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Research Article

A Smart Approach for Food Contaminants Risk Management, Complementary to Diet Nutritional Balance

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ABSTRACT

Food is usually the major source of human exposure to environmental contaminants like heavy metals and synthetic compounds. This study proposes a quick and simple approach to combine the estimate of the intake of certain pollutants with the diet, in combination with different nutritional plans (Mediterranean diet, weight loss and for athletes). The estimation of the intake of three heavy metals and two perfluoroalkyl substances was carried out by entering the type and quantity of the foods provided by each of the three selected dietary plans in the UltraBio® app. Recurring elements are high levels of Cd and Pb and very low levels of PFASs, for all the plans considered. The Mediterranean diet scheme was the one with the lowest intake of all contaminants, which, in any case, remains within the safety limits by a large margin. The high protein diet leads to exceeding the limits for two metals and critical values for the third. The advantages of this approach are mainly represented by the possibility of having a personalized risk assessment of the intake of important food contaminants for the prevention of exposures that, over time, could put health at risk.

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Introduction

Food safety perceptions are currently a widely investigated topic. Consumers' concerns about food consumption and potential health risks have substantially increased. However, risk perceptions by the general population do not always align with risk assessments provided by experts. The acute vs. chronic context of the hazard may differentially influence people's perceptions of risks, and hence their behaviours. International organizations such as EFSA (European Food Safety Authority) have collected information on the intake of contaminants through the diet to make risk assessments.

Food is usually the major source of human exposure to environmental contaminants like essential or nonessential elements and to a number of synthetic compounds, such as perfluoroalkylated substances (PFASs) [1]. Mercury is a toxic metal; introduction into the body can occur by ingestion, by inhalation of the vapours and by skin contact [2]. The most

dangerous form of mercury is organic, especially methylmercury, present mainly in fish and other foods of animal origin; methylmercury is absorbed and accumulated with greater efficiency, compared to the unbound form, by the tissues of organisms, including man [3]. Chronic exposure to methylmercury, in particular, generates accumulation phenomena in the body, which can lead to neurotoxic effects, impairment of enzymatic activities involved in detoxification processes, which, in turn, generate metabolic imbalances [3].

Furthermore, phenomena such as ataxia, insomnia, paraesthesia, narrowing of the visual field, dysarthria and hypoacusis have been related to exposure to this metal. The serious problem of the environmental toxicity of mercury, deriving from extractive activities and industrial use, has led to a series of initiatives by national and international organizations that deal with environmental protection and public health, committed to its progressive elimination from production cycles in all its forms [4].

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Fish consumption is the most important cause of exposure to ingestion of (methyl) mercury in animals and humans. Some large, terminal predatory and long-lived fish, such as tuna and swordfish, for example, may contain high levels of mercury [5]. FDA recommends for particular categories of people, such as children, women with the prospect of becoming pregnant or breastfeeding, not to consume more than 340 grams of low-mercury seafood (for example, shrimp, canned tuna, salmon or cod) per week. In the case of fish with a higher mercury content, such as fresh tuna or fish caught amateur in uncontrolled waters, the maximum recommended weekly consumption is reduced to 170 grams. However, large fish such as sharks and swordfish should be avoided [6].

A relatively rare metal that occurs naturally as a minor constituent of non-ferrous minerals. It is strongly associated with zinc, whose mines are a major source of pollution, together with the zinc, lead and copper smelting plants, the combustion of coal and the incineration of waste containing this metal [7]. Other uses are as a stabilizer of PVC plastics and as an electrode in nickel-cadmium rechargeable batteries [8]. Diet is the major source of exposure for the general population, even if smokers are particularly exposed: each cigarette contains 1 to 2 µg of cadmium and smoking one or more packets a day means doubling the daily intake of the element [9-12]. Crops grown on contaminated soils or irrigated with contaminated water may contain high concentrations of this element, as well as the meat of cattle that graze on cadmium-rich soils [13]. Cadmium in animal organisms accumulates in the liver and kidney; the latter, therefore, represent, in addition to the target organs in humans, also among the foods most contaminated by this metal [9, 12]. Other foods at risk are seafood, especially shellfish, which are strong cadmium accumulators. The main long-term effects of exposure to low concentrations are chronic lung and kidney diseases and emphysema, as well as damage to the cardiovascular and skeletal systems. Acute toxicity, due to ingestion of heavily contaminated food or drink, leads to a decrease in red blood cells and consequent damage to the bone marrow; calcium metabolism is modified, and this leads to weakening of the bone structure with consequent skeleton fractures and deformations [9].

Lead (Pb) is a nonessential trace element whose biogeochemical cycle has been greatly influenced by human activities, so much so that this metal is considered a ubiquitous pollutant. It is present in some types of paints, in lead-acid batteries and is used in the construction industry for its characteristics of resistance to corrosion and absorption of sound and radiation [14]. The main routes of exposure for humans are food and water: food contributes more to the daily dose, even if the lead present in the water is completely absorbed by the body, compared to that contained in food. The third source of exposure is air, which contributes less than about half of the diet to the introduction of the metal into the body. Almost all environmental exposure to lead concerns its inorganic forms. The metal absorbed is initially present in the blood, associated with the membrane of red blood cells or haemoglobin. At high doses, the excess amount penetrates into the soft tissues, including organs, and especially into the brain; ultimately, it is deposited in the bones, where it replaces calcium [15].

Exposures even to low doses of Pb cause anaemia in humans, inhibiting the synthesis of the heme group of haemoglobin and dysfunction of the reproductive system, such as a decrease in sperm count [16, 17]. With high doses, the central and peripheral nervous system is damaged and renal inflammation (nephritis) is one of the most common effects of long-term poisoning [18]. At the food level, it is believed that cereals, vegetables and drinking water contribute most to lead exposure for the majority of the European population [13]. Its carcinogenicity in humans has not yet found a clear demonstration: although numerous studies have been carried out on workers with occupational exposure to lead over time, the results that have emerged are controversial [19].

PFASs have been used since decades in a range of industrial and chemical application, leading to wide global distribution in the environment and tissues of organisms, including humans. Several studies towards PFASs indicated that perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS) are the chemicals with the greatest adverse effects on human health among the category [20]. Their chemical structures include a totally fluorinated carbon chain that is both hydrophobic and oleophobic, while carboxylic functional group, in the case of PFOA, and sulfonic group, in that of PFOS, add polarity. Due to these peculiarities, PFOA and PFOS are characterized by extremely chemical and thermal stability and high surface activity, with water and oil repellent properties [21].

Despite PFOA and PFOS production have been largely phased out in Europe and North America, the wide use of these compounds and their resistance to degradation processes have led to global distribution in the environment. Nowadays, in fact, they are ubiquitously present in air, water, soil, sediment, biota, outdoor and indoor dust, open ocean waters and even in human tissues [22-27]. Given the ubiquitous spread of these compounds, human exposure to PFAS is inevitable and continuous; people can be exposed mainly through food, for example, through the use of non-stick containers or with the consumption of food from contaminated environments. PFOS has been found in fish, crustaceans, molluscs and drinking water, while PFOA is present to a lesser extent in all foods, with the exception of those coming from environments characterized by specific sources of contamination: food exposure is, therefore a not negligible way, other potential sources are air and dust [1, 28, 29].

The highest concentrations were found in the liver of predators, suggesting that PFAS undergo biomagnification and bioaccumulation at the top of the food chain; a similar distribution therefore also affects the human diet. After absorption, the PFAS accumulates mainly in the blood, kidneys, liver and, to a lesser extent, in other body areas [30]. PFOA and PFOS are present in the blood of mothers and foetuses [31]. These molecules can then accumulate in maternal and foetal blood and lead to delays or changes in proper prenatal development, as they act as endocrine disruptors [32, 33]. Traces of these compounds have been found in breast milk, extending the risk even in the early stages of growth after birth [1, 28]. Many studies show the ability of these substances to interfere in the endocrine system in different ways: they can mimic or block other molecules produced by the body, alter hormone levels, and therefore have repercussions on the functions regulated by hormones [32-35].

The aim of this study is to compare different food schemes to determine any critical issues related to chemical contaminated food intake, using an easy tool for calculating the intake levels based on recent scientific literature.

Materials and Methods

The selection of specific diet plans was established since they reflected different lifestyles and dietary needs. In this study, three food schemes have been selected:

- i. a Mediterranean diet pattern (D1) (Table 1)
- ii. a fast weight-loss pattern (D2) (Table 2) and
- iii. a high-animal-protein low-carbohydrate food regimen (D3) (codified in Table 3).

Table 1: D1 - The Mediterranean diet weekly plan considered. Food quantities in grams.

Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
apple	300	almond	25	almond	25	apple	150	almond	25	almond	25	apple	150
banana	120	bread	140	aubergine	150	bread	200	apple	150	aubergine	150	banana	120
barley	80	broccoli	150	bread	100	cauliflower	150	bread	140	beans	50	barley	80
bread	210	cow milk	200	broccoli	150	chicken	120	cauliflower	150	bread	250	bread	140
cauliflower	150	Grana Padano cheese	30	yogurt	125	cow milk	200	egg	120	cod	150	cauliflower	150
cow milk	200	grapes	150	jam	40	anchovy	100	Grana Padano cheese	30	cow milk	200	cow milk	200
jam	40	honey	30	grapes	150	Grana Padano cheese	30	grape	150	escarole	150	jam	40
lentils	50	melba toast	30	ham	40	honey	30	honey	30	jam	40	lentils	50
lettuce	150	olive oil	20	mackarel	120	lettuce	150	melba toast	40	grape	150	melba toast	30
melba toast	30	pear	150	peas	50	nuts	25	olive oil	20	ham	40	nuts	25
nuts	25	red wine	125	potato	150	olive oil	20	pear	150	olive oil	20	olive oil	20
olive oil	20	ricotta cheese	80	rice	80	pear	150	tomato sauce	200	potato	150	turkey	100
salmon	100	tomato sauce	200	melba toast	40	red wine	125	wheat pasta	80	red wine	125	yogurt	125
yogurt	125	turkey	100	tomato sauce	200	tomato sauce	200	yogurt	125			courgette	150
İ		wheat pasta	80			wheat pasta	80	courgette	150				

Table 2: D2 - The fast weight loss diet weekly plan considered. Food quantities in grams.

Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
espresso		green tea	300	milk		milk	250	yogurt		milk	200	milk	200
white sugar	5	cookie	50	dried fruit muesli	30	melba toast	30	barley coffee	50	melba toast	15	melba toast	15
jam	30	grapefuit	300	kiwi	100	honey	10	white sugar	5	jam	30	jam	30
melba toast	50	bread	170	almond	10	apple	200	melba toast	30	apple	150	orange	150
yogurt	130	rocket salad	100	black rice	100	wheat pasta	80	wheat pasta	70	lettuce	150	cauliflower	100
dried fruit muesli	20	olive oil	20	tuna fish	60	fresh tomato	250	olive	20	mozzarella cheese	100	rice	30
black rice	80	beef	50	fresh tomato	200	anchovy	60	pepper	150	bread	30	olive oil	25
aubergine	200	apple	200	olive oil	20	kiwi	100	olive oil	10	olive oil	15	shrimps	100
mackarel	80	ricotta cheese	70	yogurt	130	almond	10	strawberry	160	banana	100	apple	100
olive oil	20	green beans	200	apricot	50	bread	50	red wine	125	spinach	150	salmon	120
almond	10			bread	80	olive oil	10	beef	120	turkey	100	mixed salad	120
apple	200			fennel	200	mozzarella cheese	80	carrot	130			bread	10
whole wheat bread	1 30			turkey	60	courgette	300	bread	60				
cucumber	200					asparagus	100	apple					
chicken	80												

Table 3: D3 - The high-animal-protein low-carbohydrate food regimen considered. The first table is referred to the spring/summer diet, the second to the autumn/winter diet. Food quantities in grams.

Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
bread	60	banana	110	apple	140	apple	140	bread	60	bread	70	apple	120
egg	55	beef	100	apricot	80	fresh tomato	40	chickpeas	60	chicken	150	beef	80
fresh cheese	80	boiled potato	200	basil	12	ham	30	fresh tomato	100	chocolate cake	80	bread	60
fresh peas	250	bread	60	bread	60	ham	70	green tea	5	generic fruits	120	butter	20
fresh tomato	50	carrot	100	dried fruit muesli	30	mixed salad	60	ham	80	mixed fruits	200	ice cream	90
oat flakes	30	chicken	150	ham	70	olive	20	jam	30	mixed salad	160	mixed fruits	120
olive oil	16	fennel	100	hazelnuts	30	olive oil	16	melba toast	25	oat flakes	30	mixed salad	80
Parmigiano	10	jam	30	mixed fruits	120	orange	100	mixed salad	50	olive oil	8	nuts	30
Reggiano Cheese													

peach	115	Grana Padano cheese	20	olive oil	41	pineapple	100	olive oil	16	sea bream	200	olive oil	8
tuna fish	50	green tea	5	Parmigiano Reggiano Cheese	17	ricotta cheese	60	Parmigiano Reggiano Cheese	15	yogurt	125	sauge	5
wheat pasta	70	lemon	20	Pecorino Romano Cheese	60	salmon	80	peach plum	115			stuffed pasta	150
yogurt	125	olive oil	16			strawberries	80		140			yogurt	125
		plum	140	pine nut	4	wheat pasta	70	rice	50				
		rocket salad	30	wheat pasta	60	whole wheat bread	100	vegetable pure	e 300)			
		melba toast	25	yogurt	125	breau		yogurt	125	,			
		yogurt	125										
Day 1		Day 2		Day 3		Day 4		Day 5		Day 6		Day 7	
apple	150	apple	150	barley coffee	125	apple	150	banana	200	carrot	10	artichoke	200
carrot	35	banana	200	carrot	100	carrot	30	beef	80	celery	8	aubergine	60
cauliflower	200	broccoli	150	egg	110	chicken	100	chickpeas	100	cod	150	banana	130
chickpeas	50	chicken dried	100	jam	30	curry	4	cod	170	fresh beans	25	boiled	200
fresh peas	40	fruit muesli	20	kiwi	90	espresso	7	dried fruit muesli	20	fresh peas	25	potatos carrot	35
green tea	5	fresh peas	150	melba toast	32	fresh peas	30	fresh tomato	100	fresh tomato	140	chocolate bar	20
kiwi	80	ham	60	millet	60	ham	20	green tea	7	kiwi	80	dried fruit muesli	20
olive oil	18	oat flakes	30	mozzarella cheese	80	olive oil	10	honey	7	leek mozzarella	18	fresh peas	40
Parmigiano Reggiano Cheese	5	olive oil	20	nuts	20	orange	250	linseed	15	cheese	120	fresh tomat	o70
pear	150	orange	150	olive oil	13	paprika	20	olive oil	13	olive oil	6	kiwi	80
rice	40	potato	200	Parmigiano Reggiano Cheese	25	Parmigiano Reggiano Cheese	5	plum	150	olive oil	6	oat flakes	30
ricotta cheese	30	rice	50	plum	150	pepper	100	rocket salad	50	onion	20	octopus	150
spinach	70	rice milk	125	pumpkin	250	pomegranate	100	rosemary	3	pizza	200	olive oil	13
spinach	50			yogurt	125	pumpkin	150	tangerine	140	pomegranate	100	olive oil	30
veal	100			courgette	300	rice	50	whole wheat bread	60	potato	30	onion	8
whole wheat bread	50					sea bream	150	yogurt	125	pumpkin	30	Parmigiano Reggiano Cheese	5
yogurt	125					tangerine	150			ricotta cheese	30	rice milk	125
courgette	75					wheat pasta	60			spinach	180	ricotta cheese	25
						whole wheat	50			tea	5	sea bream	130
						courgette	60			whole wheat bread	50	spinach	50
										yogurt	125	tangerine	150
												tomato	60
												sauce	
												wheat pasta	a 70
												courgette	75

The Mediterranean scheme proposed is a 2000 Kcal weight maintenance diet designed for a 75 kg sportsman, while D2 and D3 were 1200 Kcal

diets designed for a 70 kg woman. D3 was also proposed for a 60 kg woman to highlight the different inputs of contaminants in response to a

change of body mass. Tables 1-3 report detailed dietary plans considered in the study. D1 and D3, provided by nutritionists and adapted for individual tastes and needs, were two balanced diets that included an intake of carbohydrates from different sources, with the first one including mainly pasta, bread and legumes while the second characterized by consumption of various cereals according to the food pyramid.

In order to estimate the dietary contribution to the intake of contaminants, UltraBio®, the App, completely free of charges, developed by the Bioscience Research Center (BsRC), was used. UltraBio® has been developed by researchers specialized in the fields of food safety, ecotoxicology, risk assessment, environmental chemical and food contamination. The app allows to estimate, on a statistical basis, the quantities of some chemical substances potentially dangerous to health taken with the diet and to calculate the percentage of intake compared to the safety thresholds for the specific substance defined by EFSA. The basic food categories are those foreseen by the food consumption database of the European EFSA population, integrated with other foods where consolidated and scientifically reliable data are available. Chemicals considered are mercury, cadmium, lead, PFOA and PFOS. The app allows to assess weekly levels of contaminants, considering body mass and in relation to the last tolerable intake values established by EFSA. The latter are expressed on a weekly basis (tolerable weekly intakes, TWI); however, to facilitate user management of the instrument, in the UltraBio® app, these limits have been calculated on a daily basis, dividing the TWI by 7 and indicating it as 'TDI7' (tolerable daily intake deriving from TWI divided by seven) to distinguish it from a real TDI.

Weekly thresholds were also related to daily thresholds in order to monitor day-to-day contaminant intake. Each diet menu was manually entered into the app, as well as single portion sizes expressed in grams.

Results and Discussion

The three diet plans considered led to very different results in terms of contaminants' intake. At first, what emerged from the weekly reports of the three food regimes was considered; then, what could be the critical points and strengths of each diet plan (Table 4) and (Figure 1) show the results obtained with the selected diet plans.

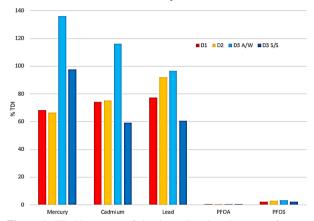


Figure 1: Weekly reports of the three diet plans in terms of percent contaminants intake in relation to TDIs. D3 is divided into autumn/winter (A/W) and spring/summer (S/S).

Table 4: Weekly reports of the three diet plans considered in terms of percent contaminants intake in relation to TDIs. D3 is divided into autumn/winter (A/W) and spring/summer (S/S).

DIET		MERCURY (%)	CADMIUM (%)	LEAD (%)	PFOA (%)	PFOS (%)
D1		68.24	74.29	77.51	0.15	2.18
D2		66.49	75.31	92.25	0.24	3.09
D2	A/W	136.27	116.06	96.47	0.21	3.37
D3	S/S	97.51	59.06	60.71	0.19	2.40

I D1-Mediterranean Diet

Following the Mediterranean diet plan (including three to nine serves of vegetables, half to two serves of fruit, one to thirteen serves of cereals and up to eight serves of olive oil daily), all the contaminants remain under the safety thresholds. The highest values were observed for Pb and Cd with almost 80% of 'TDI7'. To identify the cause of this datum, it is necessary to investigate on daily reports, which the UltraBio® app allows to consult. It has been observed that the influence is mainly due to foods such as wheat pasta for cadmium and some types of fruit such as grapes for lead.

II D2-Fast Weight-Loss Diet

Although the values remain below the threshold levels, following this scheme, Pb's levels are very close to the maximum and the Cd's near 80%. In this case, it has been observed, by daily the report, that cadmium is easily influenced by some kinds of vegetables that require the use of a lot of water for their cultivation or some crustacean meals. Contrariwise,

lead is brought by particular beverages, like barley or green tea infusions, along the whole week.

III D3-High-Animal-Protein Low-Carbohydrate Food Regimen

In this case, the diet pattern has been differentiated according to seasonality and the taste of the target subject and shows different results between A/W and S/S. In both cases, mercury is at the highest value and in A/W over the threshold, as well as cadmium that, on the other hand, is of lesser value in S/S. Daily intake shows that the highest values during the winter were mainly due to the frequency and quantity of fish consumed and the type available during the winter period that change drastically in S/S, which increase the number of edible species and reduce the quantity in favour of cold dishes based on cereal, cheese and vegetables.

IV Comparison between Diet Plans and SWOT Analysis

Mediterranean diet results in the healthiest one with the lower value of contaminants and good food variability and in agreement with other authors, the quantity of foods appears to impact health outcomes. The D2 diet appears good, but it does not present variability among foods and the food scheme is very repetitive as well as poor in animal proteins. D3 resulted to be the less healthy diet, although this can be explained by the fact that this scheme is very subjective. Indeed, it is studied for the food and sporting habits of the subject for which it is intended. Considering D3_A/W_Day 7 were subject eat fish both for lunch (130g of withe fish) and dinner (150g of octopus), it is observed that Hg, Cd and Pb are all above the threshold. In light of the fact, the subject should not discontinue eating fish but only has to defer it during the week and maybe change the species, as happens for the S/S.

Recurring elements are high levels of Cd and Pb and very low levels of PFASs. Cd and Pb levels, except for cases in which fish raise these values, are influenced by some type of vegetables like carrots or green beans. For PFASs, in general, and with minimal exceptions, only animal foods contribute to the intake and the latter is always far from levels considered harmful to health.

Conclusion

The D1 Mediterranean diet scheme was found to be the one with the lowest intake of all contaminants, which, in any case, remains within the safety limits by a large margin. Also, from SWOT analysis, considering the overall characteristics of the nutritional plans considered, the Mediterranean diet was preferable. At the opposite extreme, the D3 diet, with a high protein content formulated for athletes, shows the exceeding of the limits for two metals and critical values for the third. Recurring elements are high levels of Cd and Pb and very low levels of PFASs, for all the plans considered. The advantages of this approach, to be used in addition to the elaboration of a nutritionally balanced and personalized diet plan, are mainly represented by the possibility of having a personalized risk assessment of the intake of important food contaminants. This makes the estimate more consistent with reality, even in cases of very special diets. Furthermore, being able to modulate the assessment day by day, on the basis of real consumption data, provides a tool for the prevention of exposures that, over time, could put health at risk.

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REFERENCES

- Guerranti C, Perra G, Corsolini S, Focardi SE (2013) Pilot study on levels of perfluorooctane sulfonic acid (PFOS) and perfluorooctanoic acid (PFOA) in selected foodstuffs and human milk from Italy. Food Chem 140: 197-203. [Crossref]
- Rosenfeld PE, Feng LGH, Andrew W (2011) Risks of Hazardous Wastes. Mercury BPA, and Pesticides in Food. Elsevier 223-235.

- Grandjean P, Weihe P, White RF, Debes F, Araki S et al. (1997)
 Cognitive deficit in 7-year-old children with prenatal exposure to methylmercury. Neurotoxicol Teratol 19: 417-428. [Crossref]
- Eisler R (2004) Mercury hazards from gold mining to humans, plants, and animals. Rev Environ Contam Toxicol 181: 139-198. [Crossref]
- Hightower JM, Moore D (2003) Mercury levels in high-end consumers of fish. Environ Health Perspect 111: 604-608. [Crossref]
- U.S. Department of Health and Human Services and U.S. Department of Agriculture (2015) 2015-2020 Dietary Guidelines for Americans. 8th Edition.
- Burger J (2008) Assessment and management of risk to wildlife from cadmium. Sci Total Environ 389: 37-45. [Crossref]
- Becka F, Rüetschib P (2000) Rechargeable batteries with aqueous electrolytes. Electrochimica Acta 45: 2467.
- Perelló G, Llobet JM, Gómez Catalán J, Castell V, Centrich F et al. (2014) Human health risks derived from dietary exposure to toxic metals in Catalonia, Spain: temporal trend. *Biol Trace Elem Res* 162: 26-37. [Crossref]
- Aoki Y, Yee J, Mortensen ME (2017) Blood cadmium by race/hispanic origin: The role of smoking. *Environ Res* 155: 193-198. [Crossref]
- Fatima G, Raza AM, Hadi N, Nigam N, Mahdi AA (2019) Cadmium in Human Diseases: It's More than Just a Mere Metal. *Indian J Clin Biochem* 34: 371-378. [Crossref]
- Frank JJ, Poulakos AG, Tornero Velez R, Xue J (2019) Systematic review and meta-analyses of lead (Pb) concentrations in environmental media (soil, dust, water, food, and air) reported in the United States from 1996 to 2016. Sci Total Environ 694: 133489. [Crossref]
- Abedin MJ, Cotter Howells J, Meharg AA (2002) Arsenic uptake and accumulation in rice (*Oryza sativa* L.) irrigated with contaminated water. *Plant Soil* 240: 311-319.
- Stumm W, Morgan JJ (1995) Aquatic Chemistry: Chemical Equilibria and Rates in Natural Waters, 3rd Edition.
- Pizzol M, Thomsen M, Andersen MS (2010) Long-term human exposure to lead from different media and intake pathways. Sci Total Environ 408: 5478-5488. [Crossref]
- Walter PB, Knutson MD, Paler Martinez A, Lee S, Xu Y et al. (2002)
 Iron deficiency and iron excess damage mitochondria and mitochondrial DNA in rats. *Proc Natl Acad Sci USA* 99: 2264-2269.
 [Crossref]
- De Rosa M, Zarrilli S, Paesano L, Carbone U, Boggia B et al. (2003)
 Traffic pollutants affect fertility in men. Hum Reprod 18: 1055-1061.
 [Crossref]
- Gennart JP, Bernard A, Lauwerys R (1992) Assessment of thyroid, testes, kidney and autonomic nervous system function in lead-exposed workers. Int Arch Occup Environ Health 64: 49-57. [Crossref]
- Rahman Z, Singh VP (2019) The relative impact of toxic heavy metals (THMs) (arsenic (As), cadmium (Cd), chromium (Cr)(VI), mercury (Hg), and lead (Pb)) on the total environment: an overview. *Environ Monit Assess* 191: 419. [Crossref]
- EFSA Panel on Contaminants in the Food Chain (CONTAM), Knutsen HK, Alexander J, Barregård L, Bignami M et al. (2018) Risk to human health related to the presence of perfluorooctane sulfonic acid and perfluorooctanoic acid in food. EFSA J 16: e05194. [Crossref]
- Post GB, Cohn PD, Cooper KR (2012) Perfluorooctanoic acid (PFOA), an emerging drinking water contaminant: a critical review of recent literature. *Environ Res* 116: 93-117. [Crossref]

- Kannan K, Corsolini S, Falandysz J, Fillmann G, Kumar KS et al. (2004) Perfluorooctanesulfonate and related fluorochemicals in human blood from several countries. *Environ Sci Technol* 38: 4489-4495. [Crossref]
- Kannan K, Tao L, Sinclair E, Pastva SD, Jude DJ et al. (2005) Perfluorinated compounds in aquatic organisms at various trophic levels in a Great Lakes food chain. *Arch Environ Contam Toxicol* 48: 559-566. [Crossref]
- Perra G, Focardi SE, Guerranti C (2013) Levels and spatial distribution
 of perfluorinated compounds (PFCs) in superficial sediments from the
 marine reserves of the Tuscan Archipelago National Park (Italy). *Mar*Pollut Bull 76: 379-382. [Crossref]
- Renzi M, Guerranti C, Giovani A, Perra G, Focardi SE (2013) Perfluorinated compounds: levels, trophic web enrichments and human dietary intakes in transitional water ecosystems. *Mar Pollut Bull* 76: 146-157. [Crossref]
- ATSDR (Agency for Toxic Substances and Disease Registry) (2015)
 Draft Toxicological Profile for Perfluoroalkyls.
- Pasanisi E, Cortés Gómez AA, Pérez López M, Soler F, Hernández Moreno D et al. (2016) Levels of perfluorinated acids (PFCAs) in different tissues of Lepidochelys olivacea sea turtles from the Escobilla beach (Oaxaca, Mexico). Sci Total Environ 572: 1059-1065. [Crossref]
- Guerranti C, Cau A, Renzi M, Badini S, Grazioli E et al. (2016)
 Phthalates and perfluorinated alkylated substances in Atlantic bluefin tuna (Thunnus thynnus) specimens from Mediterranean Sea (Sardinia, Italy): Levels and risks for human consumption. *J Environ Sci Health B* 51: 661-667. [Crossref]

- Zhang B, He Y, Huang Y, Hong D, Yao Y et al. (2020) Novel and legacy poly- and perfluoroalkyl substances (PFASs) in indoor dust from urban, industrial, and e-waste dismantling areas: The emergence of PFAS alternatives in China. *Environ Pollut* 263: 114461. [Crossref]
- Giari L, Guerranti C, Perra G, Lanzoni M, Fano EA et al. (2015)
 Occurrence of perfluorooctanesulfonate and perfluorooctanoic acid and histopathology in eels from north Italian waters. *Chemosphere* 118: 117-123. [Crossref]
- Cai D, Li QQ, Chu C, Wang SZ, Tang YT et al. (2020) High transplacental transfer of perfluoroalkyl substances alternatives in the matched maternal-cord blood serum: Evidence from a birth cohort study. Sci Total Environ 705: 135885. [Crossref]
- Caserta D, Ciardo F, Bordi G, Guerranti C, Fanello E et al. (2013)
 Correlation of endocrine disrupting chemicals serum levels and white blood cells gene expression of nuclear receptors in a population of infertile women. *Int J Endocrinol* 2013: 510703. [Crossref]
- La Rocca C, Tait S, Guerranti C, Busani L, Ciardo F et al. (2015)
 Exposure to Endocrine Disruptors and Nuclear Receptors Gene
 Expression in Infertile and Fertile Men from Italian Areas with
 Different Environmental Features. Int J Environ Res Public Health 12:
 12426-12445. [Crossref]
- Predieri B, Iughetti L, Guerranti C, Bruzzi P, Perra G et al. (2015) High Levels of Perfluorooctane Sulfonate in Children at the Onset of Diabetes. *Int J Endocrinol* 2015: 234358. [Crossref]
- Guzmàn MM, Clementini C, Pérez Cárceles MD, Rejón SJ, Cascone A et al. (2016) Perfluorinated carboxylic acids in human breast milk from Spain and estimation of infant's daily intake. Sci Total Environ 544: 595-600. [Crossref]