesse Center for Clinical Environmental Medicine, Giessen; patients (e1)	"Almost 40% (N = 21) of the study participants provided findings from unconventional investigations"
Germany, 2004 Environmental medicine clinic of the Hesse Center for Clinical Environmental Medicine, Giessen; patients from September 1996 to June 1998 (e2)	Ten percent of the patients brought with them the results either of previous investigations of saliva, body fat, or feces or of mercury mobilization tests (DMPA test, chewing gum test)
Germany, 2005 Environmental medicine clinic of the Hesse Center for Clinical Environmental Medicine, Giessen; patients who introduced themselves as MCS sufferers (e3)	<ul style="list-style-type: none"> – DMPA test: 7% (N = 20) – Saliva test: 4% (N = 10) – Hair mineral analysis: 5% (N = 14) – Clinical–ecological methods (e.g., provocation/neutralization test): 3% (N = 8) – Other unconventional diagnostic procedures (electroacupuncture according to Voll, bioresonance diagnosis, etc.): 16% (N = 44)
USA, 2002 Occupational and Environmental Health Center of the Cambridge Hospital; patients in whom biomonitoring for mercury was carried out in the course of the consultation (e4)	<ul style="list-style-type: none"> – Fourteen of 71 patients had previously been told they had mercury poisoning on the strength of unconventional measurement techniques; in no case was this diagnosis confirmed by analysis of blood and urine – Eleven of 14 patients: multielement hair analysis – Three of 14 patients: DMSA/DMPA test – One of 14 patients: metal analysis in erythrocytes
USA, 2001 (21)	An average of 225 000 hair mineral analyses are carried out each year in laboratories in the USA; the costs amount to \$ 9.6 million
Australia and New Zealand, 2007 (e5)	Fifty to 70% of patients with allergies use alternative medicine methods for diagnosis and treatment (figures for diagnosis alone are not provided)

DMPA, Dimercaptopropanesulfonic acid; DMSA, dimercaptosuccinic acid; MCS, multiple chemical sensitivity

patients still had symptoms. If exposure had decreased, one would expect the symptoms to be less severe.

Overall, our cohort contained more men than women. In contrast, the study by Hornberg et al. (e25) showed a predominance of women among the patients visiting environmental medicine clinics or using information services. Inspection of the records from our own hospital for the period 1979 to 1992 revealed that 55% of the patients with complaints suspected to be of environmental origin were women. The lower proportion of women in the present collective may be due to the fact that our clinic also covers occupational and social medicine. Our group of patients with previous inappropriate investigations contained more women than men. Women form 51% of the population in Germany (e26). There are no data that might show whether the sex ratio at comparable clinics or information services has changed in the intervening years.

The proportion of privately insured patients was almost twice as high in the group of patients with previous inappropriate investigations. This may be

explained by socioeconomic factors. A number of the above-mentioned diagnostic techniques and the treatments associated with them are not covered by statutory health insurers (e27), whereas with private insurance reimbursement depends on the terms of the contract. However, the follow-up costs (further diagnostic procedures, unnecessary treatment) of inappropriate investigations are generally borne by the insurers.

A striking finding was the much higher rates of work incapacity (10.5%) and unemployment (15.8%) in the group of patients with a history of inappropriate investigations. In comparison, the unemployment rate in Germany in January 2016 was 6.7% (e28). Studies are required to determine whether the work incapacity and unemployment are causes or effects of resorting to inappropriate diagnostic procedures.

Limitations

Our study was restricted to a single center. The extent to which the results are valid for environmental medicine outpatient clinics in general is unknown. Patients cannot attend our clinic without being referred by a

TABLE 5

Statements/recommendations from leading institutions in Germany and other countries that refer to unconventional diagnostic procedures

Country/region	Institution	Title and procedure
Germany	German Society for Allergy and Immunity Research	Statement on: electroacupuncture according to Voll (EAV), bioresonance testing, pendulum divination, applied kinesiology (e6)
Germany	German Society of Allergology and Clinical Immunology (DGAKI)	In-vitro diagnosis of allergic diseases (25): → e.g., lymphocyte transformation test
Germany	RKI Committee on Methods and Quality Assurance in Environmental Medicine	<ul style="list-style-type: none"> – Guideline on diagnostic validity (6) – Amalgam: statement from an environmental medicine viewpoint (e7) → Chewing gum test, hair analysis, DMPA test – Lymphocyte transformation test (23, 24) – Role of determination of lymphocyte subpopulations in environmental medicine (e8) – Genetic polymorphisms of xenobiotic-metabolizing enzymes (e9) – Melatonin in environmental medicine diagnosis in connection with electromagnetic fields (e10)
Germany	Human Biomonitoring Commission of the German Federal Environment Agency	<ul style="list-style-type: none"> – Use of chelating agents in environmental medicine (14) – “Saliva test”—exposure to mercury from amalgam fillings (27) – Hair analysis in environmental medicine (16)
Switzerland	Expert committee of the Swiss Society of Allergology and Immunology (SGAI)	“Statement on Bioresonance and Electroacupuncture Devices in the Diagnosis and Treatment of (Suspected) Allergies: Bioresonance—Diagnostic and Therapeutic Nonsense” (in German)(28)
Europe	European Academy of Allergy and Immunology (EAACI)	“Food allergy and anaphylaxis guidelines: diagnosis and management of food allergy” (e11): bioresonance, kinesiology, iris diagnosis, hair analysis, cytotoxic foodstuffs test, IgG and IgG4 determination in food allergy
USA	American College of Medical Toxicology	“Position statement on post-chelator challenge urinary metal testing” (11): → DMPA/DMSA test
USA	FDA press release	Warning regarding over the counter sale of “chelation products” for diagnosis and treatment (e12)
USA	American Academy of Allergy	“Position statements—controversial techniques” (e13): <ul style="list-style-type: none"> – Cytotoxic food test (Bryan’s test) – Rinkel method – Subcutaneous provocation/neutralization test – Sublingual provocation test
Australia/New Zealand	Australasian Society of Clinical Immunology and Allergy (ASCI)	“Position statement—unorthodox techniques for the diagnosis and treatment of allergy, asthma and immune disorders” (e5): ALCAT, provocation/neutralization test, kinesiology, pendulum divination, and hair analysis, among others
Australia	National Allergy Strategy	„National allergy strategy: Improving the health and quality of life of Australians with allergic disease” (e14): cytotoxic food test, kinesiology, Vega test, IgG determination in food allergy, hair analysis
South Africa	Allergy Society of South Africa (ALLSA)	<ul style="list-style-type: none"> – “ALLSA consensus document: guideline for diagnostic testing in allergy—update 2014” (e15): neutralization/provocation test, hair analysis, Vega test, applied kinesiology, ALCAT – “Position statement: ALCAT and IgG allergy & intolerance tests” (e16)

ALCAT, Antigen leukocyte cellular antibody test; DMPA, dimercaptopropanesulfonic acid; DMSA, dimercaptosuccinic acid; FDA, Food and Drug Administration; IgG, immunoglobulin G; RKI, Robert Koch Institute

physician. There may therefore be a selection effect, particularly with regard to the kind of patients who place themselves in the hands of alternative medical therapists and tend to take a skeptical view of scientific, university-based medicine. Our clinic is not devoted purely to environmental medicine but also covers occupational and social medicine; as a rule, consultations involve all three aspects. Some patients with previous inappropriate investigations suspected that their symptoms arose from workplace exposure. Differences between our patients and those attending clinics dedicated to environmental medicine alone cannot be excluded.

Conclusion

Inappropriate diagnostic procedures are used in a significant proportion of environmental medicine patients. They lead to insecurity on the part of the patients and to false diagnoses. One can only speculate what the socioeconomic consequences might be.

To improve quaternary prevention, both patients and therapists must receive better information. Adequate biomonitoring requires, among other things, knowledge of the following: the validity of the analytical method involved, the appropriate investigation materials, the half-life of the xenobiotic concerned, and the relevant reference values and toxicologically derived assessment values (9).

Much more research is needed into the diagnostic procedures used in environmental medicine and the consequences of inappropriate investigations for the healthcare and social insurance systems. It is important that medical students continue to receive well-grounded basic instruction in this field. The methods used in medicine can change rapidly, so the future physician must acquire the scientific acumen required to evaluate the validity of new techniques.

University environmental medicine facilities give advice to patients who have been subjected to inappropriate procedures or are seeking diagnostic investigation of symptoms that may be of environmental origin. These clinics counter the negative effects of inappropriate investigations. Effective cooperation with the primary care physician and potentially with colleagues from other specialties is vital. University-based environmental medicine clinics generally run at a loss, but probably reduce overall expenditure on health.

Conflict of interest statement

The authors declare that no conflict of interest exists.

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BOX 2

Supplementary information

Further information on appropriate biomonitoring can be found at the following sites:

- Biomonitoring advice system of the German Federal Institute for Occupational Safety and Health: www.baua.de/de/Themen-von-A-Z/Gefahrstoffe/Biomonitoring/Auskunftsystem_content.html
- Human Biomonitoring Commission of the German Environment Agency: www.umweltbundesamt.de/themen/gesundheit/kommissionen-arbeitsgruppen/kommission-human-biomonitoring
- Occupational and environmental medicine guidelines of the German Society for Occupational Medicine and Environmental Medicine (e.g., the Environmental Medicine Guideline Human Biomonitoring : www.dgaum.de/leitlinien-qualitaetssicherung
- Detailed data on individual substances and their detectability can be found in the statements on determination of maximum workplace concentrations (MAK values) and biological tolerance values (BAT values) issued by the Permanent Senate Commission for the Investigation of Health Hazards of Chemical Compounds in the Work Area of the German Research Foundation (DFG): onlinelibrary.wiley.com/book/10.1002/3527600418/topics.

KEY MESSAGES

- The goal of quaternary prevention is to protect the patient from unnecessary and potentially harmful diagnostic and therapeutic procedures.
- In environmental medicine, knowledge of the patient's symptoms and possible exposures is fundamental in deciding how to proceed.
- Inappropriate investigations are frequently used in the field of environmental medicine, leading to incorrect diagnoses with considerable negative consequences for the patient and the healthcare system.
- University environmental medicine clinics are an important source of advice for insecure patients and aid quaternary prevention by acting as a counterweight to inappropriate investigations.
- Further research is required into diagnostic procedures in environmental medicine and the management of environmental medicine patients, including effects on the social insurance systems.

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Supplementary material
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