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Blood screening for heavy metals and organic pollutants in cancer patients exposed to toxic waste in southern Italy: A pilot study

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Abstract

In Italy, in the eastern area of the Campania region, the illegal dumping and burning of waste have been documented, which could potentially affect the local population's health. In particular, toxic waste exposure has been suggested to associate with increased cancer development/mortality in these areas, although a causal link has not yet been established. In this pilot study, we evaluated blood levels of toxic heavy metals and persistent organic pollutants (POPs) in 95 patients with different cancer types residing in this area and in 27 healthy individuals. While we did not find any significant correlation between the blood levels of POPs and the provenance of the patients, we did observe high blood concentrations of heavy metals in some municipalities, including Giugliano, where many illegal waste disposal sites have previously been documented. Our results showed that patients with different cancer types from Giugliano had higher blood levels of heavy metals than healthy controls. Despite the obvious limitations of this exploratory study, our preliminary observations encourage further research assessing the possible association between exposure to hazardous waste, increased blood metals, and increased risk of cancer.

KEYWORDS
cancer, environmental pollution, heavy metals, land of fires, POPs

Abbreviations: As, arsenic; Cd, cadmium; GC-MS, gas chromatography-mass spectrometry; Hg, mercury; IARC, International Agency for Research on Cancer; ICP-OES, inductively coupled plasma atomic emission spectrometry; MAPK, mitogen-activated protein kinase; NF-kB10, nuclear factor kB10; Pb, lead; PBDE, polybrominated diphenyl ethers; PCBs, polychlorobiphenyls; PCDD, polychlorinated dibenzo-*p*-dioxins; PCDF, polychlorinated dibenzofurans; POPs, persistent organic pollutants; WHO, World Health Organization.

1 | INTRODUCTION

Toxic environmental agents, to which anyone is involuntarily exposed, represent nonnegligible oncogenic risk factors and, therefore, the environmental contamination has become a theme of primary importance worldwide (Craft et al., 2006). However, to date, mainly owing to insufficient information about the levels and types of patients' exposure, the precise role of toxic agents in the genesis of tumors and the determination of the fraction of overall cancers attributable to pollution remain debated issues.

The International Agency for Research on Cancer (IARC) classified chemical and physical agents on the basis of their carcinogenic potential, identifying numerous substances as "certainly" carcinogenic to humans (https://monographs.iarc.fr/agents-classified-by-the-iarc/). To this category belong dioxins, benzene, furans, persistent organic pollutants (POPs), and heavy metals, which are all able to trigger complex and specific cellular pathways, modifying the genetic and epigenetic structure of the cells (Belpomme, Irigaray, Hardell, et al., 2007; Belpomme, Irigaray, Sasco, et al., 2007).

Although several studies focused on the ability of heavy metals and POPs to alter the functionality of the endocrine system (Beszterda & Franski, 2018; Buha et al., 2018; Kranthi Kumar, Uma Devi, & Neeraja, 2018; Paschoalini, Savassi, Arantes, Rizzo, & Bazzoli, 2019; Saxena, Purchase, Mulla, Saratale, & Bharagava, 2020), their involvement in cancer development is also increasingly emerging (Cao, Fan, Li, & Xiao, 2019; Leng et al., 2016; Rehman, Fatima, Waheed, & Akash, 2018).

Heavy metals are natural components of the earth's crust, which, if released into the environment, can persist for many years (Tchounwou, Yedjou, Patlolla, & Sutton, 2012; Wu et al., 2016). Metals released by incinerators, combustion of gasoline, foundries, paints, insecticides, and agricultural products can be absorbed through inhalation, skin contact or ingestion (Tchounwou et al., 2012; Yousaf et al., 2016). They can induce acute intoxications, the severity of which depend on the type of the metal accumulated, the duration of the exposure, and the individual genetic susceptibility (Jaishankar, Tseten, Anbalagan, Mathew, & Beeregowda, 2014; Tchounwou et al., 2012). Several metals have been classified as certain or probable carcinogens by IARC (https://monographs.iarc.fr/agents-classified-by-the-iarc/). The most toxic elements are arsenic (As), cadmium (Cd), cobalt (Co), chromium (Cr), copper (Cu), mercury (Hg), manganese (Mn), nickel (Ni), lead (Pb), and thallium (Tl), with the majority of them being classified as certainly or probably carcinogenic (Co, Cr, Ni, As, Cd, Pb, Hg) and/or toxic for the central nervous system (Hg, Pb, As); for liver and kidneys (Hg, Pb, Cd, Cu); for skin, bones, and teeth (Ni, Cd, Cu, Cr) (Jarup, 2003; https://monographs.iarc.fr/agents-classified-by-the-iarc/). Heavy metal carcinogenesis implicates principally the induction of oxidative stress and the interference with DNA repair mechanisms, by affecting, for instance, the activity of transcription factors involved in these processes, such as p53 or nuclear factor kB10 (NF-kB10) (Dally & Hartwig, 1997; Fatur, Lah, & Filipic, 2003; Valko, Rhodes, Moncol, Izakovic, & Mazur, 2006; Wang, Leonard, Ye, Ding, & Shi, 2000). Metals can also have a mutagenic effect by directly interacting with DNA and forming DNA-DNA and DNA-protein cross-links (Donahue et al., 1990). Moreover, metals can also activate mitogenic signals and perturb signal transduction pathways, such as that of mitogen-activated protein kinase (MAPK), thus promoting cancer development (Cavigelli et al., 1996; Chen, Zhu, & Chan, 2014; Yao & Costa, 2014). Also, metals can impact on epigenetic modulation of gene expression (Wise, Wang, Zhang, & Shi, 2017), with an example being the As-induced DNA hypomethylation (Zhao, Young, Diwan, Coogan, & Waalkes, 1997). Finally, some heavy metals are considered metalloestrogens, which can induce the development of estrogen-dependent diseases, including breast and endometrial cancers (Aquino, Sevigny, Sabangan, & Louie, 2012; Johnson et al., 2003; Martinez-Campa et al., 2006; Rzymski et al., 2014). So, overall, increasing evidence has demonstrated that metals can act as carcinogens through different mechanisms.

POPs are widely dispersed environmental contaminants, including, among others, polybrominated-diphenyl ethers (PBDEs), polychlorobiphenyls (PCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs), which are all characterized by resistance to biodegradation, environmental persistence, bioaccumulation in the food chain, and toxicity for human health (El-Shahawi, Hamza, Bashammakh, & Al-Saggaf, 2010; Lee, Kim, Jacobs, & Lee, 2017). POPs were largely used in the industry, and, despite the ban on their use by the Stockholm Convention on Persistent Organic Pollutants in 2001, they can still be released into the environment mainly owing to the industrial emission or incineration of municipal and industrial waste (Esposito et al., 2009; Hung, Katsoyiannis, & Guardans, 2016; Trivedi & Majumdar, 2013). The World Health Organization (WHO) raised awareness about POP impact on environment and human health, thus encouraging several studies, which demonstrated the association of the exposure to these compounds with cancer development, reproductive problems, neurobehavioral disorders, abnormalities in fetal development, immune alteration, and disruption of hormones (Darras, 2008; Gregoraszczuk & Ptak, 2013; Hardell, Bavel, Lindstrom, Eriksson, & Carlberg, 2006; Lim et al., 2017; Tran & Miyake, 2017).

Overall, air pollution has been found associated to different acute and chronic diseases, including neoplastic pathologies, and to premature mortality (Belpomme, Irigaray, Sasco et al., 2007; Goldman & Dominici, 2019; Lelieveld, Evans, Fnais, Giannadaki, & Pozzer, 2015; Martuzzi, Mitis, Biggeri, Terracini, & Bertollini, 2002). In Italy, a dramatic example of this situation is represented by several municipalities of the provinces of Naples and Caserta, in the Campania region. Illegal dumping and burning of waste in this region have caused an immense environmental damage, which might have affected the local population's health (Altavista et al., 2004; Cembalo et al., 2019; Mazza et al., 2018; Mazza, Piscitelli, Neglia, Della Rosa, & Iannuzzi, 2015; Pirastu et al., 2013; Rivezzi et al., 2013; Senior & Mazza, 2004; Zona et al., 2019). These areas have been referred to as the "land of fires," owing to the common practice of waste burning

(Mazza et al., 2018). Public concern regarding the Campania "waste emergency" has triggered environmental monitoring studies, documenting the critical situation in this region. For instance, an important biomonitoring study funded by the Italian National Institute of Health, the "SEBIOREC Project," evaluated the levels of environmental contaminants in blood and human milk in more than 850 healthy donors from Campania areas in the years 2008 and 2009 and suggested the possible need of interventions aimed to improve health conditions in some municipalities (De Felip et al., 2014). Indeed, toxic agent accumulation has been suggested to associate with a significant increase in cancer development and mortality in these areas (Altavista et al., 2004; Comba et al., 2006, 2014; Crispo et al., 2013; Di Lorenzo, Federico, De Placido, & Buonerba, 2015; Fazzo et al., 2011; Martuzzi et al., 2009; Petrosino et al., 2018; Zona et al., 2019).

Despite the increasing recognition of the association between exposure to environmental pollution and the development of tumors and although at present the Campania region is probably the most investigated area in Italy for the environmental contamination, the establishment of a causal link between toxic waste exposure and cancer development/mortality in this area is hampered by several confounding factors, such as unsuitable screening procedures and incorrect lifestyles, including smoking, excessive alcohol assumption, and unhealthy diet (leading to overweight and obesity), which can all increase the risk of cancer development (Barba et al., 2011; Di Lorenzo et al., 2015; Fazzo et al., 2008; Pirastu et al., 2013). Therefore, further epidemiological studies in the Campania region are urgently needed to estimate the levels of substances that are toxic to human health, by acting either alone or in combination (Belpomme, Irigaray, Hardell et al., 2007), and to exclude confounding risk factors.

In this pilot study we evaluated the blood levels of toxic heavy metals (As, Hg, Cd, Pb) and POPs (PCB, PCDD, PBDE, PCDF) in 95 patients with different cancer types residing in municipalities of the provinces of Naples and Caserta and in 27 healthy individuals, to preliminarily explore the possible association between the levels of these substances and cancer development.

2 | METHODS

2.1 | Patients

The research was carried out on two groups of volunteers enrolled from February 2018 to December 2018: (a) 95 patients with different cancer types, an age range of 5–92 years, of both sexes, and residing in municipalities of the provinces of Naples and Caserta (Table 1); (b) 27 healthy individuals of both sexes, with an age range of 17–86 years, and residing not only in these areas but also in municipalities where illegal waste dumping is not documented (Table 2). Cancer patients with a history of professional exposure to carcinogens or with well-established genetic/biologic risk factors for cancer, including mutations and oncogenic virus infections, were excluded from the study. After obtaining informed consent, the

TABLE 1 Patients' characteristics

Sex	Age	Cancer type	Place of residence	Province
M	15	Medulloblastoma	Acerra	NA
F	11	Medulloblastoma	Acerra	NA
F	43	Breast cancer	Acerra	NA
F	56	Peritoneal mesothelioma	Acerra	NA
F	55	Breast cancer	Acerra	NA
M	80	Lung cancer	Acerra	NA
F	31	Breast cancer	Acerra	NA
F	45	Breast cancer	Acerra	NA
M	45	Colon cancer	Acerra	NA
M	59	Gastric cancer	Afragola	NA
F	43	Breast cancer	Bacoli	NA
F	47	Breast cancer	Bacoli	NA
F	44	Optic nerve glioma	Boscotrecase	NA
F	28	Thyroid cancer	Caivano	NA
M	58	Kidney cancer	Caivano	NA
F	51	Breast cancer	Caivano	NA
F	48	Multiple myeloma	Cardito	NA
F	46	Leukemia	Casalnuovo	NA
M	34	Lymphoma	Casoria	NA
M	44	Kidney cancer	Castel Volturno	CE
M	26	Lymphoma	Castel Volturno	CE
M	5	Anaplastic ependymomas	Castel Volturno	CE
F	64	Bladder cancer	Frattamaggiore	NA
F	59	Breast cancer	Frattamaggiore	NA
F	55	Breast cancer	Frattamaggiore	NA
F	47	Breast cancer	Frattamaggiore	NA
M	38	Bladder cancer	Frattamaggiore	NA
F	57	Non-Hodgking lymphoma	Frattamaggiore	NA
F	47	Breast cancer	Frattamaggiore	NA
M	45	Melanoma	Frattamaggiore	NA
M	68	Colon cancer	Frattaminore	NA
F	50	Optic nerve glioma	Giugliano	NA
M	62	Colon cancer	Giugliano	NA
M	34	Testicular cancer	Giugliano	NA
F	59	Breast cancer	Giugliano	NA
M	60	Liposarcoma	Giugliano	NA
F	54	Breast cancer	Giugliano	NA
F	50	Breast cancer	Giugliano	NA
F	45	Breast cancer	Giugliano	NA
F	8	Leukemia	Giugliano	NA
M	63	Glioblastoma	Giugliano	NA
F	47	Breast cancer	Gricignano di Aversa	CE

(Continues)

TABLE 1 (Continued)

Sex	Age	Cancer type	Place of residence	Province
M	43	Thyroid cancer	Marigliano	NA
M	10	Medulloblastoma	Marigliano	NA
F	47	Ovaric cancer	Melito di Napoli	NA
F	6	Brain cancer	Melito di Napoli	NA
F	54	Kidney cancer	Melito di Napoli	NA
F	71	Breast cancer	Melito di Napoli	NA
M	73	Bladder cancer	Melito di Napoli	NA
F	50	Colon cancer	Melito di Napoli	NA
F	49	Breast cancer	Mondragone	CE
F	55	Bladder cancer	Mondragone	CE
F	55	Chronic myeloid leukemia	Mondragone	CE
M	32	Hodgking lymphoma	Mondragone	CE
F	54	Colon cancer	Mugnano di Napoli	NA
F	66	Breast cancer	Naples	NA
M	45	Testicular cancer	Naples	NA
M	43	Testicular cancer	Naples	NA
F	52	Breast cancer	Naples	NA
M	56	Prostate cancer	Naples	NA
F	63	Head and neck cancer	Naples	NA
M	46	Thyroid cancer	Naples	NA
F	11	Osteosarcoma	Naples	NA
F	62	Breast cancer	Naples	NA
M	5	Medulloblastoma	Naples	NA
F	52	Cutaneous Bowen's disease	Naples	NA
M	63	Bladder cancer	Naples	NA
F	48	Breast cancer	Naples	NA
F	72	Breast cancer	Naples	NA
M	92	Colon cancer	Naples	NA
F	62	Breast cancer	Naples	NA
F	56	Breast cancer	Naples	NA
F	72	Breast cancer	Naples	NA
M	71	Non-Hodgking lymphoma	Naples	NA
F	38	Hodgking lymphoma	Orta di Atella	CE
F	44	Breast cancer	Orta di Atella	CE
F	67	Breast cancer	Orta di Atella	CE
M	60	Lymphoma	Orta di Atella	CE
F	27	Myeloproliferative syndrome	Pianura	NA
F	15	Sarcoma	Pomigliano D'Arco	NA
F	29	Head and neck cancer	Portici	NA
F	36	Breast cancer	Pozzuoli	NA
F	52	Chronic myeloid leukemia	Qualiano	NA

(Continues)

TABLE 1 (Continued)

Sex	Age	Cancer type	Place of residence	Province
F	54	Breast cancer	Qualiano	NA
F	61	Breast cancer	Qualiano	NA
M	80	Prostate cancer	Qualiano	NA
F	64	Breast cancer	Quarto	NA
F	47	Peritoneal mesothelioma	Santa Maria a Vico	CE
F	61	Bladder cancer	Santa Maria a Vico	CE
F	59	Lung cancer	Santa Maria a Vico	CE
M	71	Bladder cancer	Santa Maria Capua a Vetere	CE
M	67	Non-Hodgking lymphoma	Santa Maria Capua a Vetere	CE
F	44	Breast cancer	Torre del Greco	NA
F	54	Breast cancer	Villa Literno	CE
M	62	Kidney cancer	Villa Literno	CE

Abbreviations: CE, Caserta; F, female; M, male; NA, Naples.

concentration of four heavy metals (As, Cd, Hg, Pb) and four POPs (PCBs, PCDDs, PBDEs, PCDFs) was determined in blood samples from all the 122 participants. All analyses were performed at the Department of Pharmacy of the University "Federico II" of Naples.

2.2 | Sample preparation and inductively coupled plasma atomic emission spectrometry (ICP-OES) for heavy metal level determination

For the determination of the blood concentration of heavy metals, all the laboratory equipment and containers were first rinsed with 10% HNO_3. Then, acid de-composition in the microwave, biological sample digestion, and ICP-OES were performed as previously described (Fathabad et al., 2018). The substance concentrations were determined using a linear calibration curve obtained by measuring the absorbance of standard solutions.

2.3 | Sample preparation and gas chromatography-mass spectrometry (GC-MS) for POP level determination

For the determination of the blood concentration of POPs, partition with acetonitrile, sulfur elimination, purification by silica gel chromatography, and GC-MS were performed as previously described (Petrosino et al., 2018).

2.4 | Statistical analysis

Statistical analysis was performed using the XLSTAT package (Addinsoft, version 2019.3.2). To compare average blood concentrations of the substances under study, we used Welch's t test. $p < .05$ was considered to be statistically significant.

TABLE 2 Healthy individuals' charachteristics

Sex	Age	Place of residence	Province
M	23	Acerra	NA
M	17	Acerra	NA
M	17	Acerra	NA
M	26	Avellino	AV
F	29	Avellino	AV
F	35	**Avellino**	**AV**
M	37	**Avellino**	**AV**
F	28	**Benevento**	**BN**
M	42	Caivano	NA
F	57	Carinaro	CE
M	23	Grumo Nevano	NA
F	56	Grumo Nevano	NA
M	64	Melito	NA
M	46	**Monteforte**	**AV**
M	35	Naples	NA
F	26	Naples	NA
M	57	Naples	NA
F	25	Naples	NA
M	33	Orta di Atella	CE
M	28	Ottaviano	NA
M	51	Pianura	NA
F	86	Ponticelli	NA
M	48	Pozzuoli	NA
M	34	**Rome**	**RM**
M	25	Sant'Arpino	CE
F	29	**Scala**	**SA**
F	30	**Vico Equense**	**NA**

Note: Municipalities where illegal waste dumping is not documented are indicated in bold fonts.
Abbreviations: A, Avellino; BN, Benevento; CE, Caserta; F, female; M, male; NA, Naples; RM, Rome; SA, Salerno.

3 | RESULTS

3.1 | Geographical distribution of hematic concentrations of heavy metals in the "land of fires"

Our analysis of blood concentrations of POPs (PBDE, PCBs, PCDD, PCDF) in the cohort of individuals from municipalities of the provinces of Naples and Caserta revealed that these compounds were homogeneously and stochastically distributed in all samples (data not shown).

Therefore, we focused our further analyses only on heavy metals (As, Cd, Hg, Pb). To represent the geographical distribution of the hematic levels of heavy metals in the "land of fires," we analyzed the average blood concentrations of these agents in municipalities of this area where at least three individuals were sampled (total individuals = 89). We observed that the overall concentration of heavy metals in blood samples of individuals from Pianura ($n = 3$), Giugliano ($n = 10$), Qualiano ($n = 4$), and Castel Volturno ($n = 3$) largely exceeded that of the other localities (Figure 1). In particular, higher blood levels of Cd and Hg were observed in all four aforementioned municipalities, whereas higher blood levels of As were found only in Pianura. Moreover, Acerra ($n = 11$) showed higher Pb blood levels. Using the measurements on individuals from Naples ($n = 23$) as control values, the only statistically significant differences were observed for Giugliano, with p = .03 for overall metal concentration and $p = .03$ and $p = .04$ for Cd and Hg, respectively (Welch's *t* test). For the other municipalities, the observed differences did not achieve statistical significance, probably because of the very small number of patients available for each of these localities.

3.2 | Blood levels of heavy metals in cancer patients residing in Giugliano were higher than in pooled healthy individuals

Since people leaving in Giugliano were the only to deviate significantly from our control sample (individual in Naples), we compared blood concentrations of As, Cd, Hg, and Pb between cancer patients residing in Giugliano and two more groups: pooled healthy individuals and pooled cancer patients, all living in localities outside Giugliano (no healthy controls from Giugliano were available). Our analyses showed that in patients from Giugliano, blood levels of Cd and Hg, as well as those of overall metals, were statistically higher than in healthy controls (Figure 2). Conversely, no statistically significant differences were observed versus the cancer patient group, except for As levels that were lower in patients from Giugliano (Figure 2).

Notably, blood levels of As and Cd were higher than the maximum reference value (according to ISTISAN 10/22, National Institute of Health) in all patients from Giugliano and the Hg levels were higher than the reference values in 9 of 10 of these patients (data not shown). Moreover, overall, the average blood concentrations of As, Cd, and Hg were higher than the reference values for all the groups analyzed (Figure 2).

4 | DISCUSSION

In recent decades, different studies have focused on the potential impact of illegal waste disposal on human health in the so-called "land of fires" in Campania (Altavista et al., 2004; Cembalo et al., 2019; Mazza et al., 2018, 2015; Pirastu et al., 2013; Rivezzi et al., 2013; Senior & Mazza, 2004; Zona et al., 2019).

In this study we performed a blood screening for heavy metals (As, Hg, Cd, Pb) and POPs (PCB, PCDD, PBDE, PCDF), which have been classified as carcinogens by IARC (https://monographs.iarc.fr/agents-classified-by-the-iarc/), in a cohort of 95 cancer patients residing in municipalities of the "land of fires" and in 27 healthy individuals, living not only in these areas but also in municipalities where illegal waste dumping is not documented.

Although exposure to pollutants is often investigated through noninvasive urine tests, these substances are rapidly degraded in urine samples, thus resulting in altered concentrations. Moreover,

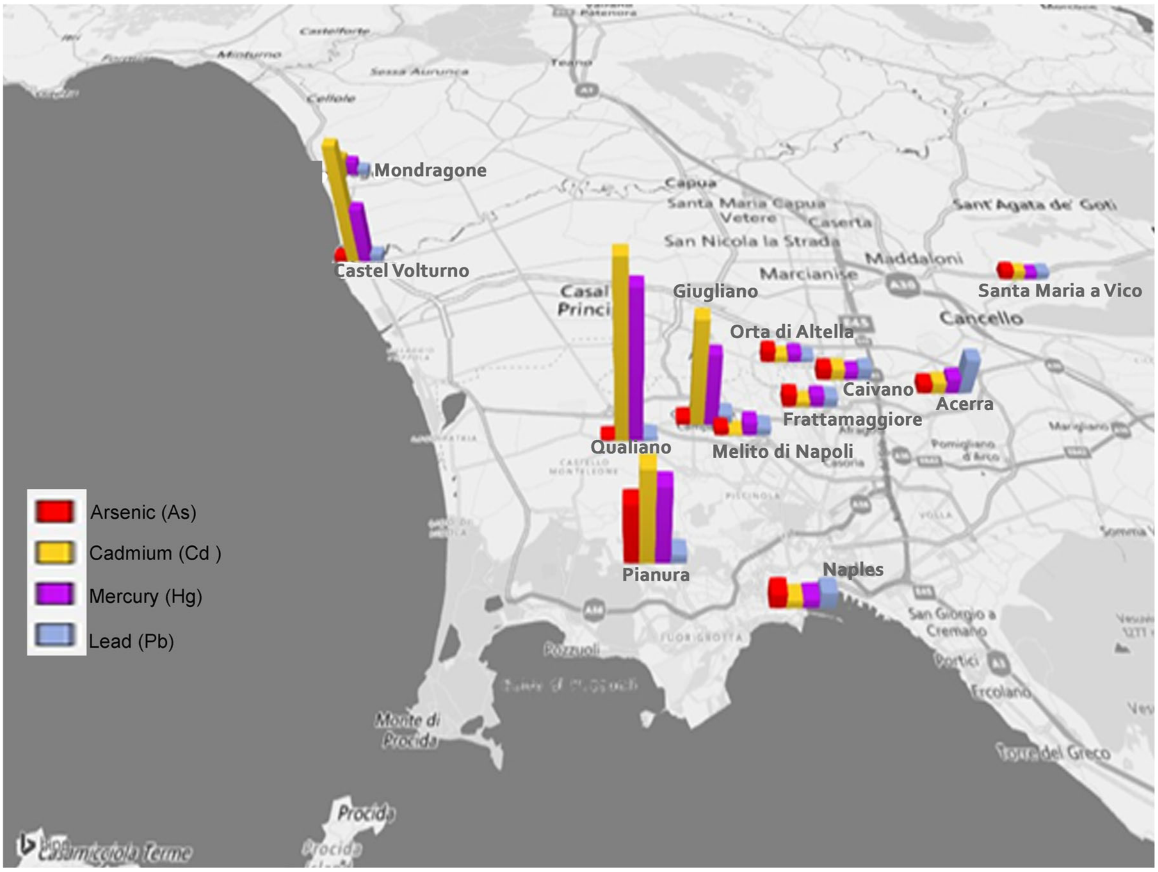
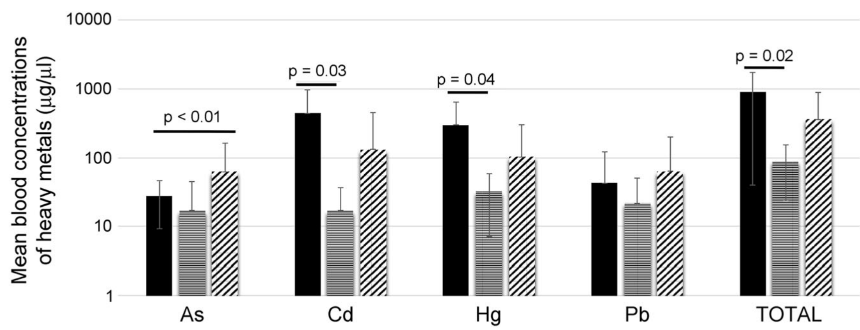


FIGURE 1 Geographical distribution of blood concentrations of heavy metals in municipalities of the provinces of Naples and Caserta. The histograms show the average blood concentrations of arsenic (As), cadmium (Cd), mercury (Hg), and lead (Pb), in municipalities where at least three individuals were sampled (total individuals = 89)



	As (0.4-11.9 µg/µl)	Cd (0.25-1.97 µg/µl)	Hg (1.7-9.9 µg/µl)	Pb (12.8-79.5 µg/µl)	TOTAL
Cancer patients, Giugliano	27.64	440.50	297.47	42.27	883.03
Healthy individuals, pooled	16.93	16.96	32.39	21.56	87.84
Cancer patients, pooled	62.42	131.26	102.41	63.33	359.83

FIGURE 2 Blood levels of heavy metals in Giugliano patients versus those of pooled healthy individuals or pooled cancer patients. The histograms show the mean blood concentrations (with standard deviations) of arsenic (As), cadmium (Cd), mercury (Hg), lead (Pb), and total heavy metals in cancer patients living in Giugliano ($n = 10$), compared with those in pooled healthy individuals ($n = 27$) and in pooled cancer patients, all from localities outside Giugliano (total individuals = 85). p values are reported for all significant differences (Welch's t test). These mean blood concentrations are also reported in the table. The reference blood values (according to ISTISAN 10/22, National Institute of Health) are shown above the table

the urine daily volume and density can also modify the results. Therefore, we performed blood measurements that reflect more precisely the real concentration. However, for a more comprehensive evaluation, multiple biological matrices should be analyzed. In particular, hair and nail analyses can provide further information, especially on long-term exposures, although, for these samples, the reference values are less standardized (Petrosino et al., 2018).

At present, we did not find any difference in the POP distribution in our sample. However, among all the numerous POPs, we analyzed only four main classes, without specifically evaluating chemicals within each of these classes. Therefore, more extensive and specific analyses are ongoing.

Conversely, we observed that the overall concentration of heavy metals in some municipalities (Pianura, Giugliano, Qualiano, and Castel Volturno) exceeded that of the other localities under study, but statistical significance was achieved only for Giugliano. In particular, using the measurements on individuals from Naples as control values, blood levels of Cd and Hg, as well as those of overall metals, were significantly higher in Giugliano patients. Moreover, in these patients, blood levels of heavy metals (As, Cd, Hg) were higher than the maximum reference value, according to ISTISAN 10/22, National Institute of Health. For other municipalities, statistical significance was not achieved, probably owing to the very low statistical power due to the very small number of patients available.

Cancer patients from Giugliano had blood levels of heavy metals and, in particular, of Cd and Hg significantly higher than those of pooled healthy individuals, which is consistent with the previously observed association between these metals and cancer development (Kresovich et al., 2019; Nersesyan et al., 2016). These observations are in line with a previous study by Altavista et al. (2004) investigating cause-specific mortality in three municipalities of Campania, including Giugliano, characterized by many illegal toxic waste dumping sites and by the widespread burning of urban waste. This study showed that the mortality rate from cancer (particularly, lung, pleura, bladder, larynx, liver, and brain cancers) among citizens of Giugliano was higher than that reported for the Campania region (Altavista et al., 2004). Our data point to the potential role of carcinogenic blood metal levels as the culprit for the higher prevalence of cancer in Giugliano.

In conclusion, we observed high blood concentrations of heavy metals in some municipalities of the “land of fires.” In particular, in Giugliano, where many illegal waste disposal sites have been documented, blood levels of Cd and Hg were significantly higher in cancer patients than in healthy controls. Owing to its exploratory nature, our study presents methodological limitations, including, in particular, the small sample size, which prevents definitive conclusions from being drawn. However, it is noteworthy that, despite the small samples used, for Giugliano the observed effect size is so high, to reach statistical significance; that is why our preliminary observations encourage further studies, involving a greater number of individuals, to investigate the possible association between exposure to hazardous waste and increased risk of cancer development in the “land of fires”. These studies could be crucial to promote interventions aimed at improving health conditions in these areas.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

I. M. F. defined the experimental design, coordinated the study, and wrote the manuscript; P. I. contributed to writing the manuscript and to the critical evaluation of data; E. B. supervised the study and performed the statistical analysis; A. G. conceived the study and supervised the whole work; A. C., C. A. I., L. C., S. M. contributed to patients’ enrollment and data acquisition and collection; A. M. and G. B. provided critical feedback and helped shape the research. All authors read and approved the final manuscript.

INFORMED CONSENT

Each volunteer has read and signed a detailed informed consent with authorization to publish the data for this study and has provided a copy of his identity document. All original consents and authorizations are available from the corresponding authors.

DATA AVAILABILITY STATEMENT

The data sets used and/or analyzed during the current study are available from the corresponding authors on reasonable request.

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REFERENCES

Altavista, P., Belli, S., Bianchi, F., Binazzi, A., Comba, P., Del Giudice, R., … Uccelli, R. (2004). Cause-specific mortality in an area of Campania with numerous waste disposal sites. *Epidemiologia e Prevenzione*, *28*(6), 311–321.

Aquino, N. B., Sevigny, M. B., Sabangan, J., & Louie, M. C. (2012). The role of cadmium and nickel in estrogen receptor signaling and breast cancer: Metalloestrogens or not? *Journal of Environmental Science and Health, Part C*, *30*(3), 189–224. https://doi.org/10.1080/10590501.2012.705159

Barba, M., Mazza, A., Guerriero, C., Di Maio, M., Romeo, F., Maranta, P., … Giordano, A. (2011). Wasting lives: The effects of toxic waste exposure on health. The case of Campania, Southern Italy. *Cancer biology & therapy*, *12*(2), 106–111. https://doi.org/10.4161/cbt.12.2.16910

Belpomme, D., Irigaray, P., Hardell, L., Clapp, R., Montagnier, L., Epstein, S., & Sasco, A. J. (2007). The multitude and diversity of environmental carcinogens. *Environmental Research*, *105*(3), 414–429. https://doi.org/10.1016/j.envres.2007.07.002

Belpomme, D., Irigaray, P., Sasco, A. J., Newby, J. A., Howard, V., Clapp, R., & Hardell, L. (2007). The growing incidence of cancer: Role of lifestyle and screening detection. *International Journal of Oncology*, *30*(5), 1037–1049. https://doi.org/10.3892/ijo.30.5.1037

Beszterda, M., & Franski, R. (2018). Endocrine disruptor compounds in environment: As a danger for children health. *Pediatric Endocrinology Diabetes and Metabolism*, *24*(2), 88–95. https://doi.org/10.18544/pedm-24.02.0107

Buha, A., Matovic, V., Antonijevic, B., Bulat, Z., Curcic, M., Renieri, E. A., … Wallace, D. (2018). Overview of cadmium thyroid disrupting effects and mechanisms. *International Journal of Molecular Sciences*, *19*(5), 1501. https://doi.org/10.3390/ijms19051501

Cao, J., Fan, T., Li, W., & Xiao, S. (2019). Association study between plasma levels of polychlorinated biphenyls and risk of cutaneous malignant melanoma. *Environment International*, *126*, 298–301. https://doi.org/10.1016/j.envint.2019.02.014

Cavigelli, M., Li, W. W., Lin, A., Su, B., Yoshioka, K., & Karin, M. (1996). The tumor promoter arsenite stimulates AP-1 activity by inhibiting a JNK phosphatase. *The EMBO Journal*, *15*(22), 6269–6279.

Cembalo, L., Caso, D., Carfora, V., Caracciolo, F., Lombardi, A., & Cicia, G. (2019). The "Land of Fires" toxic waste scandal and its effect on consumer food choices. *International Journal of Environmental Research and Public Health*, *16*(1), 165. https://doi.org/10.3390/ijerph16010165

Chen, Y. Y., Zhu, J. Y., & Chan, K. M. (2014). Effects of cadmium on cell proliferation, apoptosis, and proto-oncogene expression in zebrafish liver cells. *Aquatic Toxicology*, *157*, 196–206. https://doi.org/10.1016/j.aquatox.2014.10.018

Comba, P., Bianchi, F., Fazzo, L., Martina, L., Menegozzo, M., Minichilli, F., … Martuzzi, M. (2006). Cancer mortality in an area of Campania (Italy) characterized by multiple toxic dumping sites. *Annals of the New York Academy of Sciences*, *1076*, 449–461. https://doi.org/10.1196/annals.1371.067

Comba, P., Ricci, P., Iavarone, I., Pirastu, R., Buzzoni, C., Fusco, M., … Crocetti, E. (2014). Cancer incidence in Italian contaminated sites. *Annali Dell Istituto Superiore di Sanita*, *50*(2), 186–191. https://doi.org/10.4415/ann_14_02_13

Craft, E. S., Donnelly, K. C., Neamtiu, I., McCarty, K. M., Bruce, E., Surkova, I., … Anderson, B. (2006). Prioritizing environmental issues around the world: Opinions from an international central and eastern European environmental health conference. *Environmental Health Perspectives*, *114*(12), 1813–1817. https://doi.org/10.1289/ehp.9300

Crispo, A., Barba, M., Malvezzi, M., Arpino, G., Grimaldi, M., Rosso, T., … Montella, M. (2013). Cancer mortality trends between 1988 and 2009 in the metropolitan area of Naples and Caserta, Southern Italy: Results from a joinpoint regression analysis. *Cancer Biology and Therapy*, *14*(12), 1113–1122. https://doi.org/10.4161/cbt.26425

Dally, H., & Hartwig, A. (1997). Induction and repair inhibition of oxidative DNA damage by nickel(II) and cadmium(II) in mammalian cells. *Carcinogenesis*, *18*(5), 1021–1026. https://doi.org/10.1093/carcin/18.5.1021

Darras, V. M. (2008). Endocrine disrupting polyhalogenated organic pollutants interfere with thyroid hormone signalling in the developing brain. *Cerebellum*, *7*(1), 26–37. https://doi.org/10.1007/s12311-008-0004-5

De Felip, E., Bianchi, F., Bove, C., Cori, L., D'Argenzio, A., D'Orsi, G., … di Domenico, A. (2014). Priority persistent contaminants in people dwelling in critical areas of Campania Region, Italy (SEBIOREC biomonitoring study). *Science of the Total Environment*, *487*, 420–435. https://doi.org/10.1016/j.scitotenv.2014.04.016

Di Lorenzo, G., Federico, P., De Placido, S., & Buonerba, C. (2015). Increased risk of bladder cancer in critical areas at high pressure of pollution of the Campania region in Italy: A systematic review. *Critical Reviews in Oncology/Hematology*, *96*(3), 534–541. https://doi.org/10.1016/j.critrevonc.2015.07.004

Donahue, B. A., Augot, M., Bellon, S. F., Treiber, D. K., Toney, J. H., Lippard, S. J., & Essigmann, J. M. (1990). Characterization of a DNA damage-recognition protein from mammalian cells that binds specifically to intrastrand d(GpG) and d(ApG) DNA adducts of the anticancer drug cisplatin. *Biochemistry*, *29*(24), 5872–5880. https://doi.org/10.1021/bi00476a032

El-Shahawi, M. S., Hamza, A., Bashammakh, A. S., & Al-Saggaf, W. T. (2010). An overview on the accumulation, distribution, transformations, toxicity and analytical methods for the monitoring of persistent organic pollutants. *Talanta*, *80*(5), 1587–1597. https://doi.org/10.1016/j.talanta.2009.09.055

Esposito, M., Cavallo, S., Serpe, F. P., D'Ambrosio, R., Gallo, P., Colarusso, G., … Serpe, L. (2009). Levels and congener profiles of polychlorinated dibenzo-*p*-dioxins, polychlorinated dibenzofurans and dioxin-like polychlorinated biphenyls in cow's milk collected in Campania, Italy. *Chemosphere*, *77*(9), 1212–1216. https://doi.org/10.1016/j.chemosphere.2009.09.011

Fathabad, A. E., Shariatifar, N., Moazzen, M., Nazmara, S., Fakhri, Y., Alimohammadi, M., … Mousavi Khaneghah, A. (2018). Determination of heavy metal content of processed fruit products from Tehran's market using ICP-OES: A risk assessment study. *Food and Chemical Toxicology*, *115*, 436–446. https://doi.org/10.1016/j.fct.2018.03.044

Fatur, T., Lah, T. T., & Filipic, M. (2003). Cadmium inhibits repair of UV-, methyl methanesulfonate- and *N*-methyl-*N*-nitrosourea-induced DNA damage in Chinese hamster ovary cells. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*, *529*(1-2), 109–116. https://doi.org/10.1016/s0027-5107(03)00112-x

Fazzo, L., Belli, S., Minichilli, F., Mitis, F., Santoro, M., Martina, L., … Bianchi, F. (2008). Cluster analysis of mortality and malformations in the provinces of Naples and Caserta (Campania Region). *Annali Dell Istituto Superiore di Sanita*, *44*(1), 99–111.

Fazzo, L., De Santis, M., Mitis, F., Benedetti, M., Martuzzi, M., Comba, P., & Fusco, M. (2011). Ecological studies of cancer incidence in an area interested by dumping waste sites in Campania (Italy). *Annali Dell Istituto Superiore di Sanita*, *47*(2), 181–191. https://doi.org/10.4415/ann_11_02_10

Goldman, G. T., & Dominici, F. (2019). Don't abandon evidence and process on air pollution policy. *Science*, *363*(6434), 1398–1400. https://doi.org/10.1126/science.aaw9460

Gregoraszczuk, E. L., & Ptak, A. (2013). Endocrine-disrupting chemicals: Some actions of POPs on female reproduction. *International Journal of Endocrinology*, *2013*, 1–9. https://doi.org/10.1155/2013/828532

Hardell, L., Bavel, B., Lindstrom, G., Eriksson, M., & Carlberg, M. (2006). In utero exposure to persistent organic pollutants in relation to testicular cancer risk. *International Journal of Andrology*, *29*(1), 228–234. https://doi.org/10.1111/j.1365-2605.2005.00622.x

Hung, H., Katsoyiannis, A. A., & Guardans, R. (2016). Ten years of global monitoring under the Stockholm convention on persistent organic pollutants (POPs): Trends, sources and transport modelling. *Environmental Pollution*, *217*, 1–3. https://doi.org/10.1016/j.envpol.2016.05.035

IARC. (2019). Public health and evidence-informed policy-making: The case of a commonly used herbicide. *Scandinavian Journal of Work, Environment & Health*, https://monographs.iarc.fr/agents-classified-by-the-iarc/

Jaishankar, M., Tseten, T., Anbalagan, N., Mathew, B. B., & Beeregowda, K. N. (2014). Toxicity, mechanism and health effects of some heavy metals. *Interdisciplinary Toxicology*, *7*(2), 60–72. https://doi.org/10.2478/intox-2014-0009

Jarup, L. (2003). Hazards of heavy metal contamination. *British Medical Bulletin*, *68*, 167–182. https://doi.org/10.1093/bmb/ldg032

Johnson, M. D., Kenney, N., Stoica, A., Hilakivi-Clarke, L., Singh, B., Chepko, G., … Martin, M. B. (2003). Cadmium mimics the in vivo effects of estrogen in the uterus and mammary gland. *Nature Medicine*, *9*(8), 1081–1084. https://doi.org/10.1038/nm902

Kranthi Kumar, K., Uma Devi, B., & Neeraja, P. (2018). Elucidation of endocrine–disrupting polychlorinated biphenyls binding potency with steroidogenic genes: Integration of in silico methods and ensemble docking approaches. *Ecotoxicology and Environmental Safety*, *165*, 194–201. https://doi.org/10.1016/j.ecoenv.2018.08.112

Kresovich, J. K., Erdal, S., Chen, H. Y., Gann, P. H., Argos, M., & Rauscher, G. H. (2019). Metallic air pollutants and breast cancer heterogeneity. *Environmental Research*, *177*, 108639. https://doi.org/10.1016/j.envres.2019.108639

Lee, Y. M., Kim, K. S., Jacobs, D. R., Jr., & Lee, D. H. (2017). Persistent organic pollutants in adipose tissue should be considered in obesity research. *Obesity Reviews*, *18*(2), 129–139. https://doi.org/10.1111/obr.12481

Lelieveld, J., Evans, J. S., Fnais, M., Giannadaki, D., & Pozzer, A. (2015). The contribution of outdoor air pollution sources to premature mortality on a global scale. *Nature*, *525*(7569), 367–371. https://doi.org/10.1038/nature15371

Leng, L., Li, J., Luo, X. M., Kim, J. Y., Li, Y. M., Guo, X. M., … Tang, N. J. (2016). Polychlorinated biphenyls and breast cancer: A congener-specific meta-analysis. *Environment International*, *88*, 133–141. https://doi.org/10.1016/j.envint.2015.12.022

Lim, J. E., Nam, C., Yang, J., Rha, K. H., Lim, K. M., & Jee, S. H. (2017). Serum persistent organic pollutants (POPs) and prostate cancer risk: A case-cohort study. *International Journal of Hygiene and Environmental Health*, *220*(5), 849–856. https://doi.org/10.1016/j.ijheh.2017.03.014

Martinez-Campa, C., Alonso-Gonzalez, C., Mediavilla, M. D., Cos, S., Gonzalez, A., Ramos, S., & Sanchez-Barcelo, E. J. (2006). Melatonin inhibits both ERα activation and breast cancer cell proliferation induced by a metalloestrogen, cadmium. *Journal of Pineal Research*, *40*(4), 291–296. https://doi.org/10.1111/j.1600-079X.2006.00315.x

Martuzzi, M., Mitis, F., Bianchi, F., Minichilli, F., Comba, P., & Fazzo, L. (2009). Cancer mortality and congenital anomalies in a region of Italy with intense environmental pressure due to waste. *Occupational and Environmental Medicine*, *66*(11), 725–732. https://doi.org/10.1136/oem.2008.044115

Martuzzi, M., Mitis, F., Biggeri, A., Terracini, B., & Bertollini, R. (2002). Environment and health status of the population in areas with high risk of environmental crisis in Italy. *Epidemiologia e Prevenzione*, *26*(6 Suppl.), 1–53.

Mazza, A., Piscitelli, P., Falco, A., Santoro, M. L., Colangelo, M., Imbriani, G., … Colao, A. (2018). Heavy environmental pressure in Campania and other Italian regions: A short review of available evidence. *International Journal of Environmental Research and Public Health*, *15*(1), 105. https://doi.org/10.3390/ijerph15010105

Mazza, A., Piscitelli, P., Neglia, C., Della Rosa, G., & Iannuzzi, L. (2015). Illegal dumping of toxic waste and its effect on human health in Campania, Italy. *International Journal of Environmental Research and Public Health*, *12*(6), 6818–6831. https://doi.org/10.3390/ijerph120606818

Nersesyan, A., Kundi, M., Waldherr, M., Setayesh, T., Misik, M., Wultsch, G., … Knasmueller, S. (2016). Results of micronucleus assays with individuals who are occupationally and environmentally exposed to mercury, lead and cadmium. *Mutation Research/Reviews in Mutation Research*, *770*(Pt A), 119–139. https://doi.org/10.1016/j.mrrev.2016.04.002

Paschoalini, A. L., Savassi, L. A., Arantes, F. P., Rizzo, E., & Bazzoli, N. (2019). Heavy metals accumulation and endocrine disruption in *Prochilodus argenteus* from a polluted neotropical river. *Ecotoxicology and Environmental Safety*, *169*, 539–550. https://doi.org/10.1016/j.ecoenv.2018.11.047

Petrosino, V., Motta, G., Tenore, G., Coletta, M., Guariglia, A., & Testa, D. (2018). The role of heavy metals and polychlorinated biphenyls (PCBs) in the oncogenesis of head and neck tumors and thyroid diseases: A pilot study. *BioMetals*, *31*(2), 285–295. https://doi.org/10.1007/s10534-018-0091-9

Pirastu, R., Pasetto, R., Zona, A., Ancona, C., Iavarone, I., Martuzzi, M., & Comba, P. (2013). The health profile of populations living in contaminated sites: SENTIERI approach. *Journal of Environmental and Public Health*, *2013*, 1–13. https://doi.org/10.1155/2013/939267

Rehman, K., Fatima, F., Waheed, I., & Akash, M. S. H. (2018). Prevalence of exposure of heavy metals and their impact on health consequences. *Journal of Cellular Biochemistry*, *119*(1), 157–184. https://doi.org/10.1002/jcb.26234

Rivezzi, G., Piscitelli, P., Scortichini, G., Giovannini, A., Diletti, G., Migliorati, G., … Giani, U. (2013). A general model of dioxin contamination in breast milk: Results from a study on 94 women from the Caserta and Naples areas in Italy. *International Journal of Environmental Research and Public Health*, *10*(11), 5953–5970. https://doi.org/10.3390/ijerph10115953

Rzymski, P., Tomczyk, K., Niedzielski, P., Jakubowski, K., Poniedzialek, B., & Opala, T. (2014). Metal status in human endometrium: Relation to cigarette smoking and histological lesions. *Environmental Research*, *132*, 328–333. https://doi.org/10.1016/j.envres.2014.04.025

Saxena, G., Purchase, D., Mulla, S. I., Saratale, G. D., & Bharagava, R. N. (2020). Phytoremediation of heavy metal-contaminated sites: Eco-environmental concerns, field studies, sustainability issues, and future prospects. *Reviews of Environmental Contamination and Toxicology*, *249*, 71–131. https://doi.org/10.1007/398_2019_24

Senior, K., & Mazza, A. (2004). Italian "Triangle of death" linked to waste crisis. *The Lancet Oncology*, *5*(9), 525–527.

Tchounwou, P. B., Yedjou, C. G., Patlolla, A. K., & Sutton, D. J. (2012). Heavy metal toxicity and the environment. *Experientia Supplementum*, *101*, 133–164. https://doi.org/10.1007/978-3-7643-8340-4_6

Tran, N. Q. V., & Miyake, K. (2017). Neurodevelopmental disorders and environmental toxicants: Epigenetics as an underlying mechanism. *International Journal of Genomics*, *2017*, 1–23. https://doi.org/10.1155/2017/7526592

Trivedi, J., & Majumdar, D. (2013). Memory effect driven emissions of persistent organic pollutants from industrial thermal processes, their implications and management: A review. *Journal of Environmental Management*, *119*, 111–120. https://doi.org/10.1016/j.jenvman.2013.01.026

Valko, M., Rhodes, C. J., Moncol, J., Izakovic, M., & Mazur, M. (2006). Free radicals, metals and antioxidants in oxidative stress-induced cancer. *Chemico-Biological Interactions*, *160*(1), 1–40. https://doi.org/10.1016/j.cbi.2005.12.009

Wang, S., Leonard, S. S., Ye, J., Ding, M., & Shi, X. (2000). The role of hydroxyl radical as a messenger in Cr(VI)-induced p53 activation. *American Journal of Physiology-Cell Physiology*, *279*(3), C868–875. https://doi.org/10.1152/ajpcell.2000.279.3.C868

Wise, J. T. F., Wang, L., Zhang, Z., & Shi, X. (2017). The 9th Conference on metal toxicity and carcinogenesis: The conference overview. *Toxicology and Applied Pharmacology*, *331*, 1–5. https://doi.org/10.1016/j.taap.2017.04.007

Wu, X., Cobbina, S. J., Mao, G., Xu, H., Zhang, Z., & Yang, L. (2016). A review of toxicity and mechanisms of individual and mixtures of heavy metals in the environment. *Environmental Science and Pollution Research*, *23*(9), 8244–8259. https://doi.org/10.1007/s11356-016-6333-x

Yao, Y., & Costa, M. (2014). Toxicogenomic effect of nickel and beyond. *Archives of Toxicology*, *88*(9), 1645–1650. https://doi.org/10.1007/s00204-014-1313-8

Yousaf, B., Amina, Liu, G., Wang, R., Imtiaz, M., Rizwan, M. S., … Si, Y. (2016). The importance of evaluating metal exposure and predicting human health risks in urban-periurban environments influenced by emerging industry. *Chemosphere*, *150*, 79–89. https://doi.org/10.1016/j.chemosphere.2016.02.007

Zhao, C. Q., Young, M. R., Diwan, B. A., Coogan, T. P., & Waalkes, M. P. (1997). Association of arsenic-induced malignant transformation with DNA hypomethylation and aberrant gene expression. *Proceedings of the National Academy of Sciences*, *94*(20), 10907–10912. https://doi.org/10.1073/pnas.94.20.10907

Zona, A., Iavarone, I., Buzzoni, C., Conti, S., Santoro, M., Fazzo, L., … Comba, P. (2019). SENTIERI: Epidemiological study of residents in national priority contaminated sites. Fifth report. *Epidemiologia e Prevenzione*, *43*(2–3 Suppl. 1), 1–208. https://doi.org/10.19191/ep19.2-3.s1.032

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