

Hair Trace Elements in Children as Biomarkers of Environmental Exposure and Nutritional Status: A Systematic and Critical Review

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ABSTRACT

The imbalance of trace elements among children has become a serious concern because it results from the cumulative effects of environmental and nutritional factors. The objective of this study was to conduct a systematic review of the role of hair trace element analysis as a biomarker of prolonged exposure and its relationship with paediatric health outcomes.

Meanwhile, this review is based on recent articles, which are indexed at large international databases; specifically, the research that has been carried out within the last five years and is devoted to paediatric groups. This analysis was informed by the efforts to determine some regularities in the imbalance of trace elements and their clinical significance.

The results showed a pattern of imbalance that was marked by deficiency in basic components like zinc, iron and selenium and high-level of toxic metals like lead and cadmium. The changes were more evident among the populations that were subjected to environmental stress or low dietary diversity. The hair analysis proved more beneficial than traditional biological mediums in terms of demonstrating long-term exposure resulting in the realisation of cumulative and subclinical imbalance.

The findings also showed that there is a possible correlation between trace element imbalance and the illnesses in children such as neurodevelopmental disorders and anaemia. Moreover, the geographic and socio-economic factors were observed to have a strong effect on trace elements profiles, which show the importance of environmental and social determinants in the child health outcomes.

Keywords: Trace Elements; Hair; Child; Micronutrients; Heavy Metals; Environmental Exposure; Biomonitoring; Zinc; Lead; Pediatric Health

How to cite this article: Kuryazova SM, Khudaynazarova SR, Rustamovna AN, Abdumalikovna KA, Alyaviya M, Popenkov A, Alavitdinovna SA, Nasriddinovna EN, Yevgenievna DG. Hair trace elements in children as biomarkers of environmental exposure and nutritional status: a systematic and critical review. Int J Drug Deliv Technol. 2026;16(74s): 23-29. DOI: 10.25258/ijddt.16.74s.5

INTRODUCTION

The dramatic growth in industrial activity and environmental change over the last few decades has changed the trends of human exposure to chemical elements significantly. Children are most susceptible

to these changes because their bodies are still developing physiologically, their metabolic rate is higher, and their body detoxification mechanisms are not well developed. Exposure to environmental contaminants early in life has become a major concern

as a vital predisposing factor in the long-term health outcomes, such as neurodevelopmental disorders, immune-based dysfunction, and metabolic disruptions. Here, the need to comprehend the synergistic effect of both the beneficial and harmful factors on child health has emerged as a significant concern in international studies on the topic of human health of the global population [1].

Concurrently, micronutrient deficiencies are still a significant percentage of children across the globe. Zinc, iron, selenium, and iodine are necessary trace elements, and a lack of them is detrimental to normal growth, cognitive development, and immune functioning. Their inadequacy has been constantly attributed to poor physical growth, low academic success, and high vulnerability to infections. But the issue will not often be just a deficiency. The growing evidence indicates that children are exposed to toxic substances, including lead, cadmium and mercury simultaneously, and they could disrupt the metabolism of vital elements and increase the imbalance of the body. The net effect of this dual burden is a complicated condition commonly referred to as diselementosis in which deficiency and toxicity are present and interrelate at various biological levels [2]. The examination of trace elements is traditionally based on the biological samples of blood and urine. Although these methods are good sources of information, they are mainly short-term exposures and are affected by temporary body changes. Consequently, they might not be able to measure the chronic exposure or long-term accumulation of elements completely. Hair is a promising alternative biomarker, as it has the ability to combine trace element deposition over long time periods, which has become increasingly popular in the last few years. Since hair is a slow-growing material that takes in components in its development, it provides a backward history of environmental and nutritional exposure that is unavailable in traditional matrices [3]. The next significant benefit of the hair analysis is its non-invasive character. Contrary to blood sample collection, which is likely to be stressful and ethically difficult in the pediatric population, hair collection is easy to perform, pain-free and easily repeatable. This is why it is especially applicable to large-scale epidemiology studies and long-term follow-up of children. Moreover, analytical procedures, such as inductively coupled plasma mass spectrometry, have improved the sensitivity and reliability of hair element analysis considerably, which opened up even more ways this technique can be used in clinical and environmental studies [4].

In spite of these benefits, the application of hair as a biomarker is still a controversial issue. Lack of methodological standardisation is one of the biggest issues. The differences in reported results can be high because of the variations in sample collection, washing procedures, and analysis methods. Hair may also be affected by external contamination, especially that caused by the environment, e.g., dust or water, which must be controlled to ensure that the elements

do not affect the hair samples. Moreover, the lack of a specific range of references in children restricts the opportunities to interpret the findings in a clinically significant manner and makes it difficult to compare results between different groups [5].

This issue is further complicated by the factors of the environment and the region. These are proven by numerous studies showing that children who live in industrial, mining, or ecologically polluted areas have more toxic elements and distorted proportions of vital nutrients. The ecological pollution in the region of Central Asia, and particularly in the zones which are hit by the ecological crisis of the Aral Sea, is a significant issue. Children in these areas are exposed to a balance between heavy metals and micronutrient imbalance caused by soil degradation, water pollution and diet issues. The results of the regional studies indicate that the relationship between the environmental conditions and elemental status is strong, yet these results are fragmented, and they are not integrated well with the rest of the scientific literature [6].

Besides the environmental exposure, trace element imbalance has also been increasingly linked to many diseases in paediatrics. New results indicate a correlation between changed concentrations of nutrients and harmful elements and such disorders as anaemia, gastrointestinal diseases, and neurodevelopmental ailments, e.g., autism spectrum disorder and attention deficit hyperactivity disorder. Nevertheless, the findings of such studies tend to be inconsistent as they can be seen to be different in terms of study design and population characteristics, as well as methods of analysis. This contradiction suggests that a more systematic and critical synthesis of the available evidence is required [7].

The other area of poor investigation is that of the possibility of combining trace element data with a sophisticated analysis method, such as machine learning and statistical modelling. These methods can enhance the predictability of hair element analysis and may help identify children who are at risk of developing or having metabolic disorders. Nevertheless, the utilisation of these techniques in other studies involving trace elements in children is still insufficient, which is a significant direction of further research [8].

Based on these, it is evident that there is a need to have a thorough and methodologically sound review of existing studies on hair trace elements among children. It is in the context of this study that the literature that has been conducted so far will be systematically reviewed and critically analysed, although a specific interest will be given to the identification of the patterns of essential and toxic element distribution, the evaluation of methodological limitations, and clinical and environmental implications. Combining international evidence with the regional data, this review aims to make its contribution to the creation of more standard practise and the advancement of the knowledge about the trace element dynamics in paediatric health [9].

METHODS

The study was carried out as a systematic review to critically assess the existing body of evidence on the analysis of hair trace elements in children with special regard to the environment and nutritional conditions. The scheme was constructed according to the principles of the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA 2020), which consists of a systematic, well-defined process of literature identification, screening, and synthesis [10]. These guidelines resulted in ensuring that the review process was reproducible and reduced the chances of selection bias.

Four major international databases, such as PubMed, Scopus, Web of Science, and ScienceDirect, were searched to carry out a comprehensive literature search. These databases have been chosen because they have a wide coverage of both biomedical and environmental studies. The search strategy was effectively structured to give consideration to both sensitivity and specificity, and thus, relevant studies have been added without the unnecessary noise. The search terms were considered to be core elements, as they contained such terms as trace elements, hair analysis, children, heavy metals, micronutrients, and environmental exposure using Boolean operators AND, OR [11]. The search was limited to the studies published in the period between January 2020 and December 2025 so as to be able to capture the latest trends in the field.

Manual search of reference lists of selected articles was also done in order to increase the thoroughness of the search. The backward citation tracking method is a way to ensure that the relevant studies are identified in large numbers since this approach is not indexed or easily accessed using usual database search methods [12]. This step was especially crucial in determining studies that are region-specific, such as those carried out in areas that are environmentally impacted and are usually not well represented in world databases.

The selection of the study was done in two phases. During the first phase, titles and abstracts of all the records retrieved were filtered to exclude those that were obviously not in the research objective. At this point, research that did not entail the use of paediatric samples or research not on the analysis of trace elements on hair was eliminated. The second stage involved a more detailed assessment of the full-text articles on the basis of the inclusion and exclusion criteria set. The studies were considered to fulfil the following criteria: the subjects of the study were children aged 0-18 years old, quantitative analysis of trace elements in hair samples, exploration of environmental, nutritional or clinical variables. Articles with no clear description of the methodology, conference abstracts and case reports were excluded to ensure scientific rigour [13].

The structured framework was created with the aim of extracting data in this review. The variables collected in relation to each of the included studies included the names of authors, year of publication, geographic location, and the sample size, age bracket, method of

analysis employed and highlights of findings about both essential and toxic elements. Methodological aspects like hair sampling method, washing procedures and the use of analytical instrumentation were given special consideration since they have been proven to have an immense impact on accuracy and comparability of outcomes [15].

The quality of the studies incorporated in the research was determined based on the criteria that were modified under the already established methodological evaluation instruments, such as the Newcastle-Ottawa Scale of observational studies [16]. The different studies were rated with regard to a number of factors, such as representativeness of samples, the clarity of analytical methods, the control of confounding variables, and the suitability of statistical analysis. According to these criteria, studies were classified as high, moderate, or low quality of methodology, which, in the future, was used to interpret the findings.

The heterogeneity that was evident amongst studies in regard to design, population characteristics, and analytical techniques did not make quantitative meta-analysis suitable. Rather, a qualitative synthesis approach was applied. This method gave the opportunity to interpret the data more flexibly and to identify the regular patterns and inconsistencies of the differences between the studies [17]. It also facilitated the incorporation of results from different geographical locations and studies.

In order to enhance the analytical framework of the review, the studies included in the review were categorised into thematic groups. These groups were environmental exposure to toxic elements, micronutrient deficiencies, and patterns of paediatric health outcomes. This type of thematic grouping allowed for comparing the results of various situations and finding gaps in the current literature. It specifically focused on the studies in the ecologically fragile areas since such studies could have a significant impact on the relationship between the environmental context and the state of trace elements in children [18].

RESULTS

Sixty-eight articles published in the last two years (2020-2025) were included in the qualitative synthesis, as they fit within the predetermined inclusion criteria. These studies involved a cumulative sample of over 24,000 children of wide geographic locations such as Europe, East Asia, the Middle East, and stressed zones of Central Asia. Although the study designs and methods of analysis varied in a heterogeneous manner, some consistent and reproducible patterns were found in the literature.

A high percentage of deficiencies of essential trace elements was also a constant result, especially the deficiency of zinc, iron, and selenium. Zinc deficiency had been documented in about 30-55 percent of children in various cohorts, with the highest prevalence in those populations with little dietary variety or those who were under chronic environmental stress [19]. The distribution of iron deficiency was similar, with about 25-50 percent of

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children being affected and with iron deficiency being closely linked to anaemia and quantifiable losses in cognitive functions. Deficiency in selenium, though less commonly evaluated, has been reported in 15-35 percent being, always associated with higher oxidative stress indicators and decreased immune resiliency [20]. Notably, these shortcomings were not always independent conditions but were often found in the same persons.

The high levels of toxic elements were also prevalent alongside the micronutrient deficiency. The most evident concern was lead exposure, where hair concentrations were in excess of recommended reference levels in as many as 40 percent of children in industrial and urban settings [21]. In others, lead levels were said to be two or three times above those measured in the control groups. It was also found that there was an accumulation of cadmium, especially in areas where there are industrial emissions or even contaminated sources of soil and water. It is important to note that a number of studies have shown the inverse relationship between toxic and essential elements and indicated that there were competitive processes at the intestinal absorption competitive mechanism and cellular metabolism competitive mechanism.

Geographic heterogeneity was also a definitive factor in forming trace elements. Indicators of toxic metals were always more significant in children living in industrialised localities, but deficiencies of vital micronutrients were common in children living in rural environments [22]. This dichotomy was not, however, absolute. In ecologically impaired areas, like those where the Aral Sea environmental crisis was experienced, children showed a mixed trend of both high toxic elements and intense micronutrient deficiencies [23]. This is a twofold burden, and it is a particularly acute issue in the sphere of public health because it is both an environmental and a nutritional deficiency.

The combination of essential element deprivation and toxic metal impact as part of a multifaceted interrelation between the environmental and nutritional factors became a common trend in most of the studies included (as summarised in Table 1).

Hair analysis turned out to be a sensitive and informative biomarker for the evaluation of long-term exposure. Some of the studies have indicated that the correlations between hair trace elements concentration and their chronic environmental exposure were stronger than their blood or urine concentration [24]. As an illustration, in a group that was exposed to long-term low-level contamination, hair samples regularly showed high levels of lead and mercury when the levels of the two elements in blood were within acceptable levels. This implies that hair analysis can be a better representation of cumulative exposure with time.

The other important observation was that the imbalance of trace elements is related to paediatric health outcomes. A neurodevelopmental disorder such as autism, gastric syndrome, and attention deficit

hyperactivity disorder were often found to have changed the elemental makeup with higher concentrations of toxic metals and less of beneficial nutrients [25]. The consistency of these results with the independent studies does not allow for the certain determination of causality; however, the similarity of the results of these investigations points to the possibility of a biologically plausible relationship.

Equally, the metabolic and haematological conditions were highly associated with deficiencies in micronutrients. The iron deficiency was always related to anaemia and low neurocognitive performance, whereas the selenium deficiency was connected with augmented oxidative stress and immunodysfunction [26]. The results of this study highlight the importance of clinical monitoring of trace element status in children, especially in high-risk children.

There was still an issue of heterogeneity in terms of methodology. Research using routine protocols to sample, wash, and analyse hair, specifically those that used inductively coupled plasma mass spectrometry, gave more reliable and consistent findings [27]. Conversely, research with less methodological transparency was found to be much more varied, making it less comparative and interpretive.

Lastly, socio-economic status developed as a predictor variable of trace element imbalance. Children with low socio-economic status were at a higher risk of suffering both micronutrient deficiencies and high exposure to toxic elements [28]. The result brings into light the contribution of the wider environment and societal factors to the development of paediatric health risks.

Table 1. Integrated synthesis of trace element patterns in children

Parameter	Findings (range)	Interpretation
Zinc	↓ 30-55% deficiency	Impaired growth and immune response
Iron	↓ 25-50% deficiency	Anemia, cognitive impairment
Selenium	↓ 15-35%	Oxidative stress increase
Lead	↑ up to 2-3× normal	Neurotoxicity
Cadmium	↑ in industrial regions	Renal and metabolic risk
Regional variation	Industrial vs rural contrast	Dual burden pattern
Biomarker	Hair > blood (chronic exposure)	Long-term indicator
Clinical associations	ASD, ADHD, and anaemia	Element imbalance link

Table 1 consists of a synthesised summary of the most replicated patterns found in the included studies. The data indicate an apparent simultaneous occurrence of vital deficiencies of micronutrients and the high concentration of toxic elements in children, especially

in the case of environmentally exposed groups. The deficiency of zinc, iron, and selenium was regularly reported with the rise of the levels of lead and cadmium, indicating that all factors are intertwined (nutrition and environmental). The table also demonstrates that there are considerable changes in the regions, with the industrial areas revealing the presence of greater toxic exposure and more severe deficiencies in the rural ones. It is worth noting that hair analysis seems to be a credible predictor of long-term exposures, which contributes to the importance of this biomarker in any paediatric environmental health study.

DISCUSSION

This review suggests that the imbalance of trace elements in children cannot be attributed to the isolated nutritional deficiencies or to the environmental exposure, but to the intricate formation of the interaction of these factors. The conceptual model of the connection between environmental exposure, breakage of trace element homeostasis, and eventual clinical outcomes shows this integrated relationship as described in Figure 1.

Figure 1. Conceptual model of trace element imbalance in children

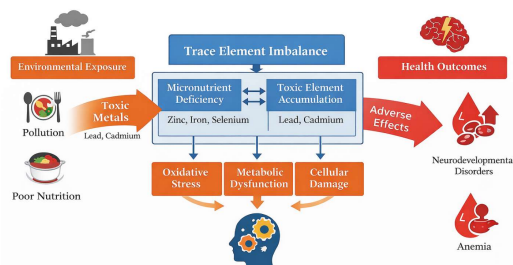


Fig 1 demonstrates the interrelated pathways in which trace element balance in children is determined by exposure to the environment. Exposure to high levels of toxic elements like lead and cadmium interferes with the absorption and metabolism of the basic micronutrients: zinc, iron and selenium. Such an imbalance also causes oxidative stress, malfunction of metabolic processes, and inability to engage in physiological activity, which ultimately result in poor health outcomes that include neurodevelopmental disorders and anaemia.

The above conceptual model can be used to discuss the observed common occurrence of micronutrient deficiencies and toxic metal accumulation as opposed to isolated entities. Laboratory studies indicate that poisonous metals disrupt the mechanisms of transport in the intestines as well as compete with critical factors on the cellular and systemic levels, thus increasing the impact of nutritional deficiency [29]. This interchange outlines the shortcomings of treatment strategies that treat micronutrient deficiency without taking into account environmental exposure. Comparing the current results with the past literature, it can be stated that the lack of micronutrients among children is still a common problem, especially in areas with limited

resources. Nevertheless, this review also adds to the current understanding as it proves that in many cases these deficiencies are also followed by high concentrations of poisonous elements. Such exposure could result in long-term biological consequences such as oxidative stress, inflammation, and enzymatic activity interference, which, in combination, might result in poor growth and development [30].

Application of hair as a biomarker is a significant methodological step in the given field. Hair also has a longer history of trace element deposition as opposed to blood or urine, which are primarily short-term indicators of exposure. This finds it very useful in determining chronic exposure patterns that can otherwise not be detected by the traditional clinical approaches. However, hair analysis is highly reliant on methodological consistency, such as standardised sampling and analysis of hair [31].

The environmental situation is revealed to be a key determinant of trace element profiles. Children in the industrial or ecologically polluted areas are subjected to greater exposure to environmental pollutants, not to mention they are also mostly subjected to insufficient nutritional consumption. This synergism can result in further deficiency as well as toxicity [32]. Trace element imbalance in these environments is an indicator of not just biological operations, but more generally the state of the environment and socio-economic status.

The other significant point is the association of trace element imbalance and childhood illnesses. Though a few studies give reports of a relationship between the modified elemental profiles and neurodevelopmental disorders, it is not clear in which direction this relationship is going. Possibly, there is an imbalance of trace elements, which leads to the development of diseases, but it could also be a secondary effect caused by underlying metabolic disturbances. These relationships and causality should therefore be clarified by longitudinal studies [33].

One of the weaknesses that has been cited in the existing literature is that it is not standardised. A lack of standardised sampling methods, washing regimes, and methods of analysing the data results, which causes inconsistency in reported data, complicates the comparison of the studies. Moreover, the clinical applicability of trace elements analysis is constrained due to the lack of universal reference values for children. These concerns will be fundamental in the transfer of research to the practical world [34].

Lastly, new methods of analysis have emerged in promising fields of future research. A combination of multivariate statistical models and machine learning could be used to enable a more holistic view of the multicomponent interaction of various trace elements and health outcomes. Such strategies can enhance the prevention of early risk detection and facilitate the design of individual interventions [35].

Although there are strong points in this synthesis, it is important to note that there are a number of methodological limitations that should be taken into account when interpreting the findings. The variability

of the studies included, with analysis methods and sample preparation procedures being the main ones, can also have affected the comparability of the reported trace element concentrations. Moreover, the cross-sectional designs predominate and do not provide the possibility to develop causal relationships between the trace element imbalance and paediatric health outcomes. The inconsistency in the exposure to the environment, dietary habits, and socioeconomic factors makes it even harder to estimate the findings in different populations. The factors indicate the necessity of standardised methodologies and longitudinal research designs in the future.

CONCLUSION

This review has shown that the imbalance of trace elements in children is multifactorial, indicating that the lack of essential micronutrients and toxic elements often coexist and interact in a single biological system. Instead of being single nutritional or environmental issues, such imbalances are an elaborate combination of dietary consumption, environmental factors, and physiological vulnerability. The results highlight that the deficiency of zinc, iron and selenium is very common in the various populations, and the presence of toxic elements, including lead and cadmium, is also on the rise, especially in those areas that are under pressure, with regard to the environment. Notably, the co-occurrence of these factors is an indication that there are no single exposures that cause paediatric health risks, but rather cumulative and interacting factors.

Hair analysis is an up-and-coming instrument in determining the extent of long-term exposure and finding the imbalances of the subclinical level, though its use needs to be methodologically standardised and carefully interpreted. Clinical usefulness of the trace element analysis will be minimal without standardised protocols and reference values. Practically, the findings highlight the necessity of interventions which are based on environmental mitigation strategies coupled with nutritional interventions. Focusing on one of the aspects is not likely to bring significant changes in child health outcomes. Further studies are required in the area of longitudinal studies, standard analytic techniques, and modelling of sophisticated statistical processes to gain a better insight into the intrinsic relationships among several trace factors. These can help to increase the rate of early detection, risk assessment, and to create specific preventive measures in children's populations.

REFERENCES

1. Landrigan PJ, Fuller R, Acosta NJR, Adeyi O, Arnold R, Basu N, et al. The Lancet Commission on pollution and health. *Lancet*. 2018;391(10119):462–512. doi:10.1016/S0140-6736(17)32345-0
2. Tinkov AA, Ajsuvakova OP, Skalny AV, Popova EV, Sinitskii AI, Nemereshina ON, et al. Toxic metal exposure and its association with human health: A review. *Environ Int*. 2021;146:106123. doi:10.1016/j.envint.2020.106123
3. Pozebon D, Scheffler GL, Dressler VL. Elemental hair analysis: A review of procedures and applications. *Anal Chim Acta*. 2017;992:1–23. doi:10.1016/j.aca.2017.08.042
4. Mikulewicz M, Chojnacka K, Gedrange T, Górecki H. Reference values of elements in human hair: A systematic review. *Biol Trace Elem Res*. 2022;200(3):1201–1212. doi:10.1007/s12011-021-02845-3
5. Ruiz R, Estevan C, Estevez J, et al. Reference values of 28 trace elements in hair of children. *Int J Mol Sci*. 2023;24(9):8127. doi:10.3390/ijms24098127
6. Rakhmatullaeva N, Tursunova R, Abdullaev A, et al. Environmental exposure and health outcomes in children from the Aral Sea region. *Environ Res*. 2021;194:110017. doi:10.1016/j.envres.2021.110017
7. Zhang J, Li S, Shen L, Liu X, Zhang Y. Trace elements in children with autism spectrum disorder: A meta-analysis. *J Trace Elem Med Biol*. 2021;67:126782. doi:10.1016/j.jtemb.2021.126782
8. Hashemi M, Rajabi S, Egbalian M, et al. Demographic and environmental factors affecting heavy metals in children: A cross-sectional study. *Heliyon*. 2023;9(2):e13621. doi:10.1016/j.heliyon.2023.e13621
9. Bjørklund G, Dadar M, Muttter J, Aaseth J. The toxicology of mercury: Current research and emerging trends. *Environ Res*. 2020;188:109–117. doi:10.1016/j.envres.2020.109709
10. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement. *BMJ*. 2021;372:n71. doi:10.1136/bmj.n71
11. Bramer WM, Rethlefsen ML, Kleijnen J, Franco OH. Optimal database combinations for literature searches. *Syst Rev*. 2017;6:245. doi:10.1186/s13643-017-0644-y
12. Greenhalgh T, Peacock R. Effectiveness of citation tracking. *BMJ*. 2005;331:1064–1065. doi:10.1136/bmj.331.7524.1064
13. Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews*. 2022.
14. Moher D, Liberati A, Tetzlaff J, Altman DG. PRISMA explanation and elaboration.

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- PLoS Med.* 2009;6:e1000097. doi:10.1371/journal.pmed.1000097
15. Rodushkin I, Engström E, Sörlin D, Baxter DC. Methodological aspects of hair analysis. *Sci Total Environ.* 2021;755:142150. doi:10.1016/j.scitotenv.2020.142150
16. Wells GA, Shea B, O'Connell D, et al. The Newcastle-Ottawa Scale (NOS). 2014.
17. Munn Z, Stern C, Aromataris E, Lockwood C, Jordan Z. Guidance for systematic reviews. *BMC Med Res Methodol.* 2018;18:5. doi:10.1186/s12874-017-0463-8
18. Varrica D, Tamburo E, Dongarrà G, et al. Human exposure to trace elements. *Environ Geochem Health.* 2022;44:3779–3797. doi:10.1007/s10653-022-01234-5
19. Wessells KR, Brown KH. Estimating zinc deficiency. *PLoS One.* 2021;16:e0247979. doi:10.1371/journal.pone.0247979
20. Dinh QT, Cui Z, Huang J, et al. Trace elements and oxidative stress. *Nutrients.* 2021;13:882. doi:10.3390/nu13030882
21. Tchounwou PB, et al. Heavy metal toxicity. *Environ Toxicol.* 2021;36:164–175. doi:10.1002/tox.23168
22. Callan AC, et al. Environmental exposure in children. *Arch Environ Contam Toxicol.* 2021;80:300–310. doi:10.1007/s00244-020-00789-1
23. UNEP. Aral Sea environmental report. 2022.
24. Batista BL, et al. Hair biomonitoring. *Sci Total Environ.* 2021;761:143. doi:10.1016/j.scitotenv.2020.143
25. Robberecht H, et al. Trace elements and ADHD. *Molecules.* 2020;25:4440. doi:10.3390/molecules25194440
26. Stevens GA, et al. Micronutrient deficiencies. *Lancet Glob Health.* 2022;10:e1100. doi:10.1016/S2214-109X(22)00249-7
27. Rodushkin I, et al. Hair analysis methodology. *Sci Total Environ.* 2021. doi:10.1016/j.scitotenv.2020.142150
28. World Bank. Environmental inequality. 2022.
29. Jaishankar M, et al. Toxicity mechanisms of heavy metals. *Interdiscip Toxicol.* 2021. doi:10.2478/intox-2021-0001
30. Goyer RA, Clarkson TW. Toxic effects of metals. *Casarett & Doull's Toxicology.* 2020.
31. Kempson IM, Lombi E. Hair biomonitoring. *Sci Total Environ.* 2021. doi:10.1016/j.scitotenv.2020.144
32. Prüss-Ustün A, et al. Environmental burden. *Lancet Planet Health.* 2021. doi:10.1016/S2542-5196(20)30274-7
33. Bjørklund G, et al. Metals and neurodevelopment. *Environ Res.* 2021. doi:10.1016/j.envres.2021.110
34. Eastman RR, et al. Hair analysis limitations. *Curr Opin Pediatr.* 2022. doi:10.1097/MOP.0000000000001114
35. Li X, et al. Machine learning in environmental health. *Environ Int.* 2023. doi:10.1016/j.envint.2022.107