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Changes with time of human exposure to toxic trace elements

Paola Borella

Senior professor

Department of Biomedical, Metabolic and Neural Sciences

University of Modena and Reggio E., Italy

A.I.S.E.T.O.V.

Key words: toxic trace elements, full test, humans, English
n. of publications

50 yrs ago	Total	exposure
1973-1975	49	7
1976-1978	69	9
1979-1981	90	21
At present	**Total**	**exposure**
2013-2015	1,700	557
2016-2018	1,973	648
2019-2021	2,534	824

50 yrs ago	Total	exposure	children
1973-1982	216	37	3
At present	**Total**	**exposure.**	**children**
2013-2022	6,207	2,029	386

50 yrs ago	Cd	Pb	Mn	Se	As
1973-1981	121	432	21	31	107
At present					
2013-2021	2,729	3,523	1130	806	3,226

The interest in the exposure and effects of toxic trace elements is being continuously increasing!

This presentation mainly focuses on:

- exposure to toxic trace elements in the Mediterranean area;
- risks of exposure for children, with special attention to possible neuropsychological effects

An excursus along 50 yrs of researches is presented

Why children?

They are more exposed:

> food and water intake relative to body weight

> respiratory rates

> contact with soil and dust

< perception of risk

Children are more vulnerable, the xenobiotic detoxification system is immature, particular susceptibility of nervous, immune, endocrine, reproductive systems that are developing even after birth.

European Union VI Framework Program (2002)

High level of quality of life and social well-being for citizens through an environment where the level of pollution does not cause harmful effects on human health

Innovative proposals

- Environment as an overall context of life: external environment, nutrition, indoor, risky behaviours
- Study of the cumulative effects of exposure to pollutants and factors related to the onset of disease (socio-economic, lifestyle)
- Specific attention to vulnerable sections of the population

Our first studies on lead exposure

We took part to the first European Campaigns on biological surveillance for lead exposure in general population (CEE Directive 29.3.77)

Population of the ceramic district	PbB (1978-1979)	PbB (1980-1981)
Adults	23.4 µg/dl	
Children	17.6 µg/dl	14.0 µg/dl
Workers	47.0 µg/dl	
Urban population	19.7 µg/dl	16.2 µg/dl

Lead exposure in general population in Sassuolo 1976-1979

- ✓ The **average level of atmospheric pollution** in residential areas was **10.3 µg/m³ of Pb** *(Olivo et al 1978)*
- ✓ the intake of Pb with diet exceeded **600 µg per day**; the most contaminated products were leafy epigeal vegetables (eg. salads 1.9-8.9 ppm) and wine (0.62 ppm) *(Borella et al., 1979)*

Up to 25% of the Pb in the diet can be absorbed by children *vs* 8-10% in adults

- ✓ **In the adults**, the mean PbB was **32.2 µg/dl** *vs* 26.0 µg/dl of Bologna, and 33% had levels > 35 µg/dl (CEE reference levels) *(Borella et al 1978)*
- ✓ In 1972 the **abortion rate** was **15.0/1,000 inhabitants**, much higher than in other areas (~ 3% in Modena) *(Aggazzotti et al., 1976)*

Effects of lead on children's health 1985-90

- ✓ Within a multicentric European study on Pb effects on CNS, about 300 children aged 8-11yrs were examined through
  - measure of ALA-D activity in blood, Pb in blood, hair and deciduous teeth
  - administration of psychometric tests to evaluate cognitive functions (WISC, QI), scholar learning, visual motor performance, memory and attention.

Results:

- **Pb in teeth** was associated with a reduction on cognitive functions
- **ALA-D and Pb in hair** were associated with two subtests of QI scale

The relationship between neuropsychological alterations and a long-term exposure indicator such as Pb in teeth suggests that the alterations were established in the first years of life, when the pollution was higher and that Pb interacts with central nervous system also during intrauterine life *(Vivoli et al. 1985, 1989)*

It is now widely accepted that lead:

- easily crosses the blood-brain barrier
- can be detrimental even at extremely low levels
- impairs brain development, particularly the prefrontal cortex, hippocampus, basal ganglia, and cerebellum
- the adverse neurological effects persist into older ages
- damages neurotransmitter systems (dopaminergic, glutamatergic, and cholinergic pathways) thus impairing cognition, attention, and impulse control
- early childhood exposure appears to be most harmful to psychological and cognitive development

Lead exposure at low levels has limited effects on neurological system, but involves attention and memory, and it is not possible to establish a threshold exposure level under which no effects are expected

2010-2018: New acquisitions on lead effects related to early exposure

The neuropsychiatric development

Goodlad et al. (2013) performed a meta-analysis of 33 studies showing that lead in blood is significantly associated with ADHD (Attention Deficit Hyperactivity Disorder) symptoms.

In summary, a multi-disciplinary literature reaches the consensus that early childhood lead exposure negatively affects cognitive development and behaviour in ways that increase the likelihood of aggressive and antisocial acts.

These links to behaviour pertain even at the moderate lead levels (5-15 µg/dL) that were common through the early 1980s.

Detrimental effect of lead on behaviour

Lead Exposure and Behaviour: Effects on Antisocial and Risky Behavior among Children and Adolescents

J. Wolpaw Reyes, National Bureau of Economic Research Working Paper No. 20366. 2014.

Using data on two cohorts of children, this paper investigates the effect of early childhood lead exposure on behaviour problems from childhood through early adulthood. Large negative consequences of early childhood lead exposure have been observed in the form of an unfolding series of adverse behavioural outcomes: **behaviour problems as a child, pregnancy and aggression as a teen, criminal behavior as a young adult**

Due to the conclusion that there is no safe level for lead exposure, preventive measures are crucial for lowering lead exposure as much as possible.

Cadmium and effects on children health

In a case-control study, high cadmium levels in blood were associated with light increase of pressure values (*Vivoli, Borella et al, 1989*)

A positive correlation between blood pressure and cadmium in hair was observed in male children hair (*Bergomi, Borella et al, 1989*)

Is cadmium as dangerous as lead for children?

Signs are emerging that children are suffering from exposure to cadmium showing learning problems at school.

Scientific American 2012

Manganese and effects on children health

NeuroToxicology 33 (2012) 872–880

Manganese exposure and cognitive deficits: A growing concern for manganese neurotoxicity☆

H.A. Roels [a,*], R.M. Bowler [b], Y. Kim [c], B. Claus Henn [d], D. Mergler [e], P. Hoet [a], V.V. Gocheva [b], D.C. Bellinger [d], R.O. Wright [d], M.G. Harris [f], Y. Chang [g], M.F. Bouchard [h], H. Riojas-Rodriguez [i], J.A. Menezes-Filho [j], Martha Maria Téllez-Rojo [k]

ABSTRACT

This symposium comprised five oral presentations dealing with recent findings on Mn-related cognitive and motor changes from epidemiological studies across the life span. The *first* contribution highlighted the usefulness of functional neuroimaging of the central nervous system (CNS) to evaluate cognitive as well as motor deficits in Mn-exposed welders. The *second* dealt with results of two prospective studies in Mn-exposed workers or welders showing that after decrease of Mn exposure the outcome of reversibility in adverse CNS effects may differ for motor and cognitive function and, in addition the issue of plasma Mn as a reliable biomarker for Mn exposure in welders has been addressed. The *third* presentation showed a brief overview of the results of an ongoing study assessing the relationship between environmental airborne Mn exposure and neurological or neuropsychological effects in adult Ohio residents living near a Mn point source. The *fourth* paper focused on the association between blood Mn and neurodevelopment in early childhood which seems to be sensitive to both low and high Mn concentrations. The *fifth* contribution gave an overview of six studies indicating a negative impact of excess environmental Mn exposure from air and drinking water on children's cognitive performance, with special attention to hair Mn as a potential biomarker of exposure. These studies highlight a series of questions about Mn neurotoxicity with respect to cognitive processes, forms and routes of exposure, adequate biomarkers of exposure, gender differences, susceptibility and exposure limits with regard to age.

CURRENT OPINION

Manganese exposure: cognitive, motor and behavioral effects on children: a review of recent findings

Silvia Zoni[a] *and Roberto G. Lucchini*[a,b]

Curr Opin Pediatr 2013, 25:255–260

Purpose of review

Manganese (Mn) is an essential element, but can be neurotoxic when exceeding the homeostatic range. We reviewed the most recent human studies (from January 2011 to July 2012) regarding the association between Mn exposure and cognitive, motor and behavioral effects on children.

Recent findings

A total of 10 articles were located; data were collected from five different countries. Six studies showed adverse effect of Mn on cognitive function. The most adopted cognitive test was the Wechsler Intelligence Scale for Children (WISC) or some subtests from it and results suggest an inverse association of higher Mn exposure with lower intellligence quotient. Three studies focused on motor effects of Mn; two of them found a direct association of higher Mn exposure with increased motor impairment. Two studies assessed Mn impact on behavior; one of them showed a correlation between higher Mn in water and both internalizing and externalizing behavioral scores. Potential limitations of these studies included the lack of validated biomarkers and the lack of consideration of mixed co-exposure with other neurotoxic agents.

Summary

Despite some potential limitations of the reviewed studies, the adverse effects of manganese exposure on the developing brain is well demonstrated and preventive strategies should be promoted.

J Trace Elem Med Biol 2014 Apr;28(2):106-116.

New insights into manganese toxicity and speciation

Bernhard Michalke*, Katharina Fernsebner

A B S T R A C T

Manganese (Mn) is known to be a neurotoxic agent for nearly 175 years now. A lot of research has therefore been carried out over the last century. From preliminary describing only symptoms of Mn-(over)exposed workers, research was preceded to more detail on toxic mechanisms of Mn. Unraveling those neurotoxic mechanisms implicated a number of studies, which were summarized partly in several reviews (e.g. Yokel RA. Neuromol Med 2009;11(4):297–310; Aschner M, et al. Toxicology Appl Pharmacol 2007;221(2):131–47; Michalke B, et al. J Environ Monit 2007;9(7):650). Since our recent review on Mn-speciation in 2007 (Michalke B, et al. J Environ Monit 2007;9(7):650), Mn-research was considerably pushed forward and several new research articles were published. The very recent years though, Mn toxicity investigating science is spreading into different fields with very detailed and complex study designs. Especially the mechanisms of Mn-induced neuronal injury on cellular and molecular level was investigated in more detail, discussing neurotransmitter and enzyme interactions, mechanisms of action on DNA level and even inclusion of genetic influences. Depicting the particular Mn-species was also a big issue to determine which molecule is transporting Mn at the cell membranes and which one is responsible for the injury of neuronal tissue. Other special foci on epidemiologic studies were becoming more and more important: These foci were directed toward environmental influences of Mn on especially Parkinson disease prevalence and the ability to carry out follow-up studies about Mn-life-span exposure. All these very far-reaching research applications may finally lead to a suitable future human Mn-biomonitoring for being able to prevent or at least detect the early onset of manganism at the right time.

Changes in the more recent studies on exposure to toxic trace elements in children 2015-2022

Arsenic studies

Environmental Research 207 (2022); 207: 112208

Prenatal arsenic exposure, arsenic methylation efficiency, and neuropsychological development among preschool children in a Spanish birth cohort

Soler-Blasco R et al, Valencia- Spain

Objectives: To explore the relationship between prenatal urinary total As (TAs) concentrations, the As species and the methylation efficiency, and child neuropsychological development in a Spanish birth cohort.
Of 807 mother–child pairs.

Methods: Urinary TAs and its metabolites, monomethylarsonic acid (MMA), dimethylarsinic acid (DMA), inorganic As (iAs) and arsenobetaine were measured in the first trimester of pregnancy.. Children's neuropsychological development was assessed at the age of 4–5 years. Modification by sex, iron status, maternal nutrients status (serum manganese and selenium, and urinary zinc), and maternal vitamins intake was studied.

Results: The geometric mean of As (sum of DMA, MMA and iAs) was 7.78 (7.41, 8.17) μg/g creatinine. MMA concentrations were inversely associated with the scores for the general, verbal, quantitative, memory, executive function and working memory scales

Discussion: An inverse association was observed between MMA concentrations and children's neuropsychological development. Maternal levels of manganese, zinc and ferritin affected the association between As methylation efficiency and MSCA scores.

Mercury studies

J. Trace Elements in Medicine and Biology 32 (2015) 122–134

Consensus document on the prevention of methylmercury exposure in Spain. Study group for the prevention of Me-Hg exposure in Spain (GEPREM-Hg)

González-Estecha M et al.

The beneficial effects of fish consumption in both children and adults are well known. However, the intake of methylmercury, mainly from contaminated fish and shellfish, can have adverse health effects. The study group on the prevention of exposure to methylmercury made up of representatives from different Spanish scientific societies, has prepared a consensus document in a question and answer format,
containing the group's main conclusions, recommendations and proposals. The objective of the document is to provide broader knowledge of factors associated with methylmercury exposure, its possible effects on health amongst the Spanish population, methods of analysis, interpretation of the results and economic costs, and to then set recommendations for fish and shellfish consumption. The group sees the merit of all initiatives aimed at reducing or prohibiting the use of mercury as well as the need to be aware of the results of contaminant analyses performed on fish and shellfish marketed in Spain. In addition, the group believes that biomonitoring systems should be set up in order to follow the evolution of methylmercury exposure in children and adults and perform studies designed to learn more about the possible health effects of concentrations found in the Spanish population, taking into account the lifestyle, eating patterns and the Mediterranean diet.

J Trace Elem Med Biol. 2020; 57:60-67.

Evaluation of blood mercury and serum selenium levels in the pregnant population of the Community of Madrid, Spain. LM Llorente Ballesteros, et al.

Objective: To describe maternal total blood mercury (THg) and serum selenium (Se) in a cohort of pregnant women living in Spain as it relates to fish intake during the three trimesters and to assess whether or not Spanish women of childbearing age follow the recommendations listed in fish advisories and choose fish species with lower Hg levels.
Methods: 141 female volunteers of childbearing age (16–45 years were interviewed about their overall eating habits and seafood intake. Hg and Se levels were tested using cold-vapor AAS and electrothermal AAS, respectively.
Results: Average THg levels in pregnant women were 2.89 µg/L (SD 2.75 µg/L, GM 2.19 µg/L), and THg GM was positively associated with fish intake. Mean Se levels in pregnant women were 73.06 µg/L (SD 13.38 µg/L), and Se levels were found to increase with tuna intake. In 16 (12%) pregnant women, THg was higher than the level recommended by the U.S. EPA (6.4 µg/L). A positive association was also found between THg and serum Se.
Conclusion: Women of childbearing age in Spain had higher Hg levels than women in other western studies: 12% of women had Hg levels above the safety limit set by the EPA (6.4 µg/L), and 31% had levels above the relevant benchmark level of 3.5 µg/L suggested by various researchers

Changes in measurement techniques to evaluate trace element concentration in both environment and biological samples

TRACE ELEMENTS ANALYTICAL EQUIPMENTS In our department

- **AAS** Air-acetylene flame atomic absorption spectrometry (Perkin-Elmer A-analyst 200)
- **GF-AAS** Graphite-furnace atomic absorption spectrometry (Perkin-Elmer A-analyst 600 equipped with an autosampler AS 800 and longitudinal Zeeman-effect background corrector)

At present

- **ICP-Mass** plasma spectrometry Series II (Thermo Fischer Scientific)

QUALITY CONTROL

All data produced are meticulously controlled through the systematic analysis of reference samples, duplicates and blanks, in order to guarantee strict control over the quality of the results. The accuracy and precision of analyses are further monitored by internally prepared standards.

Clinical Biochemistry 53 (2018) 81–87

ICP-MS measurement of toxic and essential elements in human breast milk. A comparison of alkali dilution and acid digestion sample preparation methods

Michael Levi*, Camilla Hjelm, Florencia Harari, Marie Vahter

Karolinska Institutet, Institute of Environmental Medicine, Division of Metals and Health, Box 210, S-171 77 Stockholm, Sweden

Journal of Trace Elements in Medicine and Biology 49 (2018) 157–163

External quality assessment schemes for inorganic elements in the clinical laboratory: Lessons from the OELM scheme

Arnaud, J., et al

Journal of Trace Elements in Medicine and Biology 2020, 59, 126414

Development, validation and application of an ICP-MS/MS method to quantify minerals and (ultra-)trace elements in human serum

Sören Meyera,b, Tanja Schwerdtl et al.

Actually, ICP-MS appears the most used technique

J. Trace Elements in Medicine and Biology 43 (2017) 113–120

Reference levels of trace elements in hair samples from children and adolescents in Madrid, Spain Llorente Ballesteros MT et al

Objective: To establish reference levels for trace elements in children and teenagers in Madrid, Spain. Material and methods: Inductively coupled plasma mass spectrometry (ICP-MS) was used to measure Al, As, Ag, Ba, Bi, Cd, Cr, Co, Cu, Fe, Mn, Mo, Ni, Pb, Se, Sr, Tl and Zn levels in hair samples from 648 healthy children and adolescents (253 boys and 395 girls)

Results: Median levels were as follows: Al 18.5 g/g, As 0.07 g/g, Ag 196 ng/g, Ba 0.5 g/g, Bi 0.01 g/g, Cd 18.3 ng/g, Cr 0.4 g/g, Co 14.5 ng/g, Cu 25.7 g/g, Fe 15.5 g/g, Mn 328 ng/g, Mo 0.04 g/g, Ni 0.5 g/g, Pb 0.70 g/g, Se 0.5 g/g, Sr 1.29 g/g, Tl 0.28 ng/g and Zn 121 g/g.

Conclusion: The values of trace elements here described could be considered as possible reference ranges for hair samples from children and adolescents aged 0–18 years living in the Madrid region (central Spain). These values could also be selected as a preliminary screening tool to assess exposure sources and to generate information needed to develop prevention strategies and likewise could be a complement to other diagnostic procedures.

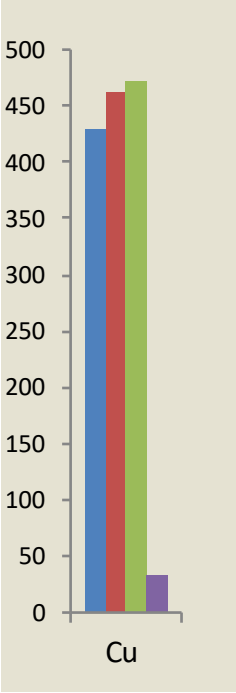
Environ Sci Pollut Res (2018) 25:2035–44

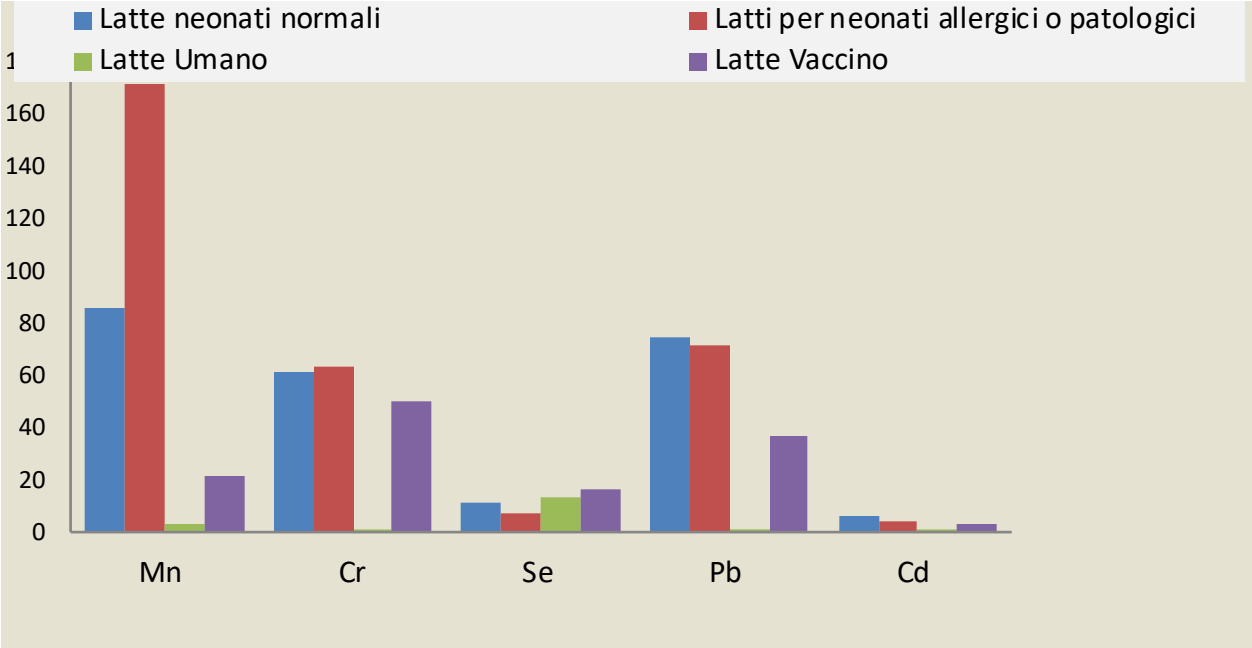
Bargellini et al. Trace elements in starter infant formula: dietary intake and safety assessment

Microelements in different milk samples

Milk type	Cu (mcg/l)	Mn (mcg/l)	Cr (mcg/l)	Se (mcg/l)	Pb (mcg/l)	Cd (mcg/l)
Healthy babies (n. 12)	428,8± 52,3	85,9± 32,1	61,2± 4,4	11,3± 5,6	74,0± 11,3	5,7± 4,1
Allergic /sick babies (n. 10)	462,6± 89,4	171,3± 124,8	63,1± 5,9	7,0± 1,5	70,9± 4,9	3,8± 1,1
Human milk (*Sweden 2012*)	471±75	3±1,4	0,3±0,2	13±2,6	1,5±0,9	0,09±0,04
Cow milk (*Polony 2013*)	32,9	21,0	50,0	16,0	36,4	3,5

Values higher than in human milk





J. of Trace Elements in Medicine and Biology 2020, 58, 126424
Martínez-Hernanz, Á., González-Estecha, M., et al

Blood lead in children and associations with trace elements and sociodemographic factors

Background: Lead can affect nearly every system in the body and is especially harmful to the developing central nervous system of children. The aim of this study is to analyze blood lead in a population of children and its association with sociodemographic variables, biochemical parameters, copper, iron, selenium and zinc.
Methods: We recruited 155 children (86 boys and 69 girls) with a mean age of 7.3 (SD:4.1). Blood lead and serum selenium concentrations were measured by eAAS. Serum copper and zinc concentrations were measured by fAAS. Serum iron levels were determined by colorimetric assay. A risk exposure questionnaire for lead was administered to the participants.
Results: The median blood lead level was 1.1 (IQR 0.7-1.6) µg/dL. Regarding risk exposure factors, the youngest children (<2 years) who played outdoors presented a median blood lead concentration of 1.1 µg/dL **IQR**: 0.48-1.48, compared to the median of 0.3 µg/dL IQR:0.2-0.48 in the children who stated they played at home (p = 0.024). Significant differences were also found when taking into account those parents who smoked (median 1.3 IQR 0.8-1.9 µg/dL vs 0.9 IQR 0.5-1.4 µg/dL of non-smokers, p = 0.002). Children who drank tap water had higher blood lead levels (median 1.2 IQR 0.7-1.6 µg/dL) than those who drank bottled water (median 0.7 IQR 0.2-1.3 µg/dL p = 0.014). In addition, children whose mothers had not finished school had higher blood lead levels (median 1.7 IQR 1.2-2.3 µg/dL) than those whose mothers had finished school (median 1.2 IQR 0.7-1.7 µg/dL) and those whose mothers had gone to university (median 0.9 IQR 0.5-1.4 µg/dL) p = 0.034. In the multivariate lineal regression analysis we continue to observe the association between mother's higher level of education and lower blood levels (p = 0.04) and the interaction between age and outdoor play (p = 0.0145).
Conclusions: In spite of the decline in blood lead concentrations, associated risk factors continue to exist in vulnerable populations such as children.

Journal of Trace Elements in Medicine and Biology 57 (2020) 126409 Fiore M , Ferrante M et al.

Metal and essential element levels in hair and association with autism severity

Background: Autism Spectrum Disorder (ASD) is a complex disorder with heterogeneous etiology and wide clinical severity which supports the needs of recognizing biological and clinical features in patient subsets. The present study aimed to understand possible associations between the hair levels of metals and essential elements and some specific features of ASD measured by the Autism Diagnostic Observation Schedule (ADOS) that represents the gold-standard instrument to objectively confirm ASD diagnosis.

Methods: A cross-sectional study was performed in the province of Catania (Sicily, South Italy). Forty-eight subjects with ASD (70.8% male), aged from 2 to 17 years were studied. Metals (Li, Be, Al, Ni, As, Mo, Cd, Hg, U, Pb) and essential trace elements (Cr, Co, Mn, Zn, Cu, Se) were quantified in hair by inductively coupled plasma mass spectrometry analysis. Participants were characterized by measuring the severity of autism symptoms and cognitive levels.

Results: A significant and positive correlation was found between hair metal burden (lead, aluminum, arsenic and cadmium levels) and severity of ASD symptoms (social communication deficits and repetitive, restrictive behaviors). Hair zinc level were inversely related with age while there was a negative, significant association between hair zinc level and severity of autistic symptoms (defective functional play and creativity and increase of stereotyped behavior). Lead, molybdenum and manganese hair levels were inversely correlated with cognitive level (full intelligence quotient) in ASD individuals.

Conclusions: The present study suggests the importance to combine metallomics analysis with pertinent disease features in ASD to identify potential environmental risk factors on an individual level possibly in the early developmental period.

Scientific Reports | (2021) 11:9898

The effects of the exposure to neurotoxic elements on Italian schoolchildren behavior

Stefano Renzetti[1,2✉], Giuseppa Cagna[1], Stefano Calza[2], Michele Conversano[3], Chiara Fedrighi[1], Giovanni Forte[4], Augusto Giorgino[3], Stefano Guazzetti[1,6], Costanza Majorani[5], Manuela Oppini[1], Marco Peli[1,7], Francesco Petrucci[4], Anna Pino[4], Donatella Placidi[1], Oreste Senofonte[4], Silvia Zoni[1], Alessandro Alimonti[4] & Roberto G. Lucchini[1,8]

Objective: a cross-sectional study to evaluate neurobehavioral effect of exposure to lead, mercury, cadmium, manganese, arsenic and selenium among 299 children living in the pollutant area of Taranto, south Italy.

Conclusion: higher blood lead, urinary arsenic concentrations and their interaction (synergic effect of Pb and As) increase the risk of neurobehavioral problems.

Relationship of trace elements with infectious diseases

Food Chem Toxicol 2021 Jun;152:112161.

The effects of some essential and toxic metals/metalloids in COVID-19: A review

Jose L. Domingo *, Montse Marques *Catalonia, Spain*

This review studies the relationship between various essential and toxic metals/metalloids and the health outcomes related with the COVID-19.

The AA conclude that particular attention must be paid to the load/levels of essential trace elements in COVID-19 patients, mainly zinc and selenium. On the other hand, the exposure to air pollutants in general, and toxic metal/metalloids in particular, should be avoided as much as possible to reduce the possibilities of viral infections, including SARS-CoV-2.

Environmental Research 204 (2022) 112375

Exposure to metal mixture and growth indicators at 4–5 years. A study in the INMA-Asturias cohort

Miguel García-Villarino et al

Exposure to toxic and non-toxic metals impacts childhood growth and development, but limited data exists on exposure to metal mixtures. Here, we investigated the effects of exposure to individual metals and a mixture of barium, cadmium, cobalt, lead, molybdenum, zinc, and arsenic on growth indicators in children 4–5 years of age.

Highlights

- Co-exposure to metals was related to childhood anthropometry at 4 years of age.
- Cd and Pb may affect children's anthropometry differently depending on levels of the other metals.
- Large head circumference is shown to be related with higher levels of Mo.
- 4-year-old children seem to have smaller head circumference when the levels of Co are low.
- High Cd exposure was associated with a decrease in children’s growth measures.

Archives de pediatrie 29 (2022) 453–458 N. Abbassia N et al.

Epidemiology, clinical features, and mortality rate of Wilson disease in Moroccan children: A pediatric case series

Wilson's disease is an autosomal recessive disorder that affects copper metabolism, leading to copper accumulation in the liver, nervous system, and cornea. Data are lacking on the epidemiology, clinical and laboratory characteristics, treatment, and survival in Morocco.

The aim of this study was to examine these features and the cause of death in a Moroccan pediatric population. The study was carried out at the University Hospital Center of Marrakesh, Morocco; 46 children were diagnosed with Wilson's disease from 2008 to 2019. The diagnosis was based on low serum ceruloplasmin, increased urinary copper concentrations, the presence of Kayser−Fleischer rings, a family history of Wilson's disease, and a Leipzig score of ≥ 4.

Results: A total of 42 patients were referred to the center for hepatic or neurological manifestations; four patients were asymptomatic. Consanguineous marriage was found in 67.4% of the cases. The mean duration of illness (42 patients) was 4.9 § 3.9 years. Kayser−Fleischer rings were found in 60.9% of 46 patients. Of the 42 symptomatic patients: 28 of 30 (93.3%) patients had low serum ceruloplasmin (<0.2 g/L), and 24 h urinary copper >100 mg/day was found in 34 of 35 (97.1%) cases. The treatment was established with D-penicillaminefor 43 of the 46 patients, with zinc acetate for one patient and with zinc sulfate in for one patient, whileone patient was not treated. D-penicillamine was discontinued in nine patients because of adverse effects such as thrombocytopenia, neurological deterioration, pancytopenia, severe vomiting and severe hypersensitivity. In total 28 patients were clinically and biologically stabilized, two patients experienced vision loss, and 16 patients died (38%). The main cause of death was diagnosis made at an advanced stage of disease and stopping treatment.

Conclusion: Wilson's disease is a rare condition associated with treatement efficacy, but late diagnosis and stopping treatment can lead to a high mortality rate.

Conclusions

In light of the uncertainties still existing on the role of toxic trace elements on human health, the studies on their presence in different matrices (food and environment) to evaluate population exposure are still numerous.

Comparing studies conducted in the last years of ‘900, we notice a significant interest in their involvement in neoplastic and neurodegenerative processes, as well as in their role in reproduction and paediatric health.

We remark on the relevance of going on with these studies to prevent excess intakes, to change current recommendations and regulations, and to better define the exposure limits able to avoid any negative biological and clinical effects on humans.

Conclusions

The most recent studies on exposure to toxic trace elements and their effects on children central nervous system

- attention to trace elements more rarely considered previously
- investigations which include numerous trace elements
- possible relationship with infectious disease

The last, but not the least…….

the significant and continuous contribution of FESTEM members in these new insights

Festem Board 2004… younger, but with the same enthusiasm for trace elements studies!

Thanks for your attention!